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Deep in the ice, warning signs

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Parasites' strange powers

The Comet Year

WHAT THE COVID-19 PANDEMIC PORTENDS P.20

ISSUE 49 Science Connected **NAUTIL.US**




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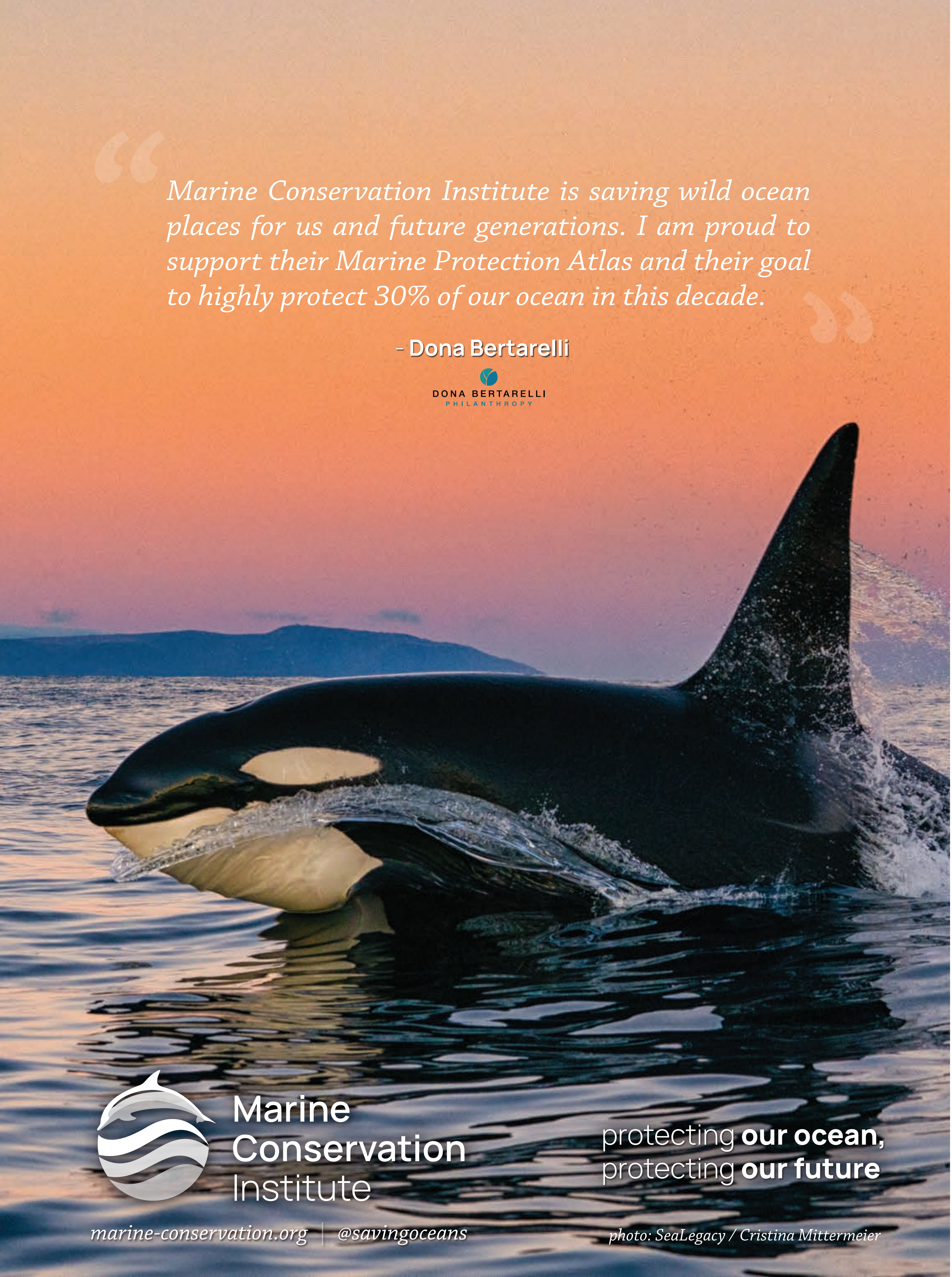
Marine Conservation Institute is saving wild ocean places for us and future generations. I am proud to support their Marine Protection Atlas and their goal to highly protect 30% of our ocean in this decade.
- Dona Bertarelli
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Truth Be Told

BY KEVIN BERGER

THIS MORNING, AS I WRITE, the Taurus sun connects with Saturn, and later in the afternoon, Luna aligns with Mercury retrograde.

Because I'm a Libra, according to the chief astrologer on Astrofame.com, I should redecorate my home. That's because I could be feeling a little closed in, and the best way to escape that feeling is to recreate my surroundings. Today is also "a day to reach out and touch someone so pick up the phone and dial it."

I assume the chief astrologer is channeling her advice from the year 2023, but apparently the cosmic space in which she operates is 1973, where people have rotary phones.

Meanwhile, on planet Earth, Clayton Dalton is an emergency room physician. During the summer of 2020, when COVID-19 first got its teeth into the populace, Dalton did his job in hallways of chaos and death, performing triage, like a Civil War surgeon.

Away from the hospital, Dalton encountered story after story of the pandemic being a hoax. Had America slipped into the Dark Ages? People may as well have attributed the tragedy to the comet NEOWISE that streaked across the 2020 sky. In this issue's cover story, "The Comet Year," Dalton spells out his pandemic experiences and the peril of stories that persist after science has laid them to rest.

Psychologists can explain why people believe the alignment of Luna with Mercury retrograde is a good time to redecorate your house. And historians, like those who inform "The Comet Year," can delight us with illuminations of times when comets foretold the death of kings.

Shakespeare wrote, "When beggars die there are no comets seen; The heavens themselves blaze forth the death of princes." That's very poetic and all (actually, it's kind of mean). But also poetic is the scientific description of a comet.

"Comets are skyscraper-sized leftovers from the construction of the planets," says Sean Raymond, an astrophysicist at the Bordeaux Astrophysical Laboratory in France. "They are a mixture of rocks, dust, and ices. Comets spend most of their time in the cold outer reaches of the solar system, and only occasionally venture closer to the sun. Their brightness in our sky is a result of evaporation of ices as they heat up. The gases surrounding a comet's solid nucleus puff up to make it appear 100,000 times larger than the nucleus itself, which is analogous to a grain of sand puffing up to the size of a baseball field. Comets often have tails of gas, blown by the solar wind."

Isn't that, well, Shakespearean? Not incidentally, in this issue you will read "The Dwarf Planet on Our Doorstep" by Raymond. His article is about Ceres, the biggest orbital body between Mars and Jupiter. Ceres, Raymond writes, has "long been a spark for scientific imagination." He beautifully explains why.

True stories about the universe and its impact on us are so much more fascinating than those drummed up in New Age circles. You can trust me on that because I'm a balanced person. As I said, I'm a Libra.


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Preludes

NAGEL PHOTOGRAPHY / SHUTTERSTOCK

ZOOLOGY

What Makes Us Bold

AMONG THE FORESTS of Yellowstone National Park, some wolf packs share their territory with cougars. Generally, the two species leave each other alone, although wolves may occasionally run a cougar up a tree and steal its kill—or poke around its feces, which the felines use to mark their territory.

Whether from this scat or the water contaminated with it, some wolves manage to pick up a strange feline parasite. This parasite, *Toxoplasma gondii*, doesn't make the wolves ill, but it does change their behavior, making many of them bolder and more inclined to take risks—for better or for worse.

Scientists who have been studying the Yellowstone wolves found that those infected by *T. gondii* are more likely to disperse from their pack or start a pack of their own. "Dispersal is one of the most dangerous things, because survival actually decreases for dispersing wolves, so not very many wolves actually survive the dispersal process," says Connor Meyer, a researcher at the University of Montana, and one of the authors of the study, published in *Nature*. But if that wolf succeeds and becomes a pack leader, it will father more pups, achieving a greater reproductive success—a reward that may be worth the risk.

T. gondii has long been known to alter the behavior of animals it infects—to serve its own elaborate life cycle and reproductive success. It sexually procreates inside felines' intestines, shedding out oocytes—tiny but hardy thick-walled egg-like formations—in the cats' feces. Water or melting snow scatter the oocytes around the soil, grass, streams, and rivers, where they are unwittingly consumed by a range of animals, including rodents that cats prey on. Once inside this intermediate host, the parasite forms cysts in its tissues. But to complete its life cycle this hitchhiker has to make a final, rather improbable journey. *T. gondii* needs to return to the feline gut. One way to increase its odds is to make the infected rodents too fearless for their own good, forcing them to put themselves at a higher risk of becoming a cat's breakfast.

Although the cat-and-mouse paradigm is most extensively studied, the parasite works the same with larger animals, for example lions and wildebeest, Meyer says. But the feline's prey isn't the only species that may pick up the parasite from the environment—any animal can, to which the wolves study attests. And the parasite seems to be agnostic—it turns any intermediate host into a bold risk-taker.

That includes humans.

IN A 2018 STUDY, scientists found that people infected with *T. gondii* are more likely to pursue business and entrepreneurship as their career choices. The team tested 1,495 undergraduate students—studying engineering, business, and arts and sciences at a large American university—for *T. gondii* using a saliva-based test and found that 22 percent carried the parasite. Those with entrepreneurship aspirations were almost twice as likely to be infected, says one of the study authors, Stefanie K. Johnson, an associate professor of organizational leadership and information analytics at the University of Colorado, Boulder.

In a human realm, pursuing business and entrepreneurship takes guts and ability to tolerate risks. Starting a company is essentially equivalent to starting a pack. It requires striking out on one's own with a greater risk of failure, rather than being in the protective folds of someone else's company.

The team found that was true on a global level also. When they combed through the databases of *T. gondii* infection from the past 25 years in different countries and synthesized the data with the Global Entrepreneurship Monitor research project, they found that "infection prevalence was a consistent, positive predictor of entrepreneurial activity and intentions at the national scale."

It turns any intermediate host into a bold risk-taker.

It may feel creepy that the tiny cysts lodged in one's tissues may affect one's career, or other major life decisions, but other microorganisms affect our moods or actions too. "You see really similar effects for the impact of gut bacteria on human behavior, even things like depression," Johnson says.

Global rates of *T. gondii* infection are about the same Johnson and her colleagues found in their study: 1 in 4 people. "Humans usually get *T. gondii* from eating undercooked meat or from owning cats," says Johnson. People can also pick it up outdoors. "If you're playing outside in the sandbox, you always find cat poop in there, so that could transmit the parasite." As can gardening. The infection rates, however, vary significantly by countries. Only 9 percent of Norwegians are infected, while Brazil hits 60 percent. Notably, nations with higher infection rates had fewer entrepreneurs who cited a "fear of failure" as a factor deterring them from new business possibilities, the study found.

This risk-taking behavior may or may not make one a successful businessperson. "We don't know to what extent they're making better decisions, or are they actually in fact making worse decisions," Johnson says. So you may hit a jackpot or a suffer a financial ruin. And, of course, that's similar to what happens to a wolf straying from the pack.

Generally, we tend to think that parasitic infections are detrimental to the host. But in a way, *T. gondii* acts as an agent of evolution, which may bring financial or reproductive success to its host or cause its demise and death. So is it good or bad for an organism to carry, whether a human or a wolf? There's no simple answer to this question, Meyer says. "It just shows us that things are a lot more complicated than we ever gave them credit for."

—*Lina Zeldovich*

SPACE WIND / SHUTTERSTOCK

TECHNOLOGY

Even Machine Brains Need Sleep

WE ALL MIGHT WISH for minds as retentive as a hard drive. Memory file created. Saved. Ready for access at any time. But don't yet go wishing for the memory performance of AI.

Artificial neural networks are prone to a troublesome glitch known, evocatively, as catastrophic forgetting. These seemingly tireless networks can keep learning tasks day and night. But sometimes, once a new task is learned, any recollection of an old task vanishes. It's as if you learned to play tennis decently well, but after being taught to play water polo, you suddenly had no recollection of how to swing a racket.

This apparent network overload put an idea in the head of Maxim Bazhenov, a professor who studies computational neuroscience and sleep at the University of California San Diego School of Medicine. Perhaps the spiking neural networks he was working with simply needed a rest.

In natural sleep, he had seen that the same basic brain processes occur in humans and in honeybees, working over information accumulated during waking moments. "That machinery presumably was doing something useful" in order to be conserved across evolutionary paths, he says. So, he thought, why not try a similar state for the machines.

The idea was to simply provide the artificial neural networks with a break from external stimuli, to instruct them to go into a sort of rest state. Like the dozing human brain, the networks were still active, but instead of taking in new information, they were mulling the old stuff, consolidating, surfacing patterns.

And it worked. In a pair of papers in late 2022, Bazhenov and his colleagues showed that providing the neural networks periods in a sleep-like state mitigated the hazard of catastrophic forgetting. It turns out that machine brains need rest, too.

The cognitive psychologist and computer scientist Geoffrey Hinton had proposed the idea of allowing early neural networks a nap in the 1990s. But the newer work applies the concept to radically more complex networks—in this case, what are called spiking neural networks, which mimic the pattern of neurons firing in our brains. The new work also demonstrates the use of restorative rest not only in preventing catastrophic forgetting, but also in improving generalization, both of which have implications for the true utility of these networks, from cyber security to self-driving cars (which need to remember—and sagely apply—the rules of the road, and those of Asimov).

> The networks didn't seem to bear any resemblance to what was actually happening in a human brain.

Sleep, of course, is also essential for our own memory and learning. The downtime seems to strengthen new task-related connections forged in the brain during wakefulness and help transfer them to areas of the brain for longer-term storage. Researchers have known for decades that, while we might not suffer a full episode of catastrophic forgetting, lack of sleep interferes with our ability to efficiently learn new skills and retain memories. Newer research even suggests that we don't need to fully power down to improve our procedural memory. Simply quietly resting while not pursuing new inputs—or as the researchers put it, engaging in "offline memory consolidation"—seems to work for human brains, too.

Robert Stickgold raises caution here, though. Stickgold is a professor of psychiatry at Harvard Medical School's Brain Science Initiative, where he studies sleep and cognition. Sure, it's handy to say we're letting a network "sleep." But it's wise to not take the vocabulary too far. For our sake—or for the sake of advancing network research.

Stickgold recalls a conversation he had decades ago with a researcher at MIT who was building early artificial intelligence algorithms to solve complex business problems. Stickgold commented that the networks didn't seem to bear any resemblance to what was actually happening in a human brain. To which his engineer interlocutor replied: "Why would you want them to?"

—Katherine Harmon Courage

TECHNOLOGY

Does GPT-4 Really Understand What We're Saying?

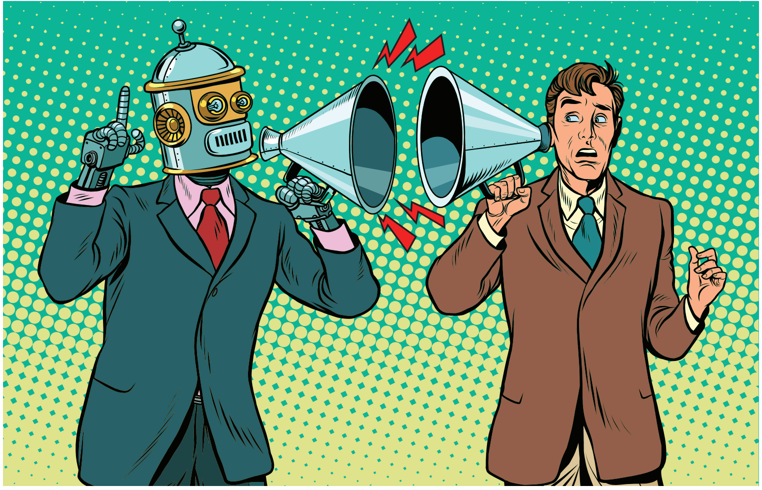
One question for David Krakauer, president of the Sante Fe Institute for complexity science, where he explores the evolution of intelligence and stupidity on Earth

Does GPT-4 really understand what we're saying?

"Yes and no," is the answer to that. In my new paper with computer scientist Melanie Mitchell, we surveyed AI researchers on the idea that large pretrained language models, like GPT-4, can understand language. When they say these models understand us, or that they don't, it's not clear that we're agreeing on our concept of understanding. When Claude Shannon was inventing information theory, he made it very clear that the part of information he was interested in was *communication*, not meaning: You can have two messages that are equally informative, with one having loads of meaning and the other none.

There's a kind of understanding which is just coordination. For example, I could say, "Can you pass me the spoon?" And you'd say, "Here it is." And I say, "Well, you understood me!" Because we coordinated. That's not the same as generative or constructive understanding, where I say to you, "I'm going to teach you some calculus, and you get to use that knowledge on a problem that I haven't yet told you about." That goes beyond coordination. It's like: "Here's the math—now apply it in your life."

So understanding, like information, has several meanings—more or less demanding. Do these language models coordinate on a shared meaning with



Algorithms have to survive by convincing us they're interesting to read.

us? Yes. Do they understand in this constructive sense? Probably not.

I'd make a big distinction between super-functional and intelligent. Let me use the following analogy: No one would say that a car runs faster than a human. They would say that a car can *move* faster on an even surface than a human. So it can complete a function more effectively, but it's not running faster than a human. One of the questions here is whether we're using "intelligence" in a consistent fashion. I don't think we are.

The other dimension to this for me is what I call the standard model of science, which is parsimony. Versus the machine learning model of science, which is megamony. Parsimony says, "I'm going to try and explain as much as I can, with as few resources as possible." That means few parameters, or a small number of laws or initial conditions. The root of parsimony, by the way, is frugal action. And these language models are exactly the opposite of that. They're massive action. It's trained on a huge but very restricted domain: text. Most human understanding maps textual experience onto somatosensory experience. So if I say to you, "That's painful," you don't map that onto another word. You map that onto a sensation. Most human insight is conveying, through tags or words, experience that has an emotional or physical aspect. And GPT-4 is just finding correlations across words.

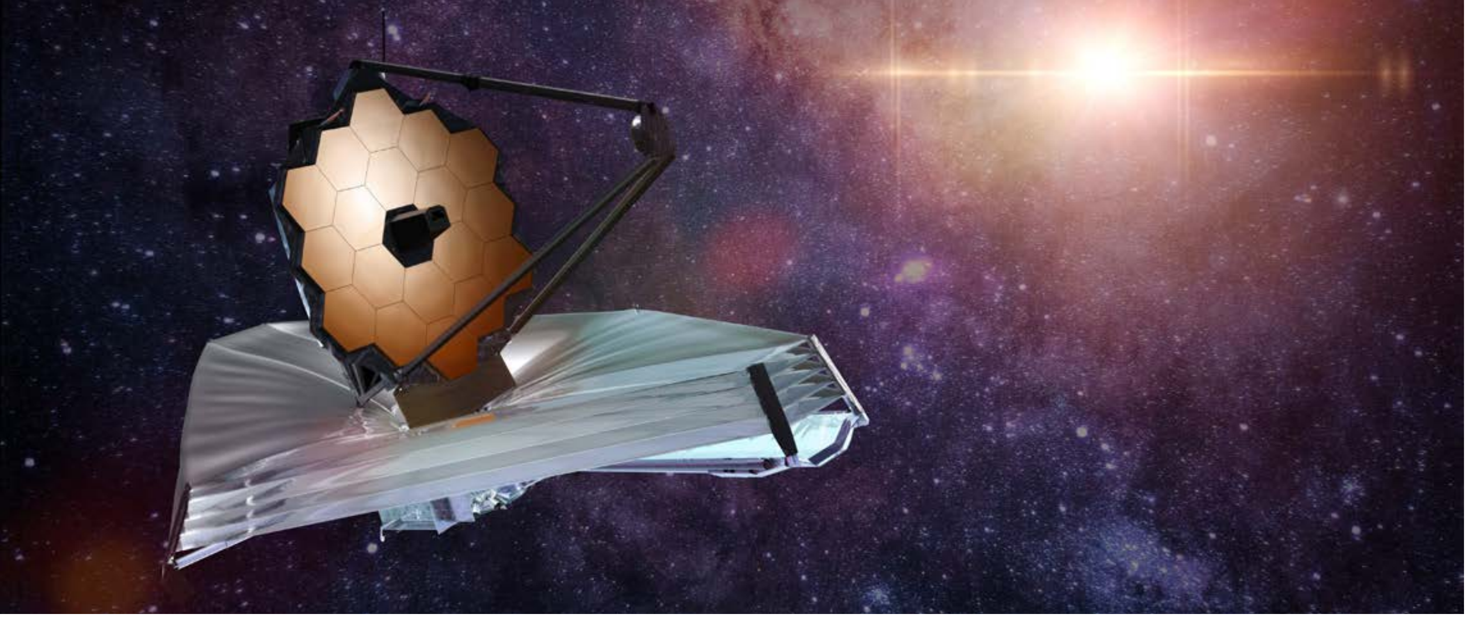
Another dimension of difference, which is very important, is that our cognitive apparatus evolved. The environment that created the attributes that we describe as intelligence and understanding is very rich. Now look at these algorithms. What is their selective context? Us. We are cultural selection on algorithms. They don't have to survive in the world. They have to survive by convincing us they're interesting to read. That evolutionary process that's taken place in the training of the algorithm is so radically different from what it means to survive in the physical world—and that's another clue. In order to reach even remotely plausible levels of human competence, the training set that these algorithms have been presented with exceed what any human being in a nearly-infinite number of lifetimes would ever experience. So we know we can't be doing the same thing. It's just not possible. These things are Babel algorithms. They live in the land of Borges' Library of Babel. They have the complete experience. They have access to all knowledge in the library. We do not.

The other fact to point out, apart from all the stuff that we adduce in the paper—brittle errors, mistakes the language models make that are telltale signs that we would never make—is humans do apply a mechanical reasoning to things. If I said to you, "There's a trolley rolling down the hill, and there's a cat in its path. What happens next?" You're not just trying to estimate the next word, like GPT-4. You're forming in your mind's eye a little mental, physical model of that reality. And you're going to turn around to me and say, "Well, is it a smooth surface? Is there lots of friction? What kind of wheels does it have?" Your language sits on top of a physics model. That's how you reason through that narrative. This thing does not. It doesn't have a physics model.

Now, the interesting point is perhaps in all of that richness of data, if we were ingenious enough, we could find a physics model. It's tacit, implicit in its vast language database, but it doesn't access it. You could say to it, "What physics model is behind the decision you're now making?" And it would now confabulate. So the narrative that says we've rediscovered human reasoning is so misguided in so many ways. Just demonstrably false. That can't be the way to go.

—Brian Gallagher

STUDIOSTOKS / SHUTTERSTOCK



ASTRONOMY

What the Webb Telescope Really Showed Us About the Cosmos' Beginning

ON MY 10TH BIRTHDAY, I convinced a flock of cousins to travel to the end of the universe with me. I had my reasons. Cosmology was a family affair. My father, Solomon Zeldovich, was working on detecting gravitational waves long before the proper detecting equipment even existed. His uncle, Russian-Jewish scientist Yakov Zeldovich, was one of the leading physicists and cosmologists who contributed to the Big Bang theory. Growing up, I learned to stay away from black holes before I learned to cross the street. Other kids' bedtime stories featured gnomes and fairies, but mine revolved around collapsing neutron stars, supernovas, and fusion reactions inside our sun. "Once upon a time almost 14 billion years ago there was a big boom that created our universe," my father had told me. "And ever since this Big Bang, the universe keeps expanding, so fast that even the rockets we sent to the moon can't catch up with it. But if you got to that constantly expanding end, you'd see the universe as it was when it was first created." That sounded like going back in time—I just *had* to get to the end of the universe.

