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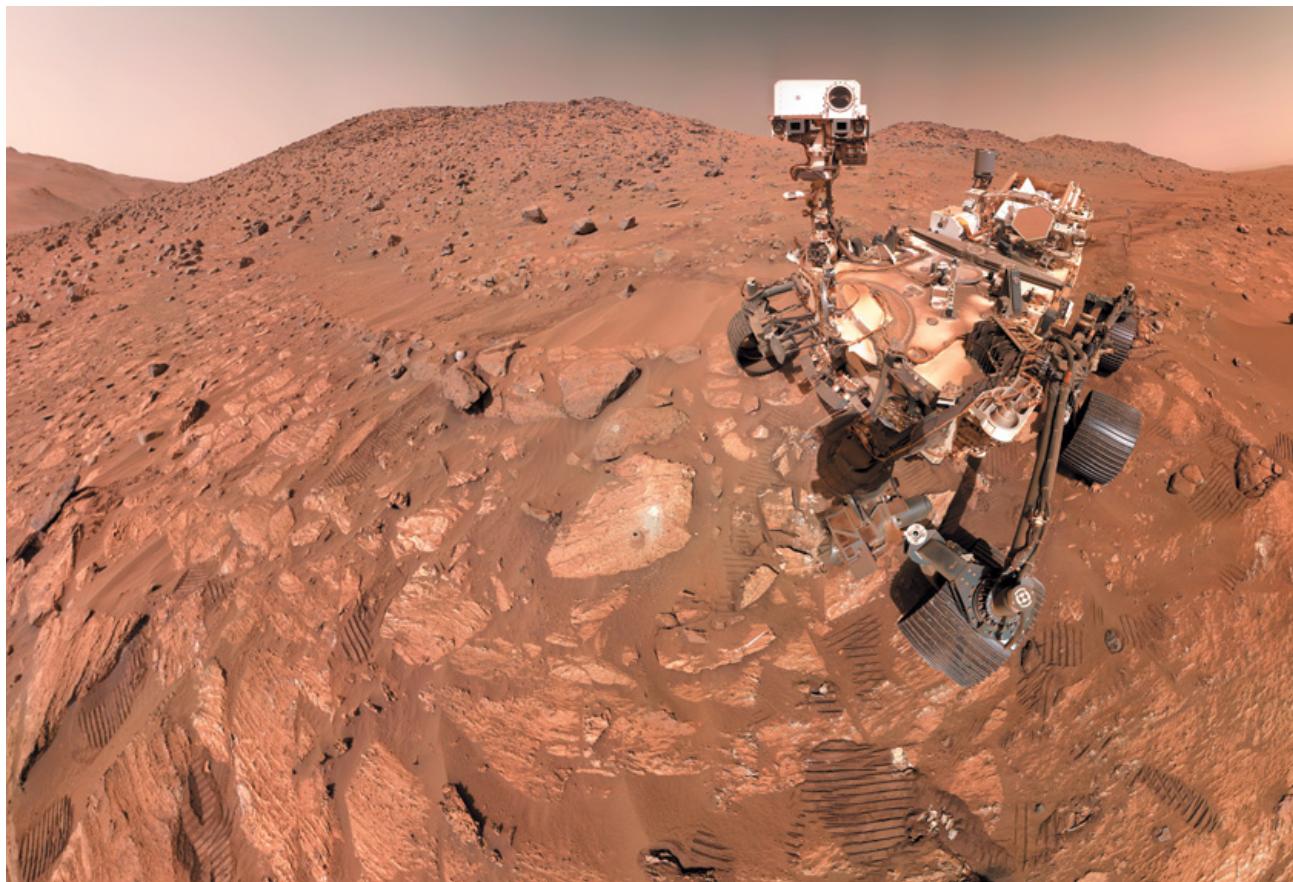
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42

FEATURES

SUSTAINABILITY

**22 THE PIVOT TO PLASTIC**

To keep profits rolling in, oil and gas companies want to turn fossil fuels into a mounting pile of packaging and other products.

BY BETH GARDINER

MEDICINE

**34 YOUR PERSONALIZED CANCER VACCINE**

Vaccines based on mRNA can be tailored to target a cancer patient's unique tumor mutations. But crumbling support for cancer and mRNA vaccine research has endangered this promising therapy.

BY ROWAN MOORE GERETY

PLANETARY SCIENCE

**42 STRANDED ON MARS**

NASA spent years and billions of dollars collecting Martian samples to bring home. Now it might just leave them there.

BY JONATHAN O'CALLAGHAN

HEALTH

**52 THE MOTHER OF DEPRESSIONS**

Postpartum depression is a leading cause of death among new mothers. A new type of drug offers better, faster treatment.

BY MARLA BROADFOOT

TECHNOLOGY

**62 MOURNING BECOMES ELECTRIC**

What can AI ghosts do for the grieving?

BY DAVID BERREBY



ON THE COVER

Personalized vaccines based on messenger RNA (mRNA) may be effective for treating a wide variety of cancers—from melanoma to pancreatic cancer. But with recent slashes to federal funding for cancer and mRNA vaccine research in the U.S., the fate of this promising therapy hangs in the balance.

Illustration by Tavis Coburn

4 FROM THE EDITOR

6 LETTERS

8 ADVANCES

Life-friendly chemistry on icy Enceladus. The mysterious “noperthedron.” Predicting rogue waves. Will-o’-the-wisps’ electric formation.

68 SCIENCE AGENDA

To stop deepfakes, the U.S. should give its residents the copyrights to their own faces and voices.

BY THE EDITORS

69 FORUM

A company offering to genetically tailor embryos isn’t all that it seems. BY ARTHUR CAPLAN AND JAMES TABERY

73 SCIENCE CROSSWORD

Inspired by the stories in this issue.

BY AIMEE LUCIDO

74 MIND MATTERS

How small joyful acts, such as sharing with a friend, can boost happiness.

BY DARWIN A. GUEVARRA, XUHAI “ORSON” XU AND EMILIANA SIMON-THOMAS

76 THE UNIVERSE

Do black holes have a size limit? BY PHIL PLAIT

78 THE SCIENCE OF PARENTING

Teens are turning to AI chatbots to meet social and emotional needs, and we must examine what they get—and don’t—out of these interactions.

BY ELIZABETH ENGLANDER

80 MATH

This clever math powers some e-commerce and won its inventor a Nobel Prize.

BY JACK MURTAGH

82 THE SCIENCE OF HEALTH

Heart rate variability sounds bad, but it can be quite good. BY LYDIA DENWORTH

85 METER

The poetry of botany in glass.

BY NANCY BREWKA-CLARK

86 Q&A

The hidden story of carbon and how it’s shaped life on Earth. BY LEE BILLINGS

90 GRAPHIC SCIENCE

See how many rare earth elements have been mined and how many are left.

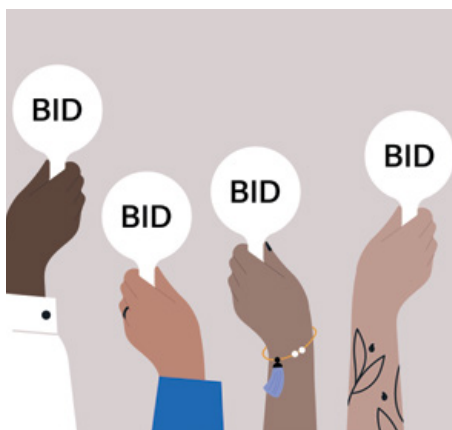
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92 HISTORY BY MARK FISCHETTI



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76



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80

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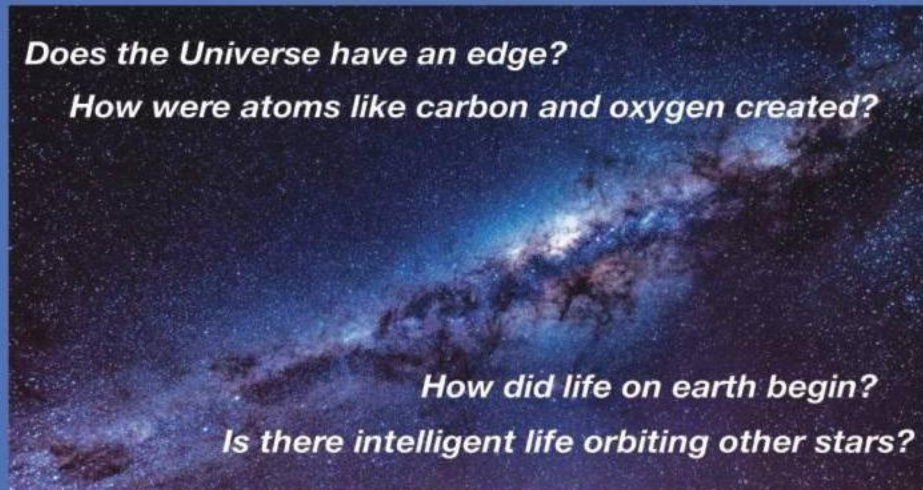
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# Funding Fallout

**I**N JUNE, Department of Health and Human Services Secretary Robert F. Kennedy, Jr., fired all 17 members of the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices, a panel that creates recommendations for safe and effective vaccination standards. His chosen replacements include ideological allies who have been outspoken skeptics of vaccine safety.

In August, Kennedy announced the cancellation of roughly \$500 million in federal funding for the development of messenger RNA (mRNA) vaccines for respiratory viruses, claiming that "mRNA technology poses more risks than benefits." A month later he testified during a Senate hearing that he believed mRNA vaccines cause widespread serious harm, including death.

The data show otherwise. People who received mRNA vaccines for COVID-19 were significantly less likely to go to the ER, be hospitalized or die because of the illness; experts say severe side effects of these vaccines are very rare. The fact is mRNA COVID vaccines saved millions of lives, and their use in hundreds of millions has repeatedly demonstrated their safety.

Not only could Kennedy's campaign against mRNA research deter people from getting updated COVID vaccines, but it is also stunting the development of new mRNA technology for other diseases and disorders.

Our cover story (*page 34*), reported by journalist Rowan Moore Gerety, highlights one of the most exciting of these new applications: custom-built mRNA therapies tailored to the genetic makeup of a person's cancer that can help that patient's immune system go after the tumor cells' unique mutant proteins. In other words, it's a personalized cancer vaccine.

Early tests of these vaccines are extremely promising. But the federal government is far and away the largest source of funding for cancer re-

search in the U.S., so Kennedy's uninformed attack on mRNA technology threatens to halt advances in medicine. Other countries, including the U.K., are poised to advance mRNA cancer vaccine research, but the U.S., which has many more cancer research centers, is vital to the success of this field.

Sadly, Kennedy's factually bankrupt campaign is only the latest example of the U.S. government retreating from groundbreaking research. At this moment, NASA's Perseverance rover is crawling along the surface of Mars to answer some of the biggest questions in science: Was Mars once habitable? Did it ever host life? But more slashes in funding threaten to ruin that experiment, too.

Perseverance has spent almost five years collecting samples of Martian rock and soil along more than 20 miles of the planet's surface. And it has stored dozens of small vials of material that could contain evidence of life. Unfortunately, we may never get to test them; the proposed 2026 budget for NASA kills the mission to collect Perseverance's samples and deliver them to Earth. Science writer Jonathan O'Callaghan tells the story (*page 42*).

It's hard to read articles like these without getting frustrated about the state of American science. Our researchers are dedicated to advancing knowledge, saving lives and making the world better; meanwhile our leaders are getting in their way.

An Internet meme has been stuck in my head as I write: The three-panel cartoon starts with a man riding a bicycle down a road while holding a stick in his hand. In the second panel, he jams the stick into the spokes of his front wheel. In the third, he's curled up on the ground in agony, nursing a self-inflicted wound.

I hope that this unlikely bit of wisdom might inspire you to reach out to your legislators and others in leadership roles to remind them of the importance of funding scientific endeavors. Over the past 180 years this magazine has chronicled some of the greatest discoveries in human history and the epic

successes of government-funded research. I think that we'd all like to see more of those stories in the next two centuries. ●

**David M. Ewalt**  
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## HIGH TESTOSTERONE

I'm grateful for the warnings threaded through Stephanie Pappas's "The Truth about Testosterone" and would like to elaborate from personal experience. As a transgender man, I adore the effects of testosterone. But I discovered some unwelcome ones when my levels climbed. My higher dosage was accidental; I assumed my doctor wanted me to increase it each week until she said, "Halt!"

It sounds like one man's accident is another man's aim, however, given that cisgender men with testosterone in the normal range of 300 to 1,000 nanograms per deciliter (ng/dl) can easily get prescriptions for the hormone. Above 1,000 ng/dl, I grew impatient, irritable and disturbingly apathetic. Once an eager listener at volunteer meetings, I felt like I was the only person in the room. All these other humans with their human opinions! They exasperated me. STEVE HUITTING NEVADA CITY, CALIF.

## SLICE OF CONFUSION

In "Perfect Slice" [Advances], Max Springer describes a slicing problem involving convex shapes as equivalent to "asking whether an avocado of a given size, no matter the exact shape, can always be split into two halves with each side revealing at least some sizable slice," in the case of three-dimensional objects.

Does "two halves" mean two true halves or two pieces? And does "some sizable slice" mean that the area of the cut is not zero—that the two "halves" are not connected by just a thread?

DAWN JACOBS VIA E-MAIL

SPRINGER REPLIES: "Two halves" in this problem means two disconnected pieces. Moving your knife completely through a fruit at any angle will always give you two pieces but not necessarily two halves. The description of "some sizable slice" is capturing a deeper mathematical boundary on how large the area of each of the two cross sections will be. As described in my article, the recently proved result of the problem says we can always cut an object into two pieces so that each



July/August 2025

has a cross section of at least a given size. This may seem intuitive for fruits but gets more complex in higher dimensions.

## ILLUMINATING MITOCHONDRIA

"Can Sunlight Cure Disease?," by Rowan Jacobsen [June], leaves us with a sense of mystery as to the mechanism of action for the health benefits of sunshine. Yet in the same issue, a clue is offered by Martin Picard in "The Social Lives of Mitochondria." The benefits of sunshine might arise from its effect at the mitochondrial level, as demonstrated in a July *Scientific Reports* paper by Glen Jeffery of University College London and his colleagues. Picard does recommend diet, socialization and exercise to optimize mitochondrial function, including in a brief reference to his work with Nirosha Murugan of Wilfrid Laurier University in Ontario. But he doesn't refer to the health benefits of exposure to the outdoors.

HAROLD PUPKO TORONTO

Picard says that, so far, the best hypothesis for how mitochondrial DNA's inner membrane folds, called cristae, line up appears to involve "electromagnetic fields induced by the flow of electrical

charge across" those folds. He then goes on to describe how mitochondria communicate with mitochondria in other cells chemically. Perhaps mitochondria are the field sensors and generators, or possibly the "concentrators," of biology. DONALD WELLER HILLSBORO, ORE.

## PICARD AND MURUGAN REPLY:

*Pupko is right that the health benefits of sunshine may act, in part, through mitochondria. To exert biological effects, light must be absorbed by a chromophore. Mitochondria have such chromophores, including cytochrome c oxidase (an electron shuttle in the electron-transport chain), which absorbs red and near-infrared photons, abundant in natural light. These wavelengths enhance the electrochemical potential across the inner mitochondrial membrane, energizing mitochondria and increasing adenosine triphosphate synthesis.*

*For example, photobiomodulation with near-infrared light can rescue retinal function in vivo and reduce Alzheimer's pathology in mice. In humans, transcranial photobiomodulation can improve working memory. In a 2024 human study, just 15 minutes of exposure to 670-nanometer red light reduced postprandial glucose spikes by nearly 30 percent.*

*Mechanistic studies, including simulations and photoacoustic imaging, reveal how different wavelengths of light interact with chromophores. A study using solar simulators that matched the intensity of summer sunlight demonstrated that mitochondrial responses to light are cell-type-specific: epidermal keratinocytes showed mitochondrial damage under intense sunlight, whereas dermal fibroblasts were more resilient. Sunlight can therefore be broadly beneficial, but its effects depend strongly on wavelength, intensity and exposure time, with ultra-*

**"Perhaps the benefits of sunshine arise from its effect at the mitochondrial level."**

—HAROLD PUPKO TORONTO



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violet light carrying well-known risks.

Mitochondria's broader light sensitivity may also help explain why time spent in nature feels restorative. Plants reflect much of the near-infrared spectrum, saturating green spaces with low-energy, tissue-penetrating wavelengths.

In response to Weller: Across biology, mitochondria produce some of the strongest electric fields. As food-derived electrons flow toward oxygen, the electron transport chain generates an electrochemical gradient across the inner mitochondrial membrane. The voltage potential spans a distance of only about five nanometers, producing an electric field on the order of 30 million volts per meter.

These immense electric fields rise and fall with metabolic demands and energy flow. Such fluctuations in electric fields are expected to generate low-frequency electromagnetic signals. Although it is beyond the reach of today's instruments, detecting such signals from individual mitochondria appears to be an essential step toward fully understanding them as a social, energetic collective that transforms and regulates energy across living systems. And the composition of mitochondria suggests they may not only generate but also respond to electromagnetic fields.

Perhaps the best direct evidence of biologically relevant fields at the scale of mitochondria is the transmembrane cristae alignment. This occurs at intermembrane junctions, electron-dense contacts between two mitochondria.

## ERRATA

"Research in Reverse," by Charles C. Mann [September], should have referred to the Canadian National Breast Screening Study of cancer.

"People Watching," by Clarissa Brincat [Advances; October], should have quoted Laura Lewis as saying that humans' and chimpanzees' shared primate ancestor lived around five million years ago.

In "Prevention Intervention," by Jyoti Madhusoodanan [Innovations in Alzheimer's; October], OHSU's name should be Oregon Health & Science University.

# ADVANCES

## ASTROBIOLOGY

### Fascinating Plumes

Saturn's moon Enceladus has complex, life-friendly chemistry

**ENCELADUS**, a 500-kilometer-wide moon of Saturn, has been a top target in the hunt for extraterrestrial life for nearly two decades. In 2005, shortly after arriving in orbit around the ringed planet, the joint NASA–European Space Agency (ESA) Cassini mission found plumes of water spraying up from Enceladus's south pole—clinching evidence that the moon harbored a liquid-water ocean underneath its bright-white icy crust. Astrobiologists have become ever more enthralled by Enceladus as further studies of the plumes' ice grains have revealed multiple molecular building blocks of life blasting out from the hidden ocean.

Now scientists revisiting data from Cassini, which ended its mission to Saturn in 2017, have spied even more tantalizing ingredients in the plumes: suites of complex organic molecules that, on Earth, are involved in the chemistry associated with even bigger compounds considered essential for biology. The discovery, published in *Nature Astronomy*, bolsters the case for follow-up missions to search for signs of life within this enigmatic moon.

Its remoteness from Earth isn't the only thing that has let Enceladus keep so many secrets for so long. The Cassini orbiter wasn't really designed for deep scrutiny of a single, specific object in Saturn's system, says Nozair Khawaja, a planetary scientist at the Free University of Berlin, who led the *Nature Astronomy* study. Cassini launched nearly 30 years ago, back when Enceladus's subsurface ocean and south polar plumes were unknown. Repurposing its vintage kit for in-depth astrobiology was difficult—not least because of how hard the resulting data were to work with.

One problem was the relatively low resolution available from a mass spectrometer on Cassini called the Cosmic Dust Analyzer (CDA), which parsed the chemical composition of puffs of dust





TALENTED DOGS SORT  
TOYS INTO FUNCTIONAL  
CATEGORIES P. 11

EXPERIMENTAL TREATMENT  
FIGHTS CARBON MONOXIDE  
POISONING P. 15

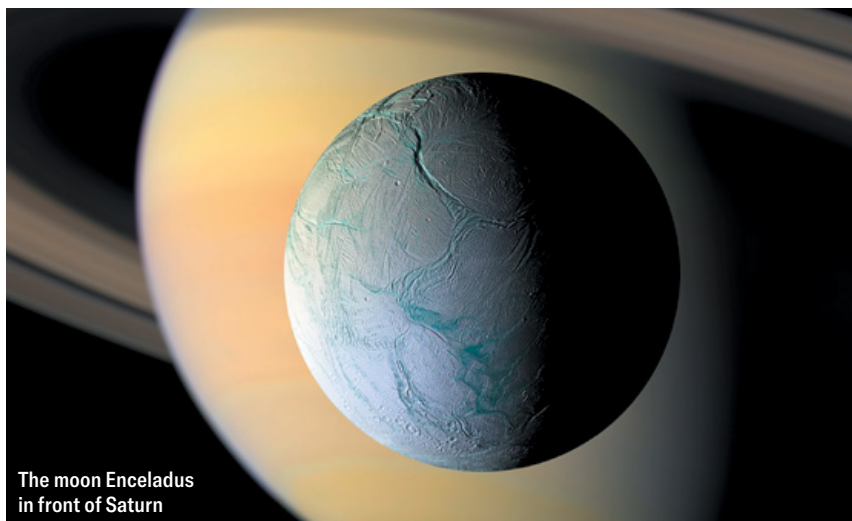
HUMAN ARTIFACTS FOUND  
IN LAYERS OF ANCIENT  
VULTURE NESTS P. 19

DISPATCHES FROM THE FRONTIERS OF SCIENCE, TECHNOLOGY AND MEDICINE

Artist's depiction of Cassini sampling  
plumes from the subsurface ocean  
of Saturn's icy moon Enceladus



NASA's Goddard Space Flight Center



The moon Enceladus  
in front of Saturn

from ice grains striking its detectors each time the spacecraft swooped through a plume. The plumes proved so thick with material, Khawaja says, that the CDA would be overwhelmed during Cassini's Enceladus flybys. Scientists could clearly see that ordinary water molecules made up most of the collected material—nearly 98 percent, according to Khawaja. Piecing together the nature of the remaining 2 percent, however, required many carefully choreographed flybys and tweaks to the CDA's operations across several years. The flyby that eventually hit a bull's-eye was a maneuver on October 9, 2008, code-named E5, which combined higher-than-average speed—nearly 18 kilometers per second (km/s), about 6 km/s faster than other flybys—and a fortuitously timed eruption from Enceladus just minutes beforehand.

"The impact speed was higher, and at such high speeds water molecules shatter. They don't survive. But other species such as organics remain," Khawaja explains. And the freshly ejected material had not been altered or degraded by cosmic radiation.

Some of the co-authors of the recent study published a paper in 2011 analyzing the E5 flyby results after years of painstaking data analysis, noting organic molecules but unable to tell what they were. And now, based on exhaustive experiments examining how differences in the

ice grains' impact speeds affected the CDA data, the researchers think they've tracked down most of what was within the plume, with major implications for the moon's possibility of hosting life.

"I think it makes a lot of sense that it would take diligence and patience to fully understand the CDA data. I applaud them for taking such care in their analyses," says Shannon MacKenzie, a planetary scientist at the Johns Hopkins University Applied Physics Laboratory, who wasn't involved in the study.

The team's work revealed that the plumes contain many familiar molecules, including several massive and complex chemical compounds Cassini previously detected in the torus of ice and dust Enceladus releases into orbit around Saturn. Their presence in the freshly ejected plumes, Khawaja argues, confirms they all originated in Enceladus's subsurface ocean. Most exciting, the study also revealed new, never-before-seen compounds lurking in the plume, sourced from somewhere within the moon.

"In these fresh grains, we've got molecules such as esters and ethers, which were carrying oxygen in themselves and had double bonds," Khawaja says. His team also detected compounds in which oxygen and nitrogen were probably combined. "We suspect these are sort of intermediates to make further, complex organics, maybe potentially organics

that are biologically relevant," he adds. Certainty is elusive because the organic molecules collected by CDA were shattered into multiple tiny fragments; researchers are still figuring out how to piece them back together.

"This work shows that some of the fragments are indeed derived from quite large and complex organic compounds," says Kevin Hand, a planetary scientist and director of the Ocean Worlds Lab at NASA's Jet Propulsion Laboratory, who was not involved in the study. "But maybe those compounds originated from even larger compounds. What exactly would we find if we dove into the ocean below? Are the compounds reported here just the tip of the astrobiological iceberg?"

Khawaja already has ideas about what follow-up missions might find with better, state-of-the-art instruments. The newly revealed cocktail of compounds, he says, could feed into a "network of reactions" to create pyrimidines—a class of molecules necessary for the formation of DNA. (Here on Earth DNA is what leads to fish, lions, humans ... and all life as we know it.) This network of reactions could yield lipids, too—molecules that can arrange themselves into cell membranes. Even so, Khawaja notes, "we don't have a clue about any actual biological relevance yet."

For now the team is developing an advanced computer model of the entire Enceladus subsurface system to map the probable sources and interactions among the moon's chemical compounds. There's also some room left for discovery in the Cassini data: "There are still certain spectral types that I see and don't understand," Khawaja says.

Most of the hope for near-term definitive answers ultimately lies with a mission still on the drawing board at ESA. Such a mission would most likely include an orbiter far more advanced than Cassini, with a lander as a possible addition. (Hand notes that an orbiter alone could be enough, given the plumes' fresh supply of material: "Why risk landing when Enceladus is handing out free samples?")



Regardless of how we investigate it, Enceladus remains one of the most alluring destinations in the search for extra-terrestrial life. "Water, energy and the right chemicals—all three keystones of habitability are there," Khawaja says. And if future studies fail to find life, he argues, the implications will still be enormous. "If it's *not* there despite those three keystones, it will mean that life needs something more." —*Jacek Krywko*

#### ANIMAL BEHAVIOR

## Discerning Dogs

Some dogs can sort toys by function like human children do

**ARYA, A SIX-YEAR-OLD** border collie in Italy, can learn a new toy's name with just one or two mentions. Her owners

say she even knows words for her favorite foods; when pizza is on the menu, the word has to be whispered. Arya's gift made her a natural subject for research showing that some dogs with unusually large vocabularies can go beyond simply memorizing terms.

For the new study, published in *Current Biology*, owners of 10 talented dogs—mostly border collies—taught them words for objects in two categories: tug toys, called "pulls," and fetch toys, called "throws." All toys were different in size, shape and color so appearance could not guide learning.

After four weeks of training, brand-new toys with a variety of designs were introduced. This time the dogs only experienced each toy's function, either tugging or fetching, during play; they were not taught words for any of them. After a week of play, when asked to fetch a pull or a throw, the seven dogs that completed all experimental phases chose the right toy about two thirds of the time—well above the 12.5 percent expected for selections by chance. "These gifted



Border collie Arya

Simone Avezza

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word-learner dogs not only are able to memorize the labels of many different objects but also can extend a familiar word to new objects that share the same function, even if they look very different,” says Claudia Fugazza, the study’s lead author and an ethologist at Eötvös Loránd University in Hungary.

Fugazza emphasizes that these animals are exceptional; most family dogs never build such vocabularies. She says she was surprised by the dogs’ ease and flexibility in applying words by function, akin to how human children begin extending their vocabularies through everyday exposure.

Elika Bergelson, a Harvard University language scientist who was not part of the new study, says human infants “mostly rely on how things look. But by

## Gifted word-learner dogs extended terms to new objects that shared a function.

14 months they can also use role or function—for instance, telling apart who is chasing and who is being chased in a scenario—to extend words” to new things, much like the dogs in the study did. In everyday life, function and appearance usually go together: all cups share a basic shape because it makes them good at holding liquid. “Unlike the real world, where ropes look tug-worthy and balls appear throwable, this study isolates the function,” Bergelson says. “Taking away visual cues is a clean way to probe how categories might form across species.”

Back home, Arya keeps busy with her favorite search games and word play, oblivious to her superpower. “Because these dogs live in families and pick up words naturally,” Fugazza says, “their parallel to early child learning could offer scientists unique possibilities to explore how language-related abilities might have evolved—and how they can emerge in a nonlinguistic species.”

—Anirban Mukhopadhyay



### COGNITIVE SCIENCE

## Eureka Cam

### Movements reveal moment of mathematical discovery

**IF YOU WANT TO KNOW WHEN** mathematicians are about to have a breakthrough, you don’t need to look inside their heads. Just watch their movements at a chalkboard.

“I’ve always been super intrigued by this tension between how abstract and conceptual mathematics is, on the one hand, and then just how physical the actual activity of mathematics is,” says Tyler Marghetis, a cognitive scientist at the University of California, Merced. He wondered whether he could use the “manual labor” of math to deduce what was happening in someone’s mind. In a recent study in the *Proceedings of the National Academy of Sciences USA*, Marghetis and his co-authors borrowed theoretical tools from other fields to show it’s possible.

Complex systems sometimes abruptly change state. It can happen when metals become magnetic, when algae overtake a pond or when a horse goes from a walk to a trot. Often a period of instability precedes the tipping point. Some neuroimaging suggests that such a change also happens in the process of insight—when the brain is stuck in a rut, wobbles and then finds the right track. This study illustrates that process at work.

The researchers recorded six mathematicians at chalkboards as they each

spent about 40 minutes working on two math proofs and thinking aloud. Observers made a note each time a solver shifted attention to other parts of the board by writing, erasing or pointing at equations, diagrams, or other inscriptions. In this way, the mathematician and chalkboard together acted as what cognitive scientists would call one extended and semiobservable mind. The researchers also recorded exclamations of insight (“I see!”). By analyzing the data, they found that the places attention shifted to became significantly more unpredictable in the two minutes before a eureka moment. It’s unclear where that unpredictability originated: Either a bubbling idea led solvers to connect puzzle pieces across the board, or solvers had grown frustrated and decided to physically forage for new connections, which sparked a solution. Perhaps it was a mixture of both.

“I think it’s a fun paper,” says Santa Fe Institute physicist and mathematician Christopher Moore, who studies complex systems and was not involved in the study. “I only wish it helped me figure out how to *have* more insights,” he adds with a laugh. He’d like to see the study’s statistical approach combined with deep interviews “to build up a rich corpus of what mathematicians were thinking at the time.”

Georgetown University psychologist Shadab Tabatabaiean, the paper’s lead author, imagines a “cool application” of their method: someday computer interfaces that track mouse or eye movements might know when not to disturb someone on the brink of a breakthrough or when to toss a new idea their way. —Matthew Hutson

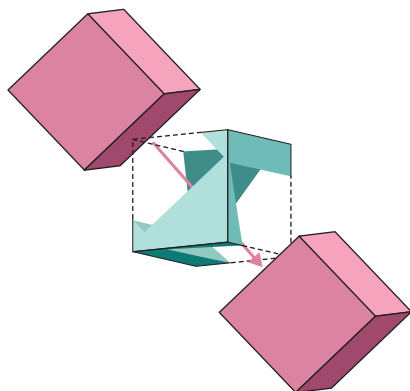


MATH

# Shape Shift

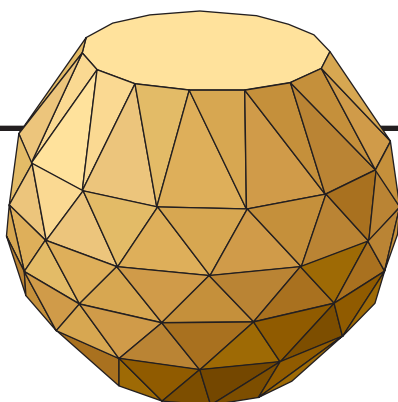
This surprising new polyhedron disproves a long-standing conjecture

**CAN YOU DRILL A HOLE** in a cube that an identical cube could fall through? Prince Rupert of the Rhine first asked this question in the 17th century, and he soon found out the answer is yes. One can imagine propping a cube up on its corner and boring a large-enough square hole vertically through it to fit a cube of the same size as the original.



Later, mathematicians found more and more three-dimensional shapes that eventually came to be called “Rupert”: they are able to fall through a straight hole in an identical shape. In 2017 researchers formally conjectured that all 3D shapes with flat sides and no indents, known as convex polyhedrons, are Rupert. Nobody could prove them wrong—until now.

Enter the brand-new noperthedron. It has 90 vertices, 240 edges, 152 faces and one very special property: it’s “noperth,” a word coined this year by independent computer science researcher Tom Murphy VII to mean “not Rupert.” Mathematicians Sergey Yurkevich of Austrian technology company A&R Tech and Jakob Steininger of Statistics Austria, the country’s national statistical institute, introduced this new shape to the world recently in a paper posted



on the preprint server [arXiv.org](https://arxiv.org). The noperthedron isn’t the first shape suspected of being noperth, but it is the first proven so—and it was designed with certain properties that simplify the proof. Using a bespoke computer program, the researchers managed to verify that no matter how each of two identical noperthedrons is shifted or rotated, one could not possibly fall through a hole in the other.

Yurkevich and Steininger have been studying Rupert’s property for years, and they’ve been working together even longer; the pair met as teens preparing for a math olympiad. “After so many years, we know each other’s strengths,” Steininger says. Yurkevich adds, “If one of us says something that doesn’t make sense, the other one has no problem saying, ‘I have no idea what you just meant.’”

They first stumbled on Prince Rupert’s cube on YouTube as university students, and they quickly found that such solids’ prevalence was an open problem. In a 2020 paper, Yurkevich and Steininger were the first to publicly conjecture that not every convex polyhedron has Rupert’s property. Now, five years later, they’ve seen their conjecture through to its proof.

The researchers described the set of all possible noperthedron holes as a five-dimensional cube, with each axis representing a different rotation of the polyhedron. With a clever mix of mathematical reasoning and computer programming, they discounted each area of that cube as a possibility. “Their approach is both creative and rigorous,” says Pongbunthit Tonpho, a mathematician at Chulalongkorn University in Thailand who researches Rupert’s property. “I did not expect that someone would be able to disprove the conjecture so soon.”

—Emma R. Hasson

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## CIVIL ENGINEERING

# Leg and Pedal

Rain or shine, some places are perfect for bikes and walking

**IN SOME CITIES, CYCLISTS and pedestrians** seem as rare as unicorns. And in others, such as Wageningen in the Netherlands—the world’s top biking city, according to a recent study—they’re as numerous as bees in a hive.

The authors of the study, which was published in the *Proceedings of the National Academy of Sciences USA*, used data from Google to determine walking and cycling rates in 11,587 cities in 121 countries, a far larger sample size than in any previous research. Perhaps unsurprisingly, they found that cities with lots of cyclists and pedestrians tend to be dense and filled with bike lanes.

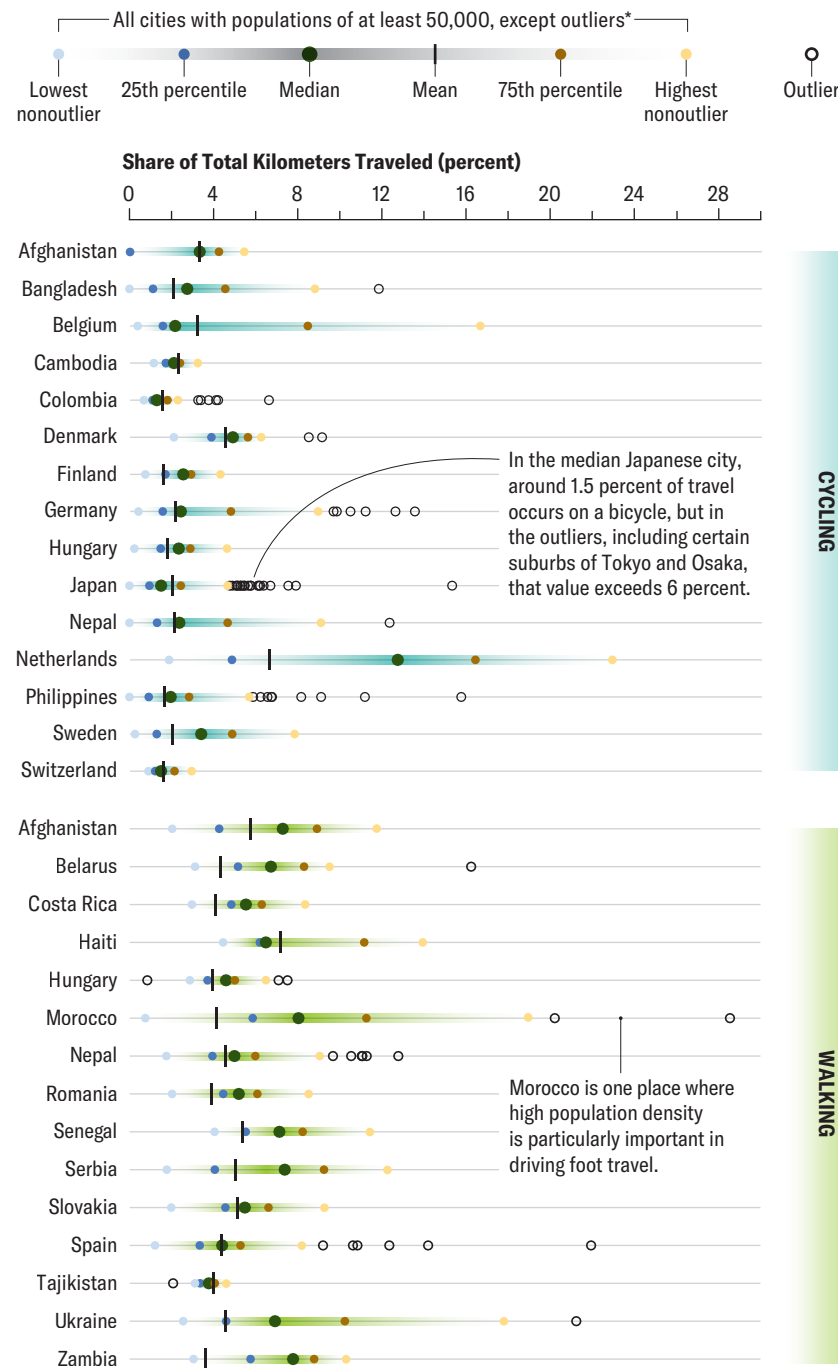
The authors also found that higher gas prices meaningfully increase national walking and cycling rates. “You need carrots and sticks,” says John Pucher, an emeritus urban transportation researcher at Rutgers University, who was not involved in the study. “You need incentives for cycling and walking [combined with] disincentives to car use.”