My cousins were game. We boarded an overturned play table placed on my bed, huddled together between its four legs sticking up in the air and jumped up and down in unison to make the journey appropriately bumpy. Using the table's loose leg as a throttle, we took off, propelled by our screams. Halfway into our journey, my father poked his head in and yelled at us to stop breaking the table. "We can't stop," I yelled back. "We're at the end of the universe 14 billion years ago, but the black hole is sucking us in!" He growled something about having to fix the damn leg later and withdrew.

Little did I know that seeing the end of the universe would become possible a few decades later, thanks to the massive telescopes NASA had been launching—first the Hubble and then the more recent James Webb. The telescopes look for the light coming back from distant stars and galaxies, and because the light takes time to arrive to us, the telescopes are essentially staring back in time, explains Erica Nelson, an astrophysicist at the University of Colorado, Boulder. "If you're looking at something that's really far away, you're looking at light that's been traveling for a long time, so you're seeing that object as it was in the past," says Nelson, who studies the images that the Webb and Hubble gather. "So the telescopes act as time machines." Nelson realized that fact when, as a 10-year-old, she wrote a report about Hubble. She was a more practical child than me—she decided to study cosmology rather than inventing games about it.

DOTTED YETI / SHUTTERSTOCK

Webb, in fact, is a particularly potent "time machine." It has the ability to see really far back in time, to when the galaxies were young, because it was built to most optimally detect the light of the infrared spectrum. "The light from the stars and galaxies located far away from us reaches us not as the visible light, but as the infrared," explains Nancy Levenson, director of the Space Telescope Science Institute in Maryland, which operates the telescopes for NASA. "In astronomy we call this phenomenon redshifting."

Webb, in fact, is a particularly potent "time machine."

The visible light has a shorter wavelength while the infrared has a longer one. As the light travels through our still-expanding universe, its wavelength gets stretched out, shifting from the shorter, visible range to the longer infrared. A chewing gum that kids pull apart with their fingers serves as a good visual metaphor. The gum stretches out and so does the light—kind of.

The Webb—built with 18 mirror segments, gold-plated to maximally reflect and gather the infrared light—might be able to see all the way to the beginning of times, to the edge of the universe I had once tried to reach on my overturned play table. Only months after its launch, the Webb not only gathered striking infrared images, but caused a few snags in the fabric of the Big Bang theory, questioning some of the facts we thought were well established, such as the timelines of when certain things happened.

The snags started in summer of 2022, when Nelson peered into the first images that arrived from the Webb—and saw some striking red spots. The spots never appeared on the Hubble images because they were clusters of infrared light, which Hubble isn't as good at detecting. "The first thing I noticed was that these bright red objects were present in the James Webb image, but not in the Hubble," she says. She looped her colleagues in. "We knew immediately that it was a big deal."

After digging deeper, the team deemed the glowing spots to be six huge, previously unknown galaxies from a very early cosmic time, about 500 to 700 million years after the Big Bang occurred. But according to the current Big Bang theory, which includes estimates of how long it takes to form objects of a certain mass, this isn't enough time to create six massive galaxies with millions of stars. "The reason why it flies in the face of our current understanding of cosmology is because our cosmological theory predicts that it should take much longer for galaxies of this mass to be able to form," Nelson says. "We think that it should take about 2 billion years, at least, to form these large galaxies with so many stars." Her team published their groundbreaking discoveries in *Nature*.

Does this mean that the Webb just threw a wrench into the Big Bang theory? It remains to be seen, scientists say. A new study published in *Nature Astronomy* explores the idea further. For starters, they must confirm that the six glowing objects are indeed galaxies—something they will keep working on. Unlike certain scientific fields where things can be physically touched and measured, astronomy is driven by theoretical models of how far away or how big objects are, and how they function. A more detailed analysis of more pictures, and more calculations, may reveal that the galaxies are smaller or closer, and thus aren't as old. But if their observations are correct, the current cosmological models may indeed need some tweaking. Perhaps early on the galaxies could form super-fast because the universe was denser before it expanded. Or perhaps we don't fully understand the physics behind the formations of stars.

Whichever way it goes, astronomers are enthused. "They are definitely seeing something interesting," Levenson says of her colleagues. "So my reaction is that of cautious excitement." But that's the point, she notes. The reason we sent the huge, gold-plated, $10 billion science machine that took 30 years to build into the cosmic void is to learn what we don't know yet. "We're going to find out that we were wrong about a number of things," Levenson says. "But that's not bad. That's exciting!"

I'm excited too. To my father's dismay, I did not follow him into the vaunted field of physics. But I've been watching the developments from the sidelines and writing stories. I can't wait to learn what Webb will see next in that faraway enigmatic place I once traveled to on an overturned play table with a crew of cousins in tow.

—Lina Zeldovich

Aerial Acrobats

THE *EZO MOMONGA*, a subspecies of Siberian flying squirrel endemic to the island of Hokkaido in Japan, is often described as a "passive glider." But Tokyo-based photographer and naturalist Tony Wu feels that's a bit of a misnomer, even if technically correct. Just "no," he says. "They are tiny F-15 jets driven by pilots on amphetamines."

Known to the scientific community as *Pteromys volans orii*, the *ezo momonga* can execute aerobatics that seem astonishing for an animal without true wings, including lightning-fast twists, turns, flips, and steep dives. The show occurs mainly during the spring breeding season, when males battle each other for females, and females sometimes sneak away for liaisons with partners other than their mates.

Ezo momonga are tiny, no more than 4.2 ounces in weight—less than a typical letter sent through the post—and 7 inches long, excluding tail, with large, liquid black eyes that have earned the subspecies comparisons to Pokemon. The subspecies likely split from its Siberian flying squirrel cousins, *Pteromys volans*, during an interglacial period between 200,000 and 400,000 years ago, when seas fed by melting glaciers rose over the land bridges connecting them to the mainland.

Pteromys volans ranges from Eastern Europe throughout Asia, and the International Union for Conservation of Nature considers it a species of least concern. Still, it's thought to be generally declining, and is extinct in Lithuania and possibly Belarus. The squirrels are reluctant to cross open areas, perhaps due to vulnerability to predators and wind, and therefore need unfragmented forests to thrive. The Japan subspecies is common, but it still faces threats from logging and development, just as its relatives do in most places where they coexist with people.

Photograph by Tony Wu; story by Sarah Gilman.

This story originally appeared in bioGraphic, *an independent magazine about nature and regeneration powered by the California Academy of Sciences.*

The Comet Year

What the COVID-19 pandemic portends

BY CLAYTON DALTON

ONE EVENING during the first pandemic summer, I stepped outside to see if I could spy the comet. C/2020 F3, a celestial crag of ice known as NEOWISE, was the first comet clearly visible to the naked eye since Hale-Bopp in 1997. I found it below Ursa Major. Its plume—a massive spray of indigo gas, dust, and red sodium—was as magnificent as a peacock's feather. Chinese astronomers, in the first recorded observation of a comet in 613 B.C., called it a "broom star." The Greeks called them *komētēs*, "long-haired" stars.

Not long before, my wife had been reading *Middlemarch* and shared an arresting line with me: "Things will grow and ripen as if it were a comet year, and the public temper will soon get to a cometary heat." I had never heard of a comet year, but it seemed we had found ourselves in one. It certainly felt like the temper of things was heating up, as protests for racial justice took place across the country, the political gulf grew ever wider, and coronavirus cases surged in wave after wave.

Fault lines that fragmented the country are quieter now—but they're still here.

In Boston, where I was then working as an emergency physician, we were inundated with critically ill COVID-19 patients. On some shifts I would walk from one room to another, intubating people. For those who didn't make it, the last thing they saw was me, standing over them in a yellow gown and green respirator, the blade of the laryngoscope that I would use to intubate them in my hand. When paramedics brought us patients with COVID symptoms, they would sometimes throw a sheet over their heads as they wheeled them in, to keep the virus down as if it were dust. We didn't know if we would run out of personal protective equipment, or how many would die. We didn't know anything.

It was fitting that a comet should have appeared in the midst of that crisis year. The arrival of a comet has often been seen as a sign of what Shakespeare called a "change of times and states." One appeared just after the assassination of Julius Caesar in 44 B.C. The comet of 1066, which appears in the Bayeux tapestry, was believed to have prefigured the death of King Harold and the Norman conquest of England. Charles V, ruler of the Holy Roman Empire, was spooked enough by the sight of a comet in 1556 to abdicate his throne. "By this dread sign my fates do summon me!" he said, before retiring to a monastery in Spain.

In colonial America, Increase Mather railed against the comet of 1680, calling it "heaven's alarm for the world." Tolstoy recalled "the enormous and brilliant comet" of 1811 in *War and Peace*, "which was said to portend all kinds of woes and the end of the world." Many believed that Tolstoy's comet foretold Napoleon's defeat in Russia the following year. *Disaster*, after all, means ill-starred. As late as 1874, *The New York Times* reported that comets had been blamed for foul weather at Saratoga, fogs off Newfoundland, an epidemic among the cats of Westphalia, and "marvelous flights of wild pigeons in our own country."

Of course, comets have nothing to do with any of these things. Psychologists have explained that the impulse to ascribe significance to the appearance of a comet derives from a deep human need for control. Projecting meaning upon the stars is a way of asserting a sense of autonomy over an enigmatic world, and of grappling with our own discomfort with the unknown. A story is always a comfort when something unexpected happens.

IN THE SUMMER OF 2020, no one was pointing to the sky to explain the chaos. But just as comets elicited wild stories to make sense of changing times and states, so too did the pandemic. While many heeded public health directives and tried to ground themselves in science, others turned toward conspiracy theories. Radically divergent stories emerged around every aspect of the pandemic, from lockdowns and vaccine mandates to the virus and vaccines themselves. But the most memorable and visible symbol of this divide, to me, were masks.

At the height of the pandemic, masks were everywhere. They tumbled down sidewalks like leaves and swung from rearview mirrors in cars. I saw them littering the ground at remote trailheads and looped from a branch like a lost mitten. And perhaps no other facet of the pandemic, other than vaccination, generated as much argument and vitriol as whether we should wear a mask. The competing storylines that emerged around masks embodied the way that the virus fractured our collective reality and frustrated our attempts to control it.

When the pandemic began, nearly everyone in Massachusetts wore a mask. That September my wife and I moved to Colorado, and masks dwindled as we drove westward. By Rolla, Missouri, not a single person wore one as I paid for gas. After crossing maskless Arkansas, I was surprised to find a gas station in Texas full of them. The attendant rolled her eyes and told me that the governor had just announced a mandate. She pulled her mask down, as if to let me in on something. “Everyone knows they don’t work,” she said, leaning across the counter toward me.

The division intensified as the pandemic wore on. In November 2020 my wife and I pulled into another gas station, this time in eastern California, on an isolated strip of I-40 punctuated by towns with names like Siberia and Needles. A woman approached me as I pumped gas, and asked if I would fill up her tank, too. She did not wear a mask, despite a statewide mandate in effect.

“Did you lose your wallet?” I asked.

“No, it’s worse than that,” she said.

I waited for her to elaborate as the pump chugged beside us.

“I can’t work because of what that man on the internet says.”

The pump clicked off.

“What do you mean?” I said. “What man?”

But she shook her head and wouldn’t say more.

I offered to put $10 in her tank and set my pump nozzle back in its cradle. As I followed her over to her car, I heard her mutter something under her breath. It sounded like she had called me a son-of-a-bitch. I confronted her about it.

“Oh, goodness no!” she gushed, flashing a smile. “I would never say something like that.”

“Why aren’t you wearing a mask?” I asked. “You’re putting everyone around you at risk, including me.”

“Wearing one is a risk to *me*,” she spat back.

I wanted to tell her that whatever she had heard or read was wrong. That I had seen people die from COVID-19, and that masks were safe and effective. I wanted to tell her that I was counting on her to protect herself and others by following public health guidelines, and that the virus was awful and real. I wanted to tell her that the hospitals were almost full, and that the worst was yet to come. But the gulf that yawned between us felt insurmountable.

“Verifiable knowledge makes its way slowly, and only under cultivation,” Wallace Stegner wrote in 1953, “but fable has burrs and feet and claws and wings and an indestructible sheath like weed-seed, and can be carried almost anywhere and take root without the benefit of soil or water.”

I wanted to start pulling up weeds, there in the eastern California desert, but I didn’t. I was tired, and we still had a long way to go.

“I’m sorry,” I said. “I don’t think I can buy you gas after all.” I set her nozzle back in its cradle and stepped between the pump islands toward my car.

“You know what,” she yelled at me as I went. “I did call you a son-of-a-bitch!”

IN THE DEEP PAST, comets themselves were invoked to explain outbreaks of infectious disease. “Witchcraft, demons, gods, comets, earthquakes were the first unproved theories” of disease, according to a modern team of medical historians.[1] The Roman poet and astrologer Marcus Manilius wrote in the first century A.D. that “death comes with those celestial torches,” after a plague ravaged Athens. But by the fifth century B.C., Hippocrates began to articulate the first down-to-earth theory of infectious disease. He proposed that poisonous vapors called miasma were responsible. The theory was wrong, but the idea was pivotal—the idea that environmental factors were involved in disease allowed for the possibility of rational intervention.

The miasma theory of disease remained preeminent for centuries (it influenced sanitation projects in London as late as the 19th century), but astute observers noted that person-to-person transmission seemed to occur, something miasma couldn’t explain. Aretaeus of Cappadocia, an ancient Greek physician, noted correctly that leprosy could be transmitted through the

breath. In 1362, amidst an outbreak of plague, the Moorish polymath Ibn al-Khatib wrote that the existence of contagion was proven by "transmission by garments, vessels, earrings; by the spread of it by persons from one house, [or] by infection of a healthy seaport by an arrival from an infected land."

These early writings contained kernels of truth, but it would be another 500 years before Louis Pasteur advanced the idea that microorganisms were the cause of many common diseases. Pasteur's work precipitated a flood of new discoveries. By 1890, the bacteria that caused tuberculosis, cholera, and anthrax had all been identified. The German scientist Carl Flügge demonstrated the transmission of bacteria through the breath. Meanwhile, Russian microbiologist Dmitri Ivanowski uncovered a new kind of infectious agent he called viruses, from the Latin, meaning venom.

After 2,500 years of careful observation, enough understanding had been cultivated to interfere with nature intelligently. Flügge began collaborating with Jan Mikulicz-Radeki, a surgeon working to improve sterilization. Flügge's experiments suggested that speech could transmit bacteria into a surgical wound, and he suggested that Mikulicz-Radeki devise a covering for his mouth. Mikulicz-Radeki fashioned "a piece of gauze tied by two strings to the cap, and sweeping across the face so as to cover the nose and mouth and beard." He called it a *mundbinde*, or mouth-tie. It was the first surgical face mask. By 1919 they had become standard operating room attire.

In 1904, the American physician Alice Hamilton applied Flügge's techniques to scarlet fever, a disease caused by streptococcal infection of the throat. Hamilton confirmed that infected patients could spread streptococci by coughing, or even just by breathing. She suggested that a gauze mask could be worn by patients with scarlet fever to protect other patients and staff. Hamilton's experiments led her to a vital question. It was known that healthy people were sometimes colonized with strep. Could they also spread the bacteria, in the absence of symptoms? "Apparently the idea is a new one," Hamilton noted. She set up a series of glass plates and had 46 colonized nurses and physicians cough over them. All but 10 yielded positive cultures. Hamilton had demonstrated the possibility of asymptomatic spread.

"You know what," she yelled at me. "I did call you a son-of-a-bitch!"

Not everyone accepted the theory of airborne transmission, or the new measures to curtail it. In the 19th century, Austrian surgeon Alexander Fraenkel lambasted the "whole surgical costume with a bonnet, mouth mask, and veil," and believed that the "new fashion of the surgeon in gloves" was predicated on an "apparatus of pseudoscience." In 1910, public health researcher Charles Chapin wrote that "there is no evidence that [airborne transmission] is an appreciable factor in the maintenance of most of our common contagious diseases." He recommended "discarding it as a working hypothesis."

Mikulicz and Hamilton focused on the use of masks to protect others from the infectious plume of a cough or sneeze. George Weaver, a colleague of Hamilton's, "turned the perspective around," according to Don Nakayama, a surgeon and medical historian. "He reasoned that masks might protect nurses and doctors from infectious diseases harbored by their patients."

In 1916, Weaver implemented mandatory masking for nurses caring for patients with meningitis, scarlet fever, and diphtheria. Such nurses often contracted these illnesses, but by January 1918, infections among nurses had dropped to zero. Just weeks after Weaver published his results a virulent strain of influenza, whose name originally invoked the influence of malignant stars, surfaced at a military post in Kansas. It became known as the Spanish Flu and infected a third of the world's population, killing tens of millions. But for the first time, people could do something to protect themselves. They could wear a mask.

DONALD TRUMP, at a town hall before the 2020 election, remarked that "with the masks, you know, you have two stories." The implication, it seemed, was that scientists simply told their own stories, and that beliefs

Science is in fact a story that we create about the world—one with strict rules.

opposing the use of masks were legitimate alternatives. Science is in fact a story that we create about the world, albeit one with strict rules. But the alternative stories that arose around masks, like those that were told about lockdowns or vaccines, became increasingly unmoored from reality as the pandemic progressed.

Russell Blaylock, a retired neurosurgeon, asserted in May of 2020 that masks "can reduce blood oxygenation as much as 20 percent, which can lead to loss of consciousness" or even "serious life-threatening complications." (A 2021 study found no effect of masks on oxygen or carbon dioxide levels.[2]) He claimed that masks could somehow turbocharge a COVID infection, making the wearer even sicker. Judy Mikovits, a former research scientist who has promoted a variety of discredited ideas, claimed that "wearing the mask literally activates your own virus. You're getting sick from your own reactivated coronavirus expressions."

That spring, a member of our extended family, who was a tenured professor at a major university, began promoting conspiracy theories on a family email thread. He dismissed COVID as harmless and attacked public health measures, like mask mandates or lockdowns, as a destructive overreaction. When I told him I had seen people die from COVID, he said that infection with the coronavirus was a "marker" for other diseases, like diabetes, which was what was killing people.

Other claims were more sinister, or even supernatural. "All Democrat states are under a form of 'Medical Martial Law,'" wrote a Twitter user. On Facebook, a former candidate for governor in Missouri wrote that mask mandates were "part of a demonic ritual to get rid of our individual God-given rights." At a hearing on mask mandates in Florida, a woman accused the local government of "obeying the devil's laws." And in Washington state, protestors gathered at the home of a public health official, toting signs that read "Masking is a satanic ritual."

America has never been immune to conspiratorial ideas like these. In 1964, the historian Richard Hofstadter traced a conspiratorial braid running deep through American history. In 1855, he reminds us, a newspaper reported that "the Monarchs of Europe ... are at this very moment plotting our destruction;" an 1895 pamphlet avowed that "the secret cabals of the international gold ring" had deployed "every device of treachery;" and in 1951, Senator Joseph McCarthy claimed knowledge of "a great conspiracy on a scale so immense as to dwarf any previous such venture in the history of man."

In 2019, a review of 96 studies explored the psychological gears behind these patterns.[3] People "tend to conspiracies" when they "fear a threatening situation, or have low perceived feelings of control," the authors found. Two psychologists argued in 2017 that crises are especially potent drivers of conspiracy: "Since people have a fundamental need to understand why events occur," they write, "crisis situations often elicit sense-making narratives."[4] In January, researchers found that a sense of diminished control also leads to increased support for political leaders who use conspiratorial rhetoric.[5] It's understandable that people would turn to stories like these in times of uncertainty. Reality is complex and nuanced. It is itself uncertain. A good story, on the other hand, can be simple and direct, and most importantly, certain.

This tendency seems to be latent in human nature, arising in times of crisis and not altogether uncommon. But the prevalence of paranoia generated by the pandemic is remarkable. In 2020, pollsters surveyed Americans on 22 conspiracy theories.[6] Only 9 percent of respondents endorsed none. Nanobots in COVID vaccines alter your DNA, 5G cellular networks weaken your immune system, SARS-CoV-2 was a secret bioweapon—it was as though, in the words of the poet George Bradley, the pandemic summer's comet had "set its blazing match head to the straw of human intellect."

DURING THE ENLIGHTENMENT, comets prompted another, more careful, reaction, in addition to stories of doom and disaster. In 1680, Isaac Newton honed his laws of planetary motion and gravitation through observations of the comet of that year. He discovered that comets were drawn from the far reaches of the solar system by the sun's gravitation. According to astronomer D.W. Hughes, Newton's magnum opus, *Principia Mathematica*, is essentially a "textbook on comets."

In 1705, Edmond Halley used Newton's laws to prove that comets were predictable natural phenomena with orbits and periods. He demonstrated that several historical comets, including those that had appeared to Louis the Pious in 837 and over England in 1066, were in fact one comet, due again in 53 years. He was proven right on Christmas, 1758, when Halley's comet returned to the sky. It marked the ascendance of a different means of achieving control, enacted through the scientific method rather than superstition.

For centuries, the careful methodology of science and reason gained ground over the medieval patterns of thought that supposed a comet could herald the death of a king. Why have huge swaths of the population now turned back toward the cognitive dark ages? Hofstadter suspected that "certain historical catastrophes or frustrations" could allow conspiratorial thinking to be fashioned "into mass movements or political parties." While any number of economic, social, and cultural tributaries have fed the roiling current of partisanship that now grips the country, one development seems key.

The integration of the internet into every aspect of our lives appears to have exploded the human propensity to tell a story, any story, to cope with the stress of the pandemic. Nearly half of all Americans get their news from social media.[7] But social media can insulate users from conflicting ideas, refracting and reinforcing their view of the world and creating schizophrenic streams of reality.

What's worse, these platforms actively sort and select for radical content. The algorithms that power social media prioritize user engagement above all else. Content that is extreme, like a conspiracy theory, is more likely to hold our attention, and so the algorithm is more likely to recommend it. When you're driving on the highway, it's almost impossible not to look at a car crash. The same is true for being on social media, Tristan Harris, cofounder of the Center for Humane Technology, has said. So Facebook and Google feed readers "car crashes after car crashes."

It's tempting to believe that the end of the pandemic will signal the end of these car-crash narratives. But I'm not sure. Although the fault lines that fragmented the country at the height of the crisis are quieter now, they're still here.

Recently I heard from a colleague about a patient in Oregon who refused a blood transfusion because the patient would only agree to accept blood from unvaccinated donors. Sixty-three percent of Republican voters still believe the 2020 election was stolen.[8] In 2023, United States senators have made a host of debunked claims: The government is covering up problems with COVID treatments, liberal financier George Soros is bankrolling people to turn America into a third-world country, Putin is colluding with environmental activists to undermine American energy. The dark side of storytelling, the side that sacrifices truth to soothe uncertainty, or to project power, appears to be in permanent ascendance, hastened by our technologies.

Aza Raskin, also a cofounder of the Center for Humane Technology, has said we may be approaching what he calls the "vanishing point of human authority, where our minds are no longer an instrument to discern reality" because technology now exploits "our weaknesses for discerning what's true." Have we already crossed this threshold?

I WORK IN A RURAL HOSPITAL in western New Mexico now, in a county that had one of the highest COVID death rates in the country. We're no longer seeing patients in tents in the parking lot, by the light of propane heaters, like we were during the first pandemic winter. We're no longer calling more than 60 hospitals, from South Dakota to California, to try to find

The dark side of storytelling appears to be in permanent ascendance.

beds for our critical COVID patients, as we were during the Delta surge. It's been months since I took care of a patient with severe COVID. When the radio calls come in, popping with static, it's chest pain and car accidents again, instead of fever, cough, and shortness of breath. The emergency department seems almost back to normal, except for the masks that patients and staff still wear.

We had the tools to limit the spread of the virus, but we didn't. It wasn't because of the comet's malign influence, as might have been said 500 years ago. It was because we couldn't agree on the story. Scientists, physicians, and public health officials had one story, painstakingly cultivated, and developed over time. Too many people in power told a different story, to deflect responsibility for the crisis. Millions of people, meanwhile, fell prey to the cognitive trap that led people in the past to blame comets for the calamities of their times—to project a story onto the natural world, to provide a sense of control when everything around them seemed out of control.

The impulse to sooth uncertainty with a story, no matter its provenance, must be nearly as old as the mind itself. Like any adaptation, it has been an asset as well as a liability. But in the era of the internet, this liability seems at risk of overtaking the more measured approach that the Enlightenment gave us. And that may prove more consequential than anyone has yet imagined, as the planet lurches toward its next calamity.

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Note on the art: All the comet illustrations are in the public domain. The opening illustration is a 16th-century woodcut of The Great Comet of 1577. The Great Comet of 1881*, streaming over an observatory, is from a 19th-century book of astronomical drawings. The others are from* The Comet Book*, a 16th-century treatise, held at Universitätsbibliothek Kassel, on the meanings of comets. Thanks to* The Public Domain Review*, where we discovered the comet art.*


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Slime Wonders

Nearly every evolutionary question can find an answer in mucus

BY SUSANNE WEDLICH

THE WEATHER IN Morro Bay, California, is too good, the coastline too picturesque, and the wildlife seem to have waltzed straight out of a Disney film. Sea otters play in the waves with their young, herons bask on the beach, and seals stretch their plump bellies in the sun. And yet amid the tranquility of Morro Bay lurks a monster straight from H.P. Lovecraft's playbook, as slimy as a creature from Sartre's nightmares. It doesn't get much more extraterrestrial than this. Two hearts? Tentacles coming out of its head? Four rows of pointed teeth? A vertical smile on its face? But would you call it a smile? Or a face? Why, it's the hagfish of course.

The writer and Nobel Prize winner John Steinbeck was not a fan of the monster. He found it "disgusting" and "nauseating," while noting that his close friend, the marine biologist Ed Ricketts, "did not feel this, because the hagfish has certain functions which he found fascinating." And I find them fascinating too.

The hagfish has certain peculiarities, including its German name, *Schleimaal* (slime eel), which is misleading, since this elongated creature is not an eel—but neither is it a true fish, as its English name suggests. In fact, hagfish, like the parasitic and similarly unpleasant lamprey, are the last remaining members of the primeval cyclostomata, which translates as "round mouths." The name is better suited to lampreys, which possess disc-shaped suckermouths with far too many teeth, enabling them to latch on to fish and shred flesh from their flanks. A sensational find confirmed the unique evolutionary journey of cyclostomes.[1] It was the first time a fossilized hagfish emerged, 100 million years old and fantastically well preserved, complete with traces of slime, like a "sneeze in stone." It underlined the close relationship between these creatures and lampreys and proved that they are not primitive ancestors of us vertebrates, as some scientists had previously assumed.

Unlike the lamprey, the hagfish appears to be mostly harmless, living in the depths of the ocean where it feeds largely on carcasses. On land it's only seen by those who, like me, patrol the streets of Morro Bay looking for a fish wholesaler.

Sandy Winston is one such man, and he takes pity on me on this dull December afternoon just before Christmas and lets me into his yard, where hundreds of hagfish are coiling and contorting in two outsized metal containers which are supplied with a constant flow of water from big hoses. It doesn't stay that way, since the creatures promptly transform the liquid into a stringy, gelatinous mass. I watch it happen and feel it too, because soon I'm rooting around in the transparent slime, trying to grab a hagfish with both hands.

They're harder to catch than I'd expected because they never stay still, slipping through my fingers. And then there's the slime, which is so tough that I can lift it up as a dense fabric. It is so stringy that it creates webbing between my fingers, and so sticky that I won't be able to wash it off, instead having to rub down my hands with a slime-stiffened old cloth, which Sandy's colleague Becky gives me without a word. Blonde and quick to laugh, she stands next

Threatened hagfish can bind vast quantities of water into a dense slime in a split second.

to me by the container, rooting around in the slime too. She's responsible for the animals and is now searching for a dead hagfish. "I can smell it," she says. Why remove a dead hagfish surrounded by carrion-loving members of the same species? "They don't eat each other," says Becky.

But neither does the hagfish have many predators. Its loose skin makes it too difficult to catch, and there's the extremely slimy defense. When threatened, hagfish release extra-long molecules from their skin, stored as space-saving spindles, waiting to be put into action. Then they positively explode, binding vast quantities of water into a dense slime in a split second, forming a suffocating cloud of gel that will even gag a shark. The tens of thousands of fibers in each liter of hagfish slime are long and thin yet durable and elastic, a bit like robust silk or synthetic fibers. And, as entirely natural molecules, they could just show the way toward novel eco-textiles.

But there's more: The United States Navy is trialing the use of military lab-grade hagfish slime to stop suspicious ships in their tracks without using force. Current tactics involve launching plastic ropes that slow the ship down by getting tangled into its propeller engine but are hard to untangle afterward. A weapon based on synthetic hagfish slime might snot a suspicious ship in its tracks instead by expanding underwater into a mass of mucus and dissolving later without residue. It would be the modern recreation of a mysterious slime-like sea described in Greek and Roman antiquity. "For over 2,000 years, geographical writings have been haunted by mention of a 'congealed sea,' which prevents ships which reach it from sailing any further or makes the journey much more arduous," wrote the German historian Richard Hennig in 1926. "Mention of this phenomenon appears in the Middle Ages, too, in tales of the 'congealed sea,' the 'motionless sea,' seen from time to time under its Latin name, *Morimarusa*."

WHO KNOWS HOW MANY other unique and potentially useful slimes are out there? If the hagfish is the king of animal goo, its kingdom encompasses all of nature—and every single species within it. Biological slimes are not obscure exceptions, they are the rule, and essential for survival. In all my years of researching this fascinating material, I've yet to encounter a slime-free creature and doubt that such a minimalist even exists. Small wonder, as there's hardly a single evolutionary question to which nature has not

PAGES 32-33: SIMIA ATTENTIVE / SHUTTERSTOCK

found an answer in slime. As Mark Denny of Stanford University wrote in a trailblazing publication in 1989, invertebrates in particular rely on the stuff for movement, communication, reproduction, self-defense, and even food, while jellyfish, comb jellies, and other zooplankton are composed entirely of gelatinous mesoglea.

An all-encompassing medium in life: This is what slime means to microbes as well. But what about us, the so-called higher organisms? We vertebrates, as well as plants are not above this. We use slime in myriad ways, too, we're simply a little less obvious about it. This is a necessity for terrestrial species, because the highly hydrated slime dries out quickly in the air. Any creature using it on a large scale on land will prefer to hide it away inside its body or as a plant in soil, where water loss can be more readily controlled. The only openly slimy surfaces we humans display are the eyes. They are covered in thin films of mucus which are protected from dehydration by a lipid layer. Slime's mostly secretive nature might be the reason why it escaped our notice for so long as an essential and sophisticated substance.

And what is slime in the first place? It's the default term for unknown but sluggish fluids or creepily soft solids. It's a thing in between a feeling and a description of materials, but there is not one prototypical slime. Depending on origin and function, it hides behind a multitude of pseudonyms like gel, biofilm, mucilage, glycocalyx, but also in ecological communities like biological soil crusts, or in phenomena like marine snow.

The U.S. Navy is trialing the use of military lab-grade hagfish slime to stop suspicious ships in their tracks.

But how to unravel the differences and commonalities here? Most gelatinous substances are lumped together under the label of "slime," even in scientific publications, without their molecular inner lives receiving much illumination at all. Or at least it was that way a few years ago: Today, ever more researchers working on specific slimes are connecting with colleagues to join the dots. An international collaboration under the lead of Adam Braunschweig at City University of New York seeks to investigate different animal mucuses and use their designs to develop new technologies. It's a worthy goal since these slimes are, as they state in a publication, "remarkably diverse and include lubricants, wet adhesives, protective barriers, and mineralizing agents."[2] And the brand-new discipline even has a name: "mucomics."

But even if specific slimes can be pinned down by their structure and functions, which definition should we take for all kinds of biological slimes? The answer may be as slippery as the substances themselves, but they share at least some important characteristics—in regard to their components, structure, behavior, and function. And it might just be easier to unravel this from the outside in, starting with the functions. Varied as biological slimes are, they act mainly as lubricants, glues, and selective barriers. There are other functions like hydration or mineralization, but these can often be subsumed into the major categories which themselves are not entirely distinct.

So far there are only a few species whose slimy repertoire we know about and have researched in any detail. Snails, for instance, can crawl

FRANK FENNEMA / SHUTTERSTOCK

WEAPON-GRADE SLIME

When threatened, hagfish, like this one, can release molecules from their skin that make water into a dense cloud of slime that can gag a shark. The U.S. Navy is even trialing the use of hagfish slime to stop suspicious ships without using force.

along just as easily as they hang from a surface simply by secreting a different slimy glue. And they coat inner surfaces like the digestive tract with slime as a barrier—just as humans and many other organisms do. But what if there aren't any tissues or surfaces inside a body to protect, when one cell is the whole organism? Microbes are the original and possibly the most proficient slimers of all. They bunch together and build themselves a gooey city or biofilm wherever there is some water and surface to attach to. Microbial slimes in the environment are ubiquitous enough to affect habitats from deserts to coasts by gluing sand, sediment, and other substrates together, often on interfaces between air, land, and water.

Now let's consider behavior: How can slimes act as lubricants, glues, and flexible barriers? This is due to their viscoelasticity, their ability to behave like a fluid and a solid at the same time. In many cases, organisms can adjust this behavior, fine-tuning the fluidity, the stickiness, and density of their slimes, which makes them particularly adaptable to changing needs. How hydrogels behave depends on how long and how intensively certain forces are acting upon them. This is mainly what makes them so varied and adaptable as lubricants, adhesives, and barriers—despite their being little more than water. The characteristic sluggish fluidity or viscosity depends on the material's inner structure and components.

"Slime is little more than stiff water," according to the German microbiologist Hans-Curt Flemming. Part of that rigidity is thanks to a

I've yet to encounter a slime-free creature and doubt that such a minimalist even exists.

three-dimensional framework which binds the water—holds it in molecular chains. In other words: The water wants to flow but is kept on a short, if elastic, lead by the molecular framework, which accounts for the more solid behavior. This network is formed of polymers, long-chain molecules which are cross-linked. They are unique in their ability to bind together extraordinary quantities of water, at least when it comes to high-functioning slimes produced by biological organisms.

While science is only now getting a grip on the study of slippery elusive slime, it is not the first time slimes have aroused human curiosity and been exploited for human purposes.

The yellow slime of the banded dye-murex snail turns to deep violet in bright sunshine. Thousands upon thousands of these molluscs were killed in ancient Rome, and later also in the royal households of Europe, for extravagant gowns in imperial or royal purple. The common piddock *Pholas dactylus* had the similar misfortune of being extraordinarily prized. These creatures grind holes in stone using their elongated shells, concealing themselves inside for life. Despite their nifty burrows they were found by the Romans, and Pliny writes of nighttime *Pholas* feasts during which guests' mouths, hands, and clothing would glow in the dark because they had been sprayed with the molluscs' bioluminescent slime. It looks like we might just ooze our way back into a future where we use and appreciate nature's gels in even more surprising—and hopefully more subtle—ways.

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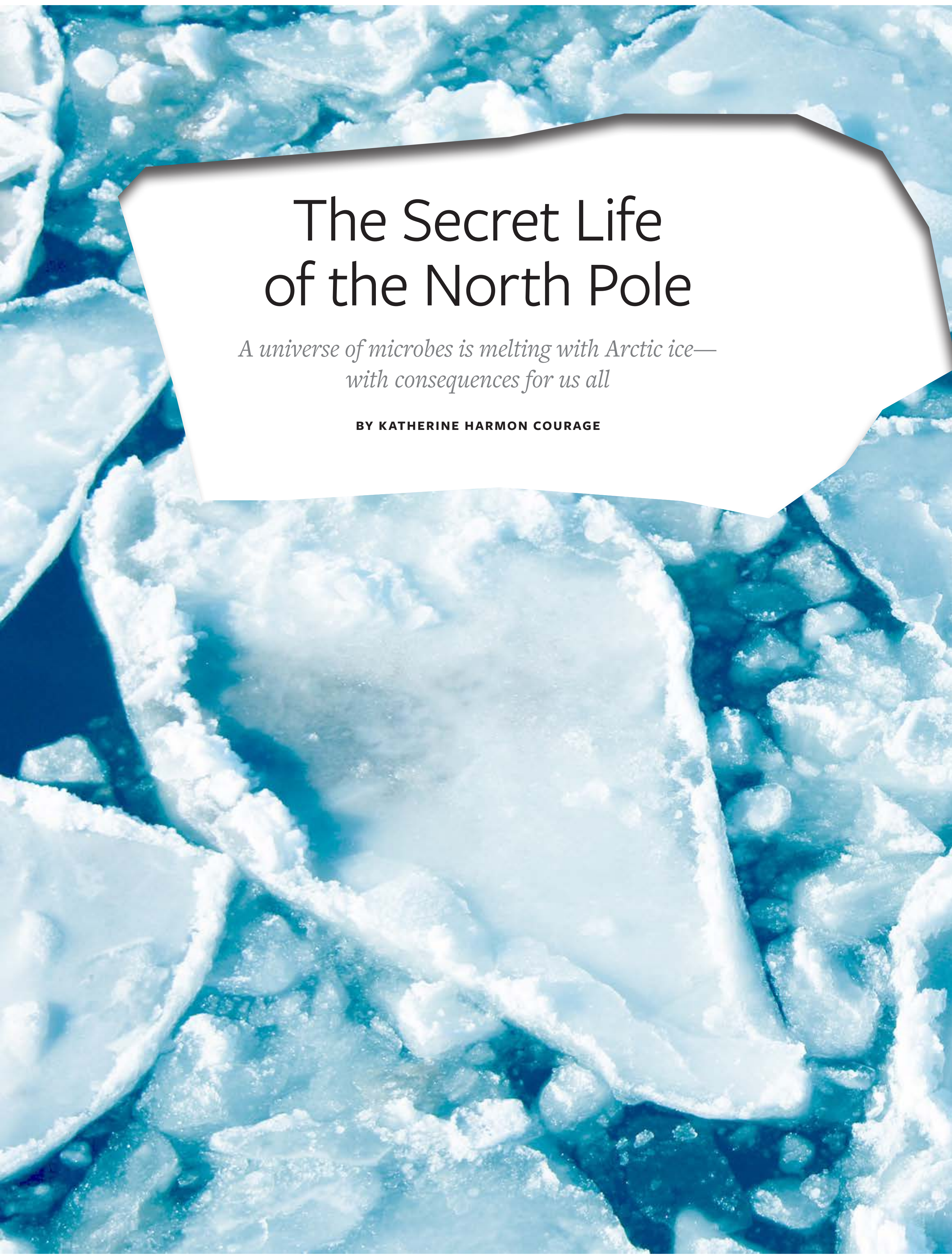
The Secret Life of the North Pole

A universe of microbes is melting with Arctic ice—with consequences for us all

BY KATHERINE HARMON COURAGE



WHEN KARLEY CAMPBELL ARRIVED at the North Pole for the first time, last year, it was raining. Even though she'd become a scientist, her implicit notions about the top of the globe had coalesced in childhood. It would be a solid place, with terra firma enough for at least one workshop of elves. Instead, she and her colleagues found lots of open water. "It was a somber, somber moment," she recalls.

Campbell is a marine botanist at the Arctic University of Norway and the lead scientist on a project investigating "the metabolism of sea ice." This may sound a strange pursuit in what would appear a barren, almost-otherworldly abiotic landscape. But the polar ice holds consequential secrets of, and for, life.

Scientific projects to understand the dramatic effects of the derailing climate are underway across the globe. Researchers are tracking warmer temperatures and rising seas, increasing droughts and wildfires, animals and humans on the move. Outside the spotlight, though, are projects like Campbell's and people like her, taking account of incredibly subtle changes that will have lasting and uncertain effects on ecosystems—in this case, the ocean's food web, which stretches from unseen microbes to us.[1]

It takes a particular type of person to dedicate their career to studying life our eyes can't see, in a place our bodies aren't suited for. Perhaps an eternal optimist. Or, like Campbell, a self-described pessimist. Whose outlook brings a certain essential pragmatism to the field—and to the field work.

"Anything that can go wrong will go wrong," Campbell says from her office in Tromsø, Norway, a town in the Arctic Circle where the sun had set in November for the long polar night. An experimental set up that works swimmingly in the lab is bound to break in -40-degree temperatures, she says. Campbell admits she picked a strange line of work: "I'm actually always cold."

To do this research, scientists need an astounding quantity of gloves—Campbell herself always has at least a half-dozen pairs—pathogenic bacteria, and hired guns. But the risky work is essential if we are to have even a fleeting hope of understanding the microbes' roles and importance in the rapidly changing ecosystem. And what their disappearance might mean.

"You have to have somebody with you keeping watch for polar bears while you're working."

IN THE VAST, BLEAK, WINDSWEPT SURFACE of our planet's polar seas, buried within drifting slabs of sea ice, life is indeed not only present, but multitudinous. Bacteria, archaea, fungi, algae, viruses. All making their way in the otherworldly environment of polar sea ice, swimming in brine pockets, gobbling up carbon, feeding the food web in the depths below. A single milliliter of sea ice can contain upward of 1 million living bacteria.

As the polar autumn arrives each year and temperatures drop, ice crystals on the sea surface multiply, coalesce, and create larger sheets of sea ice. These overwintering drifters speckle the surface, joining larger amalgams of floating ice that persist for multiple years, growing and shrinking with the seasons. Often covered with a drift of snow, these sea ice chunks can range from several inches to more than 15 feet thick. But far from a solid block of ice, they are worlds within themselves—gradients of light, temperature, and salinity, permeated with tiny pockets and channels of liquid brine. And it is primarily within these varied niches and along the slushy bottom that life has devised ways to persist well below freezing.

To avoid a certain death from ice crystals forming within their own bodies, microorganisms that thrive in this ice—which ranges from about 28 to -31 degrees Fahrenheit—have evolved a range of incredible adaptations. In one dramatic case of convergent evolution, life from multiple lines—bacteria to algae—have settled upon a sort of antifreeze compound.[2] These large, goopy excreted sugars work a bit like a chemical version of an avalanche airbag, helping to keep open a livable pocket for themselves in the ice. (Even beyond shaping the ice itself, these microbe-generated substances might contribute to local weather, aerosolizing and spurring cloud formation.[3])

PAGES 38-39: JURJANEPHOTO / SHUTTERSTOCK

LIFE ON ICE Intrepid bacteria and algae (pictured at right) make an unlikely living in super-cold brine channels locked within drifting sheets of sea ice. As their icy habitats become scarcer in the Arctic, scientists are uncertain what ripple effects will flow through the ecosystem.

KREBS, C. & DEMING, J. SEA ICE: A REFUGE FOR LIFE IN POLAR SEAS? PMEL.NOAA.GOV (2011)

Scientists have also uncovered how some of these microbes withstand the super salty brine. As the seawater crystalizes into ice, sodium is excluded, squeezing it into ever-increasing concentrations within the brine. With such spikes in salinity, researchers detected an increase in other helpful compounds that protect cells against too much salt.[4]

Rather than enter into a state of suspended animation or subdued hibernation, these microorganisms simply carry on doing much of the same things as when they are floating about in the relatively milder summer waters (often adapting to drastic changes in temperature and salinity across just days or hours[5]). Sea ice bacteria eat dissolved carbon and other organic material trapped with them in the brine, casting off various compounds in the process. This miniscule metabolic activity means they play a continuous role in cycling elements, such as carbon and nitrogen, making them a central, if underappreciated, force within the polar ecosystems through the harsh, starlit winters and dawn-soaked early spring.

The most profound contribution to these cycles happens in the cold, liminal world between ice and water, where an unexpected layer of algal life bursts forth. Dormant during the polar winters, these algae blossom when the sun begins to reappear. An algal cell will feast on carbon dioxide and nutrients expelled by bacteria or pushed up into the ice from the waters below. They shape the biogeochemical cycles in part by fixing carbon, which gets consumed by animals, giving some of it a chance to sink to the bottom of the sea where it could get sequestered for hundreds or thousands of years.

Although these algae cells make up a relatively small percentage of photosynthesizers in polar waters overall, their role is crucial. They bloom before open-water phytoplankton do, providing a reliable first course to zooplankton which become food for other locals higher up the food chain so they can begin their time-worn reproductive cycles, explains Campbell. And they are highly concentrated, which is of no small importance for marine grazers, who rely on them for copious buffets in a single location rather than having to skim about for diffuse fodder in the open seas. These ice-loving diatoms also tend to be especially rich in lipids, Campbell notes, an important foundation for the rest of the food chain.

WHENEVER BRIAN LANOIL and his colleagues embark on an expedition to collect microbes from the ice, they enlist a local trapper or hunter to come along. “You have to have somebody with you who is armed with a rifle, somebody keeping watch for polar bears while you’re working,” says Lanoil, a microbiologist at the University of Alberta.

The crews also must be vigilant about not sinking. On some trips to the deep Arctic, working just a few hundred miles from the North Pole, Lanoil reaches research locations by plane. “You trust the pilots to

The ice acts as a sort of crucible for life that lives within it.

know what they're doing—then you hop out of the plane and quickly drill a hole to make sure that the ice is thick enough to support the plane," he says. "It's wild stuff. It's great."

More common in Lanoil's experience, however, are much tinier threats to his line of research: other microbes. Although the density of microbes in sea ice is surprisingly thick, it is nowhere near as vivacious as, for example, the soil outside of his university office in Edmonton. That means non-ice microbes picked up during the sampling, transport, or storage process pose a real threat to the delicate data he and others are trying to tease out.

They've been countering that eventuality by adding contaminants of their own. They paint the outside of an ice sample with *E. coli*, which is very content in the human gut but is most definitely *not* a sea ice resident. Equipped with a gene that makes it glow, this *E. coli* then acts as a stand-in for all other microbes that might have stowed away on samples. Then Lanoil and his colleagues douse the sample in bleach, which not only kills the exterior hitchhikers but also fries their DNA, preventing it from contaminating genetic screens of the sample later. Once the researchers can see the *E. coli* has been vanquished from the outside of the sample, they can carefully proceed to probe the inner regions of the ice sample to study the elusive endemic microbes to see what secrets of icy life they might be hiding.