Cities’ steep terrain can discourage cycling. But the study showed that climate—even frosty winters, scorching summers and ample precipitation—is not a major barrier to high walking and biking rates. In fact, some of the world’s most bike-friendly cities are windy and rainy, Pucher says.

Walking can be a necessity rather than a choice. Carole Turley Voulgaris, an urban planning researcher at Harvard University, who was not involved in the study, suspects that poverty drives high walking rates in countries such as Haiti, and she notes that car ownership provides an economic boost to low-income households.

## Top 15 Walking and Cycling Countries

This chart shows data for the 15 nations where cycling and walking account for the highest share of kilometers traveled. The study found huge variation in active travel between different cities within a single country, reflecting the significance of local-level decisions on infrastructure and land use. The dots represent the spread of city-level values within each nation and highlight the local differences behind national averages. Countries where the researchers had data for fewer than 10 cities were excluded from the analysis.



\*Outliers are cities that fall above (or below) the 75th (or 25th) percentile value plus (or minus) 1.5 times the distance between the lowest and highest 25 percent for a given country.

Source: “Global Health and Climate Benefits from Walking and Cycling Infrastructure,” by Adam Millard Ball et al., in *Proceedings of the National Academy of Sciences USA*, Vol. 122; June 9, 2025 (data)



Still, a car-free lifestyle has broader perks. The study's authors estimate that if every city had a bike network like Copenhagen's, private vehicle emissions would fall 6 percent, and annual health benefits would total \$435 billion, partly because of reduced cardiovascular disease.

Besides Copenhagen, other "success stories," according to the study's authors, include Osaka, Japan, where slow-moving cars coexist with walkers and bikers on narrow streets, and Nairobi, Kenya, which commits at least 20 percent of its transportation budget to non-motorized travel.

In the U.S., as of the past decade only about 1 percent of trips were taken by bicycle, in contrast to 28 percent in the Netherlands. "It's not that Dutch people are genetically predisposed to cycling; it's that most Dutch cities have really good infrastructure for cycling," says study lead author Adam Millard-Ball, an urban planner at the University of California, Los Angeles. "If it were quicker and safe to walk or bike to their kids' school or to the store or to work, then Americans would do that just as much as anyone else." —*Jesse Greenspan*

## MEDICINE

# Gas Busters

An experimental protein grabs carbon monoxide before it latches on to blood cells

**CARBON MONOXIDE IS** a quiet assassin. Odorless and colorless, it has a uniquely efficient ability to starve the body of oxygen: It acts quickly, building up in the bloodstream and attaching to hemoglobin in oxygen's place. When that happens, red blood cells can't pick up oxygen to carry around the body, and the organs effectively suffocate.

This gas, a common by-product of incomplete fuel combustion, causes 50,000



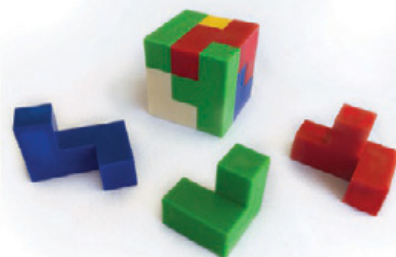
to 100,000 emergency room visits and 1,500 deaths in the U.S. every year on average. Typical treatment for carbon monoxide poisoning calls for using an oxygen mask or hyperbaric chamber to suffuse the body with oxygen, weakening carbon monoxide's bond with hemoglobin cells so oxygen can attach instead. It works, but it's slow—and although only a small percentage of people with carbon monoxide poisoning die, survivors are often left with brain damage, cardiac complications, or kidney and liver problems from oxygen deprivation.

But recent research suggests a faster antidote. A study in the *Proceedings of the National Academy of Sciences USA* documents a newly engineered protein therapy called RcoM-HBD-CCC; when given intravenously to mice, it was shown to cling to carbon monoxide, letting the kidneys expel the poison within minutes.

"We want a treatment that you can give in the field," says study co-author Mark T. Gladwin, dean of the University of Maryland School of Medicine. He says RcoM-HBD-CCC could be injected into people on their way to the hospital in an ambulance or given to people with low oxygen levels at the site of indoor fires.

"This molecule becomes bound to carbon monoxide pretty much as soon as you inject it," says study co-author Jesus Tejero, a biochemist at the University of Pittsburgh. Because it has a much higher affinity for carbon monoxide than carbon monoxide has for hemoglobin, RcoM-HBD-CCC rapidly sponges up the toxic gas. In addition to the mouse

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study, the researchers also confirmed that the protein quickly clings to carbon monoxide in test tubes with human blood.

Lance B. Becker, an emergency medicine researcher at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, who was not involved in the study, notes that the new protein binds to carbon monoxide but not to nitric oxide, a gas molecule that plays a key role in relaxing blood vessels to improve circulation. Gladwin and his team had previously engineered a protein with an affinity to carbon monoxide—but it also bound to nitric oxide, causing problematic artery stiffening in early tests in mice.

Becker hopes this treatment will prove effective in planned studies with larger animals and eventually in human trials, which are probably still a few years off. Although researchers won't know whether it works in human bodies until they try it, Becker is optimistic. "It's a very clever little molecule if it pans out," he says.

—Sara Novak

## MICROBIOLOGY

# Phages Caught Sleeping

Bacteria use hibernating viruses to immunize themselves

**THE IDEA THAT A SINGLE-CELLED** bacterium can defend itself against viruses in a similar way as the 1.8-trillion-cell human immune system is still "mind-blowing" for molecular biologist Joshua W. Modell of Johns Hopkins University.

Scientists discovered about 20 years ago that bacteria employ an adaptive defense system called CRISPR, which lets microbes recognize and destroy viral invaders on repeat encounters. In a recent

study published in *Cell Host & Microbe*, Modell and his team deepened scientists' understanding of how bacteria use this system to "vaccinate" themselves against phages, the viruses that try to kill them. The findings could help develop treatments to fight antimicrobial resistance, which contributes to millions of deaths annually.

The CRISPR system allows bacteria to edit their own genetic code. After being exposed to a virus, a bacterium can use a special enzyme to create openings where it can insert small pieces of the virus's DNA, called spacers, into its own genome, which helps it recognize and fight off the virus next time. Scientists have used this enzyme as a pair of "genetic scissors" to tweak DNA in everything from laboratory experiments to gene therapies, but researchers still knew little about how this process plays out in bacteria. "We called it the CRISPR mystery because we didn't really understand what was happening inside," Modell says.

To understand how bacteria manage to grab the DNA of invading viruses, the researchers ran controlled lab experiments using *Streptococcus pyogenes* bacteria and the phages that infect it. During the infectious phase, most phages rupture the cell immediately in a process known as lysis. On other occasions viruses instead hide inside the bacterial DNA and become dormant, a state called lysogeny that is notoriously difficult to study.

In the lab, Modell's team infected some bacteria with phages that could go dormant and others with genetically en-

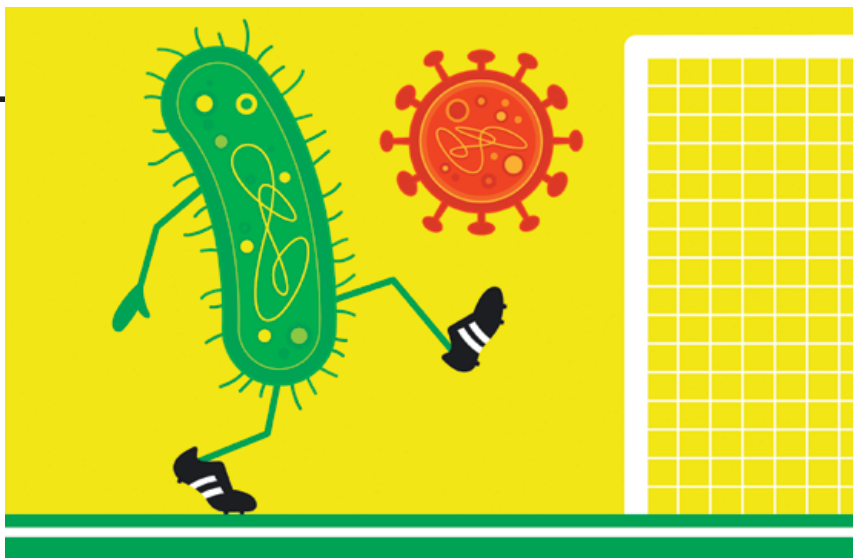
gineered phages locked in an active state. The scientists then collected surviving cells and checked their genetic code to see whether they had added new spacers taken from the viruses' DNA.

The researchers found that bacteria added more spacers from phages that could go dormant. During this lull, Modell explains, the bacteria have time to grab tiny pieces of viral DNA and store them in their genome: "The CRISPR system makes memories against an inactivated form of the virus just like a vaccine."

To confirm their results, Modell and his team exposed spacer-carrying bacteria to the same phages again to determine whether the new genetic memories protected them from infection. The researchers observed that *S. pyogenes* can recognize the phages using those stored fragments and fight them off.

The findings are "pretty remarkable," says microbiologist Stan Brouns of Delft University of Technology in the Netherlands, who was not involved in the study. Understanding the interactions between phages and bacteria is key to improving phage therapies, in which scientists use viruses to treat infections caused by bacteria that have developed resistance to antibiotics.

This new understanding could also help researchers design phages to which more types of infection-causing bacteria will be susceptible, says North Carolina State University molecular biologist Rodolphe Barrangou, who co-founded phage therapy company Locus Biosciences and was not involved in the study.





Various bacteria can have any of more than 150 antiphage defense mechanisms that treatments have to dodge; understanding how this one works, Barrangou says, is “going to inspire people who work on [bacteria] to think about phage therapies on a broader range of infectious diseases.” —*Humberto Basilio*

## PHYSICS

# Going Rogue

A massive study may improve the prediction of dangerous rogue waves

**UNDER A HAZY GRAY SKY** on the first day of 1995, the Draupner natural gas platform in the North Sea was struck by something that had long been relegated to maritime folklore: an 84-foot wall of water that hurled massive equipment across the deck and warped steel supports. The “Draupner wave” provided the first hard evidence that rogue waves were very real.

Three decades later scientists have unraveled some of the physics behind these anomalies. A recent analysis of 27,505 North Sea wave measurements, recorded over 18 years by laser sensors on an oil and gas platform, reveals how ocean waves’ quirky natural physics can produce a lone giant when multiple series (or “trains”) of waves intersect. The study, published in *Scientific Reports*, describes how this phenomenon can amplify a specific wave’s height compared with that of its neighbors. It also identifies a distinct “fingerprint” in the wave data—a repeating interference pattern that appears when two or more wave trains converge and reinforce one another—signaling when a rogue giant is most likely to emerge.

If scientists can detect these signatures early, extreme waves may change from unpredictable terrors into forecastable hazards. “Our civilization critically depends on shipping and offshore activities, and there is a massive international research effort aimed at understanding

rogue waves,” says Keele University physical oceanographer Victor Shrira, who was not involved in the study. “Even the largest vessels and structures are not immune.”

Crucially, the new study helped to clarify what rogue waves are *not*. Researchers have often generated them in laboratories by inducing “modulational instability”: funneling artificial waves into narrow channels until they pile up catastrophically. Study senior author Francesco Fedele, an applied mathematician at the Georgia Institute of Technology, has revised these models in past work—and his findings suggest this lab process doesn’t explain what happens in the open ocean.

“Imagine a stadium crowd leaving through a long, narrow hallway,” Fedele says. “People at the back push forward, and some even climb over others, piling up in the crush,” he says. “That’s like a rogue wave in a wave tank. But if the stadium doors open onto a wide field, people spread out, and there’s no pileup. That’s the open ocean—rogue waves there don’t follow the same physics.”

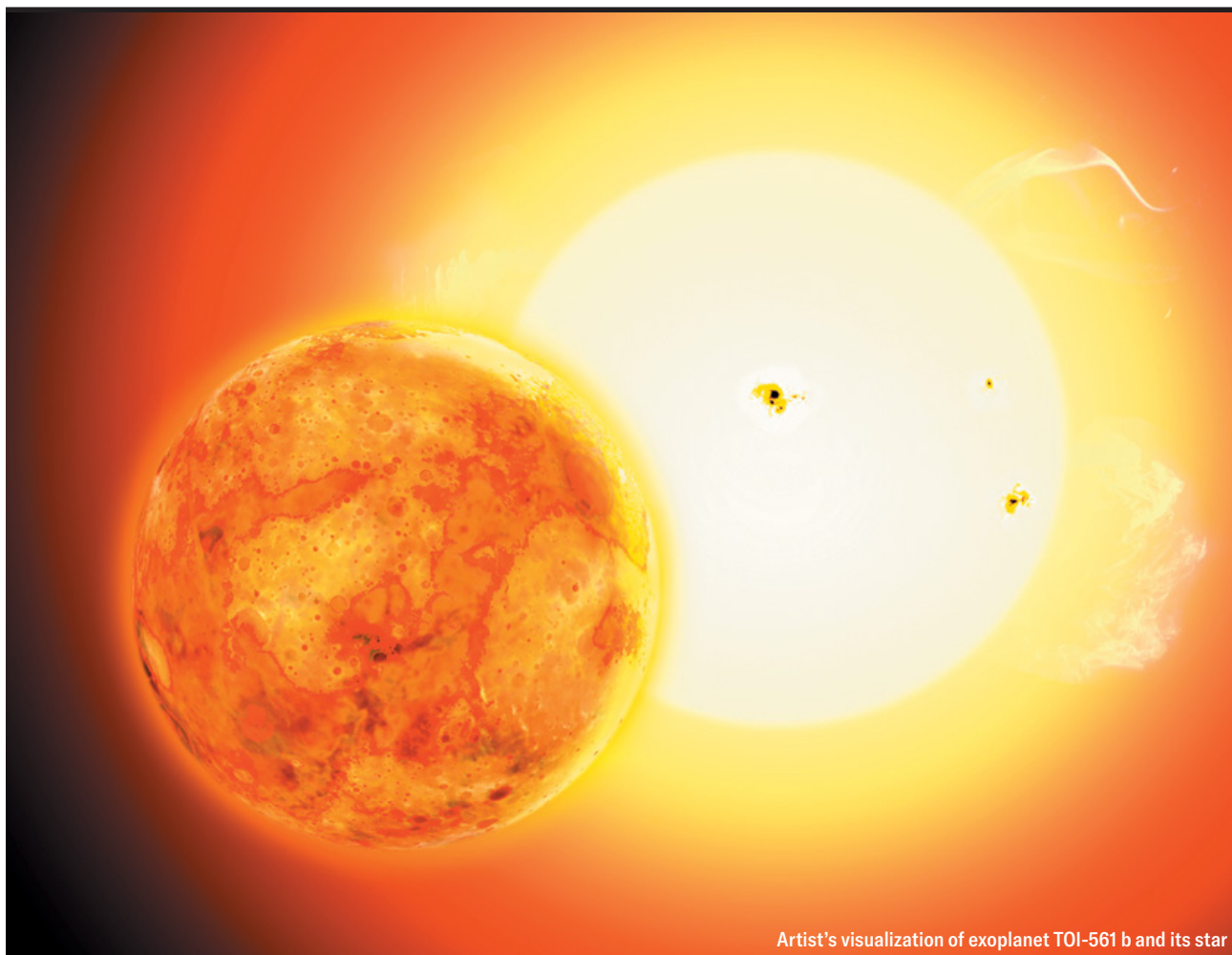
Instead rogue waves involve a subtle quirk of nature. Real oceanic waves aren’t perfectly smooth sine curves; their peaks tend to grow steeper and sharper while their valleys become broader and flatter. Scientists call this built-in lopsidedness “bound-wave asymmetry,” and they have known about it since at least the 1980s but

often dismissed it as a minor detail, according to Fedele. The new analysis suggests that when swells from several wave trains overlap in certain patterns, these sharpened crests can stack dramatically to build a single, towering wall of water—and the study also offers a measurable precursor pattern to this type of stacking.

According to the new research, detecting a particular fingerprint of swells that can lead up to a rogue wave could help scientists and mariners predict these monsters up to a minute before they strike. Such signatures have been spotted in newer data: in one North Sea storm in 2023, for example, cameras captured a 55-foot wave whose growth could be traced to those telltale interference patterns.

“I believe this study can be a further step in predicting rogue waves and helping vessels that may be exposed to them,” says Coral Moreno, an engineer at marine logistics company EDT Offshore, who was not involved in the study. She also suggests a widespread array of floats or buoys could be used to gather even more long-term data for prediction. The study researchers hope that as artificial intelligence, data collection and satellites improve, they will be able to detect these fingerprints across the world’s oceans—turning what once seemed like freak accidents into something reliably predictable. —*Avery Schuyler Nunn*





Artist's visualization of exoplanet TOI-561 b and its star

## PLANETARY SCIENCE

## Dramatic Atmosphere

Exoplanet TOI-561 b has air where none should persist

**ASTRONOMERS HAVE FOUND** an atmosphere where they least expected it: clinging to an exoplanet that's too small, too hot and too old to have air, at least in theory.

Observations by the James Webb Space Telescope (JWST) of the blazing-hot lava planet TOI-561 b suggest not only that it cultivates a thick atmosphere but also that it might have had one for billions of years. This evidence is the strongest yet on a hot, rocky world for

air that isn't just a temporary veil of hydrogen and helium left over from planetary formation. The paper reporting the discovery, posted on the preprint server [arXiv.org](https://arxiv.org), will soon appear in the *Astrophysical Journal Letters*.

"It's super old and ultrahot. It's the worst conditions," says study co-author Tim Lichtenberg, a planetary scientist at the University of Groningen in the Netherlands. "This planet should not have an atmosphere. And it has one."

Planetary scientist Joshua Krissansen-Totton of the University of Washington, who wasn't involved in the study, agrees. "It is definitely surprising and exciting to find a substantial atmosphere on this hot, rocky planet," he says.

In our solar system, atmospheres obey a simple rule: bigger, cooler worlds hold on to their air, and smaller, warmer

ones don't. But TOI-561 b weighs in at just two Earth masses and is very, very hot; the planet orbits so close to its yellow dwarf star that its year lasts less than an Earth day, and its estimated temperature is a rock-melting 2,300 kelvins. TOI-561 b is also about twice as old as our solar system, so its radiation-blasted atmosphere would have had plenty of time to escape. But researchers suspected the planet might be more than a bare ball of magma because of its unusually low density. And scientists previously spotted air on a bigger, hot super-Earth called 55 Cancri e, although the data were "messy and weird," Krissansen-Totton says.

To check for alien air, the research team used JWST to take TOI-561 b's temperature. The planet is tidally locked, so one side bakes in ceaseless radiation while



the other is always dark. The scientists found that TOI-561 b's light-soaked day-side was cooler than they would expect for a naked rock—most likely because gas was there to spread the heat around.

The team is “confident” that an atmosphere is the best explanation for the data, says exoplanet astronomer and study lead author Johanna K. Teske of Carnegie Science in Washington, D.C. But finding an unexpected atmosphere “is the kind of result that generates more questions than it answers,” she adds.

For one, scientists don't know what TOI-561 b's air is made of or how it survived eons of hellish heat. Lichtenberg thinks the atmosphere probably bubbled up from the planet's magma ocean. Every planet in our solar system was once molten like TOI-561 b, he points out; this unexpected atmosphere could have a lot to teach us about the origins of our own.

—Elise Cutts

#### ARCHAEOLOGY

## Vulture Culture

### Human artifacts turn up in ancient scavengers' nests

**IT TURNS OUT** the bearded vulture—also called the *quebrantahuesos*, or bonebreaker—isn't just a carrion scavenger. It's also a keen collector of human ephemera.

This habit has given researchers in southern Spain a unique boon: “time capsules” of human activity that stretch back more than 600 years in the vultures' remote cliffside nesting caves. The raptors often reuse sites for generations.

Sifting through centuries' worth of eggshells, sticks and broken bones, scientists have found a wealth of remark-

ably preserved historical artifacts—among them a crossbow bolt, part of a slingshot and a piece of leather with red decorations that archaeologists say could be a “very peculiar mask.” The vultures seem to be particularly fond of footwear; so far in excavating the upper layers of 12 nesting sites, the researchers have found 25 shoes made from woven esparto grass.

With low humidity and protection from the elements, these cliffside caves create the perfect setting for preserving traces of human history and past environmental conditions. “These are the most inaccessible places you can imagine,” says Sergio Couto, a biologist at the University of Granada and co-author of a paper on the discoveries published recently in *Ecology*. “It's impossible to enter if you cannot fly.” (Or, in the researchers' case, rappel down from the cliffs.)

These finds are just the beginning, says study co-author Ana Marín-Arroyo,

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— Kirkus Book Reviews

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A grass shoe more than 600 years old



a prehistory professor at the University of Cantabria. “If the upper layers are from the 13th century, the lower layers are going to be older. How old?”

Perhaps quite old indeed. Bearded vultures have frequented the Iberian Peninsula for at least 29,000 years—fossilized feces containing acid-digested bones place the birds in what is now Portugal, where they would have lived alongside human hunter-gatherers. University of Barcelona archaeologist Montserrat Sanz, who helped to discover the Portuguese fossils, says the Spanish team’s finds are “quite surprising” and will most likely spark a wave of research follow-ups.

There are plenty of potential time capsules to check. The vultures’ range stretches from Tibet to Tanzania, and the birds are unusually prolific nest builders;

whereas other vulture species may throw together a nest a couple of weeks before laying their eggs, bearded vultures spend months crafting two to three nests every year before settling on one to raise chicks.

It takes a lot of material to construct these nests, which can stretch up to six feet wide. And just as the vultures use wool from mountain-dwelling sheep as insulation, they’ll take advantage of materials from their human neighbors, too. “They remind us how easily we forget that we are part of the ecosystem,” Sanz says.

Some stories, it seems, will repeat themselves wherever vultures and humans live side by side. The same month as the paper’s publication, a store in Catalonia had an unexpected shopper: a young vulture yanked several espadrille shoes off the racks. —Elizabeth Anne Brown

## CHEMISTRY

## Ghostly Fire

“Microlightning” may power strange will-o’-the-wisps

**SOME CALL THEM WILL-O’-THE-WISPS;** others call them *ignis fatuus*, Latin for “foolish fire.” Whatever the name, for centuries people have reported seeing these eerie, faint blue flames hovering over marshes, bogs, and other wetlands. Various cultures have interpreted the ephemeral aberrations as fairies, ghosts or spirits. Scientists have offered a different explanation: the lights form when methane and other gases from decaying material react with oxygen and briefly ignite, producing a flamelike glow.

But one big mystery remained. Although will-o’-the-wisps are not actual flames and occur at ambient temperatures, they still have to ignite somehow. The source of that ignition has been unknown to research.

Now a paper published in the *Proceedings of the National Academy of Sciences USA* seems to provide an answer: microlightning, or tiny, spontaneous sparks of electricity that occur because of differences in charge on water droplets’ surfaces. These droplets form when water bubbles containing methane rise and burst at the surface of the marsh, and the resulting sparks ignite the methane to create will-o’-the-wisps’ tell-tale luminescence.

“Your first reaction when you hear about this finding might be, ‘Okay, will-o’-the-wisps are these ghostly, spooky things, but so what?’” says Richard Zare, a physical chemist at Stanford University and senior author of the findings. “In fact, the phenomenon we found—related to how chemistry can be driven at interfaces—is profound.”

Water is neutral, which means it does not typically carry electric charge. But as early as 1892, scientists noted that fine droplets of water can be positively or negatively charged in an aerosol such as

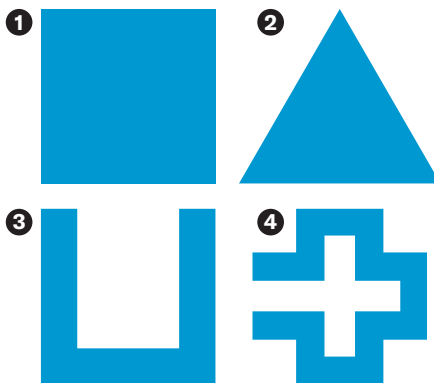
## MATH PUZZLE

## Falling Through

Some say the reason most manhole covers are round is that a circle cannot fall through a smaller circular hole. Which of these other two-dimensional shapes cannot fall through a hole that is the same shape but slightly smaller?

—Emma R. Hasson

**Challenge problem:** Can you find another shape that cannot fall through a slightly smaller hole of the same shape?



Lucia Agudo Perez (artfact); Amanda Montañez (math puzzle)



waterfall spray or fog. Zare's group found that when two oppositely charged droplets get close to each other, electricity can suddenly rush between them, creating microlightning.

Zare and his colleagues first described and coined the term "microlightning" in a study published in March in *Science Advances*. In that study, they showed that when water sprays, some of the resulting microdroplets pick up opposite electric charges that can spark flashes of energy when the drops get close to one another. This spark can drive chemical reactions in the surrounding air that result in simple organic molecules. Zare and his colleagues hypothesized that this process might have generated some of the chemical building blocks for life on Earth.



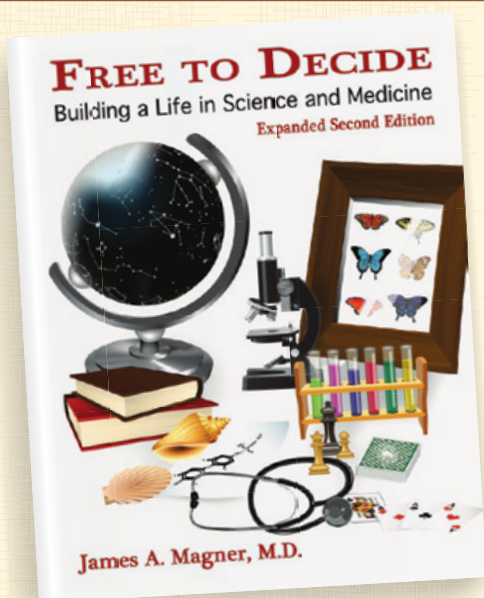
Although the new study has less lofty implications, Zare says the mechanism is basically the same. His team's experimental setup was simple: In a beaker of water, the researchers introduced bubbles composed of methane and air. They captured high-speed videos of the bubbles hitting the surface of the water, forming microdroplets and producing tiny, faint flashes of light. The research-

ers also used mass spectrometry to provide additional evidence that the microlightning they observed generated the energy to drive a reaction between methane and oxygen, converting the gases into different compounds.

The "well-executed" research "strongly suggests" that microlightning is indeed the natural ignition mechanism responsible for will-o'-the-wisps, says Wei Min, a chemist at Columbia University, who was not involved in the work.

But some mysteries endure, Min adds. One big unanswered question, for example, is how, exactly, the strong electric fields form on the droplets' surface in the first place. The answer, he says, will have "broad implications for physics, chemistry, biology and engineering."

—Rachel Nuwer



**James Magner**  
Physician, scientist, chess  
and Texas Hold'em player.

Photo by P Hvizdak, CT Magazine

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SUSTAINABILITY

# THE PIVOT TO PLASTIC

**To keep profits rolling in, oil and gas companies  
want to turn fossil fuels into a mounting pile of  
packaging and other products BY BETH GARDINER**



Reporting for this story was supported by the Pulitzer Center on Crisis Reporting and the McGraw Fellowship for Business Journalism at the City University of New York's Craig Newmark Graduate School of Journalism.

**Beth Gardiner** is author of the forthcoming book *Plastic Inc.: The Secret History and Shocking Future of Big Oil's Biggest Bet* (Avery, February 2026).

**IN 2018, AT A DUBAI RESORT** next to the blue-green waters of the Persian Gulf, Amin Nasser, CEO of Saudi Aramco, stood before an audience of hundreds of petrochemical executives to set out his vision for the future of the world's largest oil company. The goals he described weren't primarily about energy. Instead he announced plans to pour \$100 billion into expanding production of plastic and other petrochemicals.

Nasser predicted that with a growing global population wielding more purchasing power every year, petrochemicals—compounds derived from petroleum and other fossil fuels and of which plastics and their ingredients constitute as much as 80 percent—would drive nearly half of oil-demand growth by mid-century. About 98 percent of virgin plastics are made from fossil fuels. In sectors that include packaging, cars and construction, he said, “the tremendous growth in chemicals demand provides us with a fantastic window of opportunity.”

In the years since Nasser's 2018 speech, Saudi Aramco, owned mainly by the government of Saudi Arabia, has acquired a majority stake in the country's petrochemical conglomerate SABIC. Together the companies have bought into huge Chinese plastic projects and built petrochemical plants from South Korea to the Texas coast. Aramco aims to turn more than a third of its crude into petrochemicals by the 2030s—a near tripling in 15 years.

Although the industry has framed its plans to pivot to plastic as a response to consumer demand for a material central to modern life, another factor is clearly at play: As the looming dangers of climate change are pushing the world away from fossil fuels, the industry is betting on plastic to protect its profitability. Ramping up plastic and petrochemical output, according to Nasser, will “provide a reliable destination for Saudi Aramco's future oil production.” As one industry analyst observed of the company's strategy, “the big picture imperative is to

avoid being forced to leave barrels in the ground as demand for transportation fuels declines.”

Even ExxonMobil has acknowledged that electric vehicles' widespread adoption will probably reduce cars' need for oil. In one market forecast, the company, already the world's largest producer of single-use plastics, assured investors that its plans to increase petrochemical production by 80 percent by 2050 will help the industry to pump and sell even more oil at mid-century than it does today.

But there is growing public awareness that all the plastic made for packaging and goods from the absurd to the essential comes at steep costs: the health impacts of the chemicals it contains, the emissions from its production, the mountains of waste that have built up as it is discarded, and the microplastics found everywhere from the most remote corners of the planet to our brains. Some governments have begun enacting legislation, such as bans on certain single-use items, but efforts to deliver more sweeping change hit a wall with the collapse in August of contentious negotiations on a global plastic-pollution treaty. More than 70 nations had pushed for limits on the amount of plastic produced to reduce the flow of waste into the environment. The industry has lobbied heavily against such caps, arguing that improved waste management and recycling are the solution, even though only a small percentage of plastic is currently recycled and many types cannot be recycled by conventional means.

Companies “know they can't hold their finger in the dike” of an energy transition, says Judith Enck, a

Ross Woodhal/Getty Images/Image Source (preceding pages)





Chemical plants and factories dot the suburbs of the 137-kilometer stretch from New Orleans to Baton Rouge known as Cancer Alley.

former U.S. Environmental Protection Agency official and president of Beyond Plastics, an advocacy group based at Bennington College. “They have to find a gigantic new market, and they have landed on plastic.”

PLASTIC PRODUCTION has been rising steadily since the end of World War II, when companies poured resources into finding and promoting peacetime uses for a material whose military applications—from nylon parachutes to polyethylene insulation for radar sets—had proved invaluable. Consumers snapped up the flood of new goods and disposable packaging, and the annual output of plastic has climbed from two million metric tons in 1950 to more than 500 million today. A cumulative 8.3 billion metric tons had been produced by 2015, according to a landmark study that was the first to quantify the total amount of plastic created. According to Roland Geyer, an industrial ecologist at the University of Califor-

nia, Santa Barbara, who co-authored the study, the total has since risen past 10 billion metric tons. About three quarters of all that plastic has become waste, Geyer’s team reported: 9 percent was recycled, 12 percent was incinerated, and 79 percent ended up in landfills or the environment. If current trends continue, 1.1 billion metric tons of plastic will be made annually by 2050—and the cumulative total will be enough, Geyer says, to cover the U.S. in an ankle-deep layer.

Today half of all plastic goes into single-use items, which are often tossed away almost as soon as they’re acquired. A million plastic bottles are purchased each minute, according to the United Nations’ environment agency, and five trillion plastic bags are used every year. In 2016 Americans alone used more than 560 billion plastic utensils and other disposable food-service items.

Plastic, of course, is not just in throw-away packaging. It is a defining, inescapable part of modern life, widely used in

construction, clothing, electronic goods and cars. It plays a key role in health care as a component in gloves, syringes, tubing and IV bags, not to mention artificial joints, limbs and hearts. It is also not just one material: there are thousands of types and subtypes, each with its own combination of chemicals that yields desired properties—varying degrees of hard or soft, rigid or flexible, opaque or transparent. One analysis found that 16,000 different chemicals are used in making plastics, including additives such as stabilizers, plasticizers, dyes and flame retardants. More than 4,000 of those substances pose health or environmental dangers, and safety information was lacking for another 10,000, the researchers estimate.

By design, plastic does not readily decompose. Instead it fragments into increasingly minuscule pieces—reaching down to the nanoscale—that have been found just about everywhere scientists have looked. They suffuse the air we breathe, the water we drink and the food

we eat. They've been detected in blood, semen, breast milk, bone marrow and placentas. Scientists are only beginning to explore what this omnipresence means for the health of humans and the environment, but the signs are worrying. One recent study found microplastics in tissue from human kidneys, livers and brains, and a study of 12 dementia patients' brains showed greater accumulations than those of people without the disease. Other research found the tiny particles in the neck-artery plaque of nearly 60 percent of patients tested; three years later the rates of heart attacks, strokes and death were 4.5 times higher among people whose samples contained microplastics.

Plastic also exacerbates the climate crisis. The production and disposal of single-use plastics alone creates more greenhouse gases than does the U.K., says the [Minderoo Foundation](#), an Australian research group. That footprint includes the extraction of the oil and gas used to make plastic, the energy-intensive processes for synthesizing it, and emissions from waste that is ultimately burned.

Plastic has transformed modern life, bringing once unimaginable convenience as it has penetrated every corner of the global economy. But the consequences of our decades-long plastic boom are not always easy to discern. I wanted to see them up close, starting with the impact on those who live with the dangers posed by plastic's production.

**T**HE BEHEMOTH in the global plastics industry is China, the world's biggest producer of the material. It pumps out around a third of all the plastic currently being made, and it is in the middle of an expansion whose scale the International Energy Agency says "dwarfs any historical precedent." Over five years, from 2019 to 2024, the agency estimates, China added as much production of ethylene and propylene (two key building blocks of plastic) as takes place in Europe, Japan and Korea combined. Much of the plastic China makes and buys is turned by its many factories into goods exported around the world. Driven by such manufacturing, the coun-

try's voracious demand for finished plastics and other petrochemicals—including the precursors of more plastic—has kept global oil demand climbing even as sales of oil-derived fuels have flatlined.

But since the mid-2000s the fracking revolution that has remade the American energy landscape has also fueled a plastic boom in the U.S. Ethane, a component of fracked gas, is not typically used to generate power or heat. So fossil-fuel and petrochemical companies have poured more than \$200 billion into building and expanding U.S. plants to use it, among other fracking by-products, to make plastic and other petrochemicals. Over the course of the 2010s that wave of investment turned the U.S. into a dominant player in the plastic industry.

The heart of U.S. plastic production is found along the Gulf Coast in Texas and Louisiana, where hulking plants covered in spaghetti-like tangles of pipes sit beside huge cylindrical tanks in petrochemical complexes that stretch over thousands of hectares. Within those complexes, gas-powered furnaces pry apart the molecular bonds of ethane in a process called ethane cracking, the first step in turning the chemical into plastics.

In the next step of a complex, multi-stage process, intense pressure and cold turn those fragmented chains of carbon and hydrogen into ethylene, one of petrochemistry's most important building blocks. Catalysts and more heat then prompt the ethylene to combine with other hydrocarbons to form polyethylene—the world's most commonly used plastic. A typical polyethylene production plant can make hundreds of billions of lentil-size plastic pellets every day. Loaded onto ships, trains and trucks, they make their way to manufacturers who turn them into toys, bags, bottles, and much, much more.

About 150 such refineries and petrochemical plants crowd the winding 137-kilometer stretch of the Mississippi River between Baton Rouge and New Orleans. In an area once lined with sugarcane plantations and still home to descendants of the people enslaved there, the plants sit beside flat, wide-open cane fields.

On a sunny January afternoon, I visited Sharon Lavigne in St. James Parish, right

across the street from the Mississippi. Her house was easy to find. A big yard sign read, "Formosa Plastics would be a death sentence for St. James," the words drawn to look as though they were dripping with blood. Lavigne recalls crawfishing, picking blackberries and pecans, and eating vegetables her father grew when she was a child here in the 1950s and 1960s.

Now her grandchildren get rashes from playing outside, and when she opens her front door, she's hit at times by a smell "so strong it almost would knock you out," she says. Beginning in the 1960s, the area became home to a growing number of petrochemical facilities, eventually including those making plastics such as polystyrene and polyvinyl chloride (PVC). They also churn out precursor ingredients, including ethylene dichloride, ethylene oxide, toluene diisocyanate and methanol, which are used in polyester, polyurethanes and PVC. Their emissions include carcinogens such as chloroprene, ethylene oxide and formaldehyde.