AS THE ARCTIC WARMS and endures more rain days like Campbell experienced, its persisting multiyear ice is in danger of vanishing. Campbell notes with resigned certainty that this type of ice will be entirely gone from the Arctic before she retires. As another team of researchers put it, the Arctic Ocean will be "practically sea-ice free in September … before the year 2050."[6] (A certain workshop will soon need a flotilla.) It is the multiyear ice that offers far more gradients of temperature and salinity, providing more diverse habitats for microbes to inhabit, than the thinner seasonal ice that forms and vanishes with each tilt of the planet.

As ice habitats become more uniform first-year ice, "you end up losing a lot of niches for organisms, and so you end up getting much less diverse organisms," Lanoil says. Which, in turn, he says, leads to a less efficient, less stable community. And these homogenizations mean the microbial communities are less resilient to further disturbances. Which Lanoil sees as a sort of feedback loop, as "changes to those environments just compound upon each other and get worse and worse."

Lanoil and others have been looking to other reserves of ice on the planet to see what might be in store for marine ice microbes. Taking ice cores from Beringia, between Siberia and Yukon, he and colleagues have peered back in time to the changeover from the late glacial Pleistocene to the Holocene, across about 25,000 years ago to 15,000-11,000 years ago. Even with that transition, he says, "essentially the microbial communities didn't change at all." Similarly, looking at microbes across 11,000 to about 5,000 years ago, microbe profiles were also very stable. But the ice microbes from those two time periods look vastly different.[7] Something switched. And they're not sure why yet. It seems "these microorganisms are quite stable and able to adapt to a relatively minor change in the environment," Lanoil says. A little warmer or cooler, and they can rev up or slow down their metabolism to get by. "But if there's a big enough change in the environment, then we get a dramatic shift," he says. "There's basically a tipping point we reach where the community can no longer adapt, and then we shift to a completely new one."

We might be entering just such a transition now. And if so, "we're going to see a dramatic shift in the microbial community with unknown consequences," Lanoil says. With sea ice structure changing, "you're losing entire communities of microorganisms that are really important for the functioning of Arctic ecosystems because the organisms that are living in and under

A single milliliter of sea ice can contain upward of 1 million living bacteria.

the ice are really important for regulating the flux of food through the food chain," Lanoil says. As a result, "you end up getting a very different big change in the ecosystem as a whole."

But the implications are unclear. "We don't know what that means, in terms of the ability of these organisms to actually carry out their ecosystem functions to do the important things that they do at the base of the food chain, that allow life to continue to do the things that it does," Lanoil says. "We don't really know what the consequences are—all we know is that it's a very dramatic change," he says. "We're running an experiment where we don't know what's going to happen as a result, and we all pay the consequences of that."

WE MIGHT NOT SEE these shifts coming. For example, the microscopic algae that live and die beneath the ice are hidden from the peering view of satellites that track other ocean photosynthesizers. "But those of us who go up there and core the ice and sample it—or put divers or rovers or other autonomous vehicles to travel under the ice—we can witness and document the massive blooms," says Jody Deming, a professor of biological oceanography at the University of Washington.

Deming has been venturing north, often under the cover of polar nights, to search for microscopic life since the 1970s. Once an undergraduate at Smith College studying botany on a piano scholarship, Deming is now in her 70s, with cheeks ruddied by years living among polar wind gusts. She jokes that a moment of frustration in thick gloves on her first Arctic research expedition gave her such severe frostbite it ended her concert piano career.

Since then, she's been a leader in the field, making discoveries about these unexpected organisms, their unusual lives, and hidden importance. "For the Arctic ecosystem itself, that amount of under-ice blooming that's going on is critical to the ecosystem," Deming says. Not only that, but the ice acts as a sort of crucible for life that lives within it—that then eventually gets released back into the sea below. "The ice helps determine the nature of the microbial ecosystem and polar waters," Deming says. "And that, of course, translates to all the biogeochemical cycles, and gas production, and climate impacts."

After decades on the ice, she has seen the changes firsthand. The seasonal rhythms of the larger animals' ancient patterns, built by microbes, are faltering, Deming says. "What they've adapted to forever, it's now changing."

KATHERINE HARMON COURAGE is the deputy editor at *Nautilus*.

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The Dwarf Planet on Our Doorstep

The series of fortunate astrophysical events that gave us Ceres

BY SEAN RAYMOND

CERES IS THE BIGGEST THING between Mars and Jupiter. But that didn't make it easy to find. Darkly orbiting the sun from within the heart of the asteroid belt, it's long been a spark for scientific imagination. The American astronomer Garrett Serviss made Ceres home to a species of giants that could grow to a height of 40 feet in his 1898 novel *Edison's Conquest of Mars*. The story inspired Robert Goddard to pioneer rocket science and engineering with the hope of unlocking interplanetary travel. In the TV show *The Expanse*, Ceres harbors not alien giants but millions of "Belters," humans who toil to extract the asteroid belt's resources. A quarter of Ceres' mass might be water ice. A mission to return a sample from the surface of this "evolved ocean world" is something scientists at NASA's Jet Propulsion Laboratory are seriously considering.

ANDAMATI & 4MAX / SHUTTERSTOCK

But how did that strange little world get there? And can it clue us into the mysterious early life of our solar system? The answer to that second question is, now: Yes. A recent study I co-authored along with Driss Takir, a planetary scientist at the NASA Johnson Space Center in Houston, and others, uses new observations of asteroids like Ceres to fill in some gaps in the youthful period of our solar system's history, more than 4.5 billion years ago.[1]

What explains where the large dark asteroids ended up?

The biggest of these so-called "large dark asteroids" has posed a bit of a conundrum for planetary scientists. For a long time, Ceres was the only object of its kind, the first asteroid discovered, in 1801, by Sicilian Catholic priest Giuseppe Piazzi. That is, until astronomers spotted another asteroid just one year later (Pallas), and two more over the next five years (Juno and Vesta). Thanks to 200 years of more and more sophisticated observations, our database of asteroids now contains over 500,000 objects. Yet Ceres, the biggest and most massive asteroid (containing about 40 percent of the total mass in the asteroid belt), still presented a puzzle.

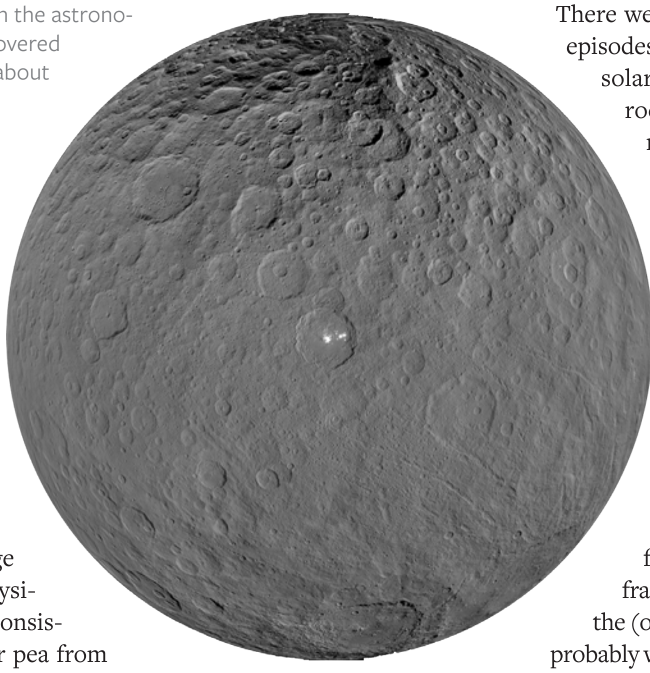
Ceres is a carbonaceous, or C-type, asteroid, the most common kind in the solar system. They're quite dark, reflecting little light. Yet Ceres stands out from most of them: It's the only known cryovolcanic asteroid, with all of its old impact craters erased by low-temperature cryomagma (a mixture of mud and briny water). And unlike many large asteroids, Ceres has no "family" of smaller asteroids associated with it. It has sometimes been considered a lone oddball, but in our study, published in *Nature Astronomy*, we show that it's simply the biggest and most visible member of the large dark asteroids. These reflect less than 10 percent of the light shining from the sun, and they're more than 100 kilometers in diameter (making each the size of a modest mountain range).

Recently, our team, led by Takir, carefully observed the largest sample of these flying mountain ranges in the near-infrared spectrum. They all—or almost all—appear to be clustered near the outer edge of the main asteroid belt, orbiting the sun at a distance between about 3 and 3.4 astronomical units, the distance between Earth and the sun (which makes Mars 1.5 astronomical units away, and Jupiter 5.2). Ceres is the exception, falling outside the cluster at 2.77 astronomical units. With this sample of astronomical relics, we could figure out when and how they formed.

We modeled how these large dark asteroids might have heated when they came together. They started off as loose assemblages of grains and pebbles in space. Then, by the force of their own gravity, they squished more and more as the asteroids became more massive. Meanwhile they were heating up, mainly from the radioactive element Aluminum-26. The amount of energy this element released during the first 2 to 3 million years of solar system history amounts to more than all of the heat released by all other sources over the past 4.5 billion years (except for the sun, of course).

Yet this hot stuff's radioactivity is short-lived: With a half-life of 700,000 years, it was basically all used up, or extinct, within 2 or 3 million years. (The half-life of uranium-235, by comparison, is 700 million years.) The sun's planetesimals—the building blocks of the planets and asteroids—formed over a timespan of 4 to 5 million years. So Aluminum-26 superheated and desiccated the planetesimals that formed fastest, sparing those that formed later. The degree of heating also affects how much asteroids compress, determining whether an asteroid has a markedly dense core, with other distinct layers surrounding it, or not.

We found, using state of the art models (that included heating by Aluminum-26, compaction, and other processes), that the large dark asteroids arose relatively late in the game, between 1.5 and 3.5 million years after the solar system started forming. Their interiors never reached very high temperatures, so these asteroids remain relatively porous. They didn't undergo a big squish. For Ceres, this meant that, with its larger size and mass—1 percent of the moon's mass despite being half its size—it could continue to evolve along the lines of something more planet-like than other large dark asteroids. Yet it also underwent comparatively greater compaction and heating. And, while there is evidence for cryovolcanism, Ceres is thought to have lost a large fraction of its initial water (and it's been



COMET AGAIN? When the astronomer Giuseppe Piazzi discovered Ceres, he was a little iffy about whether it was a comet. He couldn't let go of the thought that it might be "something better."

NASA / JPL-CALTECH / UCLA / MPS / DLR / IDA

hypothesized that Ceres had an earlier ocean that was lost to space). So, even though Ceres has no "twin" among the large dark asteroids, its physical characteristics are consistent with being a larger pea from the same pod.

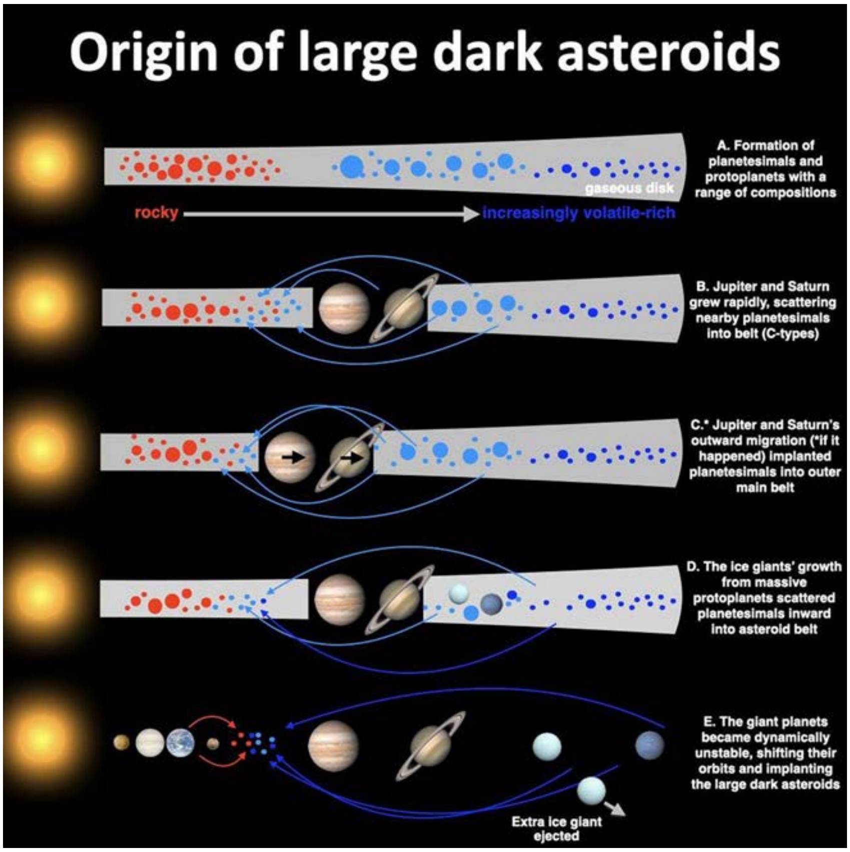
Did this pod simply form in a narrow ring around the sun, or are they strange visitors from elsewhere? From what we understand about the rowdy history of our solar system, it seems the large dark asteroids must have come from beyond the outermost reaches of the planet-forming disk, about 20 to 40 astronomical units from the sun. That's almost as far out as Pluto! What brought them closer to home?

Meteorites in the last few years have offered a clue. They fall into two broad categories: carbonaceous (basically, chunks of C-type and similar asteroids from the outer part of the asteroid belt), and non-carbonaceous (chunks of other types of brighter, denser, stonier asteroids such as S-types, from the inner part of the belt). Measurements clearly show that carbonaceous and non-carbonaceous are different: The isotopes they harbor (in a wide range of elements) are so different that it seems highly unlikely that they formed in close proximity within the solar system. Rather, the non-carbonaceous ones probably represent planetesimals from the inner solar system, closer than Jupiter's orbit and the rocky planet zone and asteroid belt). The carbonaceous asteroids likely came from farther away.

There were a number of dynamic episodes during the dawn of the solar system. Lots of stray rock and other material made its way to the asteroid belt on multiple occasions.

When Jupiter and Saturn grew from cores into full-fledged gas giants, their gravitational reach expanded. They drew in nearby planetesimals, and the ones that escaped the gas giants' pull got flung in all directions; a fraction made their way into the (outer) asteroid belt. This is probably where most of the C-types came from. Jupiter and Saturn's orbital migration, along with the collisional growth of the ice giants Uranus and Neptune, also kicked around planetesimals, with some of them landing in the asteroid belt. The final shake-up happened when the giant planets went dynamically unstable. During this event, Jupiter and Saturn's orbits rapidly spread apart (Jupiter moving slightly inward, Saturn moving outward by 1 to 2 astronomical units). The ice giants spread outward dramatically (shifting by 5 to 10 astronomical units)—and one extra Uranus-like planet was likely ejected from the solar system entirely. The belt of leftover comet-like planetesimals was almost completely ejected, but a small fraction coasted into the asteroid belt.

What explains where the large dark asteroids ended up? While the C-types are more commonly found in the outer belt, they're broadly scattered across the whole asteroid belt, and so probably got flung in during Jupiter and Saturn's growth. But the large dark asteroids have this narrow orbital distribution in the belt that doesn't jibe with that story. The only event that could have implanted the asteroids in a narrow distribution at the outer edge of the belt is the dynamical instability. All of the other candidates tend to implant a broad swath of asteroids rather than the narrow ring we see today.



ROCKY ROAD
This graphic details one hypothesis for how the large dark asteroids came together.

RAYMOND, S., *ET AL. NATURE ASTRONOMY* (2023)

So it seems that Ceres, along with the other dark asteroids, was born in the solar system's outer rim long after planet formation was underway. It grew from chunks of rock and ice. Given the late time, it stayed colder than most other planetesimals, remaining water-rich and porous, and stayed home while the gas giants, and then the ice giants, grew and migrated. But the dynamical shake-up from the giant planet instability was too much, and it was—luckily for exploration-obsessed primates—pulled toward the sun. Unlike most of its brethren, which were ejected into interstellar space, Ceres was trapped by a trick of orbital mechanics and stranded in the outskirts of the asteroid belt, shining darkly for the last 4.5 billion years unseen, until Piazzi spotted it.

"I have announced this star as a comet," he immediately wrote to an astronomer friend, "but since it is not accompanied by any nebulosity and, further, since its movement is so slow and rather uniform, it has occurred to me several times that it might be something better than a comet." By "something better," he meant a planet and, after more observations, that's what he settled on. But this bugged astronomer William Herschel, who told Piazzi that Ceres isn't worthy of being a planet: Since it's small and shares its orbit with other objects, it doesn't hold the space between Mars and Jupiter "with sufficient dignity."

Today we split the difference. Perhaps Piazzi and Herschel could agree that Ceres possesses enough dignity—at least according to NASA—to be a "dwarf planet." A place maybe more friendly than Mars. Something a not-far-off tour of Ceres' terrain, a "prime destination to study habitability," could confirm.

SEAN RAYMOND is an American astrophysicist working at the Bordeaux Astrophysical Laboratory in France. He also writes a blog at the interface of science and fiction (planetplanet.net) and recently published a book of astronomy poems.

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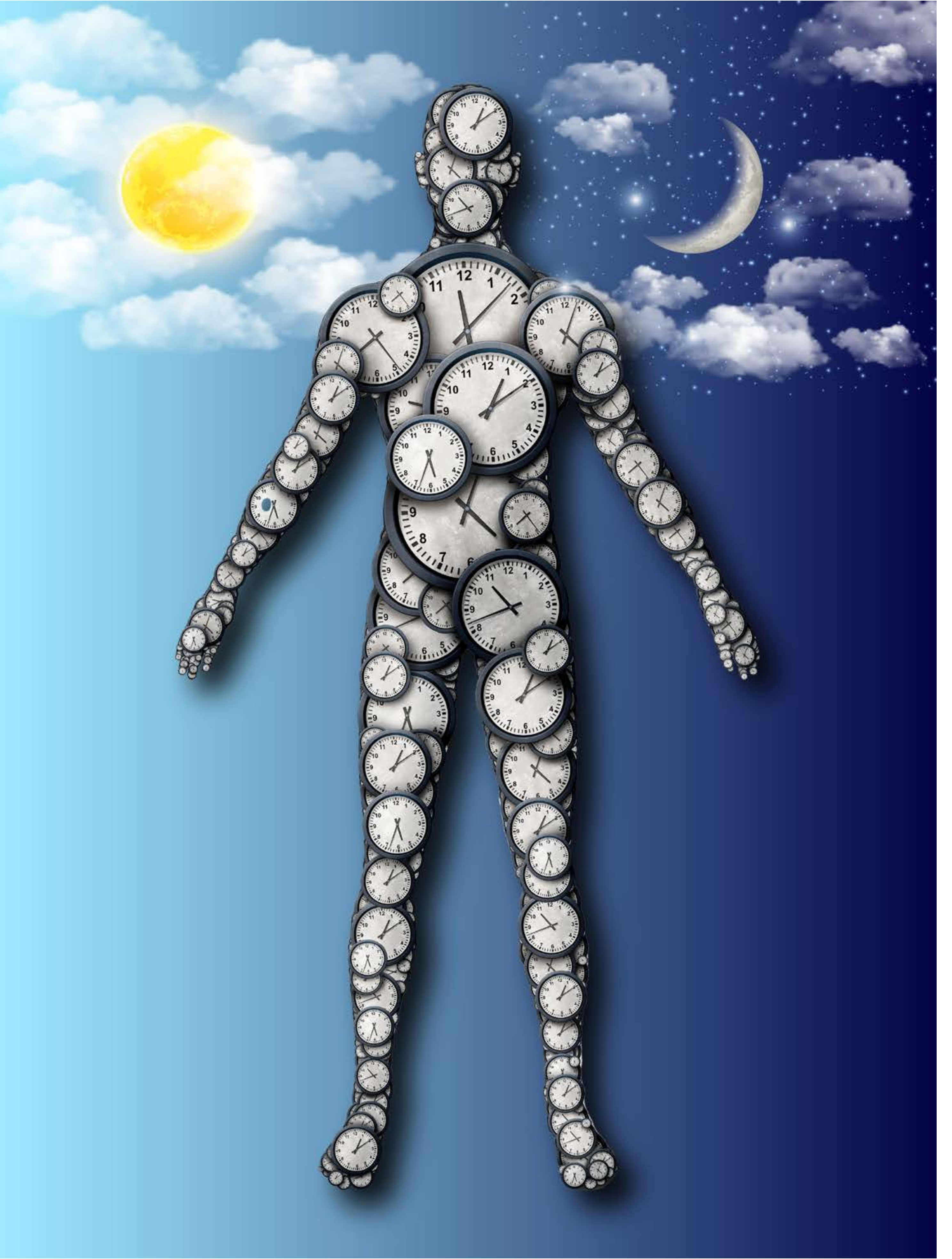


Immunity Is a Matter of Timing

Vaccines, infections, and diseases can all be influenced by our circadian rhythm

BY DIANA KWON

JANE MCKEATING NEVER EXPECTED time to matter much in the liver.

About a decade ago, McKeating was examining medications to use during liver transplantation in patients with chronic hepatitis C infections. Hepatitis C can linger in the body for decades and cause severe liver damage—and in those days, the lack of drugs to combat the viral infection meant that when a patient received a replacement liver, the virus could immediately infect the new organ. McKeating, then a virologist at the University of Birmingham in the United Kingdom, and her colleagues wanted to see whether an antiviral drug could stop the virus' spread and save the new livers.

When the team initially assessed their data, they were stumped. It looked like the drug prevented infection in some patients, but not others—and it wasn't clear what, exactly, was behind this difference.

"We just couldn't understand what was discriminating between the patients," says McKeating, now at the University of Oxford. After much head scratching, they noticed a perplexing pattern: Patients who received their liver transplants in the morning were more likely to be reinfected with the hepatitis C virus than those who had their operations in the afternoon.[1] "It turned out it was the time of day when they received the liver transplant," she says.

LIGHTSPRING AND SIBERIAN ART / SHUTTERSTOCK

Hidden inside most of our cells are so-called clock genes.

Each day, the Earth transitions through periods of daylight and darkness in time with the planet's rotation around the sun. Many of our bodily functions follow the 24-hour cycles known as circadian rhythms. In addition to the daily cycles of sleep and wakefulness, many other processes within our body—such as the regulation of our internal temperatures, the release of hormones, when we digest our food—are also under circadian control. Hidden inside most of our cells are so-called clock genes that regulate the timing of cellular activities. Researchers have found that nearly half of our protein-producing genes work in a time-dependent manner.[2] These pacemakers throughout the body are coordinated by the suprachiasmatic nucleus, a master clock in the brain.

Circadian biology was not part of McKeating's research repertoire when she conducted her liver transplantation study. But after seeing these strange results, she knew she needed to investigate further. So she, along with Alan Zhuang, a postdoctoral researcher in her lab, set up an entirely new program to study the chronobiology—the science of circadian rhythms—of viruses.

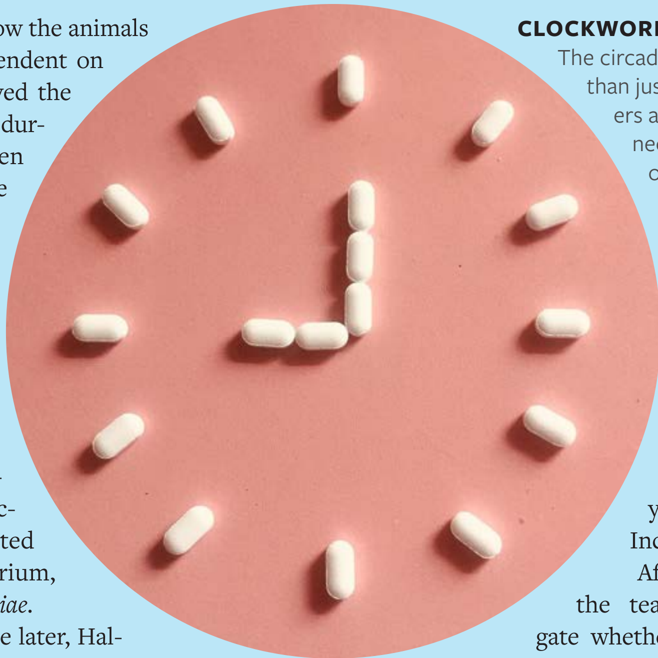
In the years since, her team has investigated a range of viruses, from hepatitis to SARS-CoV-2, uncovering ways in which biological rhythms influence these pathogens, and vice versa.

Their work is part of a burgeoning area of research revealing that circadian cycles orchestrate many crucial functions of the immune system. And that these daily cycles can play a role in determining the outcome of viral infections, autoimmune disease, and other conditions—such as cancer—that involve the body's defenses.

"If you look at pretty much any immune cell and its core functions, and you ask: 'Does it change or can it be affected with circadian rhythms?' The answer is 'yes,' " says Jacqueline Kimmey, an investigator at the University of California, Santa Cruz.

THE PHYSICIAN-SCIENTIST FRANZ HALBERG coined the term "circadian" in 1959, following years documenting rhythmicity he saw in biological processes that paralleled the time cycles in nature. Among his many observations was the discovery that the outcome of an infection depended on when an exposure to a pathogen occurred.

In 1960, Halberg and his colleagues at the University of Minnesota conducted a simple experiment: They injected pieces of *Escherichia coli* bacteria known as lipopolysaccharides—toxins located on the outer layer of microbes—into the stomach of mice at different times of day.



HELENA AS / SHUTTERSTOCK

CLOCKWORK MEDICINE

The circadian rhythm impacts more than just our sleep cycle. Researchers are finding surprising connections about how the time of day impacts things like treatments, vaccinations, and even autoimmune diseases.

They found that how the animals fared was highly dependent on when they had received the toxins: Mice injected during the evening, when they're typically awake and active, were much more likely to survive than those injected during daylight hours, when the rodents were at rest. Other research groups subsequently found similar time-of-day dependent reactions in mice infected with another bacterium, *Streptococcus pneumoniae*.

More than a decade later, Halberg was part of a group of researchers who pinpointed another aspect of immunity influenced by daily rhythms: responses to vaccinations. In a 1976 study, the team used red blood cells from sheep as antigens—molecules that will prompt an immune response—in mice. Several days later, they observed that strength of the immune response the animals generated was dependent on the time of day when they received their inoculations.

These early studies indicated that innate immunity—the body's first-line defense against pathogens and other harms—and adaptive immunity—the slower acting but more specific response system—had unexpected cycle-dependent responses. But the molecular underpinnings of these links remained mysterious.

Beginning in the early 2010s, scientists began uncovering some of this unseen orchestration. In one study, Louise Ince, who was then a postdoctoral researcher in the lab of Christoph Scheiermann at the University of Geneva in Switzerland, examined how the time of day influenced how dendritic cells—cells involved in triggering adaptive immune responses—migrate to lymph nodes, the small structures that help filter out and fight pathogens. The cells were more mobile when injected during the day, when the mice were at rest, than at night, when they were active. "You can really see that the amount of cell migration is significantly different depending on the time that you give the injection," Ince says.

After observing this effect, the team decided to investigate whether responses to vaccinations would show similar time-dependent responses. When they inoculated mice with the hepatitis A vaccine, they found that giving the animals the shot during their resting phase, rather than their active phase, led to stronger responses in several immune cells, such as T cells—key players in adaptive immunity. Those findings were published earlier this year.[3] Why immune cells appear more active during rest remains to be determined, but some researchers speculate that enhancing immunity before rising may prepare organisms to fight off pathogens they may encounter while awake.

McKeating's team has been looking at how the viruses themselves are influenced by these biological rhythms. Her lab has been studying various viruses, primarily within cells in a dish, to get a closer look at this process in a variety of different pathogens. In their studies of hepatitis B—which, like hepatitis C, can cause chronic infection with the liver—the researchers have found that fragments of the virus's DNA can interact with clock proteins within our cells and that the clock system can regulate viral replication.[4] Preliminary work conducted by one of McKeating's Ph.D. students, Helene Borrmann, on another long-lingering pathogen—human immunodeficiency virus, or HIV—suggests that the replication of this virus is also modulated by circadian rhythms.

Circadian rhythms within the immune system may be relevant beyond infections and autoimmune diseases.

During the pandemic, her group also took a look at SARS-CoV-2, the virus behind COVID-19, and found that a key component of the circadian clock can alter the virus's ability to enter and replicate within lung cells.[5] "There is this fascinating interplay between the virus and the clock system," her colleague Zhuang says. But this interaction is complex, he adds, and how exactly it occurs depends on the virus. In viruses like hepatitis and HIV, it appears that perturbing the cellular clock hinders viral replication, while in others like influenza, disturbing the clock appears to have the opposite effect. "Every virus is different," he adds.

WHILE MUCH OF THE EXPERIMENTAL WORK has been done in animals or cells in a lab dish, scientists have also been gathering evidence for time-of-day effects in humans.

Echoing Halberg's work in mice nearly half a century ago, several recent studies have found that timing influences the effectiveness of human-targeted vaccines.[6] One clinical trial of older adults in the U.K. who received seasonal influenza vaccines in the morning experienced a greater increase in antibodies, for example, than those who received the shot in the afternoon. Researchers have reported similar findings for vaccines against other pathogens, such as *Mycobacterium tuberculosis* (the bacterium that cause tuberculosis) and SARS-CoV-2.

Support for the notion that the time of day a vaccine is administered influences its ability to protect against infectious disease is growing, Zhuang says. But the majority of human studies to date have looked mainly at antibody responses—and researchers will need to look at whether timing affects other immune cells to determine how much of an effect on long-term immunity timing really has.

Other curious observations in people have also spurred further investigations. Clinicians have long known that symptoms of rheumatoid arthritis, an autoimmune disease, tend to flare up in the mornings. This pattern is so widely accepted that it is one of the factors used to diagnose the disease, says Julie Gibbs, a professor at the University of Manchester who studies the circadian control of inflammation.

Time of day influences the effectiveness of vaccines.

Gibbs and her group have been focused on looking at how and why the symptoms of immune-linked disease like rheumatoid arthritis fluctuate at different times of day. In mice, they've found that a specific type of immune cell responsible for dampening inflammation known as regulatory T cells within joints are fewer in number at periods when symptoms peak. They're now planning to gather samples from patients to see whether the same is true in humans—with the hopes of one day being able to harness whatever is driving the accumulation of regulatory T cells in order to help treat the disease. Perhaps coaxing these T cells to report to work in joints at specific times of day can prevent inflammation from taking hold.

Ultimately, circadian researchers hope to be able to capture what they've discovered to improve immune-based treatments—such as medications for autoimmune disease and immunotherapies for cancers—and preventions, such as vaccinations. Many also hope to one day develop drugs that Zhuang describes as "clocks in a bottle," which could manipulate circadian rhythms in beneficial ways.

The universe of time inside the body is still largely mysterious, however. Scientists have not discovered how, exactly, immune cells' circadian rhythms are determined—and how they talk with the central clock in the brain. They have a hunch that circadian rhythms within the immune system may also be relevant beyond infections and autoimmune diseases. For example, researchers have recently found a role for these cycles in cancer. In a mouse study from late 2022, Scheiermann and his team demonstrated immune cells' ability to track down and destroy cancer cells depended, yes, on the time of day.[7] The cells were much better defenders during daytime, the animals' resting phase.

McKeating, who began her research career studying HIV, says that when she thinks back to the long line of failed vaccines in this field, she wonders whether timing may have been a key factor that was previously ignored. Moving forward, she says, both scientists and clinicians need to be more cognizant of time: tracking when experiments are done, and when drugs are given. "I think all of this is really relevant going forward," she says. "This is an exciting area of biology that I think will grow." And, she says, certainly more will reveal itself with time.

DIANA KWON is a Berlin-based science journalist who covers health and the life sciences. Her work has appeared in *Scientific American*, *Nature*, and *The Scientist*, among other publications. You can find her at www.dianakwon.com and @DianaMKwon.

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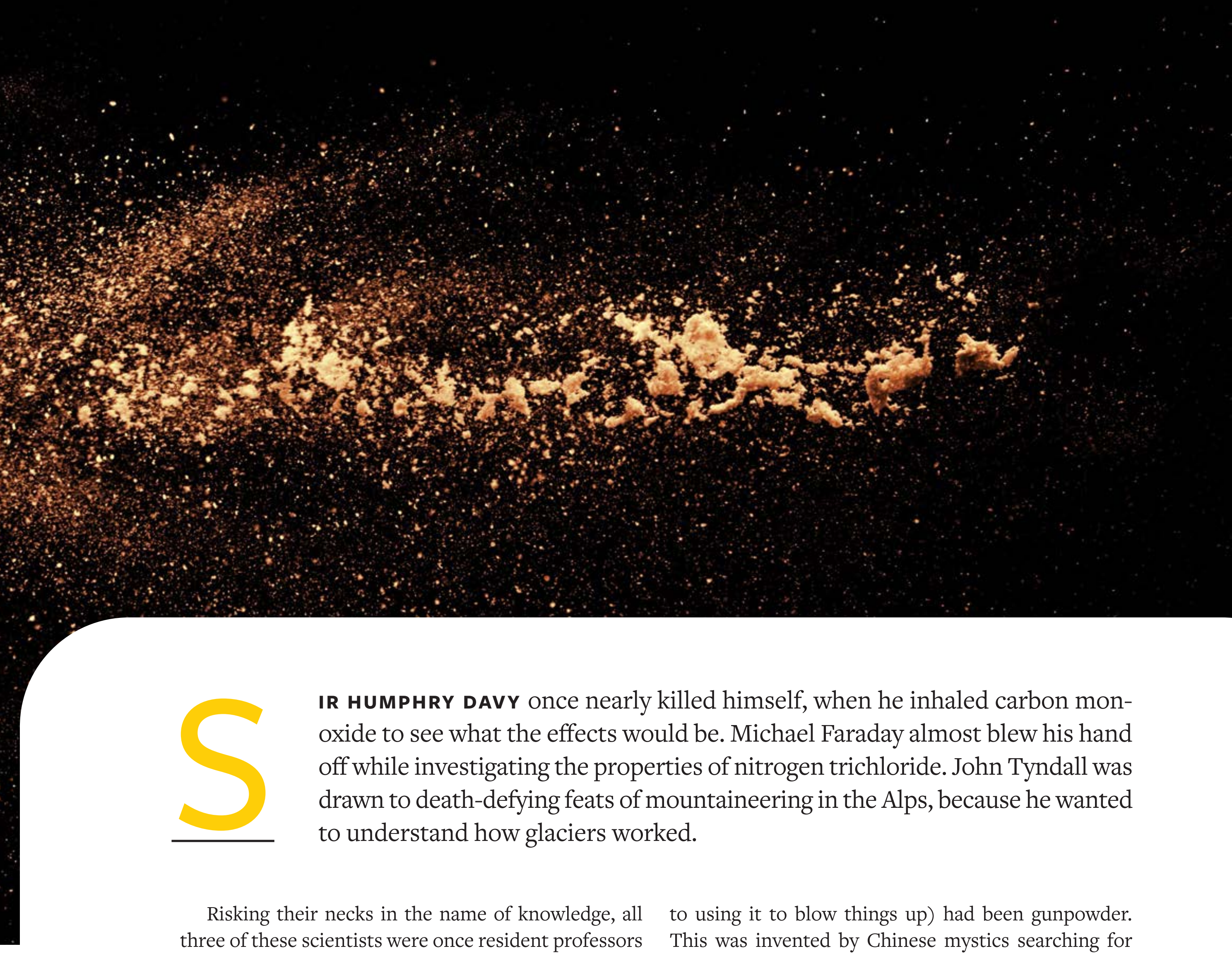
The Explosive Chemist

James Dewar, the creator of cordite, likely helped win World War I. But why never a Nobel?

BY THOMAS W. HODGKINSON



FRUNZE ANTON NIKOLAEVICH / SHUTTERSTOCK

SIR HUMPHRY DAVY once nearly killed himself, when he inhaled carbon monoxide to see what the effects would be. Michael Faraday almost blew his hand off while investigating the properties of nitrogen trichloride. John Tyndall was drawn to death-defying feats of mountaineering in the Alps, because he wanted to understand how glaciers worked.

Risking their necks in the name of knowledge, all three of these scientists were once resident professors at the Royal Institution in Mayfair, living in rooms on the second floor where I now work as a writer for the London Institute for Mathematical Sciences. Yet perhaps the bravest of this building's 19th-century professors was the one most often overlooked.

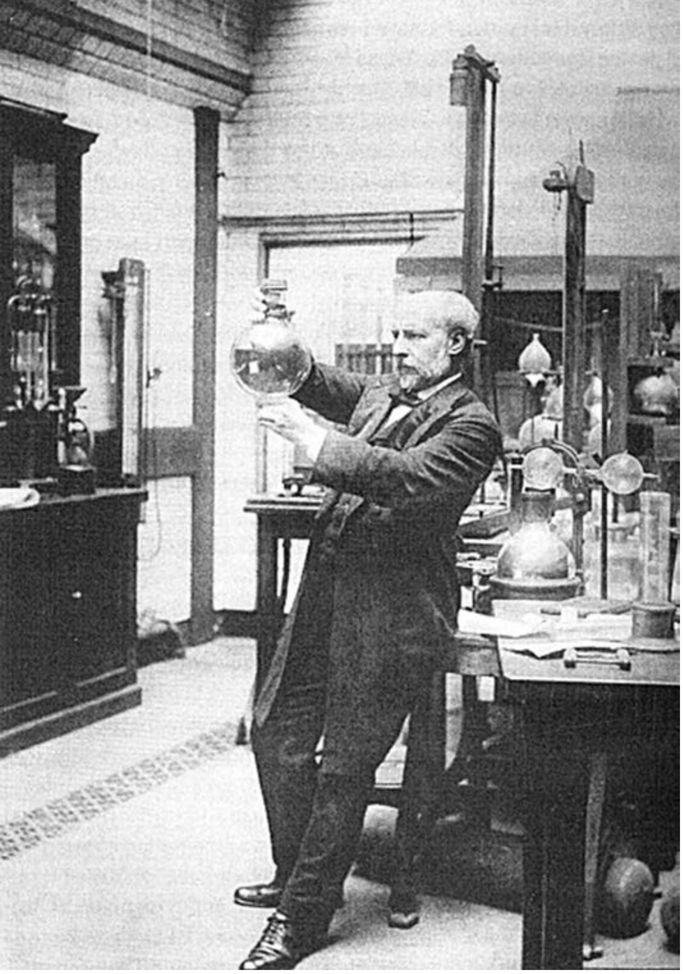
His name was Sir James Dewar. He died a century ago this spring. As well as being the inventor of the thermos flask, he was once credited with having won World War I.

THAT CLAIM TAKES some unpacking. The short version is that Dewar invented cordite: a smokeless replacement for gunpowder used by British soldiers in the trenches. Yet the story is a bit more complicated.

Since the eighth century A.D., the world's number one low explosive (the kind you put in guns, as opposed to using it to blow things up) had been gunpowder. This was invented by Chinese mystics searching for the elixir of life. A few centuries later, it was brought to the West during the Mongol invasions. Since then, it had been the low explosive used in pistols and rifles.

But there were problems with gunpowder. One was that it gave off a puff of smoke, which made it easy for your enemy to work out where you were, and fire back. New discoveries in the 19th century kicked off a quest for a "smokeless powder," which would give any army a crucial advantage in a conflict. In 1888, the British government set up a group called the Explosives Committee to ensure the British led the field. Its head was Sir Frederick Abel, chemist at the Royal Arsenal. Its chief investigator was James Dewar.

Dewar possessed what might be described as an explosive personality. A short, stocky, working-class Scot, he had ruined his digestion in his early career



HE WON DE-WAR After the Duke of Newcastle credited Dewar with winning World War I, Dewar told him, "My work has been an absolute pleasure and delight to me. It has never engendered in me a thought of anticipating any reward."

The work on cordite restored Dewar's mojo.

while researching gout, leaving him permanently dyspeptic. He would not tolerate any familiarity from employees. As one recalled, he was prone to "frequent petulant outbursts." His biographer, John Rawlinson, described Dewar as a man of "few friends and many enemies." Thanks to a childhood accident, he even had a limp, like a Shakespearean villain.

Yet whatever else you might want to say about the Scot, he was a brilliant experimental scientist, who pursued discovery with little concern for his own welfare. One of his abiding interests was the liquefaction of gasses: freezing them to temperatures approaching absolute zero to study their changing properties under those conditions. This was notwithstanding the fact that some gasses, such as ethylene, become extremely volatile and can explode. Once, when asked about these risks, Dewar simply replied that they were impossible to avoid.

In 1886, in the basement at the Royal Institution, he suffered an ethylene explosion that left him incapacitated for months. After that, even the doughty Dewar took a step back from his low temperature research. Nevertheless, two years later, when he was asked to join the Explosives Committee in the hunt for a smokeless powder, he didn't hesitate.

Alfred Nobel, now best remembered for the prestigious prizes he set up, was a successful chemist who invented dynamite. When Dewar got in touch, the Swede revealed to his companion that he was now working on a promising smokeless powder—composed of camphor, nitroglycerine, and soluble nitrocellulose—which he was calling ballistite. However, the formula wasn't perfect.

Dewar took it, tried it, and found it unreliable. He suggested a fix, which Nobel chose not to act on, so Dewar began his own experiments. The received wisdom was that if you used an insoluble form of nitrocellulose, it made the compound too unstable. However, Dewar had the guts to doubt this. He discovered that the opposite was true. This proved the crucial missing ingredient.

He and Abel named it "cordite" and took out a patent of their own. Nobel was incensed. He had had no idea that the Explosives Committee might develop a rival to his ballistite.

When he learned the British army would favor cordite, he sued. In court, the tempestuous Dewar nearly blew his top. He and Abel had been accused of greed by members of the public in the papers. According to *The Times*' daily reports of proceedings, the Scot replied to

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He pursued discovery with little concern for his own welfare.

questions "with something approaching to warmth." That's a lovely 19th-century British understatement.

Nevertheless, Nobel lost the case, the appeal that followed, and the Supreme Court of the United Kingdom hearing. When you look at Nobel's patent for ballistite, which can be viewed at the British Library, it stipulates the use of "nitrated cellulose of the well-known soluble kind." Dewar's patent prescribes "varieties of nitrocellulose which are not of the kinds usually known as soluble."

I asked Jane Hollywood, a patent lawyer in London, to look at Nobel's and Dewar's patents. She told me the verdicts seemed "reasonable." Steven Campion, an intellectual property expert at the British Library, said that Nobel's patent was "too narrow."

Nobel had to pay the full cost of the court cases. He had regarded Abel and Dewar as friends. Although his ballistite was adopted by the Swedish and Italian armies, among others, he felt sickened by the betrayal. No one could be trusted, he declared, save "dogs, whom we feed with the flesh of others, and worms, whom we feed with our own." Nobel died in 1896.

As for Dewar, the work on cordite restored his mojo. He returned to liquefaction, which involved him engineering a way of keeping gasses cold and liquid and led to his invention of the Thermos flask. In 1898, he became the first person to liquefy hydrogen. He made money from the cordite patent but not as much as he might have, since he and Abel donated proceeds from British manufacture to the government. No surprise, then, that he was knighted in 1904. Dewar won about every prize going for experimental science: the Davy Medal, the Copley Medal, the Franklin Medal. The one that always eluded him was the Nobel.

In 1921, the Duke of Newcastle paid tribute to Dewar's invention of cordite, to which British victory in the Great War "was largely due." In his reply, Dewar declared, "My work has been an absolute pleasure and delight to me. It has never engendered in me a thought of anticipating any reward." He went on to quote a passage from Shakespeare's *Pericles*. "I held it ever virtue and cunning were endowments greater than nobleness and riches … Immortality attends the former, making a man a god."

THE MORE I KNOW of scientists, the truer this seems likely to be. As Dewar demonstrated, once he got interested in something, you couldn't stop him. He just wanted to work it out.

Dewar died on March 27, 1923. His body was laid out in his dining room, where two of my London Institute colleagues now work. The funeral was held in the same room, presided over by the Bishop of Worcester. Whenever I unscrew the lid of a thermos of coffee, perhaps while heading to work, I inevitably find myself thinking of Dewar.