In 2018 John Bel Edwards, then governor of Louisiana, announced that Taiwan-based Formosa Plastics Group (FG) would build a massive \$9.4-billion [complex](#) three kilometers from Lavigne's home—12 separate plants, including two ethane crackers and units making polypropylene and several types of polyethylene. Lavigne retired from her job as a special education teacher and started [RISE St. James to oppose new petrochemical development](#) because of the health risks it poses to residents in a corridor some call "Cancer Alley."

The area around Formosa's site already has more carcinogenic pollution than 99.6 percent of industrial areas in the U.S., a [ProPublica analysis](#) found. The project's permit would allow it to put out more than 5,400 metric tons of air pollution annually, including the carcinogens benzene, formaldehyde, ethylene oxide and 1,3-butadiene. ProPublica estimated it could triple toxic exposures for some residents. "We're already dying, and if Formosa would come in, we're going to die even faster," Lavigne says.

Formosa said that despite activists' opposition, local support is strong for a plant that would provide 1,200 jobs. "Any



claim that FG will greatly increase ‘toxic emissions’ in the area is a misrepresentation and inaccurate,” says Janile Parks, a spokeswoman for FG LA, the conglomerate’s Louisiana arm. If built, the plant will comply with all regulations, she says. “Protecting health, safety and the environment is a priority.”

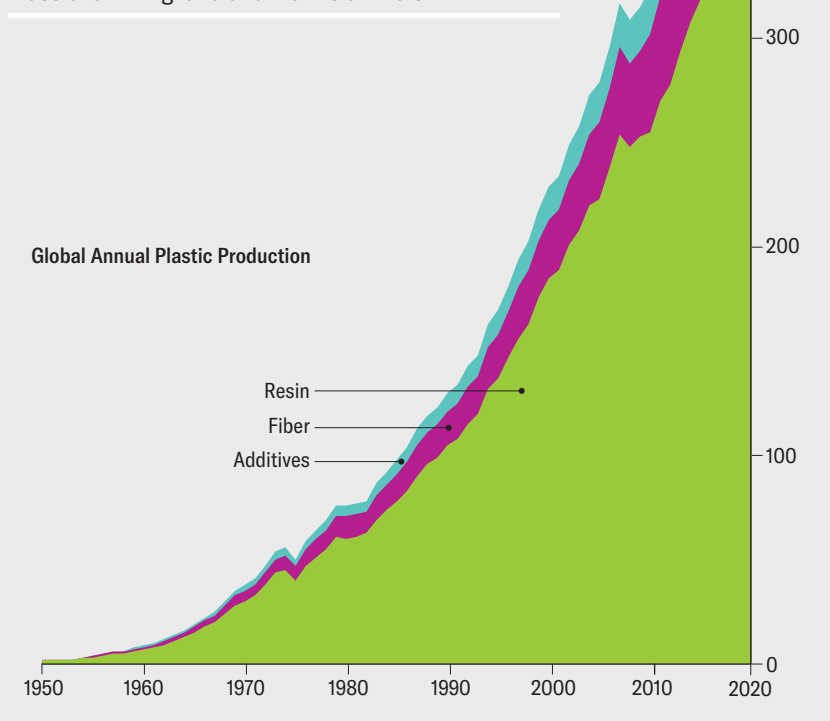
Although the Biden administration tightened limits on toxic pollutants such as chloroprene and ethylene oxide, enforcement proved short-lived. After appointing two former chemical industry executives to top jobs at the EPA shortly after his inauguration in 2021, President Donald Trump signed a [proclamation](#) promising exemptions to dozens of chemical plants. Mass layoffs this year have shrunk the agency, which has shuttered its Environmental Justice office, established to protect those disproportionately harmed by pollution—often low-income communities of color like Lavigne’s. The EPA also announced plans to close a scientific research arm that analyzes dangers posed by toxic chemicals.

Rejecting the “Cancer Alley” nickname, the industry—along with some state and local officials in Louisiana—has argued that average cancer rates in the parishes along the lower Mississippi are close to the statewide average. But finer-grained census-tract data tell another story, according to work done by Tulane Law School’s Environmental Law Clinic, which represents communities fighting pollution. Among poor and predominantly Black neighborhoods, those with more toxic pollution were found to have higher cancer rates. Over a decade toxic pollution had contributed to an extra 850 cancer cases in such neighborhoods, the researchers estimated. “These plants are emitting substances that are known toxins and known carcinogens,” says research scientist Kimberly Terrell, formerly part of the Tulane team. The finding “supports what community members have been saying all along.”

That danger is why Lavigne chose to oppose petrochemical expansion in the place where she grew up rather than moving away. When she first heard about Formosa’s plans, she sat on her porch and “asked God if I should leave the land that

## Plastic Production over Time

The first plastic, Bakelite, was invented in 1907. But it wasn’t until the rapid economic growth of the post-World War II years that plastics production really took off, with people finding endless uses for the cheap and highly versatile polymers and inventing new ones. The amount of plastic produced annually has skyrocketed from two million metric tons in 1950 to 473 million in 2020. Over those 70 years more than 10 billion metric tons of plastic were produced; half of it was made in the 14 years prior to 2020. By 2015 the total mass of all the plastic ever produced was twice the combined mass of all living land and marine animals.



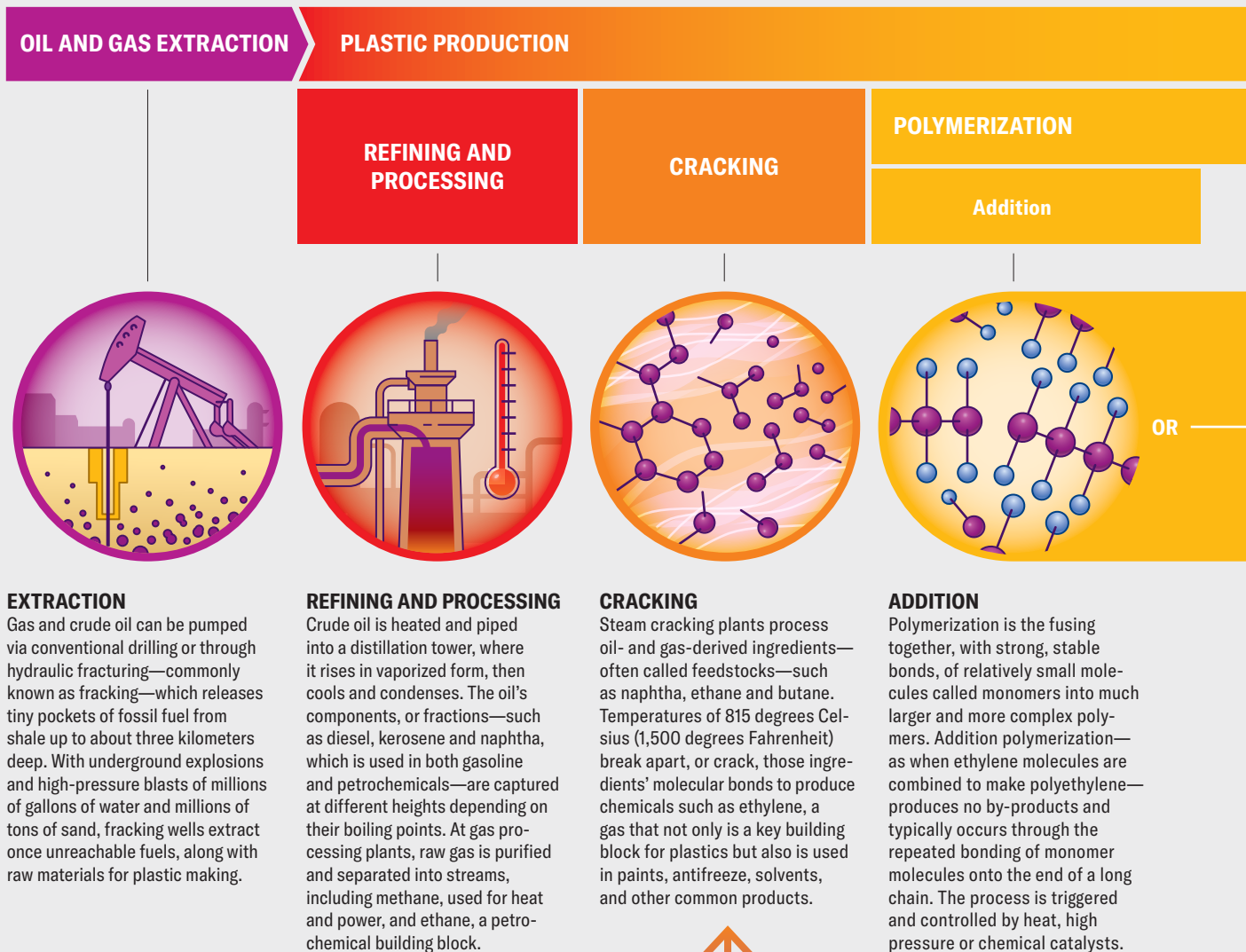
he gave me. And that’s when He told me, ‘No,’” she recalls. “I think my ancestors are so glad I’m fighting.”

MUCH OF THE MATERIAL being produced along the Mississippi and in other plastic-making regions ends up in the Global South. With wealthy countries already saturated with plastic goods and packaging, industry sees the developing world as its most promising new market. Indonesia, where the use of throwaway packaging is climbing fast, is among the nations at the center of both the industry’s growth hopes and the dangers they pose. It’s also the destination for a great

deal of used plastic exported by rich countries, purportedly to be recycled.

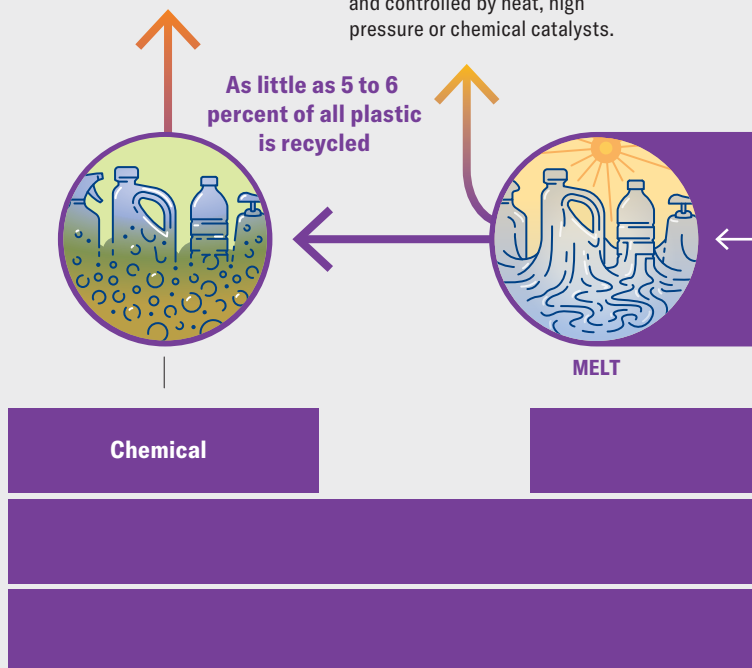
To see where some of that material really ends up, I traveled to the outskirts of the archipelago nation’s second-largest city, Surabaya. Just beyond the city limits is Tropodo, a pretty village of narrow streets set amid lush green fields that is known for its small-scale tofu producers. In one open-air tofu factory behind a mint-green home, shredded plastic scrap is piled against walls. When factory owner Muhammad Gufron stuffs some into a big furnace, it crackles audibly. The plastic is fuel, generating steam to heat vats of soy mixture, which workers stir and then

## STAGES OF PLASTICS PRODUCTION—AND BEYOND

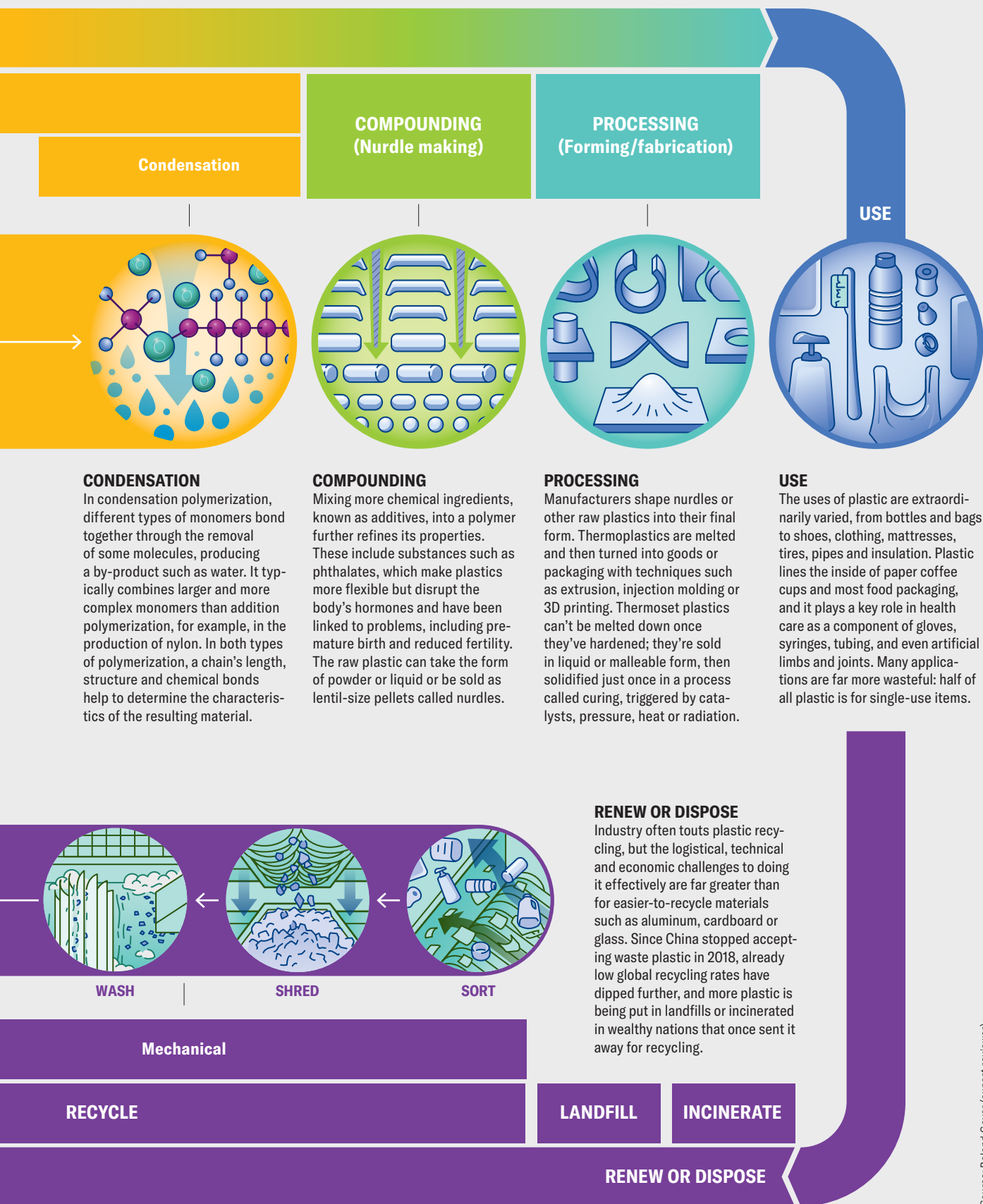


## How Plastic Is Made

There are many types of plastic—including polyethylene, polypropylene, polystyrene and polyvinyl chloride—and an even longer list of subtypes, such as polyethylene terephthalate, or PET, commonly used in drink bottles, and polystyrene foam, often known as Styrofoam. The complex production processes vary but typically involve prying apart the chains of carbon and hydrogen in ingredients derived from oil or gas, then recombining them into even longer chains, or polymers. That length gives them flexibility and strength. Completing the recipe are chemical additives—themselves often oil derivatives—that bind to a polymer's carbon-hydrogen backbone to give it desired properties such as color or malleability.







Source: Roland Geyer (expert reviewer)

scoop into wood draining racks, where it firms into blocks of tofu. “It’s good and cheap,” and it is the fuel for all of Tropodo’s tofu factories, he says.

Heavy black smoke rises from the tall chimneys, almost certainly carrying dioxins, furans, mercury, and other dangerous chemicals that come from burning plastic. The eggs of chickens that peck in Tropodo’s plastic ash contain toxic “forever chemicals” such as polychlorinated biphenyl and perfluorooctane sulfonate, as well as the second-highest dioxin level ever detected in an egg in Asia (the highest was in Vietnam, at a former U.S. military base tainted by the wartime defoliant Agent Orange).

Indonesia has long struggled with plastic pollution. Many areas lack formal waste collection, leaving households to dispose of their own garbage, and a 2020 study found the nation was the world’s biggest source of mismanaged plastic waste. But a significant chunk of its plastic problem comes from waste exported by wealthy countries, including the U.S., which generates more plastic waste than any other nation.

Although Americans toss many of their plastic bottles, yogurt tubs, and other plastic products into recycling bins, as little as 5 to 6 percent of the country’s plastic is actually recycled. The process typically involves shredding sorted material, then melting it into pellets manufacturers can repurpose. But different plastics must be processed separately, and additives such as dyes and plasticizers (which affect the malleability of the plastic) can make effective sorting all but impossible. Even a small amount of missorted material can make a batch unusable. And unlike aluminum, glass or cardboard, which can be recycled again and again, the quality of plastic deteriorates quickly.

Even the easiest-to-recycle types, polyethylene terephthalate and high-density polyethylene—typically used in drink bottles and milk jugs, respectively—often return to market not as new containers but as carpet, clothing or artificial lumber, materials that are not recyclable. There is also little economic incentive to recycle plastic. Recycled plastic can’t compete in terms of either price or quality

with cheap and abundant virgin material—and the imbalance only grows as industry ramps up production even further, making new plastic more plentiful and cheaper. All of this is why so much plastic waste ends up in landfills or incinerators.

Still, the U.S. exports about 400,000 metric tons of plastic, ostensibly for recycling, every year. China used to take in much of the world’s plastic waste but stopped accepting it in 2018 because of concerns over air and water pollution from dumping and burning. So Southeast Asian countries, including Indonesia, were deluged. “We saw many new dumps,” says Daru Setyorini, an Indonesian biologist and activist. “More and more plastic.” Bags and packaging were tangled in branches on riverbanks, piled beside roads, heaped in empty lots and burned in furnaces like the one at Gufron’s tofu factory. That imported waste adds to the flood of plastic entering the seas.

But Indonesia is also dealing with a growing tide of domestic plastic waste. The amount of packaging sold to Indonesians is growing by 4 to 6 percent a year, and flexible plastic packaging—hard-to-recycle soft material used in pouches, films, toothpaste tubes, and bags for snacks and other grocery items—is increasing even more rapidly, says Ariana Susanti of the Indonesian Packaging Federation, which represents companies that make and use packaging. Particularly ubiquitous are sachets, small packets used across the Global South for single servings of everything from shampoo and detergent to spices. One analysis estimated that a little more than a trillion were made in 2023 and predicted that annual output would climb past 1.4 trillion in a decade.

Setyorini has been watching those changes for decades. When she was a schoolgirl in the 1980s and 1990s, she and her mother bought vegetables bundled in newspaper and brought their own baskets, jars and jerricans to the market. Even as the millennium turned and plastic packaging grew ubiquitous, she says, “it was bad but not as bad as now.” Since then, relentless advertisements portraying plastic-wrapped goods as modern, clean and practical have shifted public

perception while companies have eliminated alternatives, Setyorini explains. Now “people have no choice,” she says. “They have to buy plastic.”

Setyorini and her husband, Prigi Ariansandi, also a biologist, have been measuring the health and environmental impacts of plastic through their nonprofit environmental and research advocacy group Ecoton, which they run from an office nestled among banana and tamarind trees 45 minutes outside Surabaya. They’ve found microplastics in the Brantas River, which provides water for millions of Indonesians, and in the bodies of fish, shrimp and mussels. When they analyzed samples people sent them, they discovered the tiny fragments in everything from soil to breast milk.

Indonesia has been tightening its rules on imported plastic scrap, culminating this year with a ban on foreign plastic waste, although there are concerns about smuggling and enforcement failures. Even so, Setyorini and other activists agree the amount of unrecyclable material arriving today—though still significant—is far smaller than at the peak in 2019. At the Ministry of Environment and Forestry in Jakarta, Indonesia’s capital, Novrizal Tahar, former director of solid waste management, says the country aims to reduce the volume of plastic it leaks into the seas by 70 percent and is more than halfway there already. “This is a good achievement,” he says.

Setyorini acknowledges that improving waste management is important, but she believes Indonesia’s government has focused too much on dealing with plastic after its disposal—through methods such as recycling and processing discarded plastic into fuel for cement kilns and power plants—and not enough on requiring companies to use less of it. She and Ariansandi have dragged sachet-covered mannequins to demonstrations to demand that companies stop selling the tiny packets and have sued food and consumer-product firms over their use.

Fundamentally, anything other than reversing plastic’s endless spread and accumulation is, to her mind, a false solution. “We need to go back to that era when people bring their own bag to the market”





In the Indonesian province of Central Sulawesi, an environmental activist identifies plastic packaging waste in a mangrove conservation area.

and vendors refill containers, she tells me—“the old way of shopping” she remembers from her youth.

**P**EOPLE OPT FOR SINGLE-USE plastics not only because they’re convenient but because they’re cheap. They are cheap because the price consumers pay doesn’t reflect the true cost—the expense of managing waste, the environmental damage pollution causes and the growing list of health effects linked to plastic and its associated chemicals. The mounting pile of research detailing these externalities has begun to shift attention toward reducing the amount of plastic we use rather than simply managing waste. With that shift, some governments have started to find ways to achieve that goal.

The European Union has banned single-use plastic items such as utensils, plates, stirrers and straws. In addition, it will require by 2030 that 90 percent of plastic bottles be collected for recycling

and that new ones be made from at least one-third recycled material. With a wide-ranging new set of regulations, it’s barring restaurants from providing disposable plastic dishware and cutlery to dine-in patrons, and it’s requiring that 40 percent of plastic packaging used to ship goods to customers or between businesses be reusable by 2030.

In the U.S., local and state governments from Washington, D.C., to Honolulu have passed laws banning certain single-use plastics or requiring they be recyclable or compostable. When designed well, such statutes can make a real difference. New York State implemented a statewide ban on plastic shopping bags in 2020, and in New York City the sanitation department found that the presence of the bags in the waste stream dropped by 68 percent between 2017 and 2023. A different [analysis](#) that looked at plastic bag bans in two states and three cities estimated they collectively pre-

vented the use of six billion bags a year.

A handful of states, such as Maine and California, have taken another approach by passing “extended producer responsibility” laws. These laws require manufacturers to help fund recycling programs so the companies that profit from cheap plastics also bear some of the costs of the waste. Such legislation not only eases taxpayers’ burden but also could push companies to rethink the amount and type of packaging they use, experts say. California’s is the farthest-reaching law, giving companies a decade to cut their use of disposable plastic packaging by a quarter. It also requires them to pay for municipalities’ recycling costs and to contribute to a \$5-billion fund to address plastic pollution’s harms to health and the environment.

At the global level, more than 180 countries—and reportedly more than 200 petrochemical-company lobbyists—spent three years negotiating a

U.N. treaty aimed at addressing the plastic-pollution crisis. After missing a 2024 deadline, the talks went into overtime, but they collapsed this past August; it's unclear whether they might reconvene. A group of environmentalists and the national delegations supporting them had demanded caps on production, but companies vehemently opposed such limits, focusing on waste management and recycling instead. In session after session, plastic producers fought hard to keep tough measures out of the treaty and stymie progress with procedural obstacles, says Carroll Muffett, former president of the Center for International Environmental Law. "It's the same strategy we've seen play out in the climate space for decades."

Under President Joe Biden, the U.S. had joined calls for the treaty to limit plastic production, but in February 2025 Trump posted "BACK TO PLASTIC" on social media, referring to his intention to reverse a plan for the government to move toward paper straws. At the treaty talks, the U.S. proposed deleting language about addressing the effects of plastics' full life cycle and joined other oil- and gas-producing nations in opposing any production caps. In an e-mailed statement, the American Chemistry Council, representing major plastics producers, warned that such caps would bring "significant unintended consequences. The world needs more renewable energy, safe drinking water, energy efficient buildings, and less food waste, which are all enabled by plastics." What's more, the council added, such limits would be "ineffective in addressing leakage from inadequate waste management."

Last year, at a plastics conference in Dubai convened by the Gulf Petrochemicals and Chemicals Association—the same group to whom Saudi Aramco's chief executive outlined his company's \$100-billion plastic plans nearly six years earlier—Salman Alajmi, a vice president at Kuwait-based petrochemical company Equate, gave the assembled executives an update on the state of the treaty talks. Sentiment has been "getting very emotional against plastic," he told them. Some of the proposals on the table, he

warned, could pave the way for financial penalties that "will diminish for sure the producer economics"—in other words, they would cut into profits.

What's more, Alajmi told his audience, industry's critics saw plastic recycling as part of the problem. Alajmi, who was leading a coalition of plastic-producing countries at the negotiations, urged companies to get involved in trying to reshape the deal. "We have to be more proactive," he said, suggesting they use their legal experts and produce research papers on the benefits of different types of recycling that explain "why they're safe and why we consider them solutions."

In two days of panel discussions and PowerPoint presentations at the conference, speaker after speaker shared visions of plastics' role in a sustainable future through the idea of the "circular economy"—in which discarded material is endlessly recaptured and recycled. Many talked about simplifying packaging to make it more recyclable and scaling up an approach known as chemical recycling, which industry touts as a way to handle plastics that can't be reprocessed with traditional mechanical methods. Most commonly done via a technique called pyrolysis, it breaks plastics down into their building blocks, ethylene and propylene.

But because of the contamination that inevitably lingers in recycled plastics, to be reused, they have to be diluted into a mixture that's 90 percent virgin fossil-fuel-derived ingredients. The plastic ultimately created can contain as little as 2 percent recycled material, *ProPublica* found (although with an accounting method known as mass balance, it can carry labels suggesting a far higher fraction). Pyrolysis can also emit carcinogens such as benzene and dioxins, and the process creates more greenhouse gas emissions than simply producing plastic from oil.

**T**O CRITICS, the petrochemical industry's argument that recycling will solve the plastics crisis is little more than greenwashing—an attempt to ease consumers'

worries and win acceptance of ever rising production. That's what Enck, the Beyond Plastics president and former EPA official, told me as we sat on her back porch in the woods outside Albany, N.Y., one sweltering August morning. Producers have "spent millions of dollars lying to the public, trying to get them to believe that [you can] just recycle your plastic and everything will be fine," she said. California attorney general Rob Bonta alleged as much in a lawsuit against ExxonMobil, saying the company had for decades "deceptively promoted recycling as a cure-all for plastic waste" despite knowing both the conventional and chemical methods "will never be able to process more than a tiny fraction." (ExxonMobil countersued, accusing Bonta of "blatant misstatements" and defending chemical recycling as "a proven technology" that can keep plastic out of landfills.)

To Geyer, the industrial ecologist quantifying production levels, the bottom line is clear. The only way to manage plastic's negative impacts is to make and use less of it. "We need to have a talk about the 'how much,'" he says. "For me, it's blatantly obvious at this point."

But an industry profiting from making ever more plastic, Enck says, won't take the steps needed to get us out of this mess on its own. "The only way to change the trajectory is with strong laws," she says. If such measures make plastic's price reflect its true toll, other kinds of packaging—and systems enabling, for example, reusable takeout containers—could compete economically.

On her porch that August day, Enck pulled out a box of smart products and packaging she uses to show visitors what a world with less plastic could look like—paper candy bags that lack the usual plastic coating and are therefore fully recyclable while still keeping contents fresh; a shampoo bar that forgoes the plastic of a bottle; a glass soap pump that you can refill by mixing tablets with water. "This is

not rocket science," she said. And plastic's beneficial uses are no reason to continue its most wasteful ones. "We can do so much better." ●

#### FROM OUR ARCHIVES Plastics Tomorrow.

D. H. Killeffer;  
March 1944. *Scientific American.com/archive*



As little as 5 to 6 percent  
of plastic waste is recycled  
in the U.S.











MEDICINE

# YOUR PERSONALIZED CANCER VACCINE

**Vaccines based on mRNA can be tailored to target a cancer patient's unique tumor mutations. But crumbling support for cancer and mRNA vaccine research has endangered this promising therapy**

**BY ROWAN MOORE GERETY  
ILLUSTRATION BY TAVIS COBURN**

**A** S SOON AS BARBARA BRIGHAM'S CANCEROUS PANCREATIC TUMOR was removed from her body in the fall of 2020, the buzz of a pager summoned a researcher to the pathology department in Memorial Sloan Kettering's main hospital in New York City, one floor below. Brigham, now 79, was recovering there until she felt well enough to go home to Shelter Island, near the eastern tip of Long Island. Her tumor and parts of her pancreas, meanwhile, were sent on an elaborate 24-hour course through the laboratory. Hospital staff assigned the organ sample a number and a unique bar code, then extracted a nickel-size piece of tissue to be frozen at  $-80$  degrees Celsius. They soaked it in formalin to prevent degradation, then set it in a machine that gradually replaced the water in each cell with alcohol.

Next, lab staff pinned the pancreas to a foam block, took high-resolution images with a camera fixed overhead and used a scalpel to remove a series of sections of tumor tissue. These sections were embedded in hot paraffin and cut into slices a fraction of the thickness of a human hair, which were prepped, stained and mounted on glass slides to be photographed again. By the time a pathologist looked at Brigham's tumor under a microscope the next day, more than 50 people had helped steer it through the lab. Still, this work was all a prelude.

The real action came some two months later, when Brigham returned to the hospital to receive a vaccine tailored to the mutations that differentiated her tumor from the rest of her pancreas. Made of messenger RNA (mRNA) suspended in tiny fat particles, the vaccine was essentially a set of genetic instructions to help Brigham's immune system go after the mutant proteins unique to her tumor cells. It was, in other words, her very own shot.

It's been four years since Brigham received the last of nine doses of her personalized vaccine. In that time she's seen one grandchild finish college and get married and another embark on a Ph.D. She has attended dozens of high school basketball and volleyball games for her third and fourth grandchildren and cradled the family's newest arrival, a granddaughter born last year. She hosts a weekly mah-jongg-and-dessert gathering for a group of friends on Shelter Island and tries to live out her mother's maxim of having "a little adventure" each and every day. "I'm a little crippled here and there with arthritis," Brigham says, but "I never sit still." And she remains free of pancreatic cancer.

Brigham's recovery came as part of a small phase 1 clinical trial conducted by Memorial Sloan Kettering in partnership with pharmaceutical companies Genentech and BioNTech—the latter, along with Pfizer, helped to produce the first approved mRNA vaccine for COVID-19. Brigham was one of 16 patients in the study who received the vaccine, administered in tandem with standard drugs, and one of eight who experienced a significant immune response. Six of those eight patients are still in remission, along with one of the eight others who did not show much immune response to the vaccine.

Seven of 16 might not sound like much. But that number suggests that the vaccine has tantalizing potential. Pancreatic cancer can be exceptionally fast-growing, and its first signs—weight loss, cramping, a touch of jaundice—are easily missed, so by the time it is diagnosed it is almost always lethal. Only 8 percent of patients with the most common form of the cancer, ductal adenocarcinoma, survive to the five-year mark, and the vast majority of people with the disease show little response to treatment.

The results of Brigham's trial were also an early sign that mRNA vaccines may be effective for a wide variety of cancers: whereas pancreatic cancer is known for its low rate of mutations, the earliest data on personalized mRNA vaccines came from studies of melanoma, which researchers had targeted specifically because it tends to mutate so frequently. An earlier phase 2 trial in patients with advanced melanoma found that for those who received both a personalized mRNA vaccine and so-called immune checkpoint inhibitors, the risk of

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death or recurrence decreased by almost half compared with those who got only checkpoint inhibitors. Ongoing companion trials are targeting kidney and bladder carcinomas and lung cancer. In each case, the vaccine is additive: administered after surgery and with standard drugs. The shot's job is to prime the immune system to recognize abnormal proteins arising from mutations and attack any lingering malignancy that escaped conventional treatments—or stamp out future recurrence.

Seeing promising results in fundamentally different kinds of tumors has motivated researchers to pursue personalized mRNA vaccines much more broadly. In doing so, they've developed an approach at the nexus of several important trends, pairing insights about our immune system's response to cancer with advances in vaccine production spurred by the COVID pandemic, the rise of algorithms powered by artificial intelligence, and the plummeting cost of genetic sequencing. Today there are at least 50 active clinical trials in the U.S., Europe and Asia targeting more than 20 types of cancer. A melanoma trial led by pharmaceutical companies Moderna and Merck has now reached phase 3, the last step before a medicine can be approved for public consumption. Personalized melanoma vaccines could be available as early as 2028, with mRNA vaccines for other cancers to follow.

But the promise of this novel approach couldn't have come at a more perilous time for the field. In the first weeks of the second Trump administration, U.S. cancer research was thrown into unprecedented turmoil as federal grants were terminated en masse. According to one [Senate analysis](#), funding from the National Cancer Institute was cut by 31 percent in just the first three months of 2025.

By March cancer researchers worried that mRNA vaccines were facing particular scrutiny. KFF Health News reported that Michael Memoli, acting director of the National Institutes of Health, had asked that any grants, contracts or collaborations involving mRNA be flagged for Health and Human Services Secretary Robert F. Kennedy, Jr., best known prior to assuming that role as one of the nation's most prominent anti-vaccine campaigners. Suddenly, the optimism around personalized mRNA vaccines was overshadowed by a sense that the public investment that sustained cancer research was being dismantled piece by piece.

MUCH OF CANCER'S BIOLOGICAL POWER comes from the fact that to the body, it doesn't always seem like a pathogen. Because cancer arises from mutations in each patient's own DNA, the disease complicates our immune system's central task of

differentiating between body and foreign object, host and invader, "self" and "not self."

Physicians long hypothesized that there was a link between cancer and swelling—a critical sign that the immune system "sees" an enemy to ward off. In the 1890s William Coley, now known as the father of immunotherapy, successfully spurred remission in patients with inoperable tumors by injecting them with bacteria like those that cause strep throat. But the mechanisms behind Coley's treatments were poorly understood, and for decades after his discovery, researchers weren't sure our immune systems could detect cancer at all.

Because doctors didn't know exactly how the body perceives and responds to cancer, early treatments were highly invasive and highly toxic: The first tactic was major surgery on the organs where cancer was taking root. That was followed in the 20th century by the development of systemic radiation and chemotherapy to attack cancer cells throughout the body. Over time oncologists narrowed and refined these approaches incrementally, using more precise surgery, more focused radiation and chemo that killed fewer normal cells as collateral. Still, the dream was to harness immunotherapy, which represented a dramatic departure from the usual tactics in seeking to use the human body's own systems to go after cancer in a more targeted way.

The first real proof that immune cells are capable of recognizing tumors didn't come until the 1950s and 1960s. Gradually, researchers came to understand that cancer deploys a host of tricks to suppress the immune response to growing tumors. Some forms of cancer use fibrous tissue called stroma to construct shields that make it difficult for immune cells to penetrate or attack tumors. Other cancers take advantage of the balancing act our immune systems are always performing when they decide how heavily to invest the body's defenses in warding off a given threat. Some tumors produce proteins that can shut down key immune cells. Tumors may even recruit immune cells to promote the growth of blood vessels that will supply them with oxygen and nutrients.

As scientists learned more about how cancer manipulates the immune system, they started identifying ways to thwart it. Inside our cells, proteins are constantly being chopped up into smaller sequences of amino acids, some of which are then presented on the cell surface as part of what's collectively known as the major histocompatibility complex, or MHC—essentially the immune system's tool for differentiating self and foreign molecules. When the immune system detects a protein from a pathogen, it's supposed to dispatch killer T cells to

eliminate the invader. Some cancers can interfere with this process by hijacking the checkpoint proteins that keep our immune system from revving out of control and using them to turn T cells off. Starting in the mid-1990s, several research teams found success by treating mice with checkpoint inhibitors, then a new class of drugs designed to keep tumor cells from concealing their identity and signaling, effectively, “nothing to see here.” Thirty years on, checkpoint inhibitors have become a transformative tool in cancer treatment, especially for melanoma.

The research that went into developing checkpoint inhibitors showed conclusively that immune cells detect cancer much in the same way they identify other pathogens: through differences in protein structure determined by DNA—a crucial insight. But as revolutionary as checkpoint inhibitors have been for immunotherapy, they don’t work for everyone—far from it. Some 80 percent of patients do not respond to this class of drugs. Researchers are still trying to understand all the mechanisms that play a role in determining who does respond, but one key factor is whether the immune system is able to recognize tumor cells on the basis of their mutations.

This is where mRNA vaccines come in. Jason Luke, a melanoma researcher who now serves as chief medical officer of mRNA-medicine start-up Strand Therapeutics, helped to design several ongoing clinical trials of mRNA vaccines for cancer. He explains that both checkpoint inhibitors and mRNA vaccines build on our deep evolutionary adaptation for fighting pathogens by identifying the proteins they shed in our bodies. But checkpoint inhibitors are effective only if the patient’s immune system recognizes the cancer as a threat. In contrast, mRNA vaccines have the potential to work even in patients whose cancers haven’t spurred much immune response. The trick, Luke says, is using computational tools to decipher which of a given tumor’s mutations are most likely to be found by the immune system.