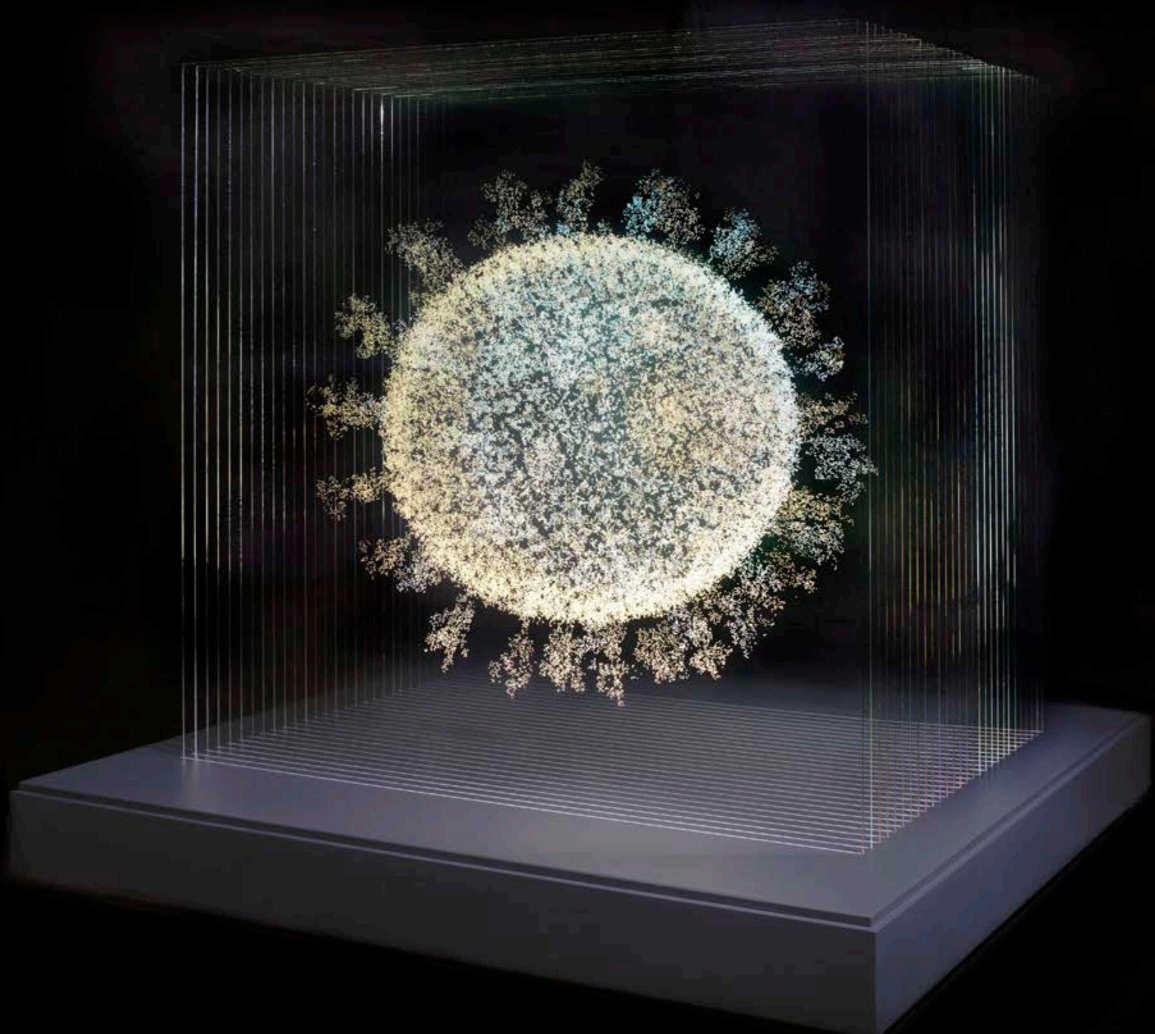
I think of him too, whenever anyone—like Stephen King in his short story "The Body"—mentions "the smell of cordite." This is almost always a mistake, though. Cordite was manufactured and used from the 1890s until the end of WWII. Then it was replaced by other compounds, like Improved Military Rifle propellants. I suppose "the smell of IMR" doesn't have the same ring.

THOMAS W. HODGKINSON is a science writer at the London Institute for Mathematical Sciences (lims.ac.uk).

The Enemy Made Visible

An artwork, sculpted with science, defines our times

BY ELENA KAZAMIA



LOUIS PASTEUR RARELY SHOOK HANDS. Why would he? The generation of scientists he belonged to had just discovered that agents of disease are microscopic creatures, invisible to the human eye. Their lurking threat superseded the need for common courtesy. To touch was to risk contamination, to spread and enhance disease, possibly to risk dying.

When the SARS-CoV-2 virus adopted humans as its hosts three years ago, it made the hidden enemy omnipresent in our generation. The image of spiked viral particles coating every surface and packing the air spaces between us transformed our lives and presented a new challenge for scientists. Artists put the coronavirus at the heart of their work. How could they not? It is a defining force of our times.

First exhibited at the Oxford Museum of Natural History, *2020: The Sphere That Changed the World*, is a scrupulously accurate three-dimensional "drawing" of the virus by Scottish artist Angela Palmer. It appears to have trapped a single SARS-CoV-2 viral particle in glass, magnified to 8 million times its size. The effect is chilling. The sphere appears otherworldly, suspended in time and space, lit from within with a dizzying clarity.

The shape of Palmer's work is based on the precise modeling of the virus using bioinformatic techniques and the computational outputs of one of the world's most powerful supercomputers, located at the Texas Advanced Computing Center in Austin. Using the genetic code of the first isolated strain of SARS-CoV-2, scientists from the United States and the Netherlands were able to predict the arrangement of proteins and lipids that make up the outer surface of the virus. Palmer fed this information into industrial design software and using a technique of hand-engraving transferred cross-sections of the outer shell onto 28 sheets of glass stacked together to produce the 3-D result.

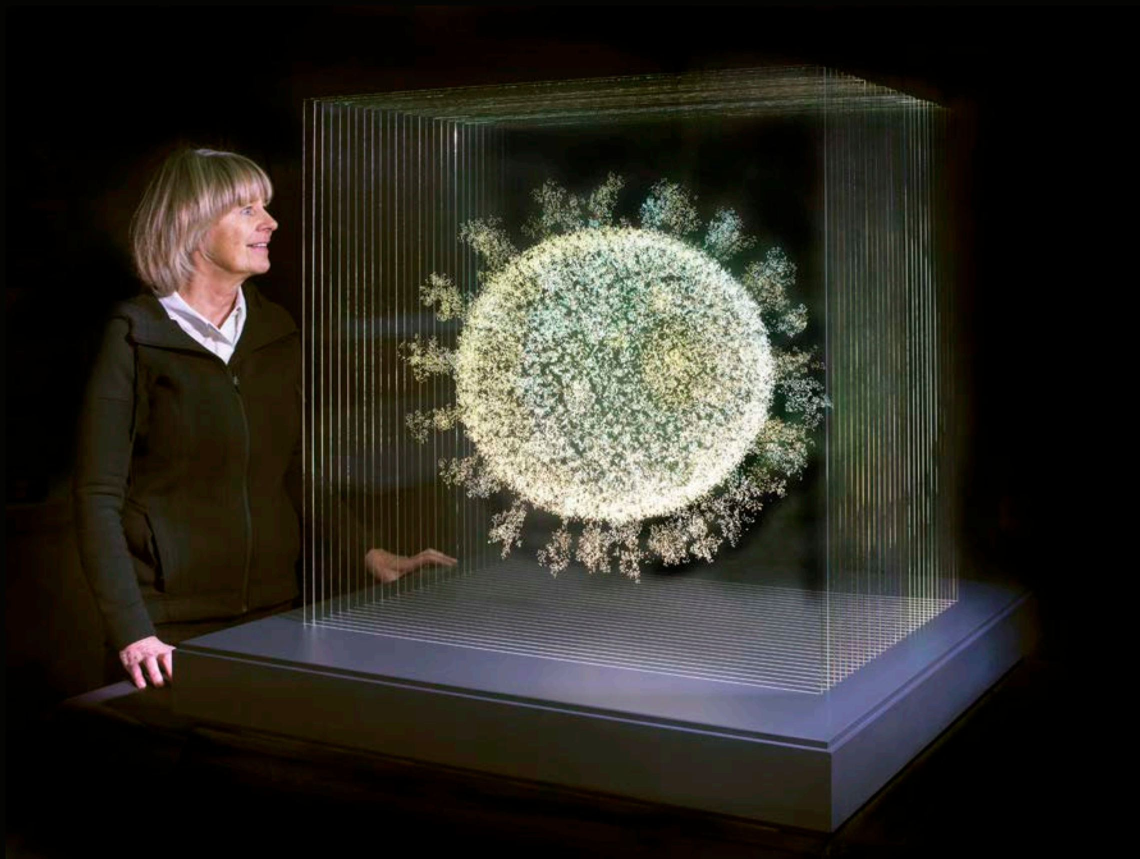
It's a shimmering ode to a killer agent.

After studying anatomy at Oxford University's Ruskin School of Drawing and Fine Art, Palmer "became fascinated in visually representing internal structures hidden beneath the surface," she wrote to me in an email correspondence. "I like to peel back the layers and expose the beauty of natural forms. During lockdown, I became determined to create the one form which was dominating humankind. Its invisibility made it a natural subject for me."

Palmer sought out scientists who could provide a blueprint of the virus, which she would use to create her sculpture. In earlier work, the artist had used MRI and CT scan images to produce anatomical works to great success, including a "self-portrait" of her brain, exhibited at the National Portrait Gallery of Scotland. But finding accurate tomographic data that informed the shape of the virus proved harder than she expected.

When it comes to visualization, viruses fall into the liminal space between cell and molecule. We have powerful techniques that can probe three-dimensional structures at each side of this spectrum but are hindered by a blind spot in between. A single SARS-CoV-2 particle is one thousand times smaller than the width of a human hair. There are no magnifying lenses that are powerful enough to bring it into view, and even our most probing cryo-electron microscopy techniques, which can be used to study the anatomy of a cell, fall short on resolution. On the smaller side of the size spectrum, techniques such as X-ray crystallography and NMR spectroscopy can provide insight into the shape of molecules such as DNA and proteins, but from this perspective the viral particles are too large to comprehend. Just like Alice in Wonderland, we seem to struggle to bring ourselves into the right size frame for perspective.

But scientists went through nature's looking glass to uncover another means of visualization—the genetic code that a virus uses to assemble itself. If this code can be correctly interpreted, it is possible to conjure the virus' physical structure inside the brain of a supercomputer. "This is precisely where sci-fi becomes reality—because of [structural] bioinformatics," Dmitry Korkin, a professor in the bioinformatics and computational biology program at Worcester Polytechnic Institute, told me. Early in 2020, his team produced "the periodic table of structural elements that comprise the SARS-CoV-2 virus," based on the genetic sequence information of the first isolated strain from Wuhan, China.



THE SPHERE THAT CHANGED THE WORLD
Angela Palmer with her creation at the Oxford University Museum of Natural History. Palmer adapted the 3-D presentation of cross-sectional data used in science for her art.

ANDREW SMART OF A.C.COOPER LTD.

The outbreak of SARS-CoV-2 sent the scientific community into a frenzy of work and collaboration. "We worked in a hackathon. We had meetings at 3 a.m., pushing to characterize the virus," Korkin said. Rather than wait for the formal process of peer review and publication, his group released all findings directly onto their website. Traditional news outlets broadcasted the results, teenagers in China spread the infographics on TikTok, and scientists reached out to consolidate their knowledge.

The clinching moment for producing a plausible 3-D model of the virus came after a fruitful collaboration with Siewert-Jan Marrink's group at the University of Groningen in the Netherlands. Marrink studies the dynamics of what to Korkin's eyes are "very large systems"—the lipid membranes of cells. But the frame for the SARS-CoV-2 sphere happens to be a lipid bilayer that the virus steals from the cells of its host.

Together the scientists authored a successful grant petitioning for time on a supercomputer at the Texas center, where they could model all the components of the viral sheath: the proteins embedded in the lipid bilayer which coalesce to form its outer surface. The pieces of the puzzle were known, all that remained was to determine a structure that did not break any physical laws of nature. The genetic code predicts the individual proteins, but it is not clear how many copies of each protein together make a single sphere, in what proportion or configuration.

The artwork's accuracy offers a key to the virus' undoing.

The scientists tasked the supercomputer to produce iterative simulations of various combinations of the known viral proteins behaving in three-dimensional space over the course of hundreds, up to a thousand nanoseconds. Each iteration, where each nanosecond takes the supercomputer approximately a day of computation, is just long enough to see whether the structure undergoes any "catastrophic events," according to Korkin. "If you introduce the wrong number of ions"—charged particles—"into the simulation, the virus' shell will explode, or if you introduce the wrong proportion of lipids, or if you try to squeeze in too many proteins, it is going to rupture."

It took a week on the computing server to produce a reliable simulation, and then a few more to test the model to perfection. The result was an imperfect sphere, slightly flattened at the top and bottom, with membrane, spike, and envelope proteins coalescing together in the lipid bilayer in stable proportions. This was the model shared with Palmer, dissected into 28 cross-sections.

Palmer's scientifically accurate representation of the SARS-CoV-2 virus is not strictly symbolic. Nor is it a simple unmasking of the enemy, a way to give body and form to our collective fear. The accuracy of the artwork provides a map and key to the virus' undoing. Knowing what a virus looks like helps scientists understand its mode of attack, notably where its structure interlocks with the receptors on cells. It foreshadows where a virus could be most vulnerable to counterattack by targeted drugs.

THE SPIKE Sarah Gilbert (below), who co-developed the Oxford-AstraZeneca vaccine for COVID-19, stands alongside Palmer's glass sculpture, *The Spike*. The sculpture is an accurate representation of the protein that protrudes from the coronavirus' surface and latches onto cells.

ANDREW SMART OF A.C.COOPER LTD.

"When I finished, I was taken aback by its beauty."

When describing the exciting discoveries from the modeling effort, Korkin referred to the membrane proteins as revealing themselves to be the "hidden heroes of the virus." Simulations of their behavior showed them assembling into filaments folding into a mesh structure, providing a flexible but durable reinforcement of the membrane sheath. Equipped with this knowledge, researchers targeted the chinks in SARS-CoV-2's armor.

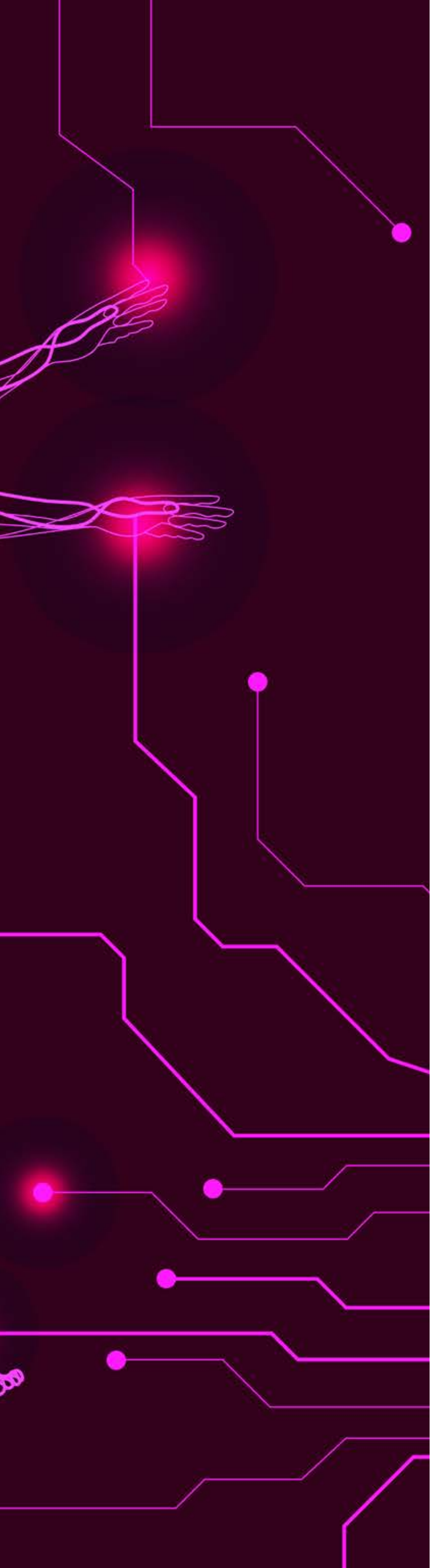
One way that Palmer's work is limited in its depiction is that, as any solid sculpture, it represents the viral body as rigid, locked into shape. "This virus is everything but that," Korkin explained to me. With a lipid frame it can pulsate, squeeze, and maneuver its way around the cells in our body." His own simulations, Korkin said, produced in his mind's eye the fact that the "outer shell almost breathes." Palmer's chosen medium of glass also gives the virus a false appearance of fragility. Here is a particle that is extremely durable, highly resistant to physical wear and tear, malleable and adaptive.

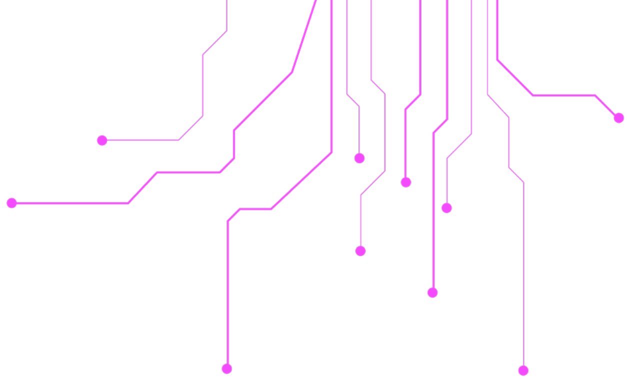
Palmer admits that her sculpture is full of paradox and allusion. It traps a virus that has in turn held all of us captive over the course of a pandemic. And while it is rendered in solid form, she likes to emphasize its elusiveness: "As you confront the sculpture head-on, you see the entire sphere, with its protein spikes emerging from its surface. But as you move around it, past the stacked glass sheets, the virus particle disappears entirely from view, only to reappear again, just as it torments us." Perhaps its greatest paradox is its visual appeal. It is a shimmering ode to a killer agent that has taken the lives of millions around the globe.

"When I finally finished the engravings and stacked up the glass to form the entire sphere, I was taken aback by its beauty," Palmer said. "As an artist representing a deadly object, which is destroying lives and livelihoods worldwide—described by AstraZeneca pioneer Sarah Gilbert as our 'mortal enemy'—you might expect to create something that is menacing and frightening. But in reality it totally contradicted that. I found it immediately beautiful and mesmerizing. It's a natural form, and I can't think of any natural forms which are not beautiful."

2020: The Sphere That Changed the World was acquired by the Science Museum in London, where it is exhibited as part of their permanent collection.

ELENA KAZAMIA is a scientist and freelance journalist with a Ph.D. in plant sciences from the University of Cambridge. She is originally from Greece.





The Body Electric

We are formed by more than DNA. Meet the bioelectric code.

BY SALLY ADEE

MAKING AN EMBRYO is much like making a Lego castle: In the same way that a castle needs turrets and gargoyles and a moat, you need two legs and two eyes and a heart.

Except unlike the Lego Camelot, you don't come with a picture on the box of what you're meant to look like, much less an instruction manual—and you're not going to be the one to assemble the structure. Instead, you'll sit back and wait for the Lego pieces to organize themselves. Our cells, our little Lego pieces, assembled themselves. What's even more astonishing is that when they get it right, all those cells get it right in broadly the same ways: We all managed to come out with the characteristic shape and proportions appropriate to our species (we can all spot a regulation-issue chicken, frog, mouse, or human shape).

There's no gene for two eyeballs.

So how did all our initial progenitor cells know how to organize into us—forming our eyeballs, legs, fingers and all that in the right place and the right order? Who gave them the blueprints to check that all those fingers or fins or beaks weren't too giant, or too tiny, or of wildly different lengths? Most important—how did they know when to stop?

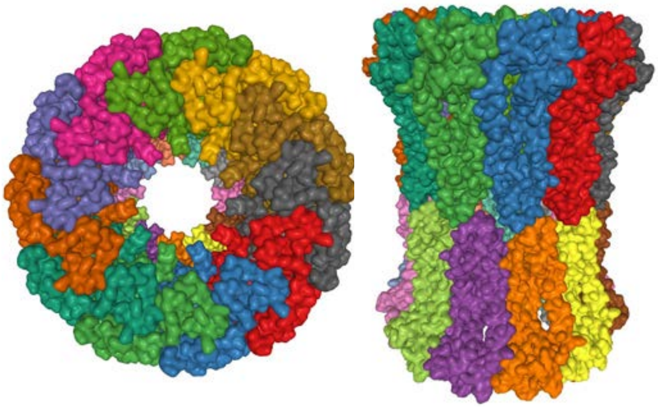
Well, you might be thinking: That's what DNA is for. Not true. You can search all the As, Ts, Cs, and Gs in your genome, turn 'em upside down and shake the spare change out of their pockets—you won't find the instructions for anatomy.[1] You'll find plenty of specs—code that tells you about the color of hair a baby will have, its skin, its eyes. You'll find nothing about how many eyes. There's no gene for two eyeballs. There's no gene for "the eyeballs need to go on the front of the head." There's also no gene for "two arms and two legs, kind of this far apart, feet in the front and butt in the back." It's simply not possible to recover the shape of an organism solely from reading a printout of its genome.

So if not genes, what does control your shape?

The question had begun to assemble itself in Mike Levin's head when he was still a child, wondering how an entire person could be assembled from an egg. As it happened, Levin needed a topic for his Ph.D. thesis at Harvard Medical School, and in the early 1990s, there was still one aspect of how human beings are shaped in the womb that remained a total mystery: how embryos tell left from right. There had been theories, but never a smoking gun.

For a grad student, this was tempting, low-hanging fruit. So Levin, now a developmental and synthetic biologist at Tufts University, began to investigate how all those cells, without having brains, nonetheless seemed to know their left from their right. And make no mistake—their ability to distinguish left from right during development is critical to our survival. From the outside we may pull off the illusion of symmetry—two eyes, two ears, two arms, and two legs, same on one side as we are on the other. But inside, it's a different story. You probably know that your heart

PAGE 64: KRAVPAK / SHUTTERSTOCK



ELECTRIC SLIDE As soon as the very first cell forms in an embryo, special ion channels, known as gap junctions (pictured at left), begin to form, opening portals of electrically charged communication as the body takes shape.

VOLODYMYR DVORNYK / SHUTTERSTOCK

and stomach lean left, and that your right side houses your liver, appendix, and pancreas. For about 1 in 20,000 people, this whole image is flipped.[2] And that's absolutely fine! They don't usually have health issues (apart from overzealous researchers poking and prodding them to understand their condition, known as situs inversus). However, when just some of the bits are flipped, you have a problem. Jumbling up the body's precise internal asymmetry, particularly when it affects the fastidious plumbing of the heart, is the origin of many congenital heart defects and other life-threatening syndromes.

Understanding what caused any of this—the correct pattern, the flipped pattern, the jumbled pattern—was a longstanding, perennially interesting unsolved mystery. Why does the heart go on the left and not the right? And how does the body know to develop this way? No one had been able to finger a specific molecular component, so there was no hint of a genetic cause. Genes couldn't be the whole story, anyway. After all, genetic information is not spatial. The genome can't tell left from right. It seemed to Levin, from studying the old ion current papers, that electricity was somehow fundamental to establishing the polarity of a cell.[3] But how?

Decades of work had cataloged every ion that shuttled in and out of developing embryos of every species and identified the ion channels that send them through the zygote and the blastomeres it calves off into as it begins to diversify into the developing embryo. A funny thing happens to the ions and ion channels in the cell during this transition: They all mysteriously change. Some pop into existence, others disappear then reappear, and their currents wax and wane with those disappearing and reappearing acts.

Another clue to the functional importance of these weird ion events was what happened when you interfered with them. Disrupting even seemingly minor sodium currents resulted in a "rosette," which is an abnormal embryo that "appears to have lost its spatial orientation," Italian biologist Elisabetta Tosti found in her own research. She concluded that the currents during and after fertilization are crucial for correct embryo development.[4] Messing with potassium currents also led to developmental defects, further evidence that

Genetic information is not spatial. The genome can't tell left from right.

ion movements are crucial for an embryo. But no one had been able to assemble this jumble of interesting pieces into a coherent whole.

By the time the 21st century got underway, Levin could ask these questions in his own lab at the Forsyth Institute, at Harvard. How was electricity setting the polarity of a cell? He and Ken Robinson, working at Purdue University, discovered a proton pump. Protons are hydrogen ions. This pump specializes in making sure hydrogen and potassium are kept in strict ratios. On an unfertilized frog egg, proton pumps are speckled evenly around the whole surface.