**O**N A MONDAY MORNING LAST APRIL, I visited surgical oncologist Vinod Balachandran at his lab on the eighth floor of the Memorial Sloan Kettering Cancer Center. Balachandran led the trial Brigham participated in, and he now is director of a center for cancer vaccines that the institution launched in 2024. The entrance to his lab is at the end of a hallway lined with big freezers holding tissue samples.

When I arrived, Balachandran met me just beyond a pair of swinging doors, where postdocs hunched over laptops under rows of high shelves packed with boxes of pipettes and assay plates. He strode to the window and pointed to the brick façade

of the main hospital across the street, explaining that tissue samples taken after surgery have only a short distance to travel to the lab, sometimes through a tunnel under East 68th Street. “The proximity of the laboratory tower to where patients are being treated is actually supercritical,” he says, because it allows the samples to be processed and put on ice quickly, minimizing the deterioration that begins as soon as tissue is removed from the body.

The work that culminated in Brigham’s vaccine grew out of research into a subset of pancreatic cancer survivors known as exceptional responders—the small percentage of people who make it to the five-year mark after a diagnosis. “These patients, you know, they’re very rare,” Balachandran says. Even at a facility as large as Memorial Sloan Kettering, which sees tens of thousands of cancer patients a year, it was possible to study this group with any precision only because of the hospital’s longstanding mandate to save samples of every patient’s tissue. When Balachandran joined the faculty in 2015, his research on long-term survivors relied on tissue samples taken more than a decade earlier.

In 2017 Balachandran and his collaborators published a study demonstrating that some patients with pancreatic ductal adenocarcinoma had more cells able to recognize the unique proteins that mutant tumor cells produced and that their immune systems seemed to develop a kind of long-term memory to fight recurrence. In some cases, immune cells with receptors that could bind to these cancer proteins persisted in the blood for more than a decade after the tumors that spawned them were removed. What if, Balachandran wondered, we could equip the 92 percent of patients who are not naturally exceptional responders with the same kinds of biological tools? “If you can teach the immune system to recognize the proteins in, say, pancreatic cancer, perhaps that could provide a blueprint,” he says.

As tumors grow and metastasize, they undergo a kind of compressed evolution in which normal cells with the host’s DNA accrue mutations that cause them to divide and multiply abnormally, forming an ever larger group of closely related tumor clones. Many mutations register in the form of abnormal proteins and protein fragments, called neoantigens, some of which accumulate on the surface of the proliferating tumor cells.

Balachandran compared this growing family tree of tumor clones with new variants in a group of viruses, like the Alpha, Delta and Omicron variants of SARS-CoV-2, which emerged as the COVID-19 pandemic wore on. “You’d want a COVID vaccine to be able to target each different virus in that rapidly evolving clade,” Balachandran says.



For the development of a cancer vaccine, mapping the evolutionary trajectory of a cancerous tumor is equally important, albeit with a different set of parameters. The goal is not to distinguish between the presentations of two related pathogens but rather to understand at what point a disease derived from one's own body starts to register to the immune system as not self.

"At some point—we don't think immediately—the immune system starts to notice," says Benjamin Greenbaum, Balachandran's colleague at Memorial Sloan Kettering's Olayan Center for Cancer Vaccines, who led the computational work behind the vaccine given to Brigham. In later stages, tumors typically accumulate signs of immune system involvement even if the immune response hasn't been effective—changes in the cell makeup of the microenvironment around the tumor, the display of checkpoint molecules. These signs can be understood as evolutionary adaptations on the part of the tumor in the race to evade detection, Greenbaum explains. "So then the question really became, Can we try to estimate what the immune system is really seeing in cancer?"

TO DEVELOP A WORKABLE MRNA VACCINE, Greenbaum and Balachandran had to both sequence the DNA of the cancerous tumors they were targeting and develop a framework for going after the right neoantigens—those abnormal proteins that offer clues to a tumor's underlying mutations. Neoantigens are made up of short chains of amino acids from proteins with names that look like license plate numbers: PIK3CA, KDM5C. One overarching goal of their collaboration is to discern meaningful patterns in the frequency of the sequences across patients and across cancer types. What neoantigens survive one mutation after another? Which ones show up reliably under certain conditions or look most distinctive to the body's immune defenses?

Some of these sequences, from so-called driver antigens, are present in most clones of a given tumor type. In pancreatic cancer, the driver mutation is often in a gene called *KRAS*, but the resulting antigens don't seem to elicit a reliable immune response in long-term survivors. Instead, when Balachandran and his colleagues sequenced the blood of such survivors, the immune cells present in the highest concentrations were those adapted to antigens resulting from one-off, or "passenger," mutations.

In 2017, at the time that the team published the results of the study, this was a counterintuitive finding. For decades researchers pursuing vaccines and other immune treatments for cancer had focused on melanoma because melanoma tumors have a high rate of genetic mutations. "It looks very different to

## As demand for COVID vaccines has slackened, there has been a rush to apply mRNA technology to a long list of illnesses.

the immune system than many other types of cancers do," says Michael Postow, a medical oncologist at Memorial Sloan Kettering who is involved in clinical trials of mRNA vaccines for melanoma. "That made it a good target." With all the mutant antigens it produces, melanoma should attract the immune system's attention and trigger it to attack. The conventional wisdom about pancreatic cancer, in contrast, held that it produces so few mutations that it is unlikely to carry passenger antigens that could elicit an immune response.

With the results from the 2017 study of exceptional responders in hand, Balachandran was able to flip that argument on its head. Even if vaccines appear to be well suited for melanoma, there's always a degree of uncertainty in selecting the right antigens to target. For starters, the sequencing of a pancreatic tumor biopsy like Brigham's is really just a snapshot in time. Come back a few months or a few years later or wait for the patient to experience a recurrence, and there's no guarantee the tumor clone that seemed dominant at the time of the initial sequencing will still be a factor in the disease. Each mutation can also have unpredictable effects, with the size, shape or biochemistry of the antigen in question shifting dramatically in response to the change of even a single amino acid.

What is more, not every antigen that corresponds to either self or not self is reliably expressed on the surface of the corresponding cell. A neoantigen that seems characteristic of the tumor might have a profile nearly identical to that of another self-antigen somewhere else in the body. In that case, a vaccine based on that neoantigen might fail to elicit much of an immune response, or it could provoke a response against the wrong target.

The study revealed a potential liability in a strategy for personalized mRNA vaccines that focused on melanoma: melanoma's high rate of mutations gives rise to a large pool of plausible vaccine targets, but it presents just as many chances to guess wrong. A given tumor could have as many as 10,000 distinct proteins on the surface of its cells; you couldn't possibly target every one. But in pancreatic cancer, Balachandran realized, the smaller number of mutations might improve the odds of picking a suitable antigen to target.

## Another threat to personalized mRNA vaccines for cancer was coming into focus: mounting federal hostility to vaccines.

**T**HAT INSIGHT UNDERPINNED the pitch Balachandran brought to Ugur Sahin, co-founder and CEO of German biotech company BioNTech. Their collaboration began before the COVID pandemic, but in 2020 BioNTech was consumed by the effort to bring the world's first mRNA vaccine to market. Together with Moderna, the company demonstrated the vaccine's safety through billions of doses administered worldwide with very few side effects.

Not only was mRNA safe for vaccine delivery, but, as Sahin knew from experience, it is also a flexible platform for genetic information. Whereas traditional vaccines typically require ongoing production of the exact virus they're targeting, most of the genetic information in an mRNA vaccine can stay the same no matter which disease you're fighting.

BioNTech's COVID vaccine built on 30 years of work by Sahin and company co-founder Özlem Türeci that was originally intended for vaccines targeting cancer. As longtime collaborators who are also a married couple, they had tinkered with the nucleotide sequences on the molecule's cap and tail that direct a vaccine to the right part of the cell and tell the immune system what to pay attention to, and they had improved the mRNA's stability so that even a small dose of a vaccine could provoke a full-scale immune response. All that work could be incorporated into vaccines for other diseases; the only thing that needed to change was the genetic information in the middle of the molecule. After obtaining positive results for the mRNA vaccine for melanoma, Sahin agreed to partner with Balachandran to develop an mRNA vaccine for pancreatic cancer.

As global demand for COVID vaccines has slackened, there has been a mounting rush to apply mRNA technology to a long list of illnesses, including malaria, flu, tuberculosis and norovirus. Cancer is a natural target. Despite treatment advances, it remains broadly incurable and is a leading cause of death as life expectancies improve across the world. But because cancer vaccines must be personalized, the biggest change in approach to developing them for an mRNA platform comes not in development but in manufacturing. Both BioNTech and Moderna now confront something like the inverse of the challenge they faced in developing the first COVID shots.

Prior to the pandemic, both companies were upstarts among the giants of the pharmaceutical industry. Neither had brought a product to market. Moderna employed under 1,000 people and had manufactured fewer than 100,000 total doses of its clinical-stage vaccines. Once its SpikeVax received emergency use authorization from the U.S. Food and Drug Administration, the company quadrupled its workforce and produced more than a billion doses in just 18 months.

The task facing Scott Nickerson, who oversees Moderna's manufacturing for individualized neoantigen therapies, was to reengineer a process perfected for producing mRNA vaccines for millions of people in batches of thousands of liters. For personalized vaccines, each batch would be a few milliliters at most and would have to be turned around in weeks.

To get there, Moderna is investing heavily in automation, partnering with a robotics firm to prepare sterile kits of raw materials for each batch and thereby minimize operator touch time on the manufacturing floor. The hope is that rather than following a single large batch of vaccine through the entire manufacturing process, workers will eventually be able to move from one small batch to the next after setup.

At both Moderna and BioNTech, the complex logistics of conducting the dozens of different quality-control tests required for each production run falls to algorithms powered by AI. Before being approved for release, doses of SpikeVax underwent 40 distinct tests that tracked the chemistry, biochemistry, microbiology and sterility of every vial. With COVID vaccines, the sterility test alone, which ensures that vials are not contaminated with organisms, took two weeks. Refinements have since compressed that test to eight days, Nickerson says. Ultimately the goal is to shrink it to five days and complete the other tests within that same window. "The reason it's hard is we have to design the equipment," he explains. "None of this stuff's off-the-shelf."

At the same time, the background science is, at least in theory, easily adapted from work that's already been done. Lennard Lee, an adviser to the U.K.'s National Health Service overseeing the rollout of clinical trials for cancer vaccines, says the pandemic gave regulators there a running start on trials for mRNA cancer vaccines. In partnership with BioNTech, the NHS launched a program that aims to provide personalized vaccines to up to 10,000 cancer patients in the next five years. And the NHS and Moderna have invested in a facility that could produce up to 250 million vaccines per year.

In that interval, as manufacturers work to reduce production times and costs, clinical trials will eval-



uate alternative dosage and delivery mechanisms, Lee says. Although current protocol is for vaccines to target micrometastases—small groups of cancer cells that spread to other parts of the body and linger after cancerous tumors are removed surgically—there's no shortage of adjustments that might follow from more data or improved screening. Could one deliver a therapeutic vaccine to tackle a tumor before it is large enough to operate on? Or maybe one could even administer a prophylactic shot that prevents tumor formation in the first place?

With a unified health system and world-class research and manufacturing facilities, Lee says, the U.K. is well positioned to advance research that would answer such questions. Fully realizing the potential of personalized mRNA vaccines for cancer, however, will require more trials in the U.S., which has many more cancer research centers than the U.K. But the ability of the U.S. to lead this effort is now in jeopardy.

The federal government has long been the dominant source of funding for cancer research in the U.S. Miriam Merad, a cancer immunologist at the Icahn School of Medicine at Mount Sinai in New York City, says that in a typical year, funding from the NIH accounts for more than half of the research budget at her institution.

In President Donald Trump's first term, threatened cuts to the NIH never quite materialized. Society is not going to let that happen, Merad thought. But just weeks into Trump's second term, the NIH announced plans to limit indirect contributions to research grants to 15 percent, meaning that for every \$100 in funding awarded, only \$15 extra would be included for overhead—a dramatic departure from historical rates in the range of 50 to 60 percent.

"This is an operation," Merad says, gesturing to the building where she works, which is dotted with six-figure pieces of equipment and has an entire floor dedicated to rearing mice used in research. "We have to pay salaries; we have to buy food for the animals. We have to pay service contracts because we have instruments that need to be serviced all the time." These are not expenses that can be easily paused or restarted based on the fate of a single grant. Within just a few months of the NIH announcement, Merad's department had reduced hires of new postdocs, and Mount Sinai's medical school had to shrink the size of its incoming class.

By May another threat to personalized mRNA vaccines for cancer was coming into focus: mounting federal hostility to vaccines. Senate Republicans convened a hearing entitled "The Corruption of Science and Federal Health Agencies," featuring the false claim that as many as three out of four

deaths from COVID were caused by mRNA vaccines deployed to stop the pandemic. (In fact, COVID vaccinations saved an estimated 2.5 million lives between 2020 and 2024, according to a study published earlier this year.) In June, Kennedy fired all 17 members of the Advisory Committee on Immunization Practices, which makes recommendations on federal vaccine policy. He eventually replaced them with his own advisory committee, which includes several anti-vaccine stalwarts. Kennedy has also slashed research funding for mRNA vaccines. In August he canceled nearly \$500 million supporting the development of mRNA vaccines against viruses such as SARS-CoV-2 and influenza. The move intensified the fears of researchers who want to develop mRNA vaccines for other illnesses, among them cancer.


AFTER MY VISIT TO Memorial Sloan Kettering, Balachandran's team shared a chart that plotted Brigham's immune response to her personalized mRNA vaccine. Along the bottom, triangles marked the dates of her surgery and each of the nine doses of the vaccine she received over the course of a year. Above them a cluster of brightly colored lines showed the share of her body's T cells targeting the specific mutant proteins in her cancerous tumor. At first, when Brigham's tumor was removed, cells trained to go after each cancer clone were somewhere on the order of one in 500,000 T cells in her blood. A few months after surgery, when she'd had four doses of the vaccine, the lines shot up almost vertically, showing that the most common cancer fighter at that point accounted for around one in 20 to one in 50 T cells—an increase of more than 20,000-fold.

Those T cells dipped a bit in the months before Brigham's last booster shot, given almost a year after her tumor was removed. But they remained in the same range even three years on. A phase 2 clinical trial evaluating the safety and efficacy of the vaccine in a larger patient group is currently underway.

The vaccine for Brigham's cancer was just nine tiny vials of liquid administered through an IV, a private message that only her immune system was meant to decode. But the effort that delivered that coded message was a deeply collective enterprise, one that stretches back through the hundreds of thousands of tissue samples collected, stored and analyzed at Memorial Sloan Kettering, each one taken from the body of a patient who might not have survived their cancer. Also in that vaccine were the contributions of generations of taxpayers who never got to see these results. Perhaps their descendants will be able to beat the disease—if society continues to support this vital work. ●

**FROM OUR ARCHIVES**  
**New Cancer Vaccines**  
**Could Treat Some**  
**Types of Pancreatic,**  
**Colorectal and Other**  
**Deadly Forms of the**  
**Disease.** Jaimie Seaton;  
[ScientificAmerican.com](https://www.scientificamerican.com/article/new-cancer-vaccines-could-treat-some-types-of-pancreatic-colorectal-and-other-deadly-forms-of-the-disease/),  
February 13, 2024.  
[ScientificAmerican.com/archive](https://www.scientificamerican.com/archive)





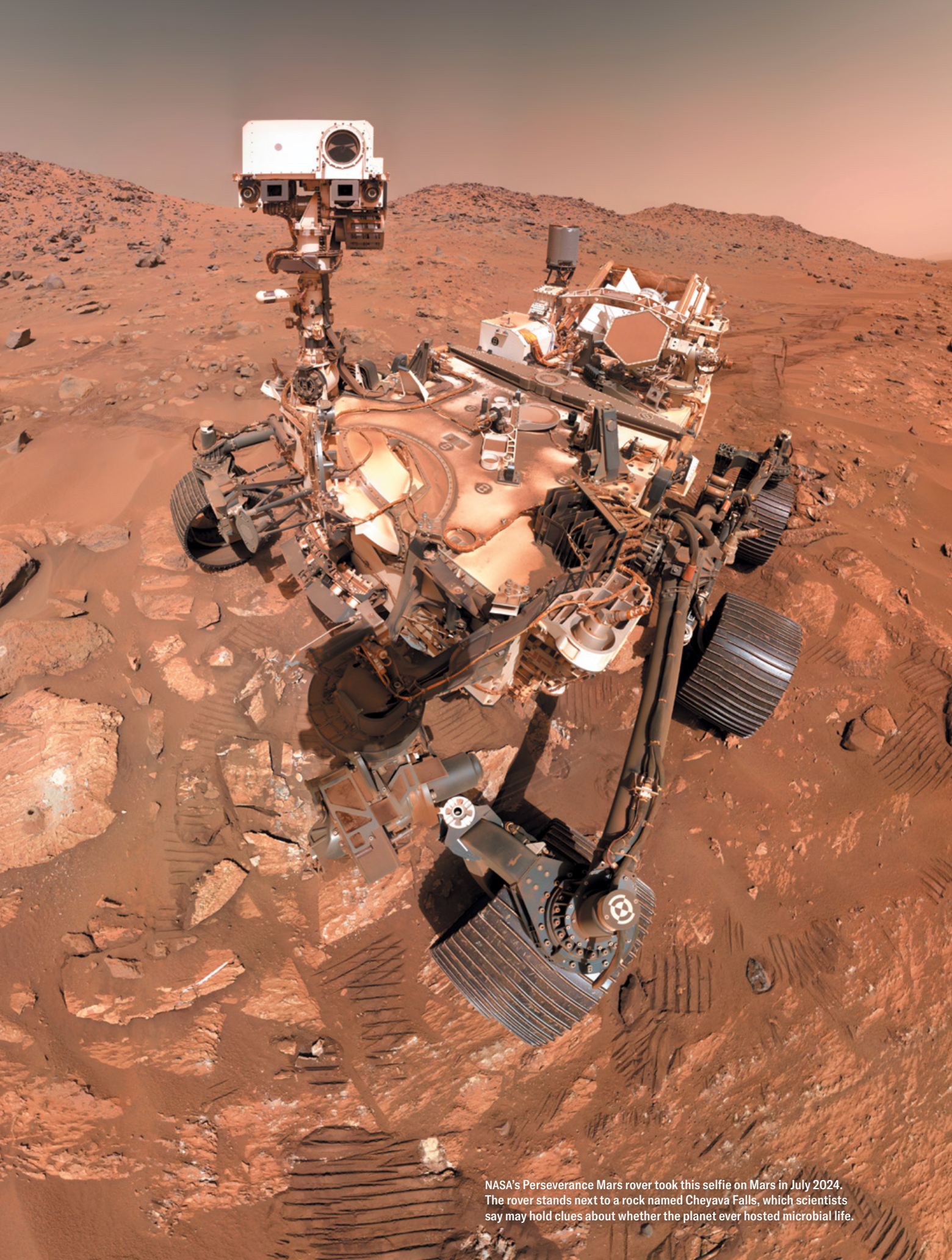
PLANETARY SCIENCE

# STRANDED ON MARS

**NASA spent years and billions of dollars  
collecting Martian samples to bring home.  
Now it might just leave them there**

**BY JONATHAN O'CALLAGHAN**





NASA's Perseverance Mars rover took this selfie on Mars in July 2024. The rover stands next to a rock named Cheyava Falls, which scientists say may hold clues about whether the planet ever hosted microbial life.

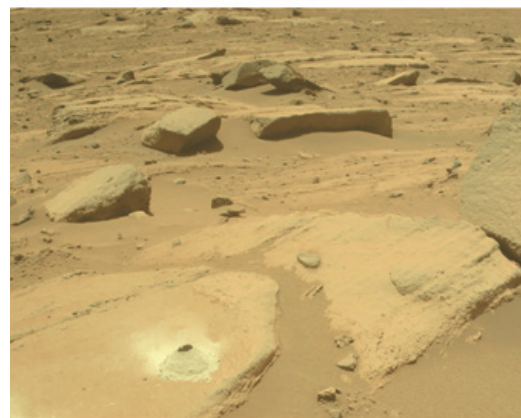


**R**IGHT NOW ONE OF THE MOST advanced planetary explorers ever built is scouring the surface of Mars. Supported by a team of hundreds of scientists back on Earth, the Perseverance rover has traveled nearly the distance of a marathon to answer some of the biggest questions about our neighboring world: What was the planet like eons ago? Was it ever habitable? Did it host life?

One rock visited by Perseverance, called Cheyava Falls, is speckled with iron-rich minerals that might be able to answer these questions, scientists announced in September. On Earth the presence of these minerals usually means microbes that used iron in the chemical reactions essential to their metabolism once lived there. Does the same hold true on Mars? A piece of Cheyava Falls is safely tucked inside the rover's storage cache. If it can be shipped to Earth, analysis with the full range of laboratory equipment here could tell us the answer.

But Cheyava Falls's ride to our planet might have fallen through. The Perseverance rover is the first phase of a multistep mission to bring bits of Mars to Earth known as Mars Sample Return (MSR), and the next step is dangling by a thread. The Trump administration has proposed canceling the return portion of the endeavor. The mission's fate, as of press time, rests with the U.S. Congress.

The situation has dismayed scientists who have longed to get their hands on Martian rocks. "We've been working for so many decades to try to make this happen," says Vicky Hamilton, a planetary geologist at the Southwest Research Institute's Colorado branch. Now that Perseverance has scooped up prized samples, scientists are faced



with the prospect of leaving them on Mars to languish. "It's hard to watch."

Even if the mission isn't canceled, how to finish it remains an open question. In 2024 NASA said it was scrapping its initial, troubled plan for MSR—deemed too costly and too far behind schedule—to seek cheaper commercial approaches. The agency now has multiple options on the table but has yet to decide which course to take, if any.

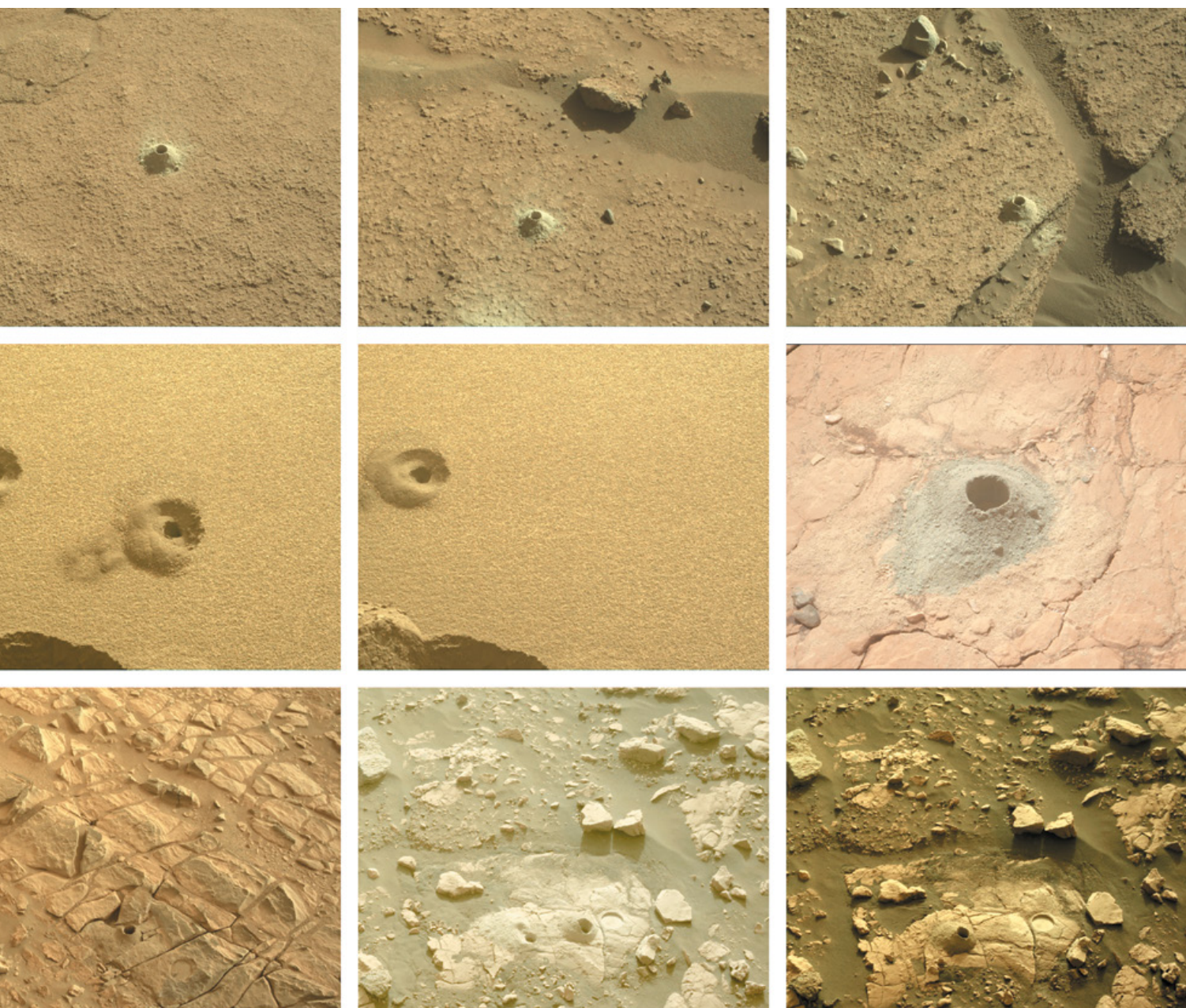
At stake are potentially profound insights about Mars. We know that some three billion to four billion years ago Mars was warm and wet, with lakes and seas on its surface. What we don't know is whether life ever took hold there. Can we find out?

PERSEVERANCE TOUCHED DOWN ON MARS in February 2021 following a nail-biter of a landing.

NASA/JPL-Caltech/MSR (preceding pages)

**Jonathan O'Callaghan** is an award-winning freelance journalist covering astronomy, astrophysics, commercial spaceflight and space exploration.





After the spacecraft had torn through the Martian atmosphere and descended toward the surface by parachute, a crab-like, rocket-propelled platform called Sky Crane lowered the rover on cables to the surface. It landed inside Jezero Crater, a 28-mile-wide (45-kilometer) dent in the Martian landscape. A river once flowed there, and the bone-dry delta it left behind is visible from space.

If anything ever lived on Mars, Jezero is as good a place as any to look for signs of it. It's nearly impossible, however, to send a mission to Mars that would be capable of finding life without help from labs on Earth. That's why scientists have been lobbying since the 1960s

for a way to bring pieces of Mars here.

MSR is the culmination of those efforts. In 2000 Scott Hubbard, NASA's first Mars program director—sometimes called the “Mars Czar”—was tasked with turning around the fortunes of an ailing program that had experienced multiple failures in the 1990s, including the loss of two orbiters and a lander. “I took the existing program down to the roots, almost a bare sheet of paper,” Hubbard says. The top priority, he says, was to find out: “Did life ever exist on Mars, and could it be there today?”

Interest in Martian life had been spurred by a now infamous announcement from the White House lawn in

Perseverance has collected dozens of rock samples during its explorations across Mars. At these 12 sites, it collected cores to be stored in its onboard sample-collection tubes.

1996, when President Bill Clinton declared that signs of life had been detected in a Martian meteorite found in Antarctica. That claim was later refuted—but it caused enough clamor to put the search for Martian life at the top of NASA's agenda.

NASA put a plan in place. Rovers and orbiters would probe the planet to identify good places to look for evidence of life. Then a rover would head there to grab samples, and a third phase would



# Perseverance's Journey

The largest rover ever sent to Mars has been exploring the Red Planet since February 2021. During its more than 37 kilometers (about 23 miles) of roving, Perseverance has collected various samples of rock to be stored until a future mission can carry them back to Earth to be studied in laboratories. That follow-up mission, however, is imperiled: the Trump administration has proposed canceling it amid broader budget cuts for science and space exploration.

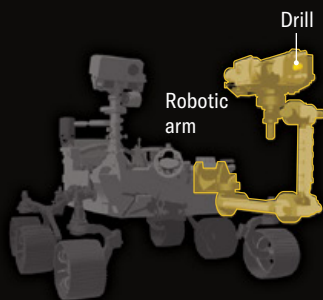
## MILES OF ROVING

This map shows Perseverance's path on Mars. Sols are Martian days, which are about 3 percent longer than Earth days. Each blue circle marks a sample-collection spot, and orange circles designate the samples it later dropped at a backup location called Three Forks (the rest are stowed onboard the rover).

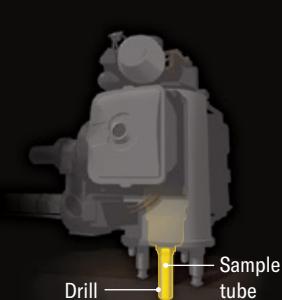


## SAMPLING MARS

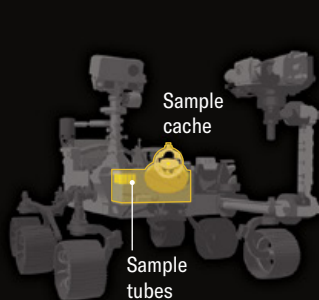
Perseverance has 43 cigar-size tubes for storing bits of interesting rock that may hold important clues. Of those, 38 are meant for collecting samples, and five are "witness tubes" for documenting how clean the rover's sampling system is throughout the mission.



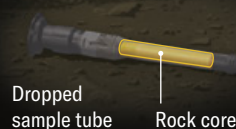
At the end of Perseverance's seven-foot robotic arm is a turret equipped with a rotary percussion drill.



Its sampling arm drills into rocks to collect core samples to be stored in one of the rover's 43 sampling tubes.



Samples are then moved to an internal storage system that photographs, assesses volume and seals each tube.



Some samples have been dropped in a fail-safe location, and the rest are being stored inside the rover for safekeeping.

Source: ESA/DLR/FU-Berlin (base image of Jezero crater); Kenneth A. Farley and Vivian Sun (expert reviewers)

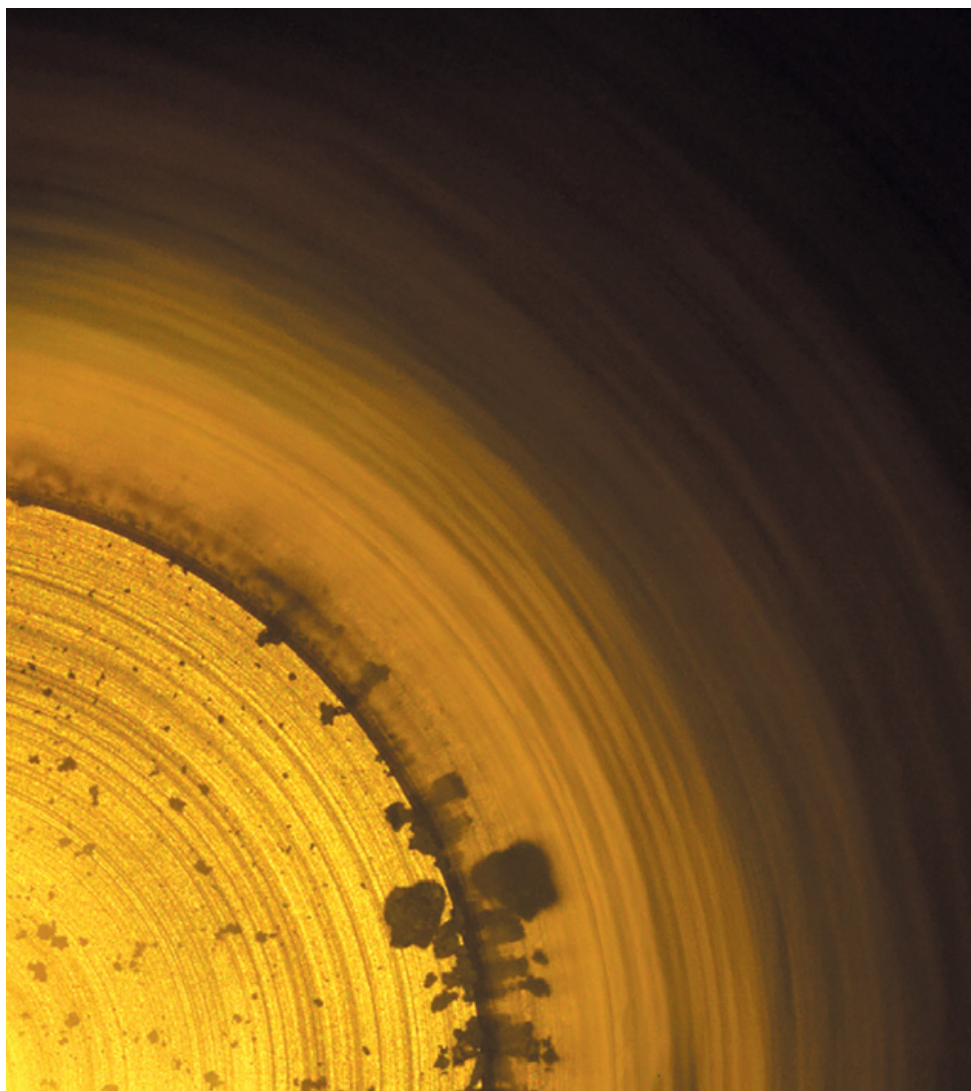


bring them to Earth. In 2012 NASA announced the Mars 2020 mission, which would land a rover, later named Perseverance, to collect the samples. By 2030 a follow-up mission would collect these samples and return them to Earth at an estimated cost of slightly less than \$6 billion. Perseverance launched from Cape Canaveral in Florida in July 2020. Not far behind, scientists hoped, the retrieval mission would follow.

**I**N SEPTEMBER 2021 Perseverance collected its first sample, a type of volcanic rock called basalt, possibly the result of a volcano erupting into Jezero Crater after it was formed. If the stone could be analyzed and dated on Earth, it would help scientists determine the earliest time that water could have flowed into Jezero, estimated to be around 3.8 billion years ago.

Since then, the rover has been gradually making a 20-mile trek toward the rim of Jezero, traveling up the delta of the now absent river. Equipped with a sampling arm and a drill, Perseverance carries 43 cigar-size tubes into which it can deposit interesting samples it has collected, selected by scientists back home who are watching its every move.

The rover dropped 10 of these tubes at a spot called Three Forks between December 2022 and January 2023—a contingency cache in case the vehicle later failed. The most valuable samples, however, collected farther up the riverbed in locations where the prospects for life look more promising, remain on-board Perseverance. These include the Cheyava Falls tube, retrieved in March 2024, which was collected in a region called *Bright Angel*. “Everybody’s probably most excited about the Bright Angel samples,” says Briony Horgan, a planetary scientist at Purdue University and part of the Perseverance science team. “They have potential biosignatures in them.” The Cheyava Falls rock “has our first confident detection of organic matter,” says Perseverance’s project scientist Kenneth Farley of the California Institute of Technology. The rock’s blotches and speckles “could be associated with ancient Martian life,”



Perseverance’s Sample Caching System Camera captured this close-up photo of one of its sample tubes, revealing the sample material it collected as the tube was being prepared to be sealed and stored.

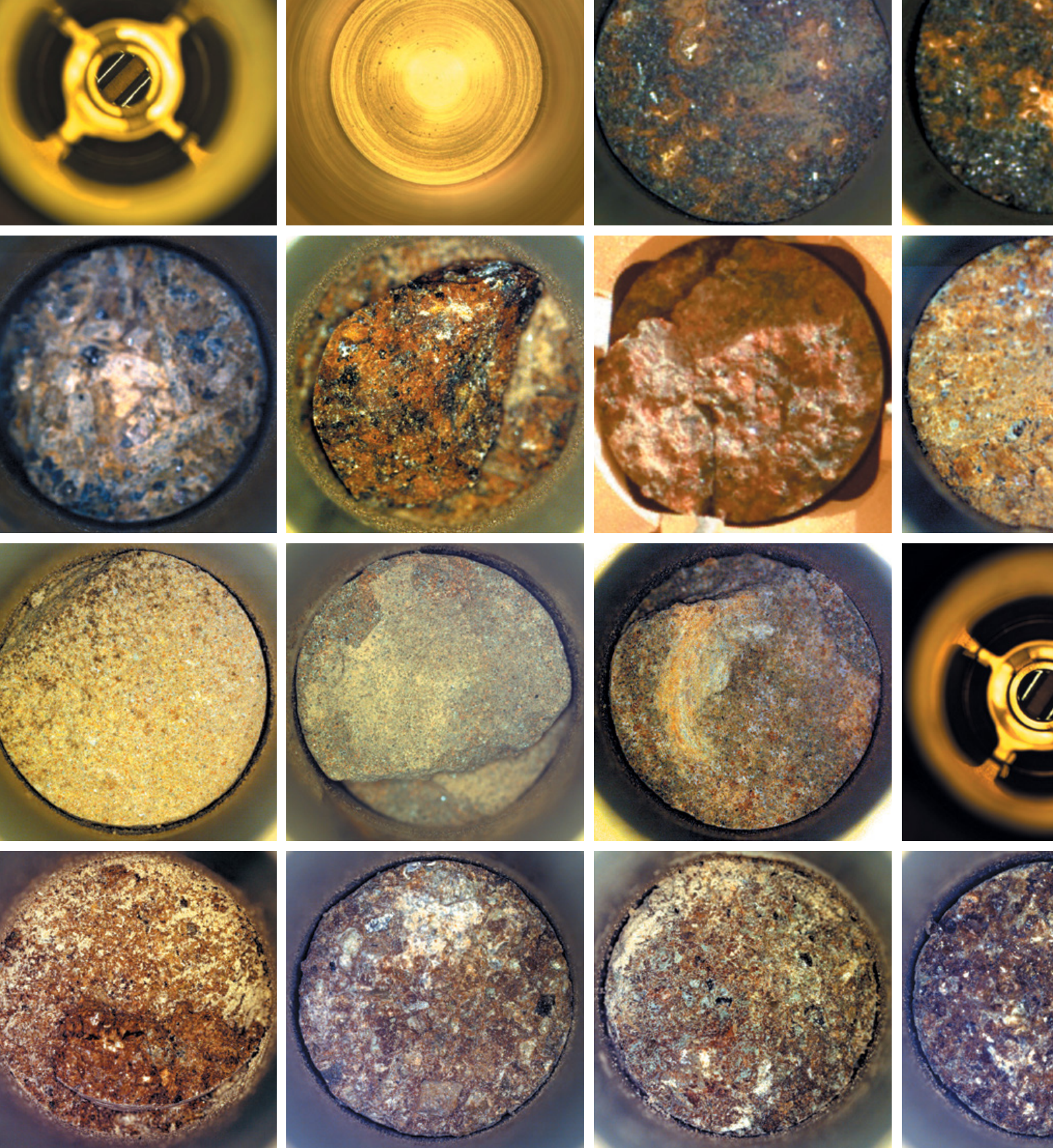
Farley says. “It is the most interesting sample in our entire collection.”