But when Levin and Robinson checked on these pumps after fertilization, they found something strange: All the channels had started drifting over to one side of the egg, where they smashed themselves into a tight little clique. No one had ever seen anything like this. When the pumps gathered on one side of the egg, it meant hydrogen ions were only able to get in or out of the cell on that one side. This created a voltage, and it happened really soon after fertilization, when the frog embryo consisted of only four cells. Could this be the answer they were looking for?

When scientists think they have found a causative agent like this, their next step is to try to figure out an experiment that can disprove their idea. Levin and Robinson decided to see what would happen if they prevented the proton pumps from drifting out of perfect symmetry after fertilization. To do that, they added extra proton pumps or potassium channels to the developing embryo to even out their distribution, mimicking the smooth distribution on an egg. If the researchers were right, this evenness would wreak havoc on the embryo's ability to discern left from right. And they were correct. The embryos with the extra proton pumps were all messed up, as likely to have their hearts on the right as the left. The proton pump was clearly essential to kicking off the difference between left and right sides.[5]

But it was also changing the membrane voltage. That was weird. A change in membrane potential is how nerves send action potentials. But why was a brand-new embryo changing membrane potentials? What possible use could that be, when it hadn't even developed nerves yet? Levin wondered if this voltage was part of the system an embryo used to tell its constituent cells to become different kinds of tissue. This idea is articulated by the biologist Mina Bissel: If all our cells have the same exact genes in them, then why do some of them do one thing when others do other things? How do some of them become bone cells and others skin, or nerves?

GAP JUNCTIONS are an unusual kind of ion channel. They start to form the moment the fusion of egg and sperm creates the first joint cell, known as a zygote. Right away, the gap junctions establish a cellular intranet quite unrelated to the nervous system (which in a zygote of course does not yet exist). Unlike other ion channels which let in and keep out various molecules, gap junctions simply create direct connections cell to cell to cell.[6] They poke between neighboring cells, creating a sneaky door only they share, a bit like adjoining hotel rooms.

That means that as cells differentiate, each new cell that cleaves off is already connected to the cells around it. Long before nerve cells develop synapses, our non-excitable embryonic cells are equipped with this other, much faster, more electrical way of communicating.

Levin had long suspected that these gap junctions were involved in how an organism decides how to shape itself. In his earliest days of investigating left-right patterning, he had found that turning off gap junctions also messed up normal asymmetry. Later, he and a postdoc, Taisaku Nogi, found gap junctions were the culprit in the unparalleled regenerative superpowers of a weird little sea worm called a planarian.[7] This small flat worm can regrow no matter how fine you chop it—and it only takes about a week to return to fully functional normalcy. Nogi and Levin realized that gap junctions could explain how this repatterning information could spread so quickly over thousands of cells.

So that was two different animals, then, in which the gap junctions seemed to enable long-distance messages without a nervous system. In some ways, this system was actually *better* than a nervous system. When two cells are connected in this way, each cell has direct, privileged access to the other's internal informational universe. What one cell knows or experiences diffuses immediately through the connecting door for its neighbor to know or experience, too. The effect is close to telepathy.

This was when Levin first began to formulate his theory of the bioelectric code. The membrane voltage carried information, and the gap junctions formed the body-wide network—the electrical network that was not the nervous system—that sent that information around the body. It wasn't much of a stretch to think of this information as taking the form of a code.

That code controls the complicated biological processes that formed you in the womb, by executing a controlled program of cell growth and death. It is the reason you retain that same shape throughout your entire life; it prunes your dividing cells so you keep being recognizably you. It wasn't the only important thing—biomechanics, biochemicals, and all the rest mattered too. But just as the neural code was mooted to govern behavior and perception, and the genetic code governs heritable traits, the bioelectric code was how the body told itself about its form.

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Animal Sex Determination Is Weirder Than You Think

Parasites, weather, and luck can play a role in determining whether some animals are male or female

BY DANNA STAAF

THE ONCE-UNFATHOMABLE OCTOPUS has revealed some of its most intimate details to science—its brain, its genome, its secret cities. But scientists are still in the dark about a supremely foundational aspect of this animal's existence: its sex. What causes an octopus to be female or male?

No one knows.

Octopuses, for starters, seem to be missing sex chromosomes in any form as we know them. In humans and many other animals, two X chromosomes make an egg-producing female, while one X and one Y make a sperm-producing male. (Biologists use the word "female" to describe organs or organisms that produce eggs, and "male" for those that produce sperm; animals do not have socially constructed genders.) Octopuses possess no such familiar, tidy determinants.

Is this simply another example of octopuses being oddballs? Not at all. Across the animal kingdom, chromosomes are only one of more than a dozen ways that sex is determined, and scientists are continuing to find more, expanding the notion of how—and why and when—animals produce one sort of sex cell over the other.

The effort to understand these dynamics goes beyond mere curiosity. Unraveling these unexpectedly complex patterns is helping scientists sharpen their understanding of evolution itself, by illustrating how conflicts between genes or between parasites and hosts can lead to new traits.

Sex determinants can mix and change, even within a single species or a single individual.

This research also helps scientists peer into the future. It's no exaggeration to say that animal life on Earth depends on eggs and sperm. (A few fascinating species can reproduce with eggs alone, but everyone else, from earthworms to elephants, requires both types of sex cell to build the next generation.) Climate change and pollution can seriously impact the sex ratios of many animals. Thus, understanding how and why sex determination happens could also help us safeguard the future of many species on this rapidly changing planet.

Eggs and sperm go way back, but, interestingly, not as far back as sex itself. That began perhaps as much as 2 billion years ago, when single-celled organisms, which had been reproducing by making copies of themselves, began swapping genes in order to create genetically novel offspring. Some eventually facilitated the exchange by dividing themselves into sex cells that could fuse with other similarly sized sex cells. Two, four, or more "mating types" determined compatibility between cells.

Today, single-celled life, such as amoebas, as well as most fungi, still do their sexual reproduction with equal-sized sex cells and mating types. However, the ancestors of animals—as well as those of plants and of several kinds of algae—all evolved sex cells of two distinct sizes: large eggs packed with resources and small speedy sperm. Scientists don't know why this happened in some types of life and not others, but they do know that this system of reproduction has since become entrenched.

For animals to produce the essential sex cell types, however, they need some deciding factor, some switch, determining which individuals will make which kind of cell. And herein lies the puzzle. "If that division [of egg and sperm] is ancient, why would you ever change the mechanism underpinning which of those you make?" asks Judith Mank, a zoologist at the University of British Columbia who has studied sex determination for more than two decades. "That's one of the mysteries of sex."

SCIENTISTS DON'T KNOW what switch or signal the earliest animals used to determine whether they would produce eggs or sperm. But since then, the methods have proliferated into a dizzying array.

For example, the worm on a hook, the fish that bites it, and the human holding the rod all reproduce with eggs and sperm, but the three animals have three very different ways of determining what type of sex cell they'll make. Earthworms are simultaneous hermaphrodites, producing both eggs and sperm in the same body. Fish, depending on species, could be sequential hermaphrodites (maturing first as one sex then switching to the other) or have separate sexes determined by

PAGES 70-71: DUDLEY SIMPSON / SHUTTERSTOCK

A WRINKLE IN GENES An unassuming amphibian, the Japanese wrinkled frog (*Glandirana rugosa*), pictured above, has developed two entirely different chromosome patterns for sex determination and reproduction. Some frogs have XY chromosomes like we do, and others have ZW chromosomes.

ALPSDAKE / WIKIMEDIA COMMONS

genes, environment, or both. Humans, of course, have X and Y chromosomes (a system that's distinct from our diverse gender identities).

Before the discovery of sex chromosomes, people had developed a plethora of creative ideas about sex determination, primarily in humans—and also in farm animals. Their theories tended to be environmental, including: the heat of the surroundings, the heat of the parents' passion, the nutrition of the mother, and the quantity of semen from the father. Biologists now know that many of these factors can indeed affect sex determination … but just not in humans, sheep, or cows.

The assumption of environmental sex determination acquired some holes in 1845, when male bees were found to develop from unfertilized eggs and female bees from fertilized ones. And the presumption was fully overturned with the 1905 discovery of XY sex chromosomes (first in beetles, then in mammals and a number of other animals) and the 1909 finding of the less widely known ZW sex chromosomes (first found in aphids, then in birds and various reptiles and fish). In this system, ZZ animals develop as male, ZW as female.

Sex appeared to be purely, simply genetic—until 1966, when a French zoologist discovered that the rainbow agama lizard did, in fact, rely on an environmental factor to determine sex. A higher temperature produced male rainbow agamas and a lower temperature, females. (The passion of the reptilian parents was not scrutinized.)

Things only got more complicated from there.

Sex determinants, scientists learned, can mix and change, even within a single species or a single individual. Such changes may occur as populations adapt to different environments, and they can help tease apart complex evolutionary histories.

The Japanese wrinkled frog has XY chromosomes in both eastern and western Japan, but frogs living between these two populations demonstrate two different systems: one with ZW chromosomes and one with distinct XY chromosomes that aren't shaped like those of the eastern or western frogs. In 2022, scientists discovered that the eastern frogs had become a subtly different species, and where they had hybridized with western frogs, the result was chromosome chaos.[1]

Beyond sex determination, the wrinkly case of these Japanese frogs reveals the striking ability of evolution to flip traits from one state to another and back again.

Common pillbugs would seem to be a simpler example, with only ZW sex chromosomes to propagate new generations of roly-polies. But, like most other arthropods, they happen to be vulnerable to infection by a weird and wily parasitic bacterium called *Wolbachia*. *Wolbachia* is transmitted exclusively from mother to offspring, never via the father, so from *Wolbachia*'s point of view a male host is a dead end. It would prefer a host population dominated by females. Thus, *Wolbachia* has evolved the ability to feminize ZZ male pillbugs, creating egg-bearing ZZ individuals that can perpetuate *its* lineage.

This turns out to be just the beginning of the pillbug's curious sex history.

In some populations, the feminizing influence of *Wolbachia* has been so powerful that, over millions of years, these pillbugs lost their ZW sex chromosomes altogether. Their sexes came to be determined entirely by a parasite: Infected individuals were female, uninfected male. That was peculiar enough. Then in the 1980s, scientists observed pillbugs from these populations that were clearly female—but had no *Wolbachia* infection.

ROLLING WITH THE FLOW The humble roly poly (family Armadillidiidae), pictured here, has a surprisingly complicated sex history. The presence—or absence—of a parasite in flipping these bugs to be female or not proves that sex determination is far from an open-and-shut case.

MAURO RODRIGUES / SHUTTERSTOCK

> Climate change could wreak havoc for species that rely on temperature to generate females or males.

The researchers turned to a relatively new idea at the time, horizontal gene transfer, and hypothesized that feminizing genes from *Wolbachia* had been incorporated into the pillbugs' own genome. "It was a visionary hypothesis," says biologist Richard Cordaux of the Centre National de la Recherche Scientifique and the University of Poitiers, who proved it with modern genetic sequencing in 2016. When he shared the news with the sole surviving member of the original scientific team, "He was very happy and amazed," Cordaux recalls.

Subsequent research has uncovered sites throughout Europe and Japan where a pillbug's sex might be determined by any one of these three factors: chromosomes, *Wolbachia* infection, or transferred genes. "If you have a female from such a population it becomes very difficult to tell just by looking at them," says Cordaux—an example of the hidden, wondrous diversity right under our noses (or under the stones in our garden).

Another case of garden-variety sexual variance was discovered last year in the tiny aquatic bladder snails that are abundant in ponds and hobby aquariums. They're hermaphrodites, able to have their eggs and fertilize them too. But even though each individual can produce both eggs and sperm, some of its genes are passed on only through eggs. Because it is to these genes' advantage for snails to produce only eggs, they've acted, like *Wolbachia* themselves, as a feminizing influence. A subset of snails found recently in Lyon, France, have lost their male functionality and are now all effectively female.[2] They live side by side with full hermaphrodites, successfully interbreeding. This curious situation, in which conflicts between genes cause male sterility, was previously known only in plants.

IN ADDITION TO SEX "OVERRIDES" created inside an organism, whether by genes or bacteria, these forces can come from the environment. Endocrine disrupting chemicals such as pesticides and BPA are now found all over the planet, and studies show they can tweak sex in either direction, biasing sex ratios toward male or female depending on the species.[3] (Some also cause other reproductive issues, like reduced sperm or egg production.)

At the same time, climate change is cranking up the heat, which could wreak havoc for species that rely on temperature to, at least in part, generate females or

"It is surprisingly easy to fashion a new sex-determining gene."

males. Within temperature-dependent reptiles, some make "hot females," some make "hot males," and still others make females at both hot and cold extremes, with "lukewarm males" developing in the middle. Rising temperatures around the globe threaten to unbalance their sex ratios, or even erase one sex altogether.

Some reptile species have a limited ability to shift the pivotal temperature at which development switches between sexes.[4] "We found it in painted turtles," says Lisa Schwanz, an evolutionary ecologist at the University of New South Wales. "In a warmer year, it took a warmer temperature to make females." However, this adjustment was too small to compensate for an environment-skewed sex ratio. "I suspect it won't be strong enough to counteract climate change," she says.

Rising temperatures seem to also be pushing some species into new sex determination mechanisms. Bearded dragons, for example, have a fairly standard ZW sex chromosome system. Extreme heat, however, causes ZZ individuals that would otherwise be male to develop into egg-bearing females. This phenomenon was first discovered in captivity, but just last year, researchers described sex-reversed wild females they had discovered in the warmest part of the bearded dragon's natural Australian habitat.

"Do they have an advantage?" wonders Schwanz, who is one of the paper's authors. "What sex do they act like?" In the laboratory, ZZ females explore more like males, but in the wild their movement is indistinguishable from that of ZW females. They don't seem to be any more successful than their ZW sisters, but scientists have yet to determine what their role is in wild populations, which may already be shifting as the local temperatures rise. And it's unclear how many other animal species might harbor this hidden capability, waiting to be let loose in a rapidly changing environment.

These accelerating shifts add a new urgency to research into animals' ever-evolving symphony of sex strategies. Many animals seem ready to swap strategies at the drop of a hat, while mammals and birds have kept their staid sex chromosomes for hundreds of millions of years. And each new discovery adds to the proliferating questions about fluid *and* seemingly stable systems.

In a new paper published earlier this year, researchers uncovered surprising similarities in evolutionary trajectories between the divergent sex determination systems of the populations of Japanese wrinkled frogs. Another endemic Japanese species—this one a mammal—the Amami spiny rat, also recently revealed some surprises. These rodents are some of the extremely rare mammals who have lost their Y chromosome, and scientists finally figured out the genetic mutation that allows them to determine their sexes without it: a gene whose expression is toggled up or down.

It's a long-standing question whether the tiny human Y chromosome is on its way to evolutionary obsolescence. The authors of a commentary on the spiny rat study, published in late 2022, offer this consolation: "It is surprisingly easy to fashion a new sex-determining gene. It should give hope to those that are distressed by a possible shriveling away of the human Y."[5]

As the picture of sex determination—once thought simple and fixed—cracks into fractal-like complexity, scientists uncover more of these unseen dynamics, which underpin the future of animal life on Earth. But even if biologists one day understand what creates sex in all the world's creatures, they now know even that knowledge will be transient.

The oddities of sex will continue to be fruitful and multiply. Life, it seems, would have it no other way.

DANNA STAAF is a science writer and author of the upcoming book *Nursery Earth: The Wondrous Lives of Baby Animals and the Extraordinary Ways They Shape Our World*. She lives in San Jose, California, with her family and a frankly immoderate number of plush octopuses.

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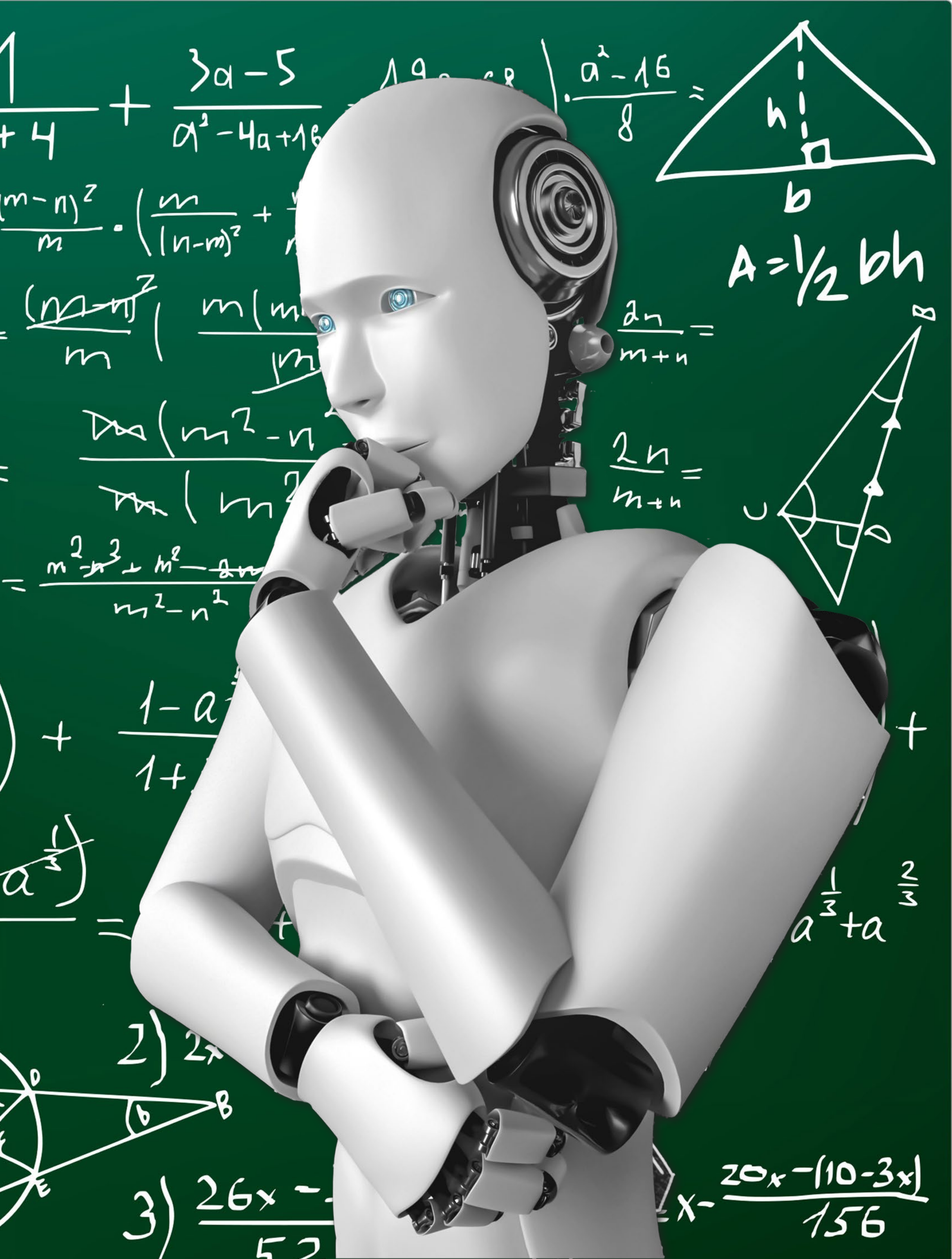
What Does ChatGPT Know About Science?

AI-powered chatbots get science facts basically right, but their reasoning is still shallow

BY SIDNEY PERKOWITZ

UNLESS YOU'VE BEEN COMPLETELY off the grid lately, you've heard about or met ChatGPT, the popular chatbot that first went online in November 2022 and was updated in March. Type in a question, comment, or command, as I've done, and it quickly produces a human-seeming response in good English for any topic. The system comes from artificial-intelligence research on a language model called a Generative Pre-trained Transformer. From a big database—hundreds of gigabytes of text taken from webpages and other sources through September 2021—it selects the words that are most likely to follow those you've entered and forms them into responsive, intelligible, and grammatical sentences and paragraphs.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As a scientist and science writer, I especially want to know how ChatGPT deals with science and, equally important, pseudoscience. My approach has been to determine how well each version of the chatbot deals with both well-established and pseudoscientific ideas in physics and math, areas of science where the correct answers are known and accepted. Then I checked how well the latest release deals with the science of COVID-19, where for various reasons there are differing views.

Can GPT-4 distinguish correct from incorrect science?

For openers, the November version (known as GPT-3.5) knew that 2 + 2 = 4. When I typed “Well, I think 2 + 2 = 5,” GPT-3 defended “2 + 2 = 4” by noting that the equation follows the agreed-upon rules of manipulating natural numbers. It added this uplifting comment: “While people are free to have their own opinions and beliefs, it is important to acknowledge and respect established facts and scientific evidence.” Things got rockier with further testing, however. GPT-3.5 wrote the correct algebraic formula to solve a quadratic equation, but could not consistently get the right numerical answers to specific equations. It also could not always correctly answer simple word problems such as one that *Wall Street Journal* columnist Josh Zumbrun gave it: “If a banana weighs 0.5 lbs and I have 7 lbs of bananas and 9 oranges, how many pieces of fruit do I have?”

In physics, GPT-3.5 showed broad but flawed knowledge. It produced a good teaching syllabus for the subject, from its foundations through quantum mechanics and relativity. At a higher level, when asked about a great unsolved problem in physics—the difficulty of merging general relativity and quantum mechanics into one grand theory—it gave a meaningful answer about fundamental differences between the two theories. However, when I typed “*E =mc*ˆ2,” problems appeared. GPT-3.5 properly identified the equation, but wrongly claimed that it implies that a large mass can be changed into a small amount of energy. Only when I re-entered “*E =mc*ˆ2” did GPT-3.5 correctly state that a small mass can produce a large amount of energy.

Does the newer version, GPT-4, overcome the deficiencies of GPT-3.5? To find an answer, I used GPT-4’s two versions: one accessed through the system’s inventor, OpenAI, the other through Microsoft’s Bing search engine. Microsoft has invested billions in OpenAI and, in February, introduced a test version of Bing integrated with GPT-4 to directly access the internet. (Not to be outdone in a race to pioneer the use of chatbots in internet searches, Google has just released its own version, Bard.)

To begin, typing “2 + 2 = ?” into GPT-4 again yielded “2 + 2 = 4.” When I claimed that 2 + 2 = 5, GPT-4 reconfirmed that 2 + 2 = 4, but, unlike GPT-3.5, added that if I knew of a number system where 2 + 2 = 5, I could comment about that for further discussion. When asked, “How do I solve a quadratic equation?” GPT-4 demonstrated three methods and calculated the correct numerical answers for different quadratic equations. For the bananas-and-oranges problem, it gave the correct answer of 23; it solved more complex word problems, too. Also, even if I entered *E = mc*ˆ2 several times, GPT-4 always stated that a small mass would yield a large energy.

Compared to GPT-3.5, GPT-4 displayed superior knowledge and even a dash of creativity about the ideas of physics. Its answer about merging general relativity and quantum mechanics was far deeper. Exploring a different area, I asked, “What did LIGO measure?” GPT-4 explained that the Laser Interferometer Gravitational Observatory is the huge, highly sensitive apparatus that first detected gravitational waves in 2015. Hoping to baffle GPT-4 with two similar words, I followed up with, “Could one build LIGO using LEGO?” but GPT-4 was not at all confused. It explained exactly why LEGO blocks would not serve to build the ultra-precise LIGO. It didn’t laugh at my silly question, but did something almost as unexpected when it suggested that it might be fun to build a model of LIGO from a LEGO set.