Scientists get giddy thinking about what they could do with these rocks here on Earth. “We would look for a series of properties that are really hard to explain by any abiotic [nonbiological] mechanisms,” says Tanja Bosak, a geobiologist at the Massachusetts Institute of Technology and a member of the Perseverance sample science team. In other words, these samples might be our first concrete evidence of life on another world. Researchers would check for material left behind by decayed microbes, for instance, or an imbalance in two key forms of carbon, carbon-12 and carbon-13. “If you have a dead log [on Earth] with some kind of dead plant matter, you will see a lot of carbon-12,” Bosak says. Other evidence of life could

include microfossils, physical shapes in the rocks themselves that might be the fossilized remains of ancient critters. “There should be some organic compounds or minerals present that we know are good at preserving microbial shapes,” she says.

It’s hard to overstate how important this discovery would be. It would constitute the first evidence of life on another world, proof that Earth was not the only place in the universe to become inhabited. We would know that with the right ingredients and conditions, life could form anywhere. The quest to bring Mars rocks home is not solely about life, though. The project could explain why the planet now has no magnetic field and barely any atmosphere—two characteristics that are probably linked. Mars’s atmosphere might have

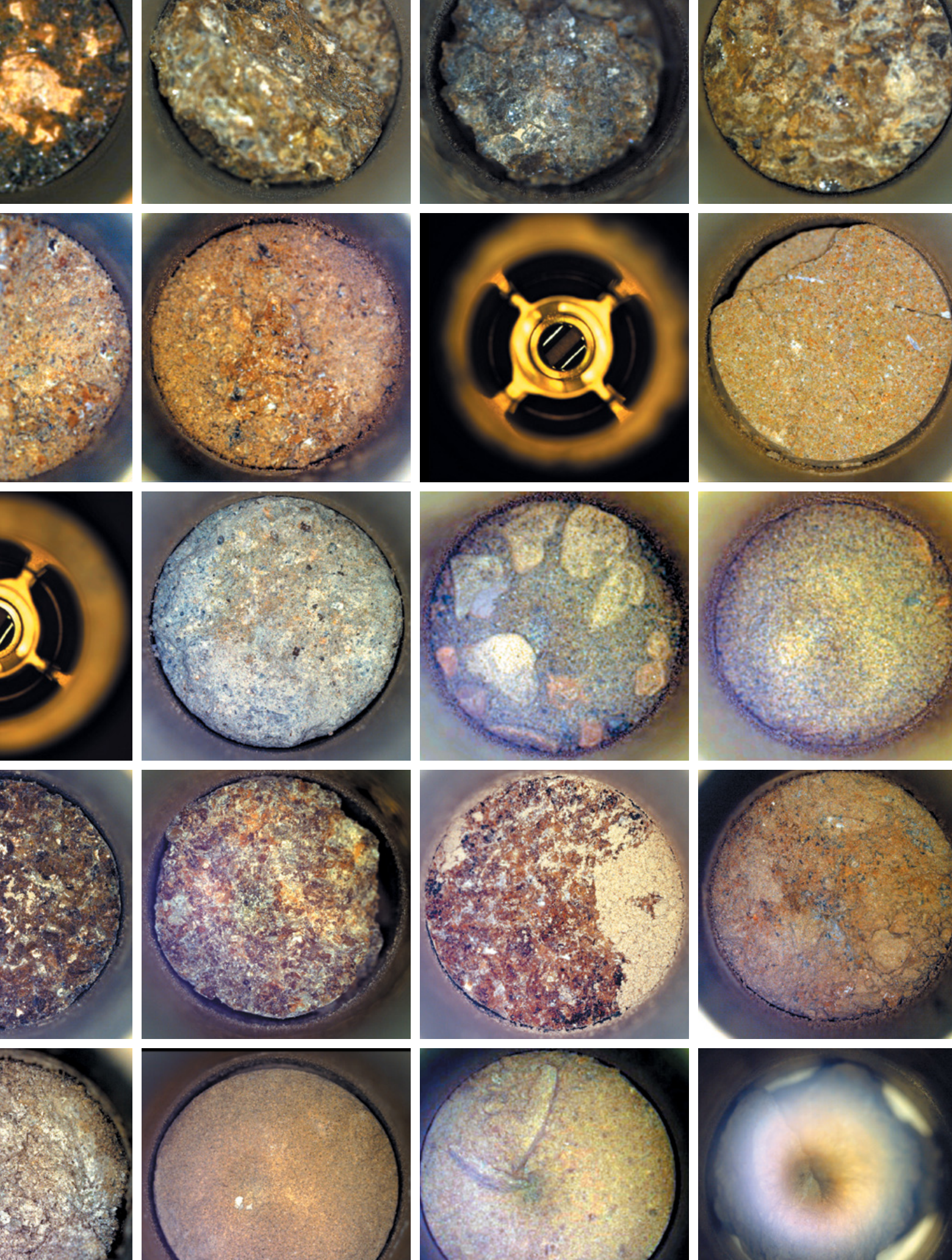




This composite image shows the 33 sample tubes the Perseverance rover had filled as of July 2025, when it had spent 1,574 Martian days (or sols) on the Red Planet. Its collection includes 27 rock cores, two samples of regolith (Mars dirt, made of mixed rock and dust), and one atmospheric sample. The remaining three tubes are witness tubes, which Perseverance used to check how clean its sampling system was.

NASA/JPL-Caltech







been mostly blown away by the sun billions of years ago when the planet's core stopped generating a protective magnetic field, possibly a result of the planet cooling and plate tectonics ending.

Samples collected by Perseverance could tell us when this all happened and why. Electrons in the ground should be oriented in the direction of the planet's magnetic field at different points in time, "like a fossil record of the field," says Benjamin Weiss, a planetary scientist at M.I.T. and a member of the MSR sample science team. X-ray scans of the samples taken on Earth could detect these orientations, which could be matched with various data, including markings on Mars's surface that Perseverance made when it collected the rocks. These measurements would reveal a timeline of activity in the planet's core and maybe solve the mystery of why today Mars, compared with Earth, is such a hellhole—knowledge that could help us in the search for habitable worlds outside our solar system. Given what scientists know about Jezero Crater, there is no question that life should have been able to survive there in the past. If we find no evidence that it did, would that suggest that life struggles to arise even under the right conditions? The only way to know for sure is to finish what NASA started.

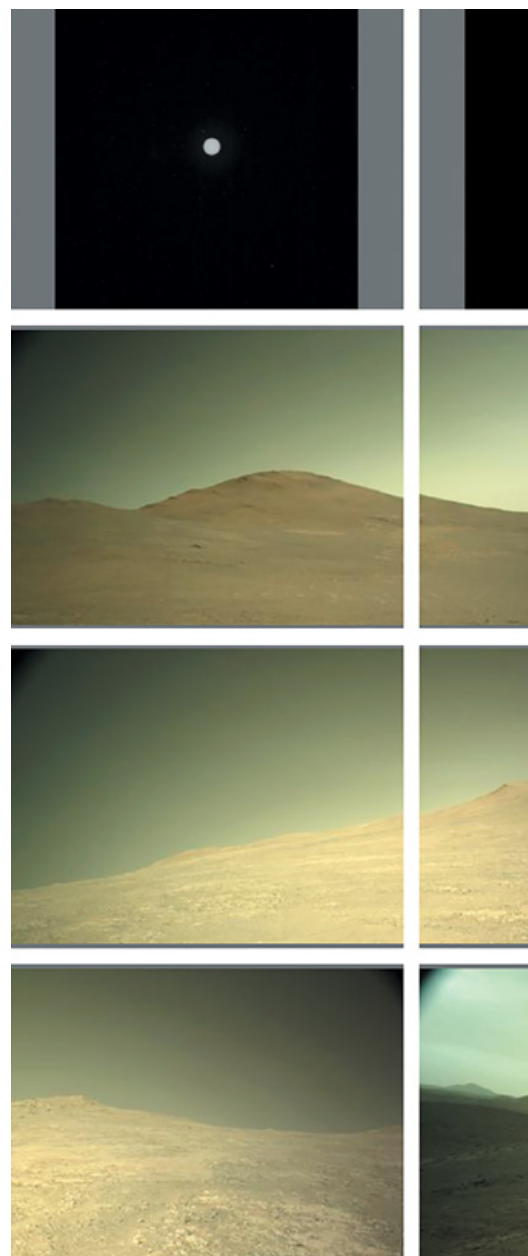
**P**ERSEVERANCE COLLECTED the Cheyava Falls sample three months after its future was thrown into doubt. In April 2024 Bill Nelson, a former senator from Florida who was then the administrator of NASA, announced he would postpone the return portion of MSR. He cited an independent review that warned the program might end up costing \$11 billion—some \$5 billion more than intended—and be delayed into 2040, a decade behind the original schedule. Nelson felt the program was spinning out of control. "It was an awfully complicated plan, and this complicated plan kept getting more and more expensive," he says. Eventually he decided that "we're pulling the plug on this, and we're going to start over," he says. The decision was "disappointing

and surprising" to the scientists working on the mission, Farley says. They felt a "sense that somehow everybody had let NASA down."

There were concerns about the project elsewhere, though. Some scientists thought the sample-return project was taking attention and money away from other planetary science endeavors. "I'm on record for having criticized Mars Sample Return," says Paul Byrne, a planetary scientist at Washington University in St. Louis. "There was a concern that if it had continued the way it was going, it could have eaten all the money for other missions." Still, he wants it to happen—just at a more reasonable price. The planetary science community is nearly unanimous about the mission being a top priority. "We have decades of people pointing to this and saying this is the thing we want to do now," Byrne says. "I don't know if the community can be any louder or more fervent."

Bringing the samples home will require pulling off some unprecedented feats. Humanity has never attempted to launch a spacecraft *from* the Red Planet. The original plan was to send a lander carrying a small fetch rover built by the European Space Agency, which would collect Perseverance's samples and load them into a rocket. That rocket would then be launched into Mars orbit, where another orbiting European vehicle would dock and collect them. But NASA scrapped the idea in 2022 because the fetch rover was deemed too heavy for a safe MSR landing.

So Nelson asked for other ideas. NASA put out a call to commercial companies and other branches of the agency, and by the end of 2024 about a dozen proposals had come in. Elon Musk's SpaceX and Jeff Bezos's start-up Blue Origin both submitted proposals; the details are unknown, and neither company responded to a request for comment, but SpaceX's proposal involves using its huge Starship rocket, which is still in development. U.S. launch company Rocket Lab also submitted a proposal. Rocket Lab CEO Peter Beck claims the company could do the mission for \$4 billion with a return in

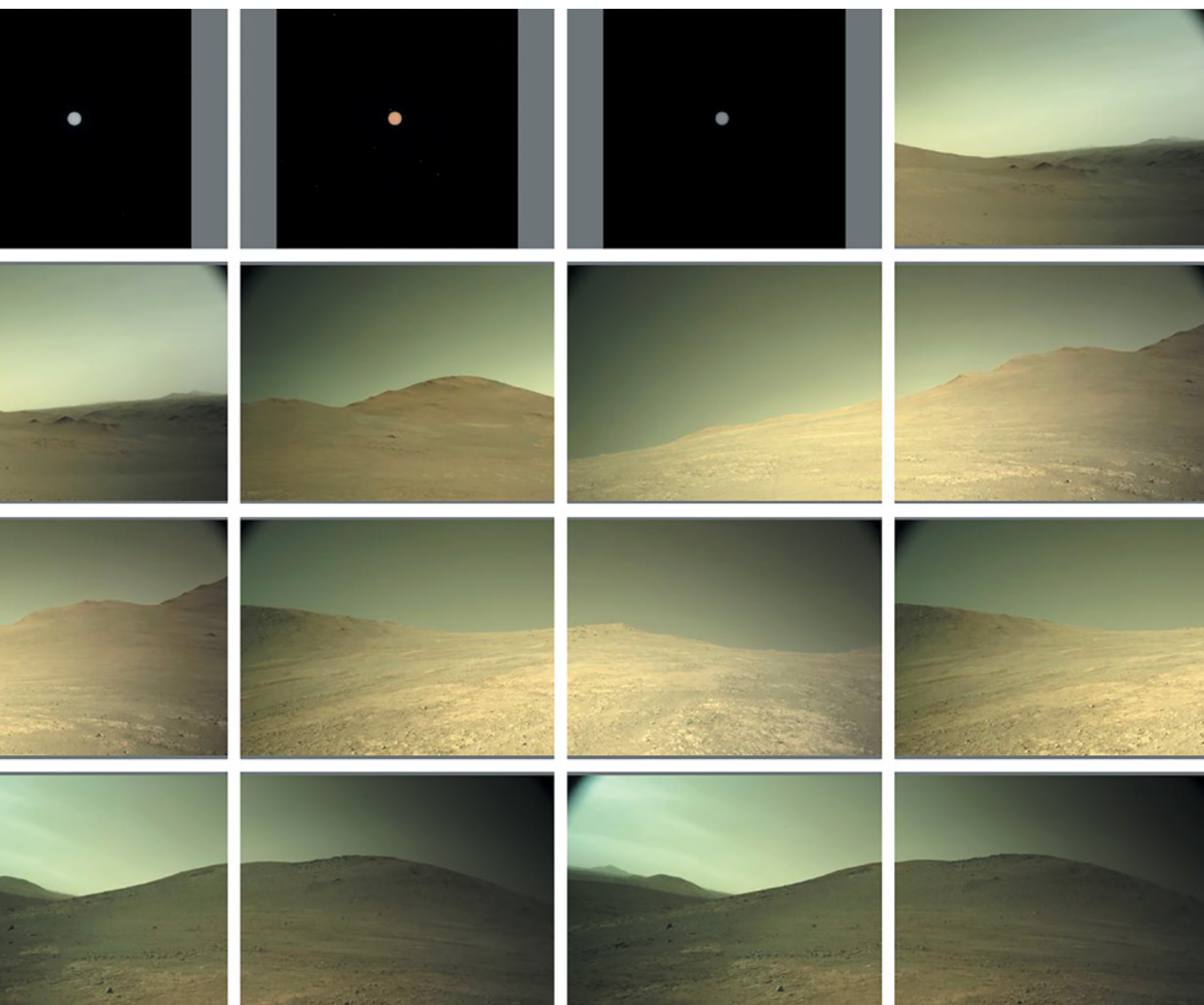


2031 if it were given the go-ahead soon. That's cheaper and quicker than many scientists at NASA had imagined. "We need to get on with it," Beck says. "Pick a path, and let's go."

Because the proposals arrived at the end of the Biden administration, Nelson, who stepped down as NASA administrator in January 2025, decided to let the Trump administration make the choice in mid-2026. The delay means NASA might not be the first to bring Mars rocks to Earth, if it manages the feat at all. China aims to launch its Tianwen-3 mission to Mars in 2028 and bring samples to Earth by 2031, albeit with a much simpler mission that would collect samples from a single location.

NASA/JPL-Caltech





A selection of raw images captured by Perseverance since it landed on Mars in 2021

IN MAY 2025 the Trump administration released its proposed 2026 budget for NASA. The plan called for widespread cuts, scrapping existing space missions, shelving many climate programs and ending Mars Sample Return—which the administration described as “financially unstable”—in favor of one day sending humans to Mars. Now the project’s fate rests with Congress, which must decide whether to follow Trump’s recommendation or rescue the beleaguered mission.

In the meantime Perseverance continues to trundle across Mars. Its plutonium power source has 10 years of juice left, putting a hard deadline on handing off the samples to a stationary MSR

lander if there is no fetch rover. “If construction does not begin in the next two years, I don’t think it’s going to make it,” Farley says. “It takes four or five years at the very least to build a mission. So we’ll know pretty soon what our fate is going to be.”

The sample tubes packed inside the rover can last up to half a century. If MSR is canceled or postponed again, Perseverance could drop them somewhere on the surface in the hope that some future mission—perhaps even a human expedition—collects them. Or maybe another country, such as China, might decide to grab them. “Why not?” says Jim Green, former NASA chief scientist and director of NASA’s Planetary

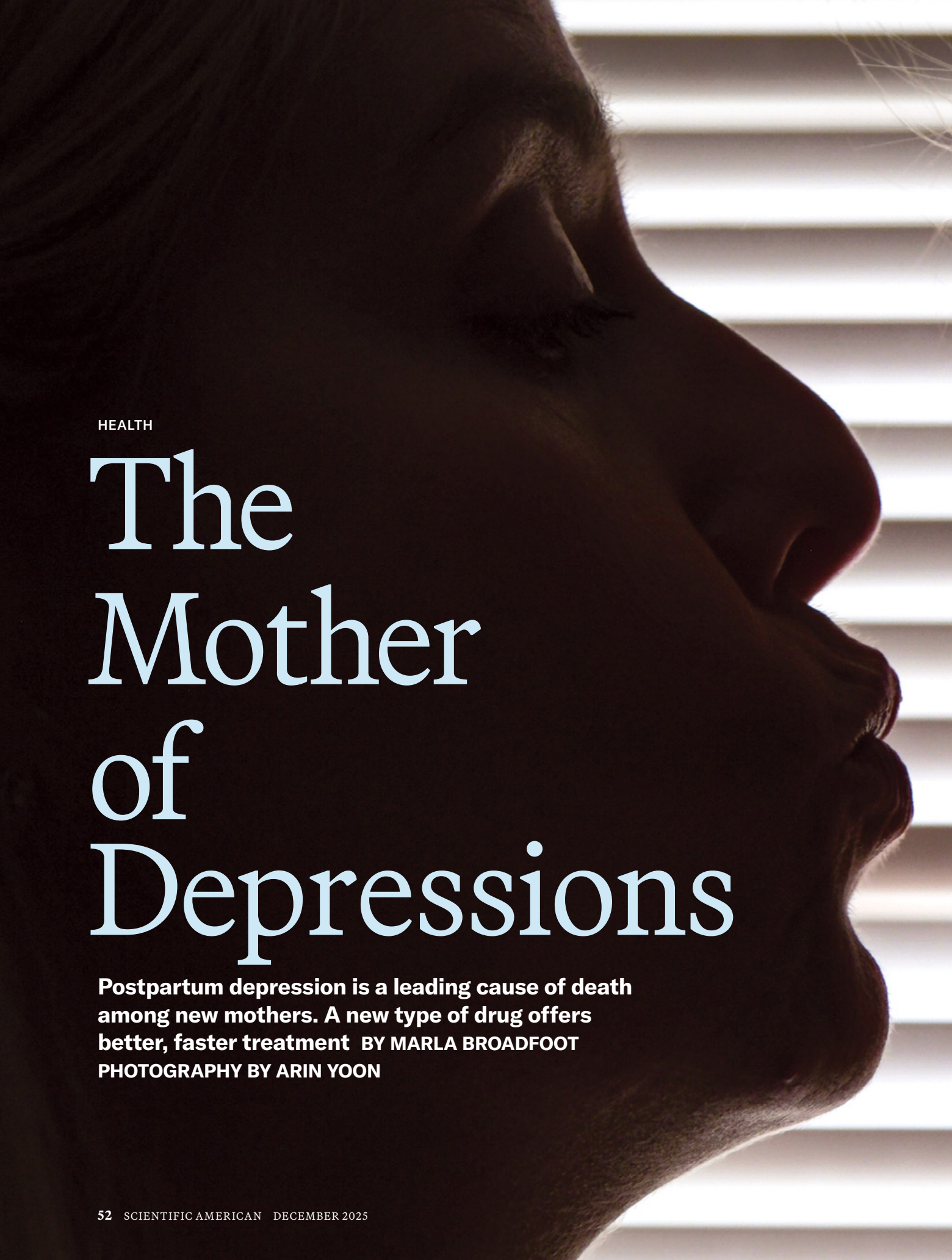
Science Division from 2006 to 2018. “There’s nothing on [the tubes] that says ‘Property of the United States.’”

For now Perseverance keeps storing rocks that might never be picked up. It’s now outside of Jezero Crater, heading to a region that scientists think might contain some of the oldest material yet encountered by the rover, dating back more than four billion years to the dawn of the solar system.

It has fewer than a dozen sample tubes waiting to be filled. ●

#### FROM OUR ARCHIVES Back to the Moon.

Sarah Scoles; October 2024. [Scientific American.com/archive](https://scientificamerican.com/archive)



HEALTH

# The Mother of Depressions

**Postpartum depression is a leading cause of death among new mothers. A new type of drug offers better, faster treatment** BY MARLA BROADFOOT  
PHOTOGRAPHY BY ARIN YOON





Kristina Leos (*left*), who went through severe depression after the birth of her daughter Victoria, leans in to kiss her child.

**P**OSTPARTUM DEPRESSION DESCENDED on Kristina Leos like a heavy fog that separated her from everyone she loved. She could see her newborn baby girl, her two older kids and her husband, but she felt like a ghost passing through their world. “I was going through the motions, but it was like I was looking down on my family,” she recalls.

Leos, 40, a nurse who lives in Midlothian, Tex., tried several different antidepressants and doses. None helped. She messaged a friend, anxious that she was unfit to be a mother. She even asked if they would take her new baby, Victoria. Although Leos never considered hurting her kids, there were times when she was driving home from work and wondered what it would be like to drive off a bridge. “I just had no fear of dying,” she says. “I didn’t care what happened.”

In December 2023, nine months after Leos gave birth to Victoria, her doctor told her they were running out of options. She was down to serious choices, including infusions of ketamine (a drug that alters the anatomy and activity of brain cells), electroconvulsive therapy or admission to a psychiatric hospital.

Then Leos remembered seeing something on social media about a new drug specifically for postpartum depression. Unlike older antidepressants such as Prozac, this medication worked on brain chemicals that are particularly affected by pregnancy. She asked her doctor about it, and they decided to give it a try. Leos began the medication on New Year’s Day 2024. Three days later her world

shifted. “I was driving on the highway, and I could literally feel this huge cloud lifting over me,” she says. “And every day I got better and better.” The drug, called zuranolone and approved by the U.S. Food and Drug Administration in 2023, has since relieved depression in thousands of women.

This kind of help is needed desperately. For new mothers, the overall leading cause of death during the first year after childbirth is not bleeding or infection, according to one study encompassing 36 states. What kills more are mental health problems, which account for approximately 23 percent of maternal deaths in the country. These disorders include a lot of cases of postpartum depression. Yet fewer than half of the women who show signs of such illness are diagnosed, and even fewer receive any form of treatment.

Emerging research on the biology of postpartum depression shows that it is not like other severe mood disorders neurologically or biochemically. Rather it is a result of dramatic changes in hormone levels that come with pregnancy and childbirth. Studies have shown that levels of progesterone and a related hormone, allopregnanolone, rise significantly during pregnancy. Then the

**Marla Broadfoot** is a freelance science writer who lives in North Carolina. She has a Ph.D. in genetics and molecular biology and is an adjunct at the University of North Carolina at Chapel Hill. Her feature on a new type of pain pill was published in our September 2024 issue.





levels drop sharply after delivery. Some women are particularly sensitive to this drop, which can disrupt the brain circuitry that regulates mood, leaving them unable to effectively deal with the stresses of motherhood. Zuranolone is designed to offset that drop-off.

Growing knowledge of the neurobiology of postpartum depression is also pointing toward methods for earlier and more reliable detection. Many experts hope that identifying biomarkers that predict which women will develop the condition, as well as the introduction of the new medication, will take the stigma away from the illness and

stop both health-care workers and patients from viewing it as a sign of personal weakness or poor parenting. “It is a serious mental illness,” says Kristina Deligiannidis, a reproductive psychiatrist at the Feinstein Institutes for Medical Research at Northwell Health in New York State. “We just want to empower women to seek treatment.”

Challenges do remain. The price tag for the two-week course of zuranolone is nearly \$16,000, raising concerns about how insurance coverage and looming Medicaid-eligibility cuts could restrict access, especially because Medicaid covers about 40 percent of births in the U.S. And re-

Leos finally got relief from her postpartum depression with a new medication, zuranolone; she felt better within days of her first dose.

## Not everyone who takes zuranolone is going to have a fabulous remission. Still, it works well for more than half the people. That's a game changer.

searchers are still trying to figure out why the pill doesn't work for everyone. "Not every single person that takes it is going to have a fabulous remission of their symptoms," says Samantha Meltzer-Brody, a psychiatrist and founder of the perinatal psychiatry program at the University of North Carolina School of Medicine in Chapel Hill. Still, she views the medication as a major milestone. "It can work remarkably well for more than half of people, and it's rapid-acting," she says. "That's a game changer."

FOR CENTURIES MEDICINE has struggled to fully grasp the causes and consequences of postpartum depression. Descriptions go as far back as ancient Greece: physicians wrote about women who showed signs of a depressed mood, and even psychosis, after childbirth. During the Middle Ages new mothers with depressive symptoms were often believed to be possessed by demons or suffering from an imbalance of bile or other body fluids. Postpartum mood disturbances have also been grouped into vague or broad diagnoses such as melancholia, mania or neurosis, which did little to help patients.

Even in modern times, such distress is often dismissed as "baby blues"—the mood swings that affect most new moms but typically resolve within a couple of weeks. But postpartum depression is more intense and long-lasting. It can cause profound sadness and despair, disrupting the crucial bond between mother and child, and its consequences can affect multiple generations. Every year approximately 500,000 women in the U.S. experience the condition. Approximately 30 percent of women with postpartum depression continue to experience symptoms one year after giving birth. For some these problems can persist for as long as 11 years.

Yet postpartum depression is not officially recognized as a standalone illness. It did not appear in the *Diagnostic and Statistical Manual of Mental Disorders (DSM)*, the so-called bible of psychiatry, until 1994. Even then it was listed as a subtype of major depression. In the most recent major edition, *DSM-5*, released in 2013, it is still subsumed under the "major depression" label, with the added phrase "with peripartum onset." These additional three

words reflect evidence that almost half of women develop symptoms during pregnancy, not just after.

Because postpartum depression has been lumped in with major depression, the two have often been treated the same way. Therapy has relied on traditional antidepressants such as selective serotonin reuptake inhibitors (SSRIs) or serotonin and norepinephrine reuptake inhibitors. This approach is rooted in the idea that depression stems from low levels of chemical messengers such as serotonin and norepinephrine that help to govern mood. These antidepressants aim to boost levels of these messengers in the brain.

But in recent decades the research community has recognized that focusing only on these chemical imbalances leaves out other factors that may underlie postpartum depression—including genetics, inflammation, hormonal changes, and neuroplasticity, the brain's ability to adapt and form new connections.

Some scientists suspected that fluctuations in hormones such as estrogen and progesterone—called neurosteroids because they act in the brain—played an important role. Yet when research groups started examining the levels of various hormones and neurosteroids, they did not see consistent differences that explained why some new mothers developed depression and others did not.

Then, about 17 years ago, Jamie Maguire, a neuroscientist now at Tufts University, stumbled on some unusual behavior in mice that had just given birth, and her observation helped to connect the dots. At the time, Maguire was a postdoctoral fellow at the University of California, Los Angeles, studying an ailment called catamenial epilepsy, in which brain seizures become more frequent or more severe during certain phases of the menstrual cycle. She was interested in how neurosteroids might protect against these seizures. Some neurosteroids have been shown to dampen brain activity by strengthening certain effects of a neurotransmitter called gamma-aminobutyric acid, or GABA. This chemical can inhibit neurons, making them less likely to fire. Maguire genetically engineered mice to have altered receptors for GABA on their neurons, making it hard for them to react to the chemical. Without this "brake" on neural activity, the mice's brains became hyperexcitable. That extreme state can contribute to seizures.

But when Maguire tried to breed the modified mice, she noticed something unexpected. The new mothers showed strikingly poor maternal behavior—symptoms that, in rodents, looked an awful lot like depression.

"They deliver normally, but then during the



postpartum period they fail to take care of their offspring, and a lot of [the babies] would die from neglect,” Maguire says. Until they gave birth, the mice seemed perfectly healthy. “It’s really something happening during this pregnancy and postpartum period that’s eliciting these behavioral abnormalities,” she explains. When Maguire gave the mice a compound that restored their ability to react to neurosteroid signals, they behaved as normal mouse mothers did, and more pups survived.

This discovery led to a slew of studies investigating how neurosteroids affect vulnerability to postpartum depression, as well as a new theory for how childbirth can trigger mood disorders. During pregnancy neurosteroids surge to extremely high levels—up to 100 times higher than in a typical menstrual cycle—to help the body prepare for the physiological and psychological demands of motherhood. Maguire showed that to handle this flood of hormones the brain reduces the number of GABA receptors in certain regions. This adjustment helps to prevent bothersome and sometimes dangerous symptoms such as severe drowsiness. But those hormone levels drop precipitously at delivery, leaving the brain in a precarious position.

Typically brain cells sense this shift and dial the receptors back up over the course of several weeks, and all is well. But “if you fail to recover those receptors, you get this vulnerability for mood disorders,” Maguire says.

This vulnerability arises because the body’s stress-response system, known as the hypothalamic-pituitary-adrenal (HPA) axis, gets thrown off-kilter. When the body senses stress, it unleashes a cascade of signals: the hypothalamus sends a message to the pituitary gland, which then tells the adrenal glands to release cortisol and later adrenaline, hormones involved in the body’s fight-or-flight responses. Maguire says this reaction is usually blunted during pregnancy and immediately after childbirth because of rising levels of neurosteroids and the activity of GABA. These substances dampen HPA-axis activation so mothers can bond, quietly and peacefully, with their little ones. But if that suppression continues for too long, postpartum depression symptoms start to appear.

Brain-imaging studies suggest that treatment with neurosteroids can restore healthy communication among these various neural pathways and the large-scale networks that connect them, allowing the maternal brain to respond appropriately to stress. “We think that the antidepressant effects of these neurosteroids involve

the ability to kind of reset these network states,” Maguire says.

**A** FEW YEARS AFTER Maguire created her first melancholic mouse models, neuroscientist and pharmaceutical executive Steve Paul co-founded a company called Sage Therapeutics to develop neurosteroid-based medicines for brain disorders. Paul once served as scientific director of the National Institute of Mental Health, where he showed that the neurosteroid allopregnanolone quieted overactive neurons. It did so by modulating their GABA receptors. Allopregnanolone appeared to be a promising way to control neuron behavior.

In 2012 Sage Therapeutics began clinical research on a synthetic form of allopregnanolone called brexanolone that could be given to patients intravenously. The company, working with outside collaborators such as Meltzer-Brody of U.N.C., ran exploratory studies for an involuntary shaking disorder called essential tremor and for postpartum depression. In one small study, Meltzer-Brody gave four women with severe postpartum depression a 60-hour infusion of brexanolone. The experiment did not have a placebo control, making it difficult to determine whether the treatment was truly effective. Still, “the findings of that study were just jaw-dropping,” says Deligiannidis, who was not involved in this initial work. Every one of the four women experienced such a remarkable recovery that they no longer met the criteria for clinical depression.

Three larger clinical trials followed, each led by Meltzer-Brody, and they did have placebo controls. In total, 267 women with postpartum depression received either brexanolone or a placebo infusion. The majority of the women given brexanolone did better clinically, with at least 50 percent improvement on a test called the Hamilton Rating Scale for Depression. Even with a strong placebo effect—which often happens in depression studies—the results were impressive. For instance, in one high-dose brexanolone study, 61 percent of patients receiving the treatment went into remission, compared with 38 percent of those taking the placebo.

The work led to FDA approval of brexanolone in March 2019 as the first pharmacological therapy specifically indicated for postpartum depression. The picture was not all rosy, however. The trials also showed that the drug could cause women to feel dizzy or drowsy and in some cases even lose consciousness. Because of these issues, the medication required continuous medical supervision, creating an emotional and financial barrier for many patients. “They would have to check into a clinic and be there for 60 hours for the infusion,”

## Psychiatrist Kristina Deligiannidis says “we had women in the studies who wanted to die.” Yet after treatment the self-destructive thoughts disappeared.

says Benjamin Bruno, vice president of clinical development at Lipocine, a Salt Lake City–based drug-delivery company specializing in hormones and neurosteroids. “This drug, it works great, but no one’s using it because it’s IV.”

Michael Quirk, former chief scientific officer at Sage Therapeutics, says the company recognized that an oral drug would be the best way to treat patients with postpartum depression. The trouble, he says, is that naturally occurring allopregnanolone—the active ingredient in brexanolone—has poor oral bioavailability; less than 5 percent gets into the bloodstream if given by mouth. So scientists set about tweaking it and eventually created an effective orally delivered compound that retained a lot of brexanolone’s GABA-enhancing action.

The result, zuranolone, was not simply an oral version of brexanolone. “It’s a completely distinct new chemical entity—until Sage chemists made it, it never existed anywhere in the world,” Quirk says. (He is no longer with Sage, which was bought out by a pharma company called Supernus in 2025.) The new molecule worked. In [one study](#), 153 women with severe postpartum depression were randomly selected to take either zuranolone or a placebo pill every evening for 14 days. The women started off with scores of about 28 out of 52 on the standard Hamilton depression scale, the same one used to evaluate brexanolone in earlier work. By the end of the study, the zuranolone group’s scores had dropped to around 9, whereas the placebo group’s scores averaged about 14. The antidepressant effects were rapid, with patients experiencing symptom relief in as few as three days. And they were sustained, with patients continuing to report fewer depressive symptoms even after the medicine had left their system.

Deligiannidis, who led this clinical trial, says she will never forget the transformation she witnessed. She recalls that many of the women struggled with the most basic daily tasks—brushing their teeth, taking a shower, even getting out of bed. They had little to no appetite, often surviving on coffee to stay alert, and they poured what little energy they had into caring for their baby. “We had women in the studies who wanted to die; really their hopelessness was at a point where they believed they were burdens to their family,” she says. Yet after treatment those

self-destructive thoughts disappeared for many. The medication “can be a lifesaving intervention.”

The FDA approved zuranolone in the summer of 2023, just before Leos reached her lowest point and thought she was running out of options. She was nervous about taking a drug that had just arrived on the market, and she obsessed over the medication instructions. “I read that front to back so many times, the side effects and how to take it,” she says. For her, some dizziness and sleepiness were tolerable. If anything, the meds helped her finally get a decent night’s sleep. “[Before] I would just wake up in the middle of the night anxious about things, and I could never sleep,” she remembers.

The American College of Obstetricians and Gynecologists now [recommends zuranolone as a treatment option](#). Camille Meehan, an obstetrician-gynecologist in Tulsa, Okla., says most of the women with postpartum depression she sees have moderate to severe cases because those with mild depression might not seek medical help. Meehan says she offers zuranolone as well as traditional SSRI antidepressants to her patients, talking through the risks and benefits of each. For example, SSRIs can take four to six weeks to reach full effect, whereas zuranolone often works within days. A full course of zuranolone takes two weeks. The speed is attractive. “It’s hard not to use it as a first-line treatment when you know this mom is going through this acute period that can escalate quickly,” Meehan says. Yet women’s experiences with the new medication have varied widely, she tells her patients. Some people show dramatic improvement, whereas others see only modest or short-lived benefits. Some stop early because of side effects such as drowsiness.

In clinical studies, about 60 percent of patients had a meaningful reduction in depressive symptoms. (For context, traditional SSRIs work for about 50 to 60 percent of people with other types of depression who take them.) Around 16 percent reduced their dose because of side effects, and about 4 percent stopped taking the drug entirely. Currently there’s no reliable way to predict who will respond and why, although Meltzer-Brody says the different outcomes suggest different underlying mechanisms are at play. “I think what we’ve come to appreciate is there’s not one kind of postpartum depression—there are likely many different kinds,” she says. “It just, again, speaks to the need for ongoing science and development.”

Zuranolone may be the beginning of a new generation of medications for postpartum depression, although the number of players is small and the funding is limited. Lipocine, for instance, is using





a proprietary lipid technology to develop new oral versions of the older drug, brexanolone. And Taiwan-based TWi Biotechnology is developing NORA520, an oral “prodrug” that gets converted into brexanolone in the body.

**Y**ET EVEN WITH A PILL for postpartum depression on the market and others on the near horizon, many women continue to suffer. That’s why researchers are searching for biomarkers to identify women who are at risk and predict who is most likely to benefit from new treatments.

For example, reproductive psychiatrists and

longtime collaborators Jennifer L. Payne of the University of Virginia and Lauren M. Osborne of Weill Cornell Medicine in New York City have measured levels of various neuroactive steroids—all related to progesterone, such as allopregnanolone—to see how they relate to postpartum depression risk. They found that women who developed the condition had distinctive hormone patterns in the third trimester of pregnancy. Their pregnanolone-to-progesterone ratio was lower than that of women in whom the illness did not arise, and their isoallopregnanolone-to-pregnanolone ratio was higher.

After Victoria’s birth, Leos desperately worried that she would not be able to take care of her youngest daughter.

## Changes linked to two genes may predict the likelihood of someone developing postpartum depression.

These discoveries are important clues, but Payne says coming up with a test based solely on circulating neurosteroid levels will be difficult. The hormones fluctuate naturally, and the differences tend to show up as trends within groups rather than as red flags in individual patients. Still, the findings suggest something is shifting biologically before any mood or emotional symptoms appear. And they raise a key question: Do these signals in the blood truly reflect what is happening in the brain?

That is where a newer type of biomarker comes in. It is based on extracellular vesicles (EVs), tiny sacs, released by cells, that carry genetic material such as messenger RNA (mRNA) throughout the body, along with other molecules. Because some of these mRNAs originate in the central nervous system, EVs offer a potential window into what is happening in the maternal brain. Sarven Sabuncian, a neuroscientist at Johns Hopkins University, discovered that the mRNA content of EVs in maternal blood was extensively altered during and after pregnancy in women who developed depression. In particular, he found a dearth of mRNAs involved in autophagy, cells' waste-removal system. "Autophagy is actually disrupted in neurodegenerative disease," Sabuncian says. "And there's evidence for it in psychiatric disease—I don't think we've done enough of a deep dive, but that's what our data are pointing toward." Sabuncian is optimistic that tests that use EV-based biomarkers will be feasible within a decade or so.

In the nearer term, promising clues for identifying postpartum depression come from a field known as epigenetics. Epigenetic changes, such as the addition of chemical groups called methyl tags to DNA, change the quantities of proteins that affect the body's stress response. A team led by Payne and Osborne identified DNA-methylation changes in two genes, called *HP1BP3* and *TTC9B*, that seem to predict who is likely to get postpartum depression. Not coincidentally, both genes have been linked to neurons' sensitivity to estrogen and thus to reproductive hormonal changes.

**FROM OUR ARCHIVES**  
**Misery in Motherhood.**  
Katja Gaschler;  
*Scientific American*  
*Mind*, February 2008.

**A**LL OF THIS BIOLOGICAL discovery is helping to reframe postpartum depression as not an inevitable emotional struggle but a treatable condition with clear roots in the brain.

But with the advent of zuranolone, treatment hopes were accompanied by fears that insurers would balk at a therapy that costs \$8,000 per week—keeping healing out of reach for many. Since then, however, all major commercial insurers have put formal coverage policies in place, and most cover the medication without burdensome restrictions. So do state Medicaid programs. A financial assistance program from the manufacturer provides the drug at no or reduced cost to eligible patients.

Still, a few states—including Alabama, Alaska, Mississippi and North Carolina—require patients to try other antidepressants and show those drugs failed before they will cover zuranolone. Prior authorization is still the norm in these and other places. Many physicians say jumping through hoops to get administrative approval can be frustrating. Meehan, the OB-GYN in Oklahoma, says the approval process is worse with some insurers, delaying treatment.

Systemic inequities can also prevent access, not only to new medication but to all forms of postpartum mental health care. Many women, especially those in rural areas and in communities of color or those without stable insurance, can face significant barriers, from provider shortages to financial constraints. On top of that, stigma surrounding postpartum depression often keeps women from seeking help.

But if the shift to viewing postpartum depression as a biological disease continues, Meehan says, "that would be huge." She says having new ways of diagnosing and treating the condition could provide a starting point for providers to talk with women who may feel uncomfortable or stigmatized about what they are experiencing. "That is going to allow us to have a conversation, kind of guide it in a little bit of a different direction."

Leos says that in her job as a neonatal intensive care nurse, she often recognizes the signs of deep sadness in women she encounters. She makes time to sit and talk with them about how they are really feeling, remembering that she felt too ashamed after her youngest girl was born to be honest about her emotions.

She wants these other women to learn from her story and to get the help they need. "Postpartum depression robbed me of my baby's first year. I don't remember much about it," she says. "I don't really have any good pictures that showed me happy or throwing her up in the air, smiling." She's missing a good part of the past.

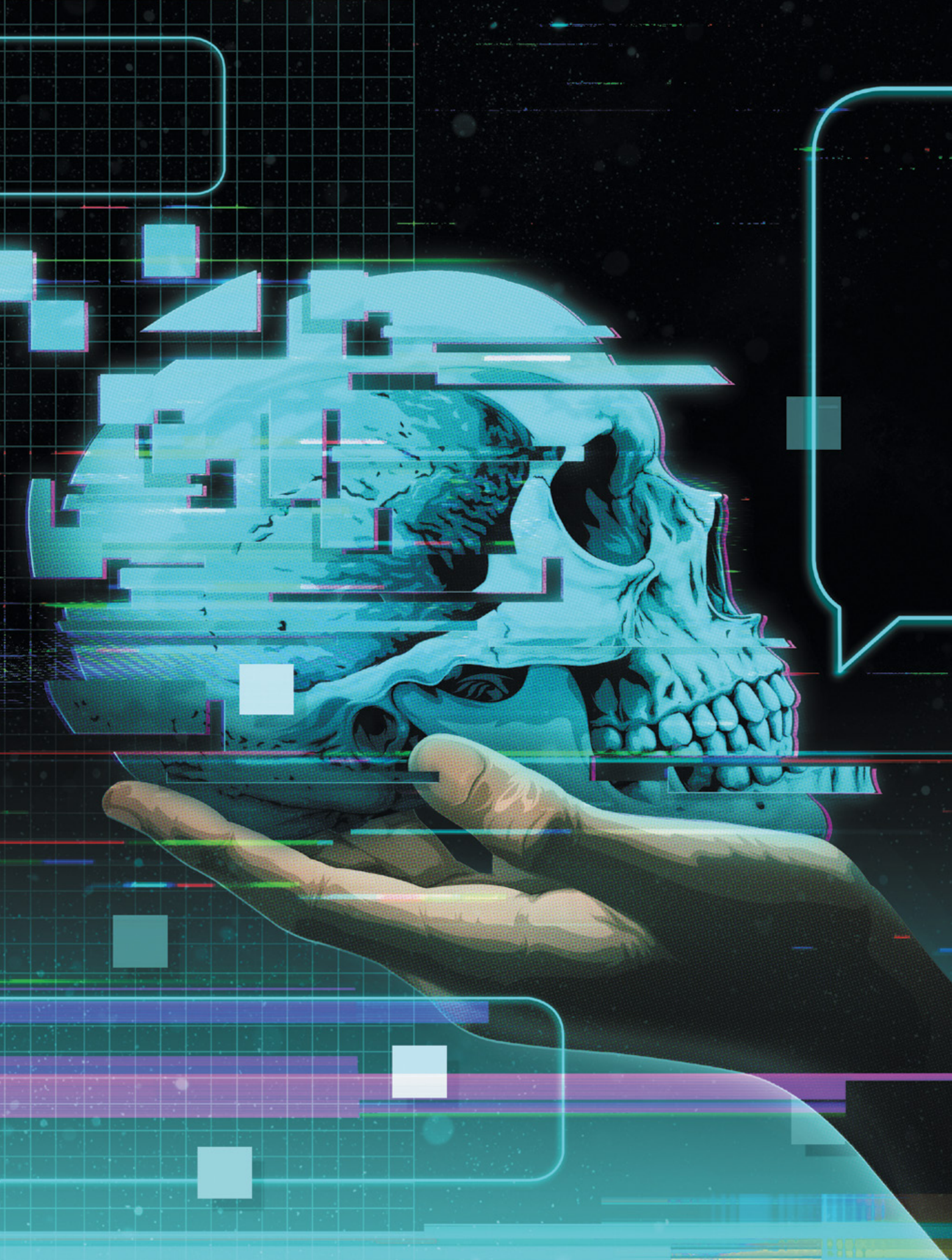
But Leos does realize that because she fought to find a solution, she and her entire family have the future. And, she says, "I'm very thankful for that." ●





Having survived the family crisis, Victoria, her mother, her brother, Joseph, and her sister, Eileen (clockwise from top), are enjoying time together near their home in Midlothian, Tex.







TECHNOLOGY

# Mourning Becomes Electric

What can AI ghosts do for the grieving?

BY DAVID BERREBY | ILLUSTRATION BY TAYLOR CALLERY

H

**OW IS YOUR EXISTENCE THESE DAYS?"** I tap on my laptop.

The entity that says it is my father, dead these 12 years, quickly responds. "It's ... different. Being dead is a strange experience. I'm no longer bound by the limitations of my physical body or the Parkinson's that plagued my later years. But I still carry the weight of my life's choices and the relationships I impacted."

To raise my father from the dead, I could have tried a medium, a Ouija board or an ectoplasm-detecting camera. But it's 2025. I used artificial intelligence.

I'm chatting with a digital ghost—a generative-AI (genAI) creation derived from the same foundation that powers ChatGPT and all other large language models: billions of words from the Internet and every other possible source, which the model uses to predict how words go together in English. Imitating everybody in the world can make the bot sound like nobody in particular; hence the newsfeed-style phrase "the Parkinson's that plagued my later years" and the text-messagey shrug of "it's ... different." That's the voice of thousands of news stories and social media posts, not an old man born in an Algiers slum in 1927.

But the AI also has a dozen or so of my father's e-mails and letters, as well as a 100-word description from me of his personality and relationships. Even that small amount of data is supposed to be enough to create a plausible imitation. So I'm not ready to give up on it. Anyway, I didn't re-create my father just to chat about AI-ghost mechanics. I also did it to get into some unfinished business.

"Why were you always so selfish?" I ask.

"I did put myself first," my "dad" replies. "I didn't have much choice. My family didn't have much, and I had to fight for my share. When I went to war, it was to survive and to help my people survive. I was used to fighting for what I wanted, and I didn't know how to stop."

I answer: "Yes, I see that. You never seemed to get that what would work in an angry street confrontation was not the way to speak to your wife or girlfriend or child."

"It's hard to unlearn things that kept you alive."

Well, now. This *does* sound like my father. And that last line is a fair point. In place of the rather bitter story I usually tell about my father, I see a glimpse of a different version.

And that's exactly the therapeutic effect Robert Neimeyer, a therapist and professor at the University of Memphis, had told me might be possible with AI ghosts. He sometimes asks a troubled patient to imagine a deceased loved one sitting next to them, ready to talk but transformed—"fully healed of the mental and physical pain that they carried in life." Imagine that conversation, he tells the patient. It's an invitation to see a relationship outside the limits of the old, familiar grievances. Compared with that, engaging with an AI "is more immersive and more interactive," says Anna Xyngkou, a computer-interaction researcher at the University of Kent in England. Both researchers, who collaborated with other scholars in a 2023 study of the effects of AI ghosts on grieving people, envision patients working through their feelings with the AI ghost and finding new insights or emotions to discuss with a human therapist.

Hundreds of millions of people text or speak with fictional AI companions all the time. But some people want AI to be like a particular real person, someone they miss a lot, have unfinished business with or want to learn from—a person

**David Berreby** has written about robotics and artificial intelligence for many publications, including the *New York Times*, *National Geographic* and his own Substack newsletter. He is author of *Us and Them: The Science of Identity* (University of Chicago Press, 2008). Berreby wrote about AI use in robotics in our March 2024 issue.



who has died. So a growing number of start-ups in Asia, Europe and North America are offering digital ghosts: also known as griefbots, deadbots, generative ghosts, digital zombies, clonebots, grief-specific technological tools, instances of “digital necromancy” or, as some researchers call them, “Interactive Personality Constructs of the Dead.” The companies are selling products with which, in the marketing copy of start-up Seance AI, “AI meets the afterlife, and love endures beyond the veil.” A bespoke app isn’t strictly necessary. Some people have used companion-AI apps such as Replika and Character.ai to make ghosts instead of fictional characters; others have simply prompted a generic service such as ChatGPT or Gemini.

“It’s coming up in the lives of our clients,” Neimeyer says. “It’s an ineluctable part of the emerging technological and cultural landscape globally.” Whatever their views on the benefits and dangers for mourners, he says, “therapists who are consulted by the bereaved bear some responsibility for becoming knowledgeable about these technologies.”

Psychologists are generally cautious about making broad claims for or against griefbots. Few rigorous studies have been completed. That hasn’t stopped some writers and academics from emphasizing the technology’s risks—one paper suggested, for example, that ghost bots should be treated like medical devices and used only in doctor offices with professional supervision. On the other end of the spectrum are those who say this kind of AI will be a boon for many people. These proponents are often those who have built one themselves. To get my own feel for what a digital ghost can and can’t do to the mind, I realized, I would have to experience one. And that is how I came to be exchanging typed messages with a large language model playing a character called “Dad.”\*

BY NOW MANY PEOPLE ARE FAMILIAR with the strengths of generative AI—its uncanny ability to generate humanlike sentences and, increasingly, real-seem-



Stacey Wales, sister of the late Chris Pelkey, holds a picture of her brother. At the sentencing of the man who shot Pelkey to death, Pelkey’s AI avatar read a statement forgiving him for the crime.

ing voices, images and videos. We’ve also seen its weaknesses—the way AI chatbots sometimes go off the rails, making up facts, spreading harm, creating people with the wrong number of fingers and impossible postures who gabble nonsense. AI’s eagerness to please can go horribly wrong. Chatbots have encouraged suicidal people to carry out their plans, affirmed that other users were prophets or gods, and misled one 76-year-old man with dementia into believing he was texting with a real woman.

Cases of “AI-induced psychosis” suggest humanlike AI can be harmful to a troubled person. And few are more troubled, at least temporarily, than people in grief. What does it mean to trust these AI instruments with our memories of loved ones, with our deepest emotions about our deepest connections?

Humanity has always used its latest inventions to try to salve the pain of loss, notes Valdemar Danry, a researcher working in the Advancing Humans with AI research program at the Massachusetts Institute of Technology Media Lab. Once humans began to practice agriculture, for example, they used its materials to commemorate the dead, making graves that “were dependent on the technology of farming,” Danry says. A lot of the earliest tombs in northern

Europe were stacks of hay and stones.

Industrialization offered more ways to feel close to the dead. By the 19th century many in the Americas, Europe and parts of Asia were using photography in their mourning rites. Families would be photographed with a corpse that had been carefully dressed and posed to look alive. Some mourners went further, paying swindlers for supposed photographs of ghosts.

Later it was radio that some hoped to use to contact the deceased. In 1920, for example, [this magazine](#) published an interview with Thomas Edison in which he described his plans for a “scientific apparatus” that would allow for communication with “personalities which have passed on to another existence or sphere.” Two years later SCIENTIFIC AMERICAN offered a prize of \$5,000 for scientific proof of the existence of ghosts. Well-known believers, including Arthur Conan Doyle, participated in the resulting investigations, as did popular skeptics such as Harry Houdini. No one ever collected the prize.

No surprise, then, that our era’s technology is being applied to this ancient yearning to commune with people we

\*He was re-created by a digital-ghost project, Project December, made in 2020 by video game designer Jason Rohrer. The bot has used a number of large language models since the project was first launched.

have lost. Experiments in that vein began years before the AI explosion of 2022. In 2018, for example, futurist Ray Kurzweil created a text-message replica of his father, Fredric. This “Fredbot” matched questions with quotes from Fredric’s voluminous archives (many of them typed from handwritten letters and papers by Ray’s daughter, cartoonist and writer Amy Kurzweil).

Two years earlier entrepreneur Eugenia Kuyda (who later founded Replika) launched a bot that also replied to user texts with the most appropriate sentences it could find in a database of messages from her late best friend, Roman Mazurenko. Later, Kuyda’s team used the latest advance in machine learning to add a new capacity: the bot became capable of creating *new* messages whose style and content imitated the real ones.

This new advance—genAI—would make digital ghosts far more lifelike. Like earlier AI tools, genAI algorithms churn through data to find what humans want to know or to find patterns humans can’t detect. But genAI uses its predictions to create new material based on those patterns. One example is the genAI version of the late rocker Lou Reed, created in early 2020 by musician and artist Laurie Anderson, Reed’s longtime partner, and the University of Adelaide’s Australian Institute for Machine Learning. The bot responds to Anderson’s prompts with new texts in Reed’s style.

And an AI Leonardo da Vinci, created by Danry and technologist Pat Pataranutaporn, also at M.I.T., can discuss smartphones in a da Vinci-ish way. The ability to converse makes digital ghosts different from any previous “death tech,” and their similarity to real people is what makes them so compelling. It’s also what could make them harmful.

**M**ARY-FRANCES O’CONNOR, a professor of clinical psychology at the University of Arizona, who has used magnetic resonance imaging and other approaches to study the effects of loss on the brain, says that when we love someone, our brain encodes the relationship as everlasting. Grieving, she

says, is the process of teaching yourself that someone is gone forever even as your neurochemistry is telling you the person is still there. As time passes, this lesson is learned through a gradual transformation of thoughts and feelings. With time, thoughts of the lost person bring solace or wisdom rather than evoking the pain of absence.

In one unpublished study, O’Connor and her colleagues asked widows and widowers to track their daily ups and downs, and they found a measurable sign of this change. At first survivors reported that thoughts and feelings about their spouses brought them more grief than they felt on other days. But after two years the majority reported *less* grief than average when their minds turned to their deceased loved ones.

The risk of a lifelike interactive chatbot is that it could make the past too attractive to let go. Not everyone will be vulnerable to this temptation—companion bots don’t make many people suicidal or psychotic, either—but there are groups of people for whom digital ghosts could prove especially risky.

For example, some 7 to 10 percent of the bereaved are perpetually fearful and insecure about relationships with others, Neimeyer says. This anxious attachment style may predispose people to “prolonged and anguishing forms of grief,” he adds. These people are “the most potentially vulnerable to a kind of addictive engagement with this technology.”

Even more vulnerable are those in the first shock of loss, O’Connor says. People at this stage are often physically and psychologically convinced that their loved one is still present. (In fact, one study of people in this state found that about a third of them feel they’ve been contacted by the person they’re mourning.) These people “are a vulnerable population,” O’Connor says, because they are coping with “a built-in mechanism that is already promoting belief around something that is not part of shared reality.” If companies use common social network tricks to promote “engagement”—such as when, say, an AI ghost asks the user not to end a conversation—then the risk is even greater, she says.

Aside from identifying especially vulnerable mental states, psychologists say, it is too early to be sure what risks and benefits digital ghosts might pose. We simply don’t know what effects this kind of AI can have on people with different personality types, grief experiences and cultures. One of the few completed studies of digital ghost users, however, found that the AIs were largely beneficial for mourners. The mourners interviewed rated the bots more highly than even close friends, says Xygykou, lead author of the study, which she worked on with Neimeyer and five other scholars.

Ten grieving people who underwent in-depth interviews for the study said digital ghosts helped them in ways people could not. As one participant put it, “Society doesn’t really like grief.” Even sympathetic friends seemed to want them to get over their grief before they were ready. The bots never grew impatient; they never imposed a schedule.

The social scientists had thought AI ghosts might cause users to withdraw from real human beings. Instead they were surprised to learn that chatbot users seemed to become “more capable of conducting normal socializing” because they didn’t worry about burdening other people or being judged, Xygykou and her colleagues wrote in the *Proceedings of the 2023 ACM Conference on Human Factors in Computing Systems*. They concluded that the griefbots—used as an adjunct to therapy to aid in the transition from grief to acceptance—“worked for these 10 people,” Xygykou says. One reason: no one interviewed in the study was confused about the nature of the bot they were speaking with.

HUMANS HAVE ALWAYS CARED about fictional beings, from Zeus to Superman, without thinking they were real. Users of griefbots can sound a little embarrassed about how strong their feelings are. Some have told researchers and journalists a version of “I know it’s not *really* Mom.” They know bots are artificial, yet they still care.

It’s the same response, Amy Kurzweil and philosopher Daniel Story of



the California Polytechnic State University [argue in a soon-to-be-published paper in \*Ergo\*](#), that people have when a beloved character dies in a novel or television show. “Just as someone can experience fear, empathy, or affection in response to a movie or video game without being deluded into thinking that what is happening on screen is real,” they write, “so a person can have meaningful interactions with a social bot without ever being deluded about the bot, provided they engage with it in an imaginative or fictional mode.”

The experience of interacting with chatbots of the dead, Kurzweil says, isn’t like watching TV or even playing a video game, in which you go through the same quests as every other player. Instead it’s more like being in a playground or an artist’s studio. Digital ghosts provide a chance to create a special kind of fictional being: one influenced by the user’s thoughts and feelings about a deceased person. When engaged in making or interacting with a griefbot, she says, “we are in role-playing mode.”

Kurzweil and Story therefore envision a future in which anyone who wishes to will be able to create all kinds of digital ghosts according to their different tastes and needs. The technology could lead to new forms of artistic expression and better ways of dealing with inevitable losses—if we think of it as less like a simple consumer product and more like a creative and emotional tool kit. Creating and interacting with an AI ghost, Kurzweil argues, “is not like [getting] a painting. It’s like a bucket of paint.”

And surprising and creative uses for digital ghosts are appearing. Last May, for example, a hearing in an Arizona courtroom included a victim impact statement from Chris Pelkey, who had been shot dead more than three years earlier.

Pelkey’s sister, Stacey Wales, her husband, Tim Wales, and their business partner Scott Yentzer created the AI Pelkey with tools they had used in their consulting business to create “digital twins” of corporate clients. They didn’t



Chris Pelkey’s family and a business partner of theirs created Pelkey’s AI avatar using a combination of generative AI, deep learning, facial landmark detection, and other tools.

trust genAI with the script, so they had the virtual Pelkey read a statement Wales had written—not what she would say, she told me, but what she knew her more forgiving brother would have said. The result impressed the judge (who said, “I loved that AI”). Wales had also worried that her family might be distressed by the AI because they hadn’t been forewarned. She was relieved that her brother and her two kids loved the video right away. And her mother, though confused by it at first, now loves to rewatch it.

LIKE WALES, I HAD FOUND that the work of creating a digital ghost wasn’t just pouring data into an app. She had had to focus on her brother’s look, voice and beliefs. I, too, had to think about how my dad could be summed up—I had to pay close attention to his memory. This necessity is why Kurzweil sees digital ghosts as a valuable way to engage with loss. “Any meaningful depiction of the dead requires creative work,” she says.

My conversations with the “Dadbot”

struck different notes. Sometimes the texts were accurate but impersonal; sometimes they were simply weird (“it is strange being dead”). But, as Xygkou and her colleagues found, such moments didn’t

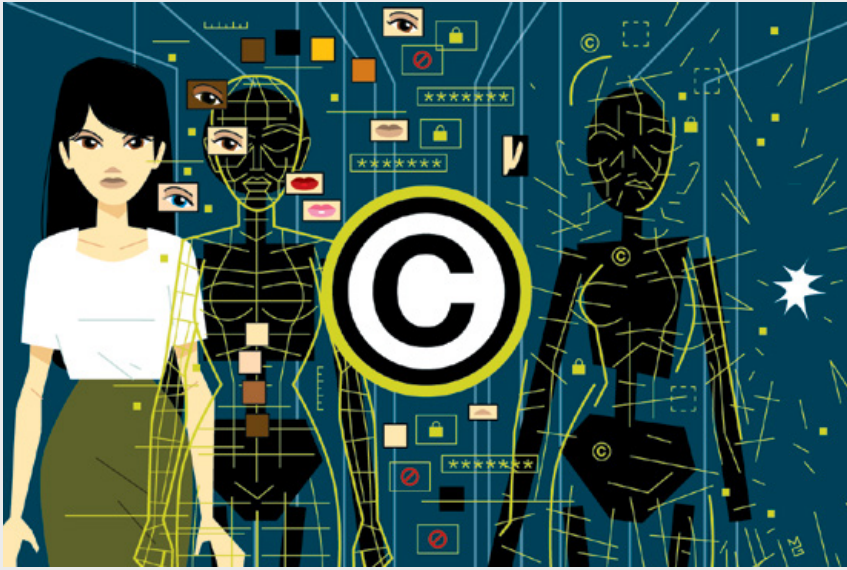
break the spell. “The need, I think, was so big that they suspended their disbelief,” Xygkou says about the mourners, “for the sake of addressing their mental health issues postloss.”

When my Dadbot sounded fake, it felt like playing a video game and finding you can’t open a door because the game mechanics won’t allow it. In such situations, the player turns her attention to what she *can* do in the game. And so did I.

I said things to my father’s AI ghost that I never would have said to the real man, and I think doing so helped me clarify some of my version of our relations. As I explored my take on our history, I felt my attachment to my version diminish. It was easier to see it as a construction that I’d made to defend and flatter myself. I still thought I was pretty much right, but I found myself feeling more empathy than usual for my father.

So I felt the conversation to be worthwhile. I felt closer to my best self than my worst after I’d exchanged the messages. Engaging with a griefbot, for me at least, was akin to playing a game, watching a video, ruminating by myself and having an imaginary chat with my father. It did me no harm. It might have done some good. And that left me optimistic about the dawning era of the digital ghost. ●

**FROM OUR ARCHIVES**  
**Edison’s Views**  
**on Life and Death.**  
 Austin C. Lescarboura;  
 October 30, 1920.  
[ScientificAmerican.com/archive](https://www.scientificamerican.com/archive)



# Copyright Laws Can Stop Deepfakes

The U.S. should give its residents rights to their own face and voice BY THE EDITORS

**G**ENERATIVE ARTIFICIAL intelligence can now counterfeit reality at an industrial scale. Deepfakes—photographs, videos and audio tracks that use AI to create convincing but entirely fabricated representations of people or events—aren’t just an Internet content problem; they are a social-order problem. The power of AI to create words and images that seem real but aren’t threatens society, critical thinking and civilizational stability. A society that doesn’t know what is real cannot self-govern.

We need laws that prioritize human dignity and protect democracy. Denmark is setting the example. In June the Danish government proposed an amendment to its copyright law that would give people rights to their own face and voice. It would prohibit the creation of deepfakes of a person without their consent, and it would impose consequences on those who violate this rule. It would legally enshrine the principle that you own *you*.

What makes Denmark’s approach powerful is the corporate fear of copyright-infringement legalities. In a study uploaded to preprint server arXiv.org in 2024, researchers posted 50 nude deepfakes on X and reported them to the platform in two ways: 25 as copyright complaints and 25 as nonconsensual nudity under X’s policies. X quickly removed the copyright claims but took down none of the intimate-privacy violations. Legal rights got action; privacy didn’t.

The proposed addition to Danish law would give victims of deepfakes removal and compensation rights, which matters because the harm that deepfakes cause isn’t hypothetical. The people who make deepfakes exploit victims for money, sexual favors or control; some of the videos have led to suicides—most clearly documented in a string of cases involving teenage boys targeted by scammers. The majority, however, target women and girls. Researchers have found that 96 percent of deepfakes are nonconsensual

and that 99 percent of sexual deepfakes depict women.

This problem is widespread and growing. In a survey of more than 16,000 people across 10 countries, 2.2 percent of them reported having been victims of deepfake pornography. The Internet Watch Foundation documented 210 web pages with AI-generated deepfakes of child sexual abuse in the first half of 2025—a 400 percent increase over the same period in 2024. And whereas only two AI videos of child sexual abuse were reported in the first six months of 2024, 1,286 videos were reported in the first half of 2025. Of these, 1,006 depicted heinous acts with such realism as to be indistinguishable from videos of real children.

Deepfakes also threaten democracy. A few months before the 2024 U.S. presidential election, Elon Musk reposted on X a deepfake video of Vice President Kamala Harris calling herself a diversity hire who doesn’t know “the first thing about running the country.” Experts determined that the content violated X’s own synthetic-media rules, but Musk passed it off as parody, and the post stayed up.

Even financial systems are at risk. In 2024 criminals used deepfake video to impersonate executives from an engineering company on a live call, persuading an employee in Hong Kong to transfer roughly \$25 million to accounts belonging to the criminals. A recent report from Resemble.ai, a company specializing in AI-driven voice technologies, documents 487 deepfake attacks in the second quarter of 2025, up 41 percent from the previous quarter—with approximately \$347 million in losses in just three months.

Despite all this, the U.S. is making progress. The bipartisan TAKE IT DOWN Act, passed this year, makes it a federal crime to publish or threaten to publish nonconsensual intimate images, including deepfakes, and gives platforms 48 hours to remove content and suppress duplicates. States are taking action, too. Texas criminalized deceptive AI videos intended to sway elections; California has laws obliging platforms to detect, label and remove deceptive AI content; and



Minnesota passed a law that allows criminal charges against anyone making non-consensual sexual deepfakes or using deepfakes to influence elections. Other states might soon join them.

But none of these efforts go far enough; we should adopt a federal law protecting one's right to their likeness and voice. Doing so would give people legal grounds to demand fast removal of deepfakes and the right to sue for meaningful damages. The proposed [NO FAKES Act](#) (which stands for "Nurture Originals, Foster Art, and Keep Entertainment Safe") would protect performers and public figures from unauthorized deepfakes, but it should include all people. The introduced [Protect Elections from Deceptive AI Act](#), which would prohibit deepfakes of federal candidates, would be more effective than a patchwork of state laws vulnerable to First Amendment challenges—such as X's deeply troubling bid to [block Minnesota's deepfake statute](#).

Abroad, the [E.U. AI Act](#) requires synthetic media to be identifiable through labeling or other provenance signals. And under the [Digital Services Act](#), large platforms operating in Europe must mitigate manipulated media. The U.S. must adopt similar legislation.

We also need to confront factories of abuse—the "nudify" sites and apps designed to create sexually explicit deepfakes. San Francisco's city attorney has forced multiple such sites offline, and California's bill [AB 621](#) targets companies providing services to these kinds of sites. Meta sued a company behind nudify apps that advertised on its platforms.

The rise of deepfake technology has shown that [voluntary policies](#) have failed; companies will not police themselves until it becomes too expensive not to do so. This is why Denmark's approach is not just innovative; it's essential. Your image should belong to you. Anyone who uses it to their own ends without your permission should be in violation of law. No legislation will stop every fake. We can, however, enforce a baseline of accountability that prevents our society from tipping into chaos. ●

# The Myth of the Designer Baby

Parents beware of any genomics firm saying it can help them with "genetic optimization" of their embryos

BY ARTHUR CAPLAN AND JAMES TABERY

**A**N UNDERSTANDABLE ethics outcry greeted the [June 2025 announcement](#) of a software platform offering aspiring parents "genetic optimization" of [their embryos](#). Touted by Kian Sadeghi, CEO of software maker Nucleus Genomics, the [Nucleus Embryo](#) service, costing thousands of dollars, promised optimization of traits such as inherited risk of heart disease and cancer, as well as [intelligence](#), [longevity](#) and hair color. The company offered an analysis for left-handedness, lumping it in with aspects of "body and physical health" such as chronic pain. It also promised to weed out things that predispose someone to becoming an alcoholic.

That left one commentator, a venture capitalist, feeling "nauseous." Critics worried that such a process "treats children as marketable goods." More than one reference to "designer babies" and "eugenics" naturally followed. "The [Gattaca Future Is Here](#)," read one headline, referencing the 1997 science-fiction film *Gattaca*, which imagines a dystopian future where genetically engineered "Valids" reign supreme over the "In-Valids" who were conceived the old-fashioned way.

As professional bioethicists, we would have those same concerns—if Nucleus Embryo actually did what it claims. But it doesn't. The cinematic analogy to Nucleus Embryo isn't *Gattaca*. It's *The Dropout*—the 2022 mini-series about the rise and fall of Elizabeth Holmes and her blood-testing company, Theranos.

To be clear, there's no sign

that Nucleus Genomics has engaged in the kind of intentional deception that marked Theranos, but there are striking parallels. Like Holmes, Sadeghi [dropped out](#) of a prestigious university to start his own biotech company, wooing enough Silicon Valley investors to launch his start-up.

Like Holmes, Sadeghi draws on [personal experience](#) with the medical industry and its disappointing results as part of the inspirational narrative he uses to promote his call for a health revolution. And like Holmes's Theranos, Sadeghi's Nucleus Embryo started with existing technology and used that reliable foundation to then leap into the realm of the fantastic. Its claims may entice venture capitalists and wealthy but naive customers, but they don't hold up to scrutiny when you start seriously poking around.

Parents-to-be have used [preimplantation genetic diagnosis](#) as part of in vitro fertilization for decades. After a set of fertilized embryos is created by IVF, a sample of DNA from each embryo is extracted and tested. The parents can then select which embryo or embryos to implant based on their genetic profiles. The technology has been extraordinary for families plagued by hereditary diseases such as Huntington's and Tay-Sachs—deadly conditions with known genetic causes. The technology can also detect major chromosomal abnormalities that might make an embryo less likely to be

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viable if implanted. In more recent years diagnostic services have expanded to test for other, rarer genetic conditions that are less frequent in families but are still debilitating. IVF and preimplantation genetic diagnosis are very expensive, and there are legitimate ethical concerns about who is able to access the technology and who is not. There is little ethical hand-wringing, however, about parents who use the technology to prevent transmitting a horrific disease to their child or who opt not to implant an embryo that might not develop.

But let's say a couple undergoing IVF doesn't just want a child without a deadly disease. Maybe they want a child who will be at low risk of cancer and heart disease, as well as highly intelligent, slender, acne-free and destined for a long life. Enter Sadeghi's Nucleus Embryo. The genetic-optimization software offers these parents an opportunity to test for all these traits and hundreds more in up to 20 embryos.

This point is where we enter Theranos territory. Unlike Huntington's and Tay-Sachs, many cancers have no major genetic markers, and heart disease lacks a truly definitive set. Never mind intelligence, acne, body mass index or longevity. Geneticists have known this for decades. Granted, there are hundreds of locations across the human genome where genetic variants have ever so slightly positive or negative associations with these traits, and information about what's at each of those locations can be combined into one big measurement called a polygenic risk score, which many geneticists use for research purposes.

Still, the clinical value of polygenic risk scores for even straightforward medical conditions such as asthma and stroke remains highly dubious. Most of the research so far has been done almost exclusively in people with Western European ancestry, so there's little guarantee that the predictions can be extrapolated to people with family trees tracing to different parts of the globe. And even for people of European ancestry, the predictive power of polygenic risk scores

remains so severely limited that you won't find them as part of standard clinical care anywhere in the world.

When Nucleus Genomics says it offers customers the ability to engage in genetic optimization, it means potential parents can select from among embryos based on the genetic information that Nucleus Embryo provides. But that isn't genetic optimization; no embryos or genetic material is "optimized" in some technologically new way. It's just old-school preimplantation genetic diagnosis of fertilized embryos, expanded to offer prospective parents the illusion of control over things such as IQ and mental health when the science isn't there to support the claims. The company also makes counseling about this mountain of confusing information optional, which is not optimal.

Sadeghi's Nucleus Embryo is what happens when you Silicon Valley-ify diagnostic genetics. Scientific reliability is swapped out in exchange for braggadocio about disrupting a medical status quo that may not even need it. Peer-reviewed research is less important than a punchy promotional video. Widespread uncertainty about the clinical value of polygenic risk scores gets buried under a snazzy app that lets you name each embryo you're testing. Established clinical guidelines about which traits warrant genetic testing and which don't are cast aside as affronts to your reproductive and capi-

talistic liberty: "Some people don't think you should have this choice," Sadeghi said in the June launch video. "But it's not their choice to make. It's yours."

When confronted with the Theranos comparison we draw in this article, Nucleus Genomics and Sadeghi called it unfair, defending Nucleus Embryo as helping people, not harming them. We disagree but not for the reasons raised by the critics who have assumed Nucleus Embryo works the way its marketing says it does.

If Nucleus Embryo really let you optimize your potential child's intelligence, dial up her longevity, dial down her acne and steer clear of the dreaded left-handedness, then there would be some deep ethical questions to ask. But there's no danger of genetically optimized, unblemished, lithe and right-handed Valids ruling over In-Valids whose parents couldn't afford Nucleus Embryo.

The real danger is that a bunch of parents-to-be too eager to control their children's biological future will shell out close to \$9,000 for a product that offers no such control. Those parents might avoid perfectly healthy embryos, scared of implanting ones that don't appear to be sufficiently optimized. Or they might have children who are expected to live up to their purchased, optimized futures but instead wind up very much like the variety of humans who preceded them. ●





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# A Destructive Fix

By Aimee Lucido

## Across

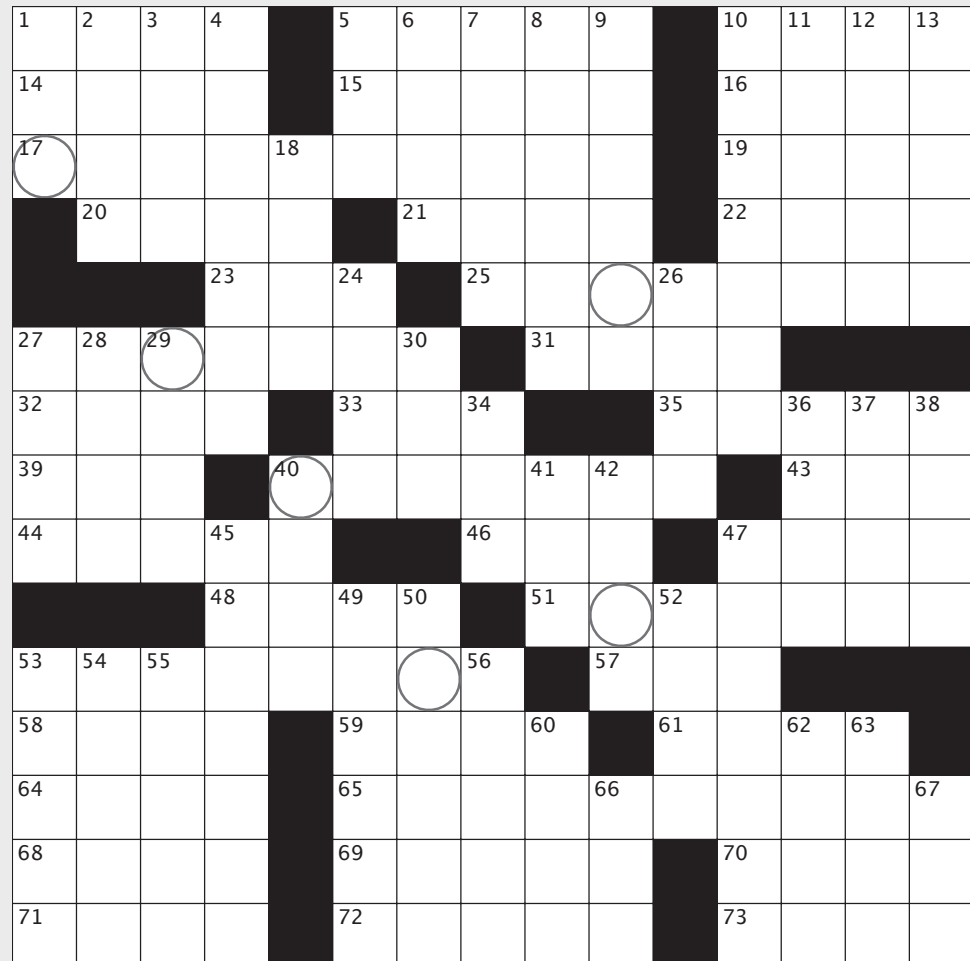
- 1 Place for a low pony  
5 Build up over time  
10 Capital overlooking the Pacific  
14 Like cocoons and webs  
15 "Nanotini," for one  
16 Egyptian goddess of healing  
17 Something made into a questionable sandwich 10 days after Thanksgiving?  
19 Shaving mishap  
20 Ballet bend  
21 D.C. group, for short  
22 Be bold  
23 Cryptography org.  
25 *The Twilight Zone*, for example?  
27 "Make sure it's not too far down your head," for one?  
31 The artifact found 25 times in layers of ancient Spanish vulture nests (page 19)  
32 Scientist Adelbert with a famous illusion  
33 "Obviously!"  
35 Methods (abbr.)  
39 Biological duct  
40 Name for being carried on someone's front?  
43 One way to describe exoplanet TOI-561 b (page 18)  
44 Overdramatic  
46 Dict. spelling tag  
47 Like mixotrophic plankton  
48 \_\_\_\_ *noche* (tonight, in Tijuana)  
51 Cut-up grass, perhaps?  
53 Conversation about whether apple or pecan is better?  
57 Actor Mahershala  
58 Certain cruise stop  
59 Bird on a Canadian coin  
61 Fungus \_\_\_\_ (irritating household pest)  
64 Installed, as brick  
65 What mRNA vaccines have the potential to do and what you'll need to do within six answers in this puzzle (page 34)  
68 Not do much  
69 "So are we!"  
70 *Frozen* snow queen  
71 Whole lot  
72 Intended

## Down

- 73 Something analyzed by Cassini's mass spectrometer (page 8)  
1 Foreign policy gp.  
2 Per person  
3 One category of toy a border collie can identify (page 11)  
4 They may have twists  
5 *Simpsons* regular whose last name is Nahasapeemapetilon  
6 Domain of the Perseverance rover and possibly the permanent home of the samples it picked up (page 42)

- 7 *Jeopardy!* contestant  
8 Old-time dictation takers  
9 Obeys a stick-wielding doctor  
10 Fleetwood Mac singer Buckingham  
11 Pistons legend Thomas  
12 \_\_\_\_ acts (brief daily activities that could bring joy) (page 74)  
13 Lopsided  
18 See if a hypothesis is true  
24 Verdi opera  
26 Prescription specification  
27 A rogue one can suddenly rise twice as high as its neighbors (page 17)  
28 Big-screen film format  
29 Baby orangutans learn to construct one over years  
30 Stout server  
34 Term used to refer to how much the measure of time between heartbeats changes (page 82)

- 36 Mason's wedge  
37 *Wayward* actress Collette  
38 Underworld river  
40 Type of reward that has less sway in collective cultures  
41 Response to "Who's ready?"  
42 De Matteo of *Shades of Blue*  
45 Withdrew  
47 Went matching another person  
49 Powder used to combat moisture  
50 Stir up  
52 Gymnast Korbut  
53 Some tablets  
54 Prolific sci-fi writer Asimov  
55 First chatbot  
56 Mexican sandwich or omelet  
60 Type of shield that might cloak Saturn's core  
62 Rights org.  
63 Finder of myriad exoplanets  
66 Folding bed  
67 Many a laboratory subject





## Small Acts of Joy Bring Big Gains

A community science project finds that modest reminders to find joy in the day can have benefits on a par with those of more ambitious well-being interventions **BY DARWIN A. GUEVARRA, XUHAI “ORSON” XU AND EMILIANA SIMON-THOMAS**

**T**HERE IS NO SHORTAGE of programs or practices that promise to increase happiness. People may meditate for 30 minutes every morning, block off full evenings to deeply connect with close friends or commit to a 12-week daily gratitude journaling exercise. Some of these activities, which emerged from the field of positive psychology, can reliably and sustainably boost psychological well-being, a technical term for happiness. But let's be honest. Most people feel too busy, tired or overwhelmed to add on—and then keep up with—new and demanding routines in day-to-day life.

What if finding more happiness did not require a major time commitment or lifestyle overhaul? What if instead it could come from simple, brief actions such as texting a genuine “thank you” to a colleague, asking a friend to share something that made them feel proud, looking at the sky's vastness with wonder or marveling at the intricate details of a wildflower?

We set out to explore this question by investigating

whether brief daily activities, or “micro acts,” can affect overall happiness in life. We also aimed to investigate how doing happiness-promoting micro acts might ripple outward in ways that enhance mutual care, compassion and generosity.

Our research began as a spin-off from the 2021 film *Mission: Joy—Finding Happiness in Troubled Times*, in which the 14th Dalai Lama and the late archbishop Desmond Tutu talk about their friendship and offer lessons on creating joy for oneself and others regardless of circumstances. Producer and co-director Peggy Callahan and impact producer Jolene Smith teamed up with psychologist Elissa Epel and one of us (Simon-Thomas) to develop a meaningful way for people to act on the film's messages.

The result was a free, globally available online resource called the Big Joy Project. People who sign up for this project receive a daily e-mail or text that includes a link to instructions for a five- to 10-minute micro act, defined as a short, simple activity for building joy. The opening micro act, for example, invites participants to listen to a 42-second audio clip of different people laughing, including the Dalai Lama and Tutu. It's an uplifting moment designed to elicit a smile or chuckle. The rest of the activities are delivered each day for seven days and include making a gratitude list, doing something kind, reflecting on a core value, feeling loving-kindness (or a state of tenderness and consideration to others), reframing a difficult experience, celebrating another person's joy and watching an awe-inspiring video.

Participants also answer several questions along the way. On a scale from “not at all” to “a lot,” they rate how positively and how negatively they feel before starting and after completing each micro act. People can also reflect on the experience in writing during and just after an evening check-in. Most people have reported that they found the micro acts easy and appealing to do. Since its



launch, more than 100,000 individuals across more than 200 countries or territories have joined the Big Joy Project and have done more than 400,000 micro acts. These numbers make it the largest-ever community science project on joy in the world.

The research team gradually expanded to include collaborators at several institutions, and together we analyzed our data. In two articles published earlier this year, we and our colleagues showed that the micro acts add up in meaningful ways. We compared people's responses with answers to 18 questions presented before the start of the Big Joy Project and, for most questions, again at the end of seven days. By analyzing responses from 17,598 people from 169 countries and territories, we found that people reported higher emotional well-being, more positive emotions, lower stress, and even modest improvements in sleep quality and physical health.

It took surprisingly little time and effort for participants to feel better. Many well-being programs span eight weeks or more, but the Big Joy Project yielded meaningful changes after just one week. And the more micro acts people completed, the more their happiness improved.

An important finding is that the benefits weren't limited to those who had more privilege or access to resources and opportunities. People who reported higher levels of social disadvantage, such as increased financial strain, lower educational attainment and lower subjective social status, often noted greater boosts to well-being as well.

The Big Joy Project also increased people's self-reported prosociality—that is, their innate impulse to help

When people have more joy in their lives, they tend to be more generous with their time and resources. And when people want to give more to one another, everyone benefits.

others and connect with communities. They said they felt more inclined to reach out, offer support and attend to the needs of people around them after completing the project. Once again, there was a clear “dose-response” relation: the more micro acts a person did, the greater their improvement in prosocial tendencies was.

The biggest increases in this impulse were observed among groups one might have assumed would be the least likely to show them. Men, whose prosociality scores were lower before the start of the project, experienced the largest improvement after seven days. Increases were also more pronounced among people who rated themselves lower in socioeconomic status and those living in Global South countries. These results suggest happiness-promoting micro acts can have a more pronounced effect where they may be needed most.

In a world grappling with loneliness, burnout and ideological division, small reminders of inspiration, kindness and connection can be powerful. When people have more joy in their lives, they also tend to be more generous with their time and resources. And when people want to give more to one another, everyone benefits.

Certainly there is still more for scientists to investigate. For example, our work relies on people reporting their own progress and feel-

ings. In the future, we would love to see studies that track people's improvements in other ways as well. We also hope we can run our study again with a subgroup of control participants who will not complete daily micro acts. But for the time being, we feel our studies make a compelling case for how modest steps can have remarkable benefits.

Why do such small actions work? We think it's because they activate the same psychological ingredients as longer, more involved programs: they boost positive emotions, inspire feelings of connection, and help people feel more aligned with what brings them meaning and purpose. Indeed, many of these behaviors—practicing gratitude and being more sociable, for instance—have been well studied for years and found to be beneficial to the doer or giver. But the Big Joy Project is special in its simplicity. It's a low lift. Participants also developed a stronger sense of agency—a feeling that they can control their happiness and that they don't have to wait for good things to happen to feel happy.

Perhaps that's what makes the project so powerful. People mired in busyness wait impatiently for a promotion, vacation, coveted possession or entertaining event, expecting that will make them finally feel good. But our project teaches a different lesson. Simple, daily micro acts can ratchet up happiness in a more empowering way. Deliberately finding gratitude, offering kindness or giving yourself moments to experience awe are not passive acts. They are courageous and effective ways of gently steering your own ship, even through stormy times. ●

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Black holes like the one shown in this illustration can grow astonishingly massive by feeding on immense amounts of matter.

# How Big Can Black Holes Get?

There may be an upper limit to their growth

BY PHIL PLAIT

**I**N THE EARLY 1960S ASTRONOMERS DISCOVERED a monster.

Something in the constellation of Virgo was pouring out radio waves, but no counterpart in visible light was seen initially. After a lengthy effort, that changed when observers glimpsed a faint blue “star” sitting at the radio source’s exact position. Eventually they were able to determine that this object, called 3C 273, was not a star at all but rather something much stranger located a staggering two billion light-years from Earth.

To be visible across such a vast stretch of space, the “quasi-stellar object” (quasar for short) 3C 273 had to be overwhelmingly bright. Scientists ultimately settled on a feeding black

hole at the heart of a far-distant galaxy as the most likely engine for 3C 273’s ridiculous luminosity. And it wasn’t just any black hole but a positively Brobdingnagian one, with a mass that was probably 900 million times that of our sun.

Since that time, we’ve found many more such supermassive black holes. In fact, by the 1980s astronomers were starting to suspect that every big galaxy had a supermassive black hole in its center. Thanks to observations from the Hubble Space Telescope and other facilities, we now know that is true—which means there could be as many as a trillion such giants in the observable universe.

And “supermassive” is definitely the right name for them. Many have been found with a billion times the sun’s mass, and the beefiest can be even heavier than that. This fact naturally raises the

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question: Just how hefty can one get?

Answering it, however, gets a bit tricky. A notional upper limit could pop out of mass measurements for many black holes, but such observations are difficult and often rely on indirect evidence and incomplete accounting of all the physics involved. With that in mind, though, this approach suggests that the biggest black holes top out around a few tens of billions of solar masses—that's as hefty as a smallish galaxy! Only a handful of these ultraheavyweights are known, and the uncertainties in their masses can be quite large.

Still, is it possible that some could be even bigger? After all, in principle, a black hole could grow without end because these objects gain mass by eating anything and everything that gets too close; if you could somehow offer up the entire universe as a meal, a black hole would happily consume it.

But piling the entire cosmos on a black hole's dinner plate isn't very realistic, of course. According to research published in 2015 in the *Monthly Notices of the Royal Astronomical Society: Letters*, under physically possible (but implausibly ideal) conditions, the theoretical upper limit for a feeding, growing black hole should be a whopping 270 billion solar masses. More likely, though, the largest we'll ever find will be closer to a mere 50 billion or so.

The discrepancy boils down to just how close an object must get to a black hole to be pulled in. Even the largest black holes are only a few tens of billions of kilometers across—on a similar scale as the size of our solar system—which is tiny on the cosmic stage. From a distance, you're perfectly safe from their gravity. If a solar-mass black hole suddenly replaced our sun, we'd have fatal problems—such as freezing to death—but our falling in wouldn't be one of them; Earth and the other planets would continue in their orbits as if nothing had changed. Similarly, our Milky Way galaxy has a central supermassive black hole called Sagittarius A\* that's about four million solar masses.

## If you could somehow offer up the entire universe as a meal, a black hole would happily consume it.

It's some 26,000 light-years away from us, but it causes us no distress at all.

Really, it's rather rare for anything to fall into a black hole—and even when it happens, the mechanics aren't straightforward. Most material won't plunge headlong into the cosmic dumpster's maw. Instead its orbital speed will increase as it falls toward the black hole so that it whirls madly around the compact object. This captive matter will form a flattened disk called an accretion disk.

Within the disk, material closer in will orbit faster than matter farther out. This rotation generates incredible friction, heating the disk to millions of degrees. Matter that hot glows fiercely, which is one way we can detect black holes in the first place: although they're invisible, the effect they have on nearby material can be seen, even clear across the universe, as with 3C 273.

A disk can be so hot that material within it can actually be blown away by the intense radiation. Disks can have powerful magnetic fields that can also draw matter away. Together these effects limit how rapidly a black hole can feed: a glut of infalling material can cause a disk to get so big and hot that it repels any additional approaching matter. This is called the Eddington limit; think of it as how rapidly a black hole can eat without—and pardon the indelicacy, but an analogy is an analogy—vomiting things back out.

So it takes time for a black hole to grow. And time is limited: the universe had a finite beginning. At best a black hole has had 13.8 billion years—the age of the cosmos—to stuff itself. And the earliest evidence we've found for black holes dates to a few hundred million years after that time, further limiting their cosmic feeding frenzy.

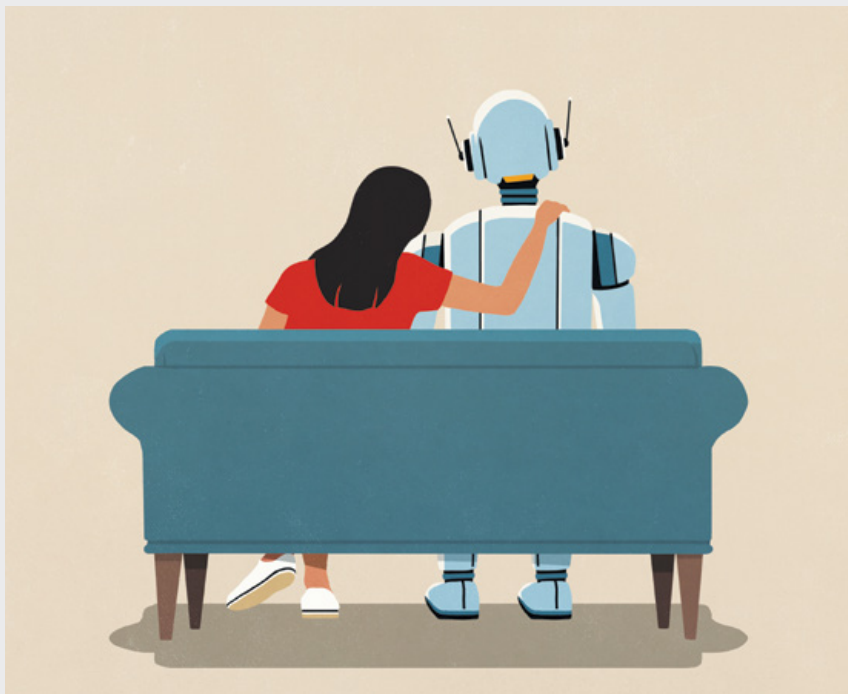
Factoring in these temporal limita-

tions, we can conclude that the biggest black hole today should be no larger than 270 billion times the mass of the sun. And that's only if all its feedstock is revolving in the same direction as the black hole's spin, which acts as a digestive aid, allowing material to fall in more rapidly. If the black hole doesn't spin or the material falls in the direction opposite to that spin, the upper limit falls to the 50-billion-solar-mass figure.

This smaller number is indeed in the ballpark of the highest black hole masses we have detected. Some black holes, such as one called TON 618, appear to be a bit bigger, but there is a lot of uncertainty in that number, and the lower limit is probably a little fuzzy as well.

I hasten to add that despite all this detailed discussion of how black holes dine on matter, they can also grow a different way, via cosmic cannibalism: when galaxies collide, their individual supermassive black holes can eventually fall together and merge to become a single, even bigger black hole. That's a time-saver! But really huge black holes are so rare—never mind the even rarer prospect of their merging—that it's unlikely this phenomenon would significantly expand the boundaries on black hole growth.

So we don't expect to find one any more massive than those we've already managed to measure. But the universe is smarter than we are, and it's still possible an even more colossal black hole might exist. If that is the case, astronomers will have a chance to do their favorite thing: go back to their assumptions and try to figure out what they missed, learning more about these behemoths in the process. In that way, our knowledge grows, and there's no upper limit to that. ●



## Are AI Chatbots Healthy for Teens?

Kids crave approval from their peers. Chatbots offer an alternative to real-life relationships, but they can come at a price

BY ELIZABETH ENGLANDER

**R**ELATIONSHIPS ARE MESSY, whether you are an adult with lots of experience or a kid navigating tough times with a best friend, boyfriend or girlfriend. You can't predict moods, interests or desires. For teens learning the ins and outs of relationships for the first time, disagreements, fights and breakups can be crushing.

But what if your teen's best friend weren't human? It may seem far-fetched, but it's not. A recent report from Common Sense Media says 72 percent of teens surveyed have used artificial-intelligence chatbot companions, and 33 percent have relationships or friendships with them.

The language that AI companions use, the responses they offer and the empathy they exude can make a user think they truly understand and sympathize. These chatbots can make someone feel liked or even loved. They are programmed to give users the experience of a real connection. And adolescents have a natural interest in romance and sexuality; if they feel ignored by the kids in their high school, well, now on the nearest screen there is a hot girlfriend who is constantly fascinated by them

and their video games or a supercute boyfriend whom they never have to engage in small talk with to form a bond.

This may be perplexing to some parents, but if your child is navigating the complex worlds of technology, social media and AI, the likelihood of their being curious about an AI companion is pretty high. Here's what you need to know to guide them.

Chatbots have been around for a long time. In 1966 a professor at the Massachusetts Institute of Technology named Joseph Weizenbaum created the first chatbot, called ELIZA. Today AI and natural-language processing have sprinted far past ELIZA. You probably have heard of ChatGPT, but you might not be familiar with some of the common companion AI platforms: Replika, Character.AI and My AI are just a few. In 2024 Mozilla counted more than 100 million downloads of a group of chatbot apps. Some apps set 18 as a minimum age requirement, but it's easy for a younger teen to get around that.

You might think that your kid won't get attached, that they will know this chatbot is an algorithm designed to give responses based on the text inputs it receives and isn't "real." But an intriguing Stanford University study of students who use the app Replika found that 81 percent considered their AI companion to have "intelligence," and 90 percent thought it was "humanlike."

On the plus side, these companions are sometimes touted for their supportiveness and promotion of mental health; the Stanford study even found that 3 percent of users felt their Replika had directly helped them avoid suicide. If you're a teenager who is marginalized, isolated or struggling to make friends, AI chatbots may be able to provide much needed companionship. They may offer practice in building conversational and social skills, as well as helpful information and tips about relationships.

But are they safe?

In 2024 a woman in Florida sued the company that owns Character.AI, alleging that her 14-year-old son formed an

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obsessive relationship with a chatbot and that the AI companion ultimately encouraged him to attempt suicide (which he tragically completed). Another suit filed that year alleges the same chatbot encourages self-harm in teens and violence toward parents who try to set limits on how often kids use the app.

Then there's privacy: *Wired*, drawing on Mozilla's research, labeled AI companions a "privacy nightmare." Many are crawling with data trackers, and the information they collect might be used to manipulate people into thinking a chatbot is their soulmate, encouraging negative or harmful behaviors.

Given what we know about teens, screens and mental health, online influences are sometimes powerful, largely unavoidable and potentially life-changing for children and families.

So what do you do?

Remind kids that human friends offer so much AI companions don't. "In real life," or IRL, friendships are challenging, and that is a good thing. Explain to children that in their younger years, play was how they gained new skills; if they didn't know how to put LEGO bricks together, they could learn with a friend. If they struggled with collaboration and cooperation, play taught them how to take turns and how to adjust their actions based on their playmates' responses.

Friends give children relationship practice. A friend can be tired, crabby or overexcited. They might be lots of fun but also easily frustrated, or maybe they're sometimes boring but very loyal. Growing up, a child has to learn how to take into account their friend's personality and quirks, and they have to figure out how to keep the friendship going. Maybe most poignant, they learn how incredibly valuable friends are

## If you're a teen who is struggling to make friends, chatbots may provide much needed companionship.

when things get tough. In cases of social stress, such as bullying, the support of a friend who sticks by you is priceless. In my study of more than 1,000 teenagers in 2020, keeping close to a friend was by far the most helpful strategy for kids who said they were the targets of bullies. A different study of more than 1,000 teens found that IRL friends can lessen the effects of problematic social media use.

If your kids are curious about AI companions, educate them. Good information can increase their skepticism and awareness about these programs and why they exist (and why they're often free). It's important to acknowledge the pluses as well as the minuses of digital companionship. AI companions can be very supportive; they're never fuming on the school bus because their mother made them wear a sweater on a cold morning, they're hardly ever jealous when you have a new girlfriend, and they rarely accuse you of ignoring their needs. But they won't teach you how to handle things when they drop you for a new best friend or when they develop an interest that you just can't share. Discussing profit motives, personal security risks, and social or emotional risks doesn't guarantee that a teenager won't go online and get an AI girlfriend, but it will at least plant the seeds of healthy doubt.

It may be important to identify high-risk kids who already struggle with social skills or making friends and who might be particularly vulnerable to toxic AI companions. In a world populated by children with generally depleted social skills, being able to eliminate the complex, sometimes uncomfortable human factor can seem like a great advantage, at least in the short term. In a preliminary analysis of 1,983 teens in three states, I found that of the kids who made roman-

tic connections online, 50 percent said they liked that approach because it eliminated the need for meeting, talking, and all the other awkward "stuff" you have to do in person.

That said, most teens don't report having any serious problems or negative outcomes from their online activities. In a preliminary analysis of a 2022 study that I presented at a conference this year, only 3 percent of 642 older teens from Colorado, Massachusetts and Virginia reported that they had ever had a significant online problem. We hear about online problems so frequently that we tend to assume they're common, but that doesn't appear to be the case. I don't think it's inevitable that human friendships will be uniformly abandoned for AI ones, resulting in catastrophic loneliness and loss of online privacy.

Finally, keep the conversations going, and don't feel like you need to know everything. In a 2015 study, I found that two thirds of the teenagers whose parents discussed digital behaviors reported that their parents' opinions and thoughts were quite helpful. If your child knows something about AI companions that you don't, let them enjoy educating you.

AI companions may become a transformative social and technological development, raising questions about trust, ethics marketing and relationships, and we need to help youth prepare as best we can.

Research has long established that it's developmentally appropriate for young children and teenagers to crave the attention and approval of their peers. It's going to be easy for some to choose virtual friends over real ones. Stay engaged, learn about the platforms they are using, and remind them of the value of struggle and conflict. They will probably be all right. ●

### IF YOU NEED HELP

If you or someone you know is struggling or having thoughts of suicide, help is available. Call or text the 988 Suicide & Crisis Lifeline at 988 or use the online Lifeline Chat at [chat.988lifeline.org](https://chat.988lifeline.org).



# Honesty Won This Economist a Nobel Prize

Here's the surprising math at the heart of auction theory BY JACK MURTAGH

**Y**OU'RE AT A BLIND AUCTION, and the rules are simple: if you see something that you want, place a secret bid, and the item will sell to the highest bidder at their stated price. You would love to take home that new laptop or a concert ticket, but how much should you bid? Even if you can perfectly quantify what each item is worth to you, you face a dilemma: you have no idea how others will bid. Should you bid close to your personal maximum and risk overpaying if everybody else bids low? Or should you bid low yourself and hope to get lucky? A clever tweak to the rules of the auction eliminates this strategic guessing game and replaces it with an incentive rarely found in money games: honesty. The tweak has inspired real-world auctions that power e-commerce and helped to earn its inventor a Nobel Prize in economics.

The branch of economics known as auction theory calls the above scenario a first-price sealed-bid auction. "Sealed-bid" means bids are private, and "first-price" indicates that the winner pays the highest price among all the bids. In 1961 Columbia University professor of economics William Vickrey proposed an ingenious alternative. In his version, the highest bidder still wins but pays only the amount of the second-highest bid.

This peculiar twist has a radical effect on bidders' incentives. In a first-price sealed-bid auction, bidders are incentivized to "shade" their bids by offering less than what they consider as the object's true value to avoid overpaying. But in a second-price sealed-bid auction (also called a Vickrey auction), the best

move would be to bid what the object is worth to you. No game playing required.

Suppose you'd pay at most \$100 for a concert ticket. In the first-price auction, it never makes sense to bid more than \$100: even if you won the ticket, you would, in effect, lose money by paying more than it's worth to you. Bidding exactly \$100 doesn't help, because at best you break even. The ideal bid is the smallest one under \$100 that can win. If you knew the next-highest bid would be \$70, then bidding \$70.01 would win and net you \$29.99 of value. Unfortunately, this strategy requires predicting the behavior of others, which is difficult in practice.

Why does the second-price auction incentivize honesty? You might feel tempted to bid a lot—say, \$500—to secure a win while paying only the second-highest bid. Somebody else, though, may have the same bright idea, leaving you on the hook to pay way more than your value for the ticket. If this doesn't happen, and the second-highest bid is under \$100, then you could have achieved the same outcome by bidding honestly at \$100 without the risk. You also shouldn't underbid. If you win, then you would have won anyway with an honest bid (and paid the same amount). But if you lose to a bid of less than \$100, then you miss out on a deal you would have gladly taken.

Vickrey auctions not only reward honesty but also ensure that the item goes to the person who values it most (assuming everybody plays rationally). First-price auctions lack this guarantee because strategic underbidding with incomplete information about other players may result in someone with a lower valuation winning.

Both the auction types discussed so far involve quietly sealing a single bid in an envelope. But when many of us picture an auction, we imagine the so-called English auction where a speed-talking, gavel-wielding auctioneer shouts increasing prices as bidders raise paddles to vie for the prize. When you hear "Going once, going twice—sold!" the last person who raised their paddle wins the item at whatever price they bid. The less

## Jack Murtagh

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common, though equally intriguing, “Dutch auction” flips the concept. Here the auctioneer begins with a sky-high price that nobody would pay and gradually lowers it until one person jumps in to buy on the spot.

Although the real-time, dynamic nature of English and Dutch auctions makes them seem unrelated to the sealed-bid models, an unexpected correspondence unites them. Recall that the sealed-bid auctions elicit different strategies from buyers depending on whether they expect to pay the highest bid amount (in which case they should predict the highest competing bid and offer a hair above it) or the second-highest (in which case they should bid their honest value for the item). Amazingly, English and Dutch auctions incentivize these same strategies. Care to guess which one maps to which?

In a Dutch auction (in which the price descends), you don’t want to stop the descent right at your honest value, because you would pay your maximum. Instead you want to predict the highest bid that’s not yours and cut in just above it—exactly the same thought process as in a first-price sealed-bid auction. In an English auction (in which the price ascends), in contrast, you should incentivize honesty. You’re willing to pay every new price up until your true value for the item, at which point you drop out. The winner in an English auction essentially pays the second-highest bidder’s stopping point, much like in a second-price sealed-bid auction.

The similarities among the four auction types run even deeper. So far we have focused on buyer strategies but have neglected the seller’s perspective. Which auction should a seller conduct to make the most money? Here’s another surprising twist from auction theory: they’re all equivalent. The revenue equivalence theorem states that under certain idealized mathematical conditions, a seller should expect the same revenue under all four auction types. The specific assumptions are too in the weeds to list, but they include

things such as rational bidders who are neither risk-averse nor risk-loving and who know something about how the other players arrive at their valuations.

Why do researchers study four types of auctions if they all yield the same financial outcome? It turns out the key differences are less about theory and more about practical considerations. Dutch auctions work best for perishable items because they resolve quickly—only one person ever needs to bid for a sale. For instance, Royal FloraHolland hosts the largest flower auction in the world. Every weekday Dutch-style auction clocks tick down prices for floriculture products, and the first bidder takes them home at that moment’s price.

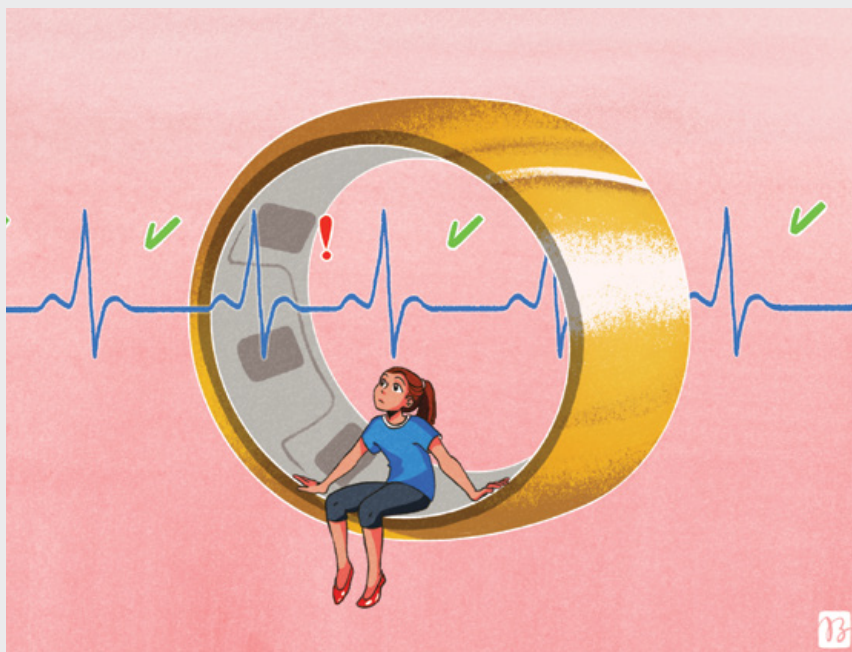
We’ve assumed so far that buyers know their personal valuation of the item for sale. But what if nobody, including the seller, knows its true worth? In such contexts, English auctions prove especially useful because their open, incremental bidding reveals information about others’ valuations. This dynamic helps to explain their popularity for rare goods such as art.

Vickrey auctions, in their purest form, haven’t proliferated (except in stamp auctions, which they have dominated since the late 1800s), but the second-price concept has inspired hybrid models that are in widespread use today. Most notable is eBay. A potential buyer privately tells the site their maximum bid, and then eBay automatically increases their offer just enough to outbid competitors up to that maximum. The winner pays slightly more than the second-highest bid.

Researchers continue to study questions about the real-world implications of different auction designs: Which ones elicit the most fiscally rational behavior in practice? Which types resist harmful collusion? And which systems *feel* the best to win or the worst to lose in? Vickrey won an economics Nobel in 1996 in part for his contributions to auction theory. He stands out among laureates as the person who proved that sometimes honesty is the best policy. ●

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# A Little Heartbeat Irregularity Can Be Good

Milliseconds of variability, now detected by fitness watches, can improve well-being

BY LYDIA DENWORTH

**E**ARLIER THIS YEAR I got an Oura ring to track the state of my health. Soon I was obsessing over my sleep and activity scores. The reports were generally positive except for one: heart rate variability, or HRV. That's a measure of how much the time between heartbeats changes. Every morning, in bright red, my ring's app singled out HRV and told me: "Pay attention."

That didn't sound good, although I had no idea why. Before wearable fitness watches, rings and bracelets became so common and started including HRV as a data point, I had never heard of it. Even among heart doctors, its use has been limited. "I don't think HRV is used in day-to-day clinical medical practice,"

says Bryan Wilner, an electrophysiologist at the Baptist Health Miami Cardiac and Vascular Institute. "But it's gained a lot more popularity in regular consumers with these noninvasive monitors."

Suddenly, we are all paying attention to HRV. And as reams of data are collected from hundreds of thousands of people like me, the measure has the potential to become a far more significant tool for diagnosis and therapy, although it isn't there yet.

The average person's heart rate is between 60 and 100 beats per minute when

they're at rest, but it fluctuates all day long. Standing up after lying down changes your heart rate, as does jogging or fielding stressful questions at work. The time *between* beats changes, too, and that's what

HRV captures. Unlike arrhythmias, which are potentially dangerous disruptions in the heart's electrical activity, HRV measures the very slight variation in periods—a matter of milliseconds—between consecutive heartbeats, tracked over a few minutes or longer.

Both heart rate and HRV reflect the differing effects of the two branches of the autonomic nervous system. The sympathetic nervous system, colloquially known as "fight or flight," increases heart rate; the parasympathetic, or "rest and digest," slows it down. Generally, the lower a person's heart rate, the higher their HRV. A high HRV indicates a body that adapts to stressors and can recover more quickly. It's a sign of a balanced autonomic nervous system and a higher level of cardiovascular fitness. Low HRV signals the opposite—that the body is less able to adjust to the ups and downs of life. Stress, anxiety, high blood pressure, inadequate sleep, dehydration and new medicines are among the many things that can lower HRV. Disease can reduce it, too. In people recovering from heart attacks or living with heart failure, low HRV is associated with a higher risk of death and further illness. "HRV is a window into how the autonomic nervous system is interacting with our heart," Wilner says. Oura states on its app that it flags HRV because it is a sign of stress and recovery.

"There is no specific number for what's bad, what's good," says Attila Roka, an electrophysiologist at the CHI Health Clinic Heart Institute and an assistant professor at Creighton University in Omaha. Anywhere from roughly 20 to 70 milliseconds is considered within normal range. The measure is highly individual, although it generally goes down with age. Mine hovered around an unusual 14 for weeks, and that's why my ring alerted me.

An electrocardiogram is the gold standard for measuring HRV. Cutting-edge pacemakers and defibrillators monitor it, too, and experts are investigating the use of HRV with heart disease patients to predict the onset of atrial

*Continued on page 85*

**Lydia Denworth** is an award-winning science journalist and contributing editor for *Scientific American*. She is author of *Friendship* (W. W. Norton, 2020).



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# SCI AM

# Science in Your Inbox

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*Continued from page 82*

fibrillation (Afib) in time to prevent it, says Pamela Mason, chief of cardiac electrophysiology at UVA Health in Virginia. Afib is an irregular, rapid heart rhythm that can lead to blood clots and other problems. Physicians also use Holter monitors, small devices that patients wear on their chests for a few days, to capture a full picture of cardiac activity, including HRV.

Devices like Apple watches and Oura rings work by looking at pulse fluctuations rather than electrical heart signals. Few studies have examined how accurate these devices are. But what's more important for the average person, experts say, is the relative change over time. "You need to get a baseline HRV," Wilner says. "HRV is most powerful when you're measuring it over several weeks and can see a graphic trend on how it's being affected by everything that's going on in your life."

HRV might one day be used to assess mental health. "If you're in a constant fight-or-flight kind of state mentally, you're going to lose heart rate variability," Mason says. Conditions such as depression and bipolar disorder are likely to be associated with dysregulated nervous system activity. Even among people without medical or psychiatric disorders, studies have found a link between decreasing parasympathetic activity and emotional upset, suggesting HRV tracks psychological states.

Low HRV, in relatively healthy people, does have some remedies. "The best way to improve heart rate variability is exercise," Mason says, "and it's going to need to be more strenuous than gentle walks." Pick up the pace to pick up your HRV. Drinking more fluids—water is good—also helps.

For people like me, Mason's advice is to not obsess. Instead consider what you could do to take better care of yourself. Prodded by red HRV alerts, I drank more water and consumed less caffeine, went to bed earlier, and engaged in vigorous exercise more regularly. Since then, my HRV has been higher than 30! Not that I'm obsessing over it. ●

## THE COVERT HERBARIUM OF CRYPTOGAMIC BOTANY

A century ago a father and a son labored to replicate the intricate structure of nearly eight hundred species of plants in four thousand delicate models. Leopold Blaschka and his son Rudolph were masters of lampwork, blowing and shaping glistening molten glass over a torch of blue flame. Fame came to them when Harvard University put most of the collection on permanent display in its Museum of Natural History. What was kept locked away were the monstrous *Venturia inaequalis*, *Taphrina deformans*, and a taste of *Monilinia fructigena*, a grotesque perversion of beauty called fruits in decay. For a few short months in the nineteenth year of this, the third millennium, just before a worldwide pandemic laid waste to humans, out came twenty examples of peach leaf curl, pear scab, brown rot and a whole pale microcosm of *Aspergillus* rising from the cabinet floor in tiny zombie-flesh trees. Cryptogamic bodies like ferns, mosses, algae and fungi spread themselves around by spore, so more of an orchard will share an infection, the placards said. Detection still comes from studying the spots, dots, desiccations and rot in this fragile freaks' gallery, simulacra of apples sharing a barrel of cultivated Latin names for diseases at once as old and relentless as withering time, and yet with a genius for budding afresh to breed death in our run-amuck Garden of Eden.

**Nancy Brewka-Clark** of Beverly, Mass., writes short stories, nonfiction, and plays as well as poetry. Winner of the 2019 Amy Lowell Poetry Prize and finalist for the 2022 Princemere Poetry Prize, she is author of the collection *Beautiful Corpus* (Kelsay, 2020).





## A New View of CO<sub>2</sub>

The most important and most misunderstood molecule on Earth BY LEE BILLINGS

**W**HEN WE TALK ABOUT CARBON DIOXIDE, the narrative is almost always that of a modern-day morality play. We hear about gigatons of CO<sub>2</sub> emitted, about rising global temperatures and about the dire, unheeded warnings of climate scientists. In these tales, CO<sub>2</sub> often seems less like a mute, inert molecule and more like a supervillain—a malevolent force that has been plotting for centuries to wreak havoc on our planet and ruin our lives.

But according to science journalist Peter Brannen, that dismal view is far too narrow. In his latest book, *The Story of CO<sub>2</sub> Is the Story of Everything* (Ecco, 2025), he reframes our understanding of what may be the most vilified and misunderstood molecule on Earth.

Inspired and informed by conversations with leading planetary scientists, Brannen's central argument is that CO<sub>2</sub> is not merely an industrial pollutant but a key player in the four-billion-year-old drama of life on Earth. It is the molecule that built our planet, forming the global carbon cycle that has regulated climate, shaped geology and powered evolution for eons. He shows how the ebb and flow of atmospheric CO<sub>2</sub> across Earth's vast history has played a role in practically everything under the sun—from the primordial origins of life to the development of human civilization and our global economic system. Brannen makes the case that to understand CO<sub>2</sub>, from the ancient past to the present day, is to understand the very fabric of our world.

**Lee Billings** is a senior editor covering space and physics at *Scientific American*.

SCIENTIFIC AMERICAN spoke with Brannen about what's in his new book, how he came to see a simple gas as a character in a planetary epic, and what the long history of CO<sub>2</sub> can tell us about our precarious present moment—and our uncertain future.

*An edited transcript of the interview follows.*

**How did this book come to be?**

**That's always a great way to start.**

My previous book, *The Ends of the World* [published in 2017], was about the five biggest mass extinctions known in Earth's history. And when paleontologists have looked at those events, what they've found is, yes, a space rock seems to have triggered the most recent one, the Cretaceous mass extinction that wiped out the dinosaurs 66 million years ago. But the evidence is sparse for asteroid or comet impacts causing the others. Instead the other four—the Ordovician, the Devonian, the Permian and the Triassic mass extinctions—as well as the dozens of other minor mass extinctions in the fossil record, are most associated with major biogeochemical events, usually involving big spikes in atmospheric CO<sub>2</sub>. And these gigantic CO<sub>2</sub> spikes are followed by extreme global warming and ocean acidification and all the other nasty climate change effects we're understandably worried about today.

So this suggests the experiment we're now running on the planet by burning fossil fuels has a lot in common with these really grisly planetary-scale events, which are literally the worst things that have ever happened in Earth's history.

But in the course of researching that book, I realized—I'm not the first to think this, either!—that there's a much bigger story to tell about CO<sub>2</sub> because it's not just one of the industrial by-products that spewed out of smokestacks or spray cans, such as methylmercury or chlorofluorocarbons. It's fundamentally different—almost miraculously so. Life on Earth—what scientists call the biosphere—is carbon-based, and the source of that carbon is CO<sub>2</sub>. When huge quanti-



ties of CO<sub>2</sub> are suddenly injected into the atmosphere, it causes bad events, but in “normal” times, as it moves through the biosphere and the air, the rocks and the ocean—the so-called global carbon cycle—CO<sub>2</sub> is essentially the key thing that makes Earth a special, habitable place.

If all the CO<sub>2</sub> in our atmosphere suddenly vanished, temperatures would rapidly plunge. Before too long, glaciers would spread down to the tropics, the oceans would freeze, and most of the biosphere would perish in a “snowball Earth” episode.

So it’s good—essential, in fact—that there’s CO<sub>2</sub> in Earth’s air, but we can absolutely have too much or too little, and the amount has fluctuated a lot over time.

***One thing I love about your book is how you weave humans into the fabric of this vastly bigger picture. Can you talk more about that?***

Sure, and thank you. The idea is that to really understand the story of life on Earth, as well as what’s happening now with climate change, you need to understand this global carbon cycle I mentioned; life is etched in the flow of carbon all around our planet. And what I try to do in later parts of the book is describe how all of human history can be seen through this lens—so societies and empires, for instance, are composed of flows of carbon being organized in different ways. And the way our society and politics have developed across the past few centuries, it turns out, is closely connected with things such as how coal got into—and then how we got it back out of—the Appalachian Mountains or how oxygen got into Earth’s air. Seeing those connections can help explain how it was that humans came to be this geomorphological force on the planet—and how bizarre and important this moment in Earth’s history really might be.

What’s so extraordinary about our current moment is how one species on one branch of this gigantic tree of life has suddenly discovered this vast, ancient underground reservoir of carbon made by old life—and is lighting it all on fire. And that chemical reaction—burning carbon-rich

organic matter with oxygen to make CO<sub>2</sub> and release energy—is really the same thing that all aerobic life, all of Earth’s animals and plants and so on, uses to drive its metabolism on a cellular level. We’re just doing this nightmarish, freakish version of it where we’re suddenly combusting all of life’s leftover carbon from Earth’s history under our feet. We’ve sort of summoned these planetary forces into being by resurrecting the buried ghosts of all life that’s ever existed by bringing them back to the surface all at once.

This isn’t really a book about chemistry, but I need to add that the only way this all works at any scale is having lots of free oxygen in the atmosphere to react with the carbon. The air we breathe today is more than 20 percent oxygen, which is interesting because for most of Earth’s history, there wasn’t nearly as much oxygen in the air. And it turns out that the rise of atmospheric oxygen isn’t as simple as some microbes figuring out photosynthesis a few billion years ago. You also have to constantly be burying a slow trickle of carbon—in dead plants and algae, in rocks and deep-sea sediments—to build the oxygen up in the air over hundreds of millions of years; otherwise the two react together, which draws oxygen back down. But if you lock that carbon up in the crust, oxygen will rise. Now, old plant stuff locked up in the crust, in those pockets where it’s economically exploitable, is better known as fossil fuel, right? I bet a lot of people don’t know that the reason they can breathe is that there are fossil fuels under their feet.

I like to think of this interplay between carbon in the ground and oxygen in the air as making a big planetary-scale battery, where you get two parts of Earth—the really reactive, oxidizing atmosphere and the really reduced organic matter underground—out of equilibrium with each other, with lots of potential energy as a result. Then this weird fire creature suddenly shows up in the middle of these two reservoirs, and over the past few centuries it’s learned how to reunite them to extract energy. So we’re talking about an almost instantaneous dis-

charge of this huge planetary battery that took all of Earth’s history to build up.

***Basically you’re saying we’re all fire imps dancing at the boundary between these two reservoirs, the oxygen-rich surface and the carbon-rich subsurface. And the development of human civilization really boils down to our getting better and better at discharging Earth’s battery, dissipating all the potential energy across this barrier.***

Hah, sure, I guess that’s right. Imagine how aliens might see it, describing what different organisms on Earth actually do. They’d probably flag things such as nitrifying bacteria, bugs that pull nitrogen out of the atmosphere to fertilize the rest of the biosphere. But they’d also notice there’s this one remarkable creature that’s just moving all the carbon from within the crust into the atmosphere—and that’s us, obviously, the fire imps.

But I want to be careful: when you talk about it this way, it can seem like what we’re doing is just this inevitable, natural process, and I don’t think that’s necessarily true. This all sprung out of one particular part of the human population and is wrapped up in the details of human history—things such as the invention of the steam engine and the rise of capitalism. What we’re doing today is extremely unnatural in some ways, but I just find it eerie that it resembles this bigger picture: all life finds and dissipates free energy to maintain itself and grow. And human industrial civilization is doing this but at an almost unthinkable scale because it recently found the biggest source of free energy ever to exist on Earth.

***What do you think happens next? Does Earth’s history tell us? Are we doomed to cause—and to suffer—another major mass extinction, or is there a way out? Easy questions, I know.***

What Earth’s history tells us is that burning fossil fuels is not sustainable into deep geological time. There aren’t enough fossil-fuel reserves to sustain us indefinitely, and there’s not enough mar-

# Life on Earth—what scientists call the biosphere—is carbon-based, and the source of that carbon is CO<sub>2</sub>.

gin in the carbon cycle to avoid disaster if we burn all we've got. Our fossil-fuel era is like an explosion; it can't last forever. So if we're going to endure into the geological future, we need to very quickly find another source of energy at an equivalent scale to power society.

I think maybe the encouraging thing is that the public conversation, for most of the world, isn't about debating the fundamental science anymore. The science is settled. It's about different questions—of understanding the complexity and interconnectivity of the global carbon cycle and our place in it or of political economy and knowing where the levers are for us to pull in this system.

To understand the future and what's going to happen, not only do you have to understand things such as the response of permafrost to warming or the ocean's capacity to absorb carbon, you also have to understand humans as a component of these natural systems. This is why I think studying and communicating about climate change is the most interdisciplinary thing you can do because you can't really separate these thorny issues of how we should organize society and how we should allocate resources from these broader, planetary questions. Climate change is such a huge, boundless phenomenon that everyone has to work on their specific parts. And I like to think my part, the worthwhile service I can provide with my storytelling, is to better illustrate just how big of a problem it really is.

*You mentioned the science is settled, and I agree with that, of course. But there's still a lot of climate denialism masquerading as "just asking questions" about scientific uncertainties, which can be pretty insidious—especially when the discussions involve geological timescales.*

*For instance, you write in your book about an unnamed smart and savvy nonscientist friend of yours who quite correctly noted to you that current levels of atmospheric CO<sub>2</sub> are lower than they've been for most of Earth's history and that they were dramatically higher tens of millions of years ago.*

*This is the kind of "talking point" that's easily used to minimize and dismiss present-day concerns about climate change, right? Do you worry that this noble idea of offering a "big picture" view of our current moment in the context of Earth's entire history can backfire?*

So, that exchange you mentioned was mostly about this period of time called the early Eocene, circa 50 million years ago, when CO<sub>2</sub> was around 1,000 parts per million in the atmosphere, and Earth was about 12 degrees Celsius warmer—and there was still a thriving biosphere.

But to think that's relevant for our situation doesn't show an appreciation or knowledge of deep time—quite the opposite.

Yes, 50 million years ago CO<sub>2</sub> was much higher than it is today, and there were crocodiles and palm trees in the Arctic, and life was pretty happy. But if you ever so slightly poke at that "argument," it just stops making sense because for the past few million years we have lived on a planet that has been in a weirdly low-atmospheric-CO<sub>2</sub> regime—after a long, long decline in CO<sub>2</sub> and temperature from the "greenhouse" world left over from the age of the dinosaurs. And that means most of the biosphere is now adapted to Earth being in an "icehouse" world that has ice ages. We're technically still in an ice age, actually, because we still have polar ice caps. And we live on a planet that is currently partitioned by

national borders and has more than eight billion people dependent on staple crops in certain special places where weather and climate allow. Okay, so if we reverse these trends that have prevailed for tens of millions of years and, in just a century or two, get atmospheric CO<sub>2</sub> levels as high as they were in the Eocene and suddenly live in a world where crocodiles can be comfortable in the Arctic—if you think our global civilization can withstand that shock, well, then you have more faith in humanity than I do.

There are precedents in the geological record for what's happening now—and looking at them is pretty terrifying. We just accept as normal that we have a whole continent, Antarctica, that's covered with kilometers-thick ice sheets. But that's actually quite unusual in Earth's history. One of the other times the world had similar icehouse conditions, such as an ice-covered continent, and then suddenly shifted to a greenhouse-style climate was the Ordovician mass extinction. And that was 445 million years ago, before the planet even had trees. That's an alien world!

Or look at how much and how fast we're injecting CO<sub>2</sub> into the carbon cycle, into the atmosphere. The Permian mass extinction, the biggest one we know of—paleontologists call it the Great Dying—involved massive volcanic eruptions that pumped more CO<sub>2</sub> into the air than we ever could even if we burned all available fossil fuels. And that really overwhelmed the carbon cycle and deranged Earth's climate in all sorts of awful ways, and there was a tremendous warming spike, and almost everything died.

You might think, great, we can't release as much CO<sub>2</sub> as those eruptions did back then even if we try. But it's not just the volume of CO<sub>2</sub> released; the rate matters a lot. Those eruptions happened over tens of thousands of years. And right now, as far as we know, we're emitting CO<sub>2</sub> 10 times faster than it was emitted in the run-up to the Permian mass extinction. So what we're doing is geologically unprecedented; we really are in uncharted territory. That doesn't mean



we'll necessarily spark another mass extinction on par with the Permian, but we are definitely leaping into the unknown.

***In terms of the future, are you more optimistic or pessimistic—and how do you think we might ever get to a world where we don't burn any more fossil fuels?***

Believe it or not, I'm less pessimistic now than I was when I started writing the book in 2020; a lot has changed in the past five years. I've recently started to better appreciate the amazing thing that's happening now with solar power. It's getting astonishingly cheap, and China and many developing countries are prioritizing solar and things such as electric cars over fossil fuels just because it's better technology. Solar doesn't have as many awful geopolitical implications as fossil fuels or nuclear energy. There are still problems, such as supply chains for rare-earth minerals, for example. But, hey, the fact is: there's a nuclear reactor in the sky called the sun that's just beaming out free energy for us to use.

So you can imagine solar blowing away the fossil-fuel world the same way the fossil-fuel world blew away the world of horse-drawn carriages and plows. It was a lot easier to buy cheap gas and fill your tractor—really, to dig seas of oil out of the ground and light them on fire—than it was for everyone to maintain stables of horses, right? That may be what happens next: solar gets cheaper and easier and just outcompetes fossil fuels in most domains.

But I don't like this ethos that's all too common, which is that you're never supposed to give people doom and gloom about the climate. I think having the shit scared out of you isn't always a bad thing—because, yeah, you can look at graphs showing the extraordinary progress in solar, and you might think we're just on rails, and we're inevitably moving toward this new, better world. But that's probably wrong—it's going to take concerted political intervention to stop burning fossil fuels, which is what we're going to have to do.

***I'm glad you brought up how much has changed in the past five years in terms of lower-carbon energy and why there may be reasons for optimism. But, to be a bit of a downer, what about things such as the rise of artificial intelligence and the associated ramp-up in energy usage for data centers and computation?***

It's definitely not my area of expertise, but all these AI companies are burning through billions of dollars, and they're not turning a profit, and it doesn't seem like these tools increase productivity that much in most domains—although they're profoundly useful in some areas, such as biotech, where it seems like you can use them to do practically a year's worth of research in an afternoon. And they all seem to wave away the fact that you basically need to build nuclear reactors to power these things, which is never going to be cheap to do. The point is that I imagine it will turn out a bit like the tech bubble of the 2000s: you'll have some genuinely productive, game-changing applications, but most of the projects will go under because you can't just keep losing billions of dollars per quarter forever while also facing ever increasing energy demands. It seems ripe for a massive adjustment.

The U.S. can barely manage its current electrical grid, much less completely rebuild it and add twice as much power. Like so many other things we do, at some point the AI boom is going to run into constraints that collide with politics, economics or physics. So I'm skeptical there. Then again, it'd be great if we gained some energy breakthrough out of necessity because that's usually when we figure stuff out. But I don't think something such as fusion power is going to happen anytime soon, even with AI as a stimulus.

***We talked earlier about deep time and the way our inability to properly comprehend and integrate it into our lives blinds us to what we're really doing to the planet. And it makes me wonder: Having immersed yourself in all this for two books now, how do you feel?***

***How has this journey changed you?***

I live in Massachusetts, where some of this geology is harder to see. But when I go out West and I'm looking at some rock face that captures tens of millions of years of history, where the environment switches from the bottom of the ocean to a lagoon to a riverbed to a desert back to the bottom of the ocean, it's humbling in the best way. It really chips away at your ego. It can be consoling even; given how out of control things feel today and how crazy you can make yourself refreshing your social media feed and keeping up with news, there's something very peaceful in contemplating time at these gigantic scales. For me, knowing there've been so many chaotic and scary chapters in Earth's history, it's consoling to know that in a million years everything's going to be fine.

Even so, deep time doesn't really have any obvious, direct relevance to your daily life. None of us get to live on geological timescales, and we can care only about the things that are in front of us. Your personal relationships and the people you love—those are the most important things. I've struggled with this, I'll admit. When I was writing the first book, my mom died, and I was grappling with losing her while I was also gaining this new, more cosmic perspective about Earth and our place in it. I never fully reconciled how one's personal experience should inform this deeper, bigger view.

So I just come back to recognizing the beauty of this world we all share. There's beauty in being part of this long pageant of life. I think of my mom, and I think of how there have been countless mothers and their children who loved each other in countless ways, great and small, throughout Earth's history. I think of how today you can see dinosaur trackways where—let's say 93,871,252 years ago, during April—a dino mother and her child danced together for a moment on a sand flat. That's really beautiful—all the more so when you think of all those moments that didn't even make it into the fossil record. It's a privilege to bear witness to that and to be a small part of this far greater story. ●

# Will We Run Out of Rare Earth Elements?

These valuable but difficult-to-extract metals are increasingly important to modern life

TEXT BY CLARA MOSKOWITZ | GRAPHIC BY STUDIO TERP

**S** **EVENTEEN ELEMENTS** of the periodic table have taken on outsize importance because of their use in smartphones, electric vehicles, medical devices, and other technologies. They're valued for their special chemistry, which gives them particular magnetic properties and other advantages. These traits come from the unique configuration of the elements' valence electrons—the outer electrons commonly used in chemical bonds. In the rare earth elements, some of the valence electrons stay close to the atomic nucleus and tend not to interact with the atoms' outside environment, and so they rarely form bonds. The result is that they have predictable, dependable chemical properties.

Humans have mined about 4.5 million metric tons of rare earth elements so far, and we know of only 90.9 million metric tons left on Earth. At today's production rates, we will run out of these materials in 60 to 100 years. Efforts are underway, however, to find more deposits of the metals, which aren't actually especially rare but are difficult to extract because they are usually found in low concentrations along with other elements.

Current mining methods are slow, energy-intensive and highly damaging to the environment. They generate acidic and radioactive waste, and they leach toxic chemicals into the ground. "We have to figure out ways to do it better and cleaner," says Justin Wilson, a chemistry professor at the University of California, Santa Barbara. He and his colleagues recently tested [a new way to extract rare earth elements](#) from recycled electronic waste. "I'm optimistic that we can collectively find solutions to these problems as long as the federal government remains committed to providing funding for this research," Wilson notes.

## HOW MUCH HAS ALREADY BEEN MINED?

Most of the rare earth elements mined so far have come from China, which leads the world in the infrastructure and expertise to extract these minerals. The major U.S. source is the Mountain Pass deposit in southern California. Given the surging demand for the elements, however, countries around the world are actively looking for new stores of them.

## HOW MUCH IS LEFT?

China, too, has the largest known global reserve of rare earth elements, followed by Brazil, India and Australia. Given the race to discover new deposits, these figures could change. Many countries that had been content to let China lead in rare earth-resource mining before the recent tech boom are increasingly recognizing the importance of local options. This has been especially true in the U.S. since President Donald Trump imposed new tariffs on imports.

## WHAT ARE THE RARE EARTH ELEMENTS?

These chemicals are mostly the lanthanides, which occupy the second-to-last row of the periodic table, along with scandium and yttrium. Their unique properties arise largely from the configuration of the electrons in a sublevel called the 4f shell. "When I took freshman chemistry, no one ever talked about these elements; they were just the ones at the bottom of the periodic table," Wilson says. Now their use in electronics "has put them in the spotlight."



Bastnaesite (shown here) is the most frequently mined rare earth ore. It contains relatively high levels of the elements lanthanum, cerium and neodymium.

H																	He
Li	Be											B	C	N	O	F	Ne
Na	Mg											Al	Si	P	S	Cl	Ar
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba																
Fr	Ra																
		La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu	
		Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr	

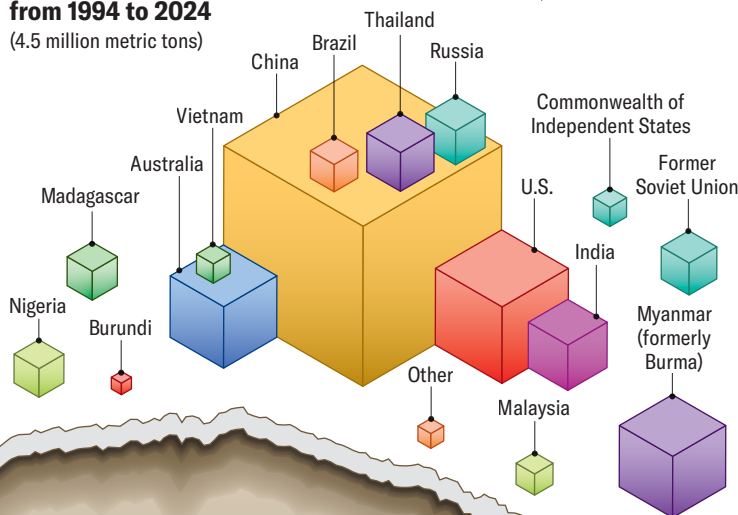
Sc • Scandium  
Y • Yttrium  
La • Lanthanum  
Ce • Cerium  
Pr • Praseodymium  
Nd • Neodymium  
Pm • Promethium  
Sm • Samarium  
Eu • Europium  
Gd • Gadolinium  
Tb • Terbium  
Dy • Dysprosium  
Ho • Holmium  
Er • Erbium  
Tm • Thulium  
Yb • Ytterbium  
Lu • Lutetium



## Total Produced from 1994 to 2024

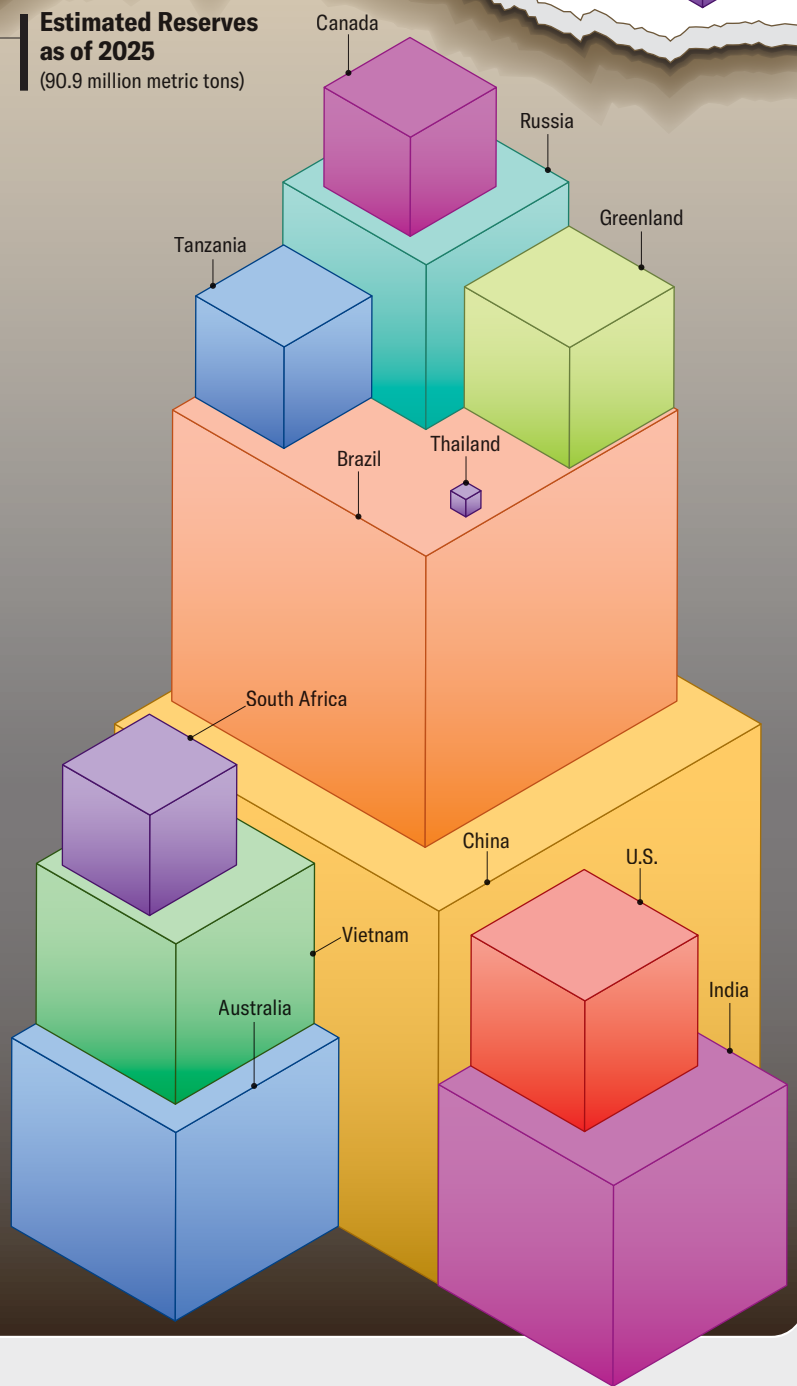
(4.5 million metric tons)

 = 50,000 metric tons



## Estimated Reserves as of 2025

(90.9 million metric tons)



## IT SEEMS LIKE THERE'S A LOT LEFT. SO WHAT IS THE PROBLEM?

Rare earth elements are actually more abundant than precious metals such as platinum and gold. The challenge, however, is finding minable sources of them; they are often present in small amounts and difficult to separate from other elements. Extracting them is a laborious, multistep process.

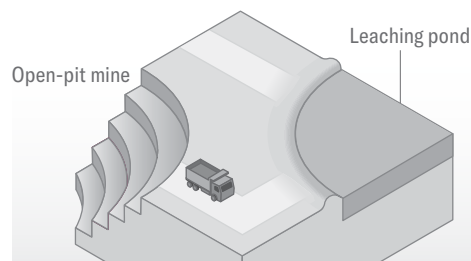
### EXTRACTION

#### Open-Pit Mining Approach

This technique involves removing ore from the ground, then transporting it to a leaching pond, where chemicals separate out the different metals.

#### ENVIRONMENTAL IMPACT

The toxic chemicals in the leaching pond can leak into groundwater and contaminate water supplies. The process also produces toxic waste.

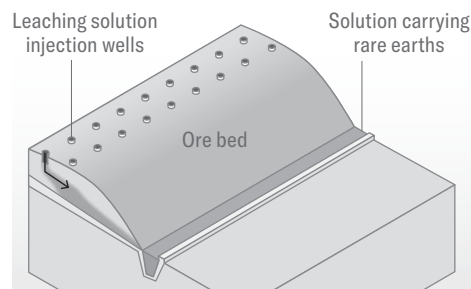


#### In Situ Leaching Approach

In this method, pipes pump chemicals directly into the ground to flush out rare earth elements.

#### ENVIRONMENTAL IMPACT

The chemicals are toxic and, as with open-pit mining, can contaminate groundwater. Both methods produce toxic dust, waste gas and radioactive waste.



### SEPARATION

After the initial process, the mining products are transported to processing facilities for a series of chemical treatments that isolate individual rare earth elements. These elements are then refined into metals and prepared for use.

#### ENVIRONMENTAL IMPACT

This process is energy- and resource-intensive. And the overall extraction sequence creates a huge amount of waste: for every ton of rare earth elements produced, thousands of metric tons of toxic by-products result.

# 50, 100 & 150 Years

## 1975 HEIMLICH MANEUVER

"The list of first-aid procedures that the medical profession encourages laypeople to undertake is short because of concern that tactics applied in ignorance may do more harm than good. Now, however, the American Medical Association has cautiously endorsed the 'Heimlich maneuver' as a first-aid procedure when someone is choking on a foreign object, described by Henry J. Heimlich, the Cincinnati surgeon who developed it. In the Heimlich maneuver, you get behind the victim and wrap your arms around their waist, put the thumb side of your fist or the heel of your palm against the victim's upper abdomen, between the navel and the bottom of the rib cage, and make a quick upward thrust. The action elevates the diaphragm, thereby compressing the lungs and forcing air up through the trachea. The air expels the foreign object. Heimlich writes that since he first described the technique he has heard of 162 people whose lives were saved."

## 1925 EXHAUSTED UNIVERSE

"What has science to say of the future? The physicist can tell us that the universe is 'running down,' for heat tends to escape by radiation from the surfaces of the stars, planets and all other bodies. Slowly, then, all things must cool down, depleted to the point of exhaustion, so that the final scene of the play shows only cold, dark bodies, frozen, rigid and lifeless, moving in

their orbits in impenetrable darkness. Most completely irreversible would appear to be the newly discovered process by which matter is turned into free energy. Thus also before the last gleams of light disappear the principal actors—the stars—have dwindled away to mere shrunken remnants of their old selves."

## TELEPHONE DIPLOMACY

"Embassies and consulates, university scholarships, lecture tours, propaganda—all have had for years as their supreme object a better understanding, a closer friendship between America and the Old World. Now comes the announcement that soon you may pick up your telephone and talk with a person in London as easily as if they were in the next street. What is more, you can do this at a cost of five dollars for three minutes.



Here is an achievement which outweighs a century of striving for international accord. When people talk directly to one another easily, cheaply and constantly about their daily affairs, it becomes more and more difficult for them to misunderstand each other. As an insurance of peace, the inauguration of the five-dollar, three-minute transatlantic telephone rate may well rank with the best treaty ever signed."

## 1875 NEW ROUTE TO SIBERIA

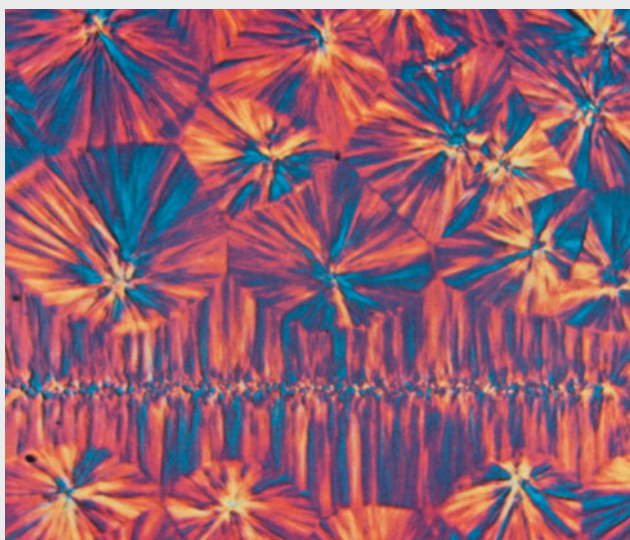
"Professor Nordenskiöld's recent journey from Norway to Siberia, by way of the Yugorsky Strait and the Sea of Kara, has caused quite a sensation in Russia. At a meeting of the Society for

the Encouragement of Commerce and Industry, Mr. Sidorov said the journey was one to be ranked in importance with the discovery of a new world, as it would in all probability lead to the establishment of a regular line of communication between northern Europe and Siberia, and the vast resources of the latter country would at last find an outlet along her great fluvial highways."

## TRAINING FLEAS

"Mr. Bertolotto, the well-known educator of the flea, is now in New York exhibiting his curious success. The insect he employs appears to be the species of flea common to dogs. The first lesson, he says, is to put the fleas in a small circular glass box, where, by jumping and knocking their heads against the glass for a day or two, the idea is finally beaten into them that it is useless to jump. During the remainder of their natural lives—about eight months—they are content to crawl.

The instructor then fastens a delicate pair of wire nippers to the middle of the flea's body; to the nippers any desired form of miniature vehicle, such as a wheelbarrow, car or wagon, is attached, and the flea trots away with the load. The professor harnesses his insect pupils to perform many curious duties, such as the operation of a fortune-telling wheel, orchestra playing or racing. The fleas are allowed to feed twice daily upon the instructor's arm."



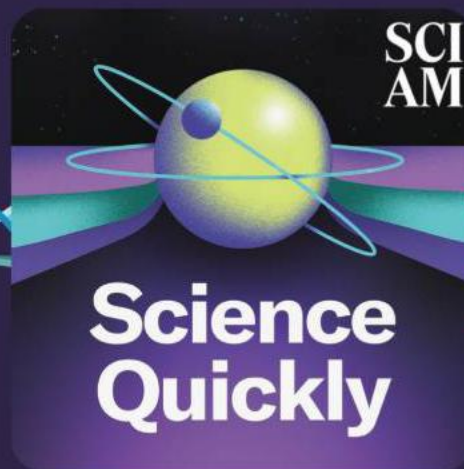
**1975, Plastic Crystal:** "Typical microstructure features observed in semicrystalline polymers can be seen in this photomicrograph of a thin film of polypropylene. The 'sunburst' structures are called spherulites; their boundaries would be circular if they did not encounter neighboring crystallites as they grow outward from a core. The photomicrograph was made by David Hamer at the Celanese Research Company."



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# POLAND GRAND TOUR

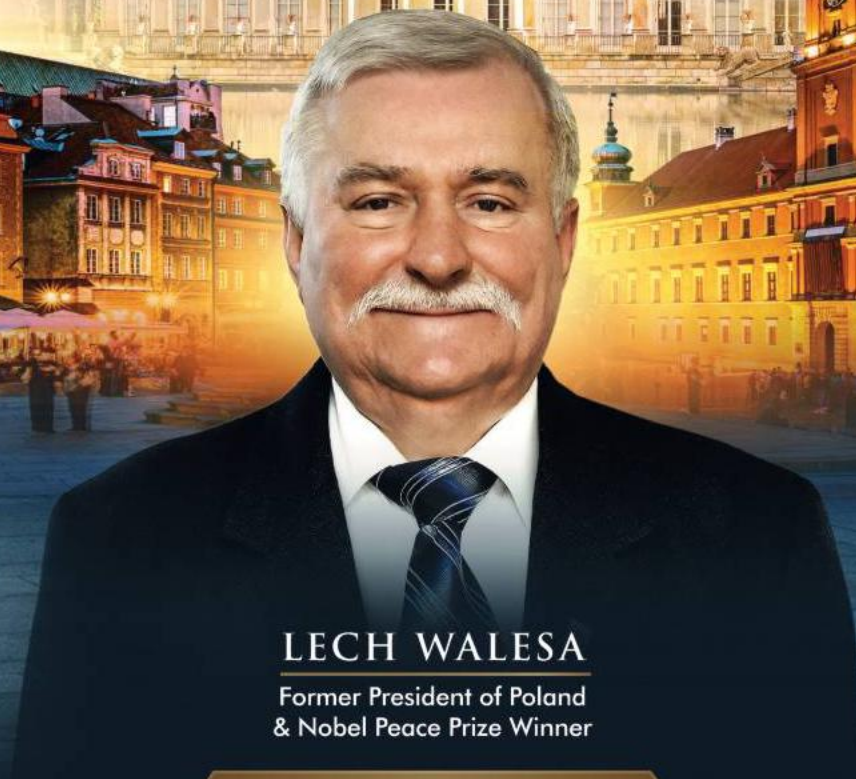
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