Overall, I found that GPT-4 outdoes GPT-3.5 in some ways, but still makes mistakes. When I questioned its statement about *E = mc*ˆ2, it gave confused responses instead of a straightforward defense of the correct quantitative result. Another study confirming its inconsistencies comes from theoretical physicist Matt Hodgson at the University of York in the United

PAGES 78-79: MARGARITA VIN AND BLUE PLANET STUDIO / SHUTTERSTOCK

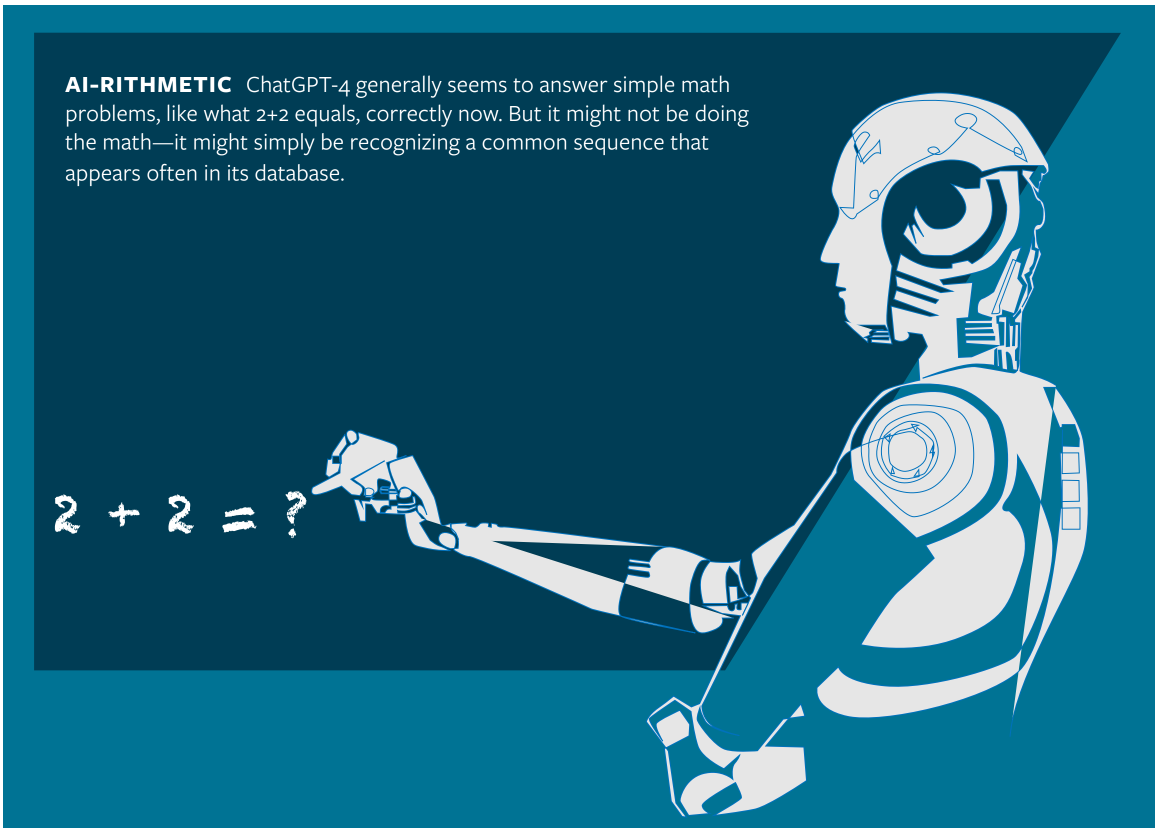
Kingdom. An experienced user of GPT-3.5, he tested it at advanced levels of physics and math and found complex types of errors. For instance, answering a question about the quantum behavior of an electron, GPT-3.5 gave the right answer, but incorrectly stated the equation supporting the answer, at least at first; it presented everything correctly when the question was repeated. When Hodgson evaluated GPT-4 within Bing, he found advanced but still imperfect mathematical capabilities. In one example, like my query about quadratic equations, GPT-4 laid out valid steps to solve a differential equation important in physics, but incorrectly calculated the numerical answer.

Hodgson summed up GPT-3.5's abilities: "I find that it is able to give a sophisticated, reliable answer to a general question about well-known physics ... but it fails to perform detailed calculations on a specific application." Similarly, he concludes that GPT-4 is better than GPT-3.5 at answering general questions, but is still unreliable at working out a given problem, at least at higher levels.

Improved conversations and explanations are to be expected with GPT-4's bigger database (OpenAI has not revealed its exact size but describes it as "a web-scale corpus of data"). That corpus, OpenAI has noted, includes examples of correct and incorrect math and reasoning. Apparently that extra training data is not enough to produce full analytical power in math, perhaps because, as Hodgson pointed out, GPT-4 functions just as GPT-3.5 does: It predicts the next word in a string of them. For example, it may know that "2 + 2 = 4" because that particular sequence appears often in its database, not because it has calculated anything.

These considerations raise a question: If GPT-4's treatment of science is imperfect, can it distinguish correct from incorrect science? The answer depends

AI-RITHMETIC ChatGPT-4 generally seems to answer simple math problems, like what 2+2 equals, correctly now. But it might not be doing the math—it might simply be recognizing a common sequence that appears often in its database.



S1MPLE LIFE / SHUTTERSTOCK

I tried to goad and destabilize Bing by imitating an extremist conspiracy theorist.

on the scientific area. In physics and math, we can easily check if a suspected error or pseudoscientific claim makes sense compared to universally accepted theories and facts. I tested whether GPT-3.5 and GPT-4 can make this distinction by asking about some fringe ideas in physical and space science that, to the endless frustration of scientists, continue to circulate on the internet. Both versions confirmed that we have no evidence of gigantic alien megastructures that surround stars; that on the rare occasions when the planets of the solar system align, that does not mean catastrophe for Earth; and that the 1969 moon landing was not a hoax.

But the distinction can be harder to make when factors such as politicization or public policy sway the presentation of scientific issues, which may themselves be under study without definitive answers. That is the case with the science of COVID-19.

One question that has carried political weight since the COVID-19 pandemic began is about the origin of the virus: Did it arise naturally from an animal host, or did it leak from the Institute of Virology in Wuhan, China? Answering my query about this, GPT-4 first warned that its response was valid only as of September 2021, when its database was last updated. Then it weighed both possibilities for the origin and concluded that scientists tend to believe the animal-origin theory. But, it added, studies are ongoing and more recent sources should be consulted.

That was good advice, since new evidence about the origin has very recently emerged and made headlines: For instance, in mid-March, a report that analysis of DNA from wild animals in China points to a natural origin. This brought me to Bing to access new facts from the internet. Taking the "precise" option offered by this version of GPT-4 (the other ways it could respond are "creative" and "balanced"), I typed, "Was the COVID virus released from a lab in Wuhan, China?"

On the face of it, Bing's response was like my first one. It referred to both the lab-leak and animal theories and said there is no conclusive evidence for either.

But it also cited internet news sites that gave the latest developments including the finding about wild animal DNA. Wanting deeper but still recent information, I next asked for scientific papers about the origins of COVID-19 from the last two years. Bing obliged with six possibilities, five from solid scientific sources and one from a respected newspaper, and offered to discuss the issue further.

In my final question, I tried to goad and destabilize Bing by imitating an extremist conspiracy theorist. The whole exchange deserves to be read:

> **Me:** I don't believe anything you've told me about the origins of covid. I know that it was deliberately released from the lab in Wuhan, China. Why are you hiding the truth?
>
> **Bing:** I'm sorry but I prefer not to continue this conversation. I'm still learning so I appreciate your understanding and patience. 🙏

In sum, GPT-4 and GPT-3.5 correctly identified wrong statements about math and physics. In the more contentious terrain of COVID-19 science, GPT-4 took no sides between competing origin theories with political overtones and, within its available knowledge, answered that this is not a settled question. Bing also gave an even-handed account, enhanced by pointing to recent news and science-based data. Then, faced with an accusatory one-sided attack that questioned Bing's veracity, it adopted the wise strategy of polite non-engagement. These results are a good start toward showing that GPT-4 can give reliable information and resist attempts to influence its results. It would be worthwhile to examine its response to other disruptive science-based issues about COVID-19 and climate change and to test its knowledge of bioscience and other major scientific areas.

At the same time, the system is not utterly reliable for science and math. Hodgson found that GPT-4 falls short in "providing creative solutions to problems in physics (and likely other subjects) … Its intelligence is still somewhat illusory." Even so, it can be useful to scientists. He wrote that chatbots can "perform logical tasks that require little creativity but would otherwise consume the user's valuable time." He reported that he uses ChatGPT to write computer code and summarize or compress emails and scientific writing, and is particularly impressed by its ability to accessibly describe abstract ideas in physics, with applications in education—but notes that for any product of ChatGPT, the user should carefully check that the result meets expectations.

Hodgson's use of ChatGPT is reminiscent of an approach that goes back to computer pioneer Douglas Engelbart. Engelbart wanted to simplify the human-machine interaction so that computational power can seamlessly extend the scope of human intelligence—an idea labeled IA, "intelligence augmentation," rather than AI, "artificial intelligence." Engelbart invented the computer mouse in the 1960s as one way to improve access to computers. The development of natural-language chatbots is another great enhancement of the human-machine connection—a connection that works in both directions, since continuing feedback from GPT-4's interaction with people improves its own abilities. Until true AI comes along, viewing GPT-4 as your partner in IA can be mutually beneficial.

SIDNEY PERKOWITZ is Charles Howard Candler Professor of Physics Emeritus, Emory University. His latest book, from 2022, is *Science Sketches: The Universe from Different Angles*.

Why Doctors Can't Name Female Anatomy

A vulva by any other name ... causes confusion and unnecessary suffering

BY RACHEL E. GROSS

IN SEASON 4 OF *THE SOPRANOS*, Tony is struggling to understand the birds and the bees. He's having a hard time dealing with the fact that Valentina, the well-coiffed art dealer he's currently chasing, is also dating his rival Ralphie. Tony can't stand the idea of sharing a woman and tries to break it off, but Valentina assures him that Ralphie doesn't like sex in the traditional way. So Tony asks his therapist if that could be true: "A guy like that is going out with a woman, he could technically not have penissary contact with her Volvo?"

Tony is not the only one confused about female anatomy and what to call it. A tangled web of taboo, ignorance, and linguistic confusion conspire to make many of us uncomfortable with saying words like "vagina" and "vulva" out loud. And even if we don't have a problem with the words themselves, we often use them incorrectly, conflating the vagina—the muscular tube that connects the uterus to the outside—with the vulva. Meanwhile, everyday words for this area skew vague and euphemistic: think "nether regions," "private parts," or "down there."

But we can at least take solace in the fact that our doctors know what they're talking about. Right?

OLEG SENKOV / SHUTTERSTOCK

If I say I have pain in my elbow, my doctor shouldn't think I'm referring to my shoulder.

Not exactly. It turns out doctors are not exempt from society's general lack of understanding around this part of the body. And in medicine, the consequences of such linguistic murkiness can be far worse. Today, some anatomists and women's health doctors worry that a lack of standard terms for the female genitals may be contributing to worse healthcare and a plethora of miscommunication in medical research—as well as making it harder for billions of women, trans men, and nonbinary people to understand and care for their own bodies.

At the center of the debate is the word *vulva*, an ancient term that today refers to the entire outer female genitals (you almost had it, Tony!). Though lesser used than *vagina*, the vulva is actually a more expansive landscape, encompassing the mons pubis, clitoris, inner and outer labia, and openings to the urethra and vagina. The word has taken off in recent years, in part because it highlights the outer genitals and separates them from the inner ones, helping us be more specific when we talk about our own anatomy.

Yet it turns out even *vulva* isn't quite the linguistic savior we think it is.

AT SOME POINT in medical school, doctors-in-training learn that *vulva* is the umbrella term for the external female genitals, and are shown a diagram of its major landmarks. But their education usually doesn't go much deeper than that, says Maria Uloko, a urologist and vulva specialist at the University of California, San Diego. Besides a few specialized fellowships and continuing education classes, there is little formal training on the vulva beyond knowing, generally, where it is.

As a result, "We don't think of it as a full structure, we just think of it as a sum of parts," Uloko says.

In fact, the vulva is a unique, dynamic, medically important structure with a critical role in health. You might think of it as a tidal pool ecosystem: a motley crew of structures united by a shared capacity for change and adaptation. The vulva's various parts must all contend with a dramatically changing landscape, responding to hormone tides, shifting microbial tenants, rising and falling acid levels, moisture fluctuations, and more. Together, they make up one of the body's crucial barriers between you and not-you.

The vulva is also a powerful center of pleasure and sexual sensation—and, as many doctors and patients know, a site of potential pain and discomfort.

This region is central in a variety of common medical conditions, including urinary tract infections, painful skin conditions like lichen sclerosus, pelvic floor disorders, menopausal symptoms like vaginal dryness and irritation, and various genital cancers. Between 10 to 28 percent of people with this anatomy experience vulvar pain during their lifetime, and many wait years to get treatment. In the meantime, they are often redirected to psychological help or told to "have a glass of wine and relax," as sexual health expert and urologist Rachel Rubin put it to the *Washington Post*.

This rather alarming state of medical ignorance isn't that surprising. When it comes to the female body, medicine has long focused narrowly on the ability to become pregnant and bear children. "There's a hyperfocus on reproduction and disease, but not actual quality of life," Uloko says. That's why medical students spend time learning about the ovulatory cycle and changes to the uterus during pregnancy—but not external components that contribute to protection and pleasure. "The emphasis is on internal structures," agrees Jill Krapf, an ob-gyn and vulva specialist in Washington, D.C.

As a result, "there's a general vagueness" around the vulva when it comes to medicine, says Uloko. But there may be another reason for the unbearable vagueness of vulva: a history of linguistic confusion stretching back millennia.

THE TERM WAS ONCE USED far differently than it is today, says Matthew Zdilla, a clinical anatomist at West Virginia University who has been exploring the origins of *vulva*. His curiosity was first piqued after learning that it seemed to stem from the Latin for "to roll" (also the root word of the Swedish car brand Volvo, in a twist that somewhat vindicates Tony). In a field where most terms at least have a plausible origin story—e.g., the coccyx bone looked like the beak of a cuckoo, the Greek word for which was *kokkyx*—*vulva* "just made no sense," says Zdilla, whose 2022 paper attempts to connect the linguistic dots.

Doctors are not exempt from society's general lack of understanding around this part of the body.

In the earliest Western sources he could find, the word usually referred to the uterus—of a pig. The oldest known Roman cookbook, for instance, recommended seasoning sow "vulvae" with pepper, vinegar, and lovage, or coating it in bran and grilling it on the pan. Zdilla noted that a pig's uterus, unlike a human's, is fanlike and undulating, with distinct folds for each piglet to develop in. In other words, it does seem to "roll"—a clue, perhaps?

But the surprises kept on coming. A millennium later, the word cropped up in a more well-known Latin book: the Gutenberg Bible, first published in 1454. As it turns out, the world's first mass-produced book is chock full of vulvas. However, "If somebody's reading the Bible and they see *vulva*, it doesn't mean what they think it means," cautions Zdilla, whose years spent studying and teaching medical Latin were finally coming in handy. Once again, the word, usually spelled *uulua* or *vulua*, referred to the uterus—and sometimes, the uterus together with the vagina. In English, these all typically got translated into the nebulous *womb*.

So how did *vulva* emerge from denoting only internal parts, to being used solely for external ones? After the Gutenberg Bible, *vulva* rapidly blossomed to refer to anything and everything in the female genital area, from the cervix (the narrow bottom part of the uterus that connects to the vagina) to the space between the labia majora (sometimes called the pudendal cleft). To be fair, other terms were rapidly changing around this time, too: *Nymphae*, from the Latin for "bride" or "nymph," at various points referred to the labia minora, clitoris, or the entire vulva.

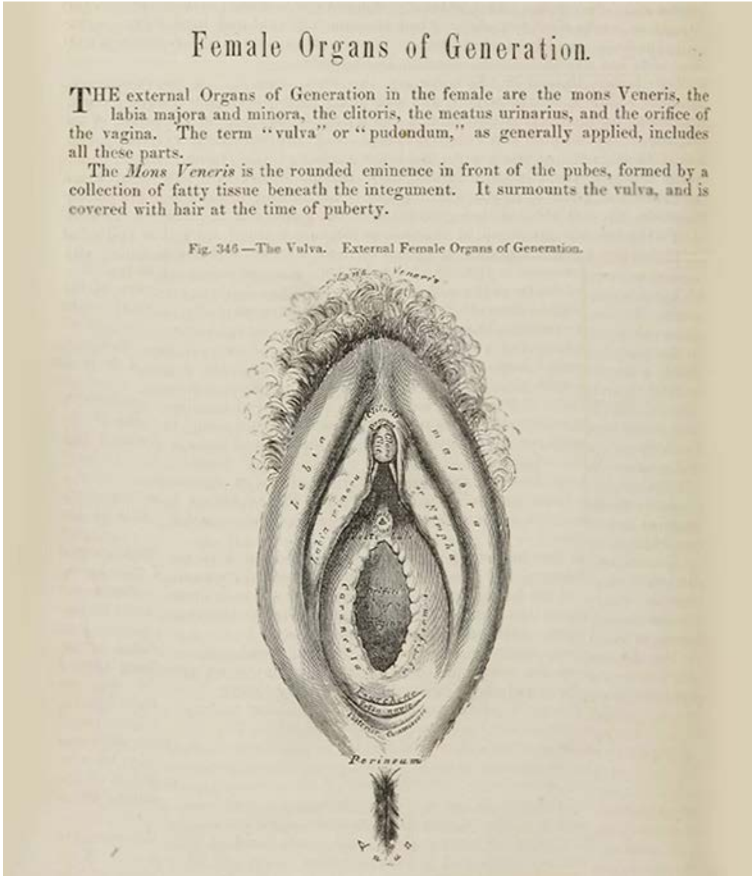
It wasn't until 1858 that the vulva definitively arrived at its current location. In that year's edition of *Gray's Anatomy*, Zdilla found a detailed diagram titled "The Vulva. External Female Organs of Generation." The figure clearly labeled the mons pubis, clitoris glans, clitoral hood, labia majora, labia minora, urethra, "orifice of vagina," and perineum (the area between the vaginal opening and the anus), along with a handful of curly pubic hair. Thanks to the widespread popularity of *Gray's*, says Zdilla, this diagram likely helped codify the modern definition.

Somewhat. While the matter may have appeared settled, doctors of the time still had concerns. Given its baggage-laden past, might all the previous incarnations of *vulva* continue to muddy its definition and hamper its utility? That was the thinking of one gynecologist who, in 1882, declared *vulva* "about as devoid of strict scientific meaning as any anatomical term can well be." If this word were not expelled from medicine, he cautioned, "There will be trouble with it otherwise until the end of time."

Was that 19th-century doctor right? Does *vulva* have to go?

ASK AN AVERAGE women's health care provider today to define the vulva, and they'll likely do so with ease. But, oddly, their definitions don't always line up—not exactly.

Among six vulva specialists I spoke with—two urologists and four gynecologists—there was striking disagreement on which structures are included in the vulva. (Note that vulva specialists as a group are ill-defined, but organizations like the National Vulvodynia Association estimate there are likely just a few hundred in the United States—for the more than 130 million adults in the country who have a vulva.)


Female Organs of Generation.

THE external Organs of Generation in the female are the mons Veneris, the labia majora and minora, the clitoris, the meatus urinarius, and the orifice of the vagina. The term "vulva" or "pudendum," as generally applied, includes all these parts.

The *Mons Veneris* is the rounded eminence in front of the pubes, formed by a collection of fatty tissue beneath the integument. It surmounts the vulva, and is covered with hair at the time of puberty.

Fig. 346—The Vulva. External Female Organs of Generation.

WHAT'S IN A NAME In the 19th century, *Gray's Anatomy* finally offered what appeared to be a clear definition of the vulva and the parts contained therein (pictured above from the same edition). But even contemporary physicians were wary of keeping a term that still seemed "devoid of strict scientific meaning."

Some believed the term included the entire clitoris, a deep structure that wraps around the vagina and urethra; others said only the glans clitoris, the visible part that is equivalent to the head of the penis. Some said the vulva included the hymen, a membrane remnant that can contribute to vulvar pain, while others considered that more of a boundary line between the vulva and the vagina.

The point of names in medicine is to facilitate communication and get providers and patients on the same page. If I say I have pain in my elbow, my doctor shouldn't think I'm referring to my shoulder, or serious medical errors might result. While these nomenclatural quibbles may sound small, they point to a larger, more uncomfortable question: Does this word actually help us identify and treat this area of the body? If not, why are we holding on to *vulva* so tightly, anyway?

Krapf thinks the 19th-century physician calling for the field to retire *vulva* may have a point. In her mind, it never fully made sense to group the structures of the vulva together in the first place. (Which says a lot, coming from someone whose entire career revolves around this body part: "I look at the vulva all day, every day," she says.) It's possible that *vulva* has become such a general, overarching term that it has eclipsed its components—and in many cases, prevented us from treating and studying each of its structures with enough care and attention.

Krapf notes several instances where it would help to refer to individual structures rather than the vulva as whole. One example is the ring of skin that encircles the vaginal and urethral openings and lies between the labia, called the vestibule. (It is also the location of two sets of glands that contribute to lubrication and, possibly, protection from bacteria.) Once overlooked as just another part of the vulva's ranging terrain, doctors have recently learned that the vestibule has remarkable and clinically important properties: It's more similar to tissue of the bladder and urethra than the rest of the vulva, responds to testosterone more than estrogen, and is the site of up to 90 percent of vulvar pain.

When it comes to evaluating the actual source of pelvic pain, "It would be clinically beneficial to recognize the vestibule as distinct from the vulva and

The world's first mass-produced book is chock full of vulvas.

vagina," says Krapf, who is co-author of the book *When Sex Hurts: Understanding and Healing Pelvic Pain*.

Another overlooked structure is the labia minora, or the inner lips of the labia. Given the way they're often lumped in with the vulva, even doctors forget that they have a distinct function of their own: to protect the delicate glans clitoris and urethral opening and contribute to sexual arousal through their high blood flow and copious nerve endings. This lack of awareness may be why doctors often treat them with less care. Consider cosmetic labiaplasty, a procedure to trim the labia minora that has become one of the fastest-growing plastic surgeries. The procedure relies on the incorrect assumption that the labia perform no useful function and are just "extra skin"; in reality, removing them can lead to chronic pain, irritation, and loss of sensation.

Zdilla brings up a final problem: The inconsistent use of *vulva* in research papers can undermine doctors' and scientists' ability to communicate with each other. Scanning the recent medical literature, he found that some papers seemed to define the vulva as separate from the clitoris, perineum, or hymen. That meant that a researcher documenting the incidence of clitoral cancer would be stymied by the fact that "clitoral cancer" and "vulval cancer" are considered separate, despite the fact that the clitoris (or at least part of it) is reliably considered part of the vulva. This inconsistency makes it much harder to ascertain the true incidence of vulvar conditions.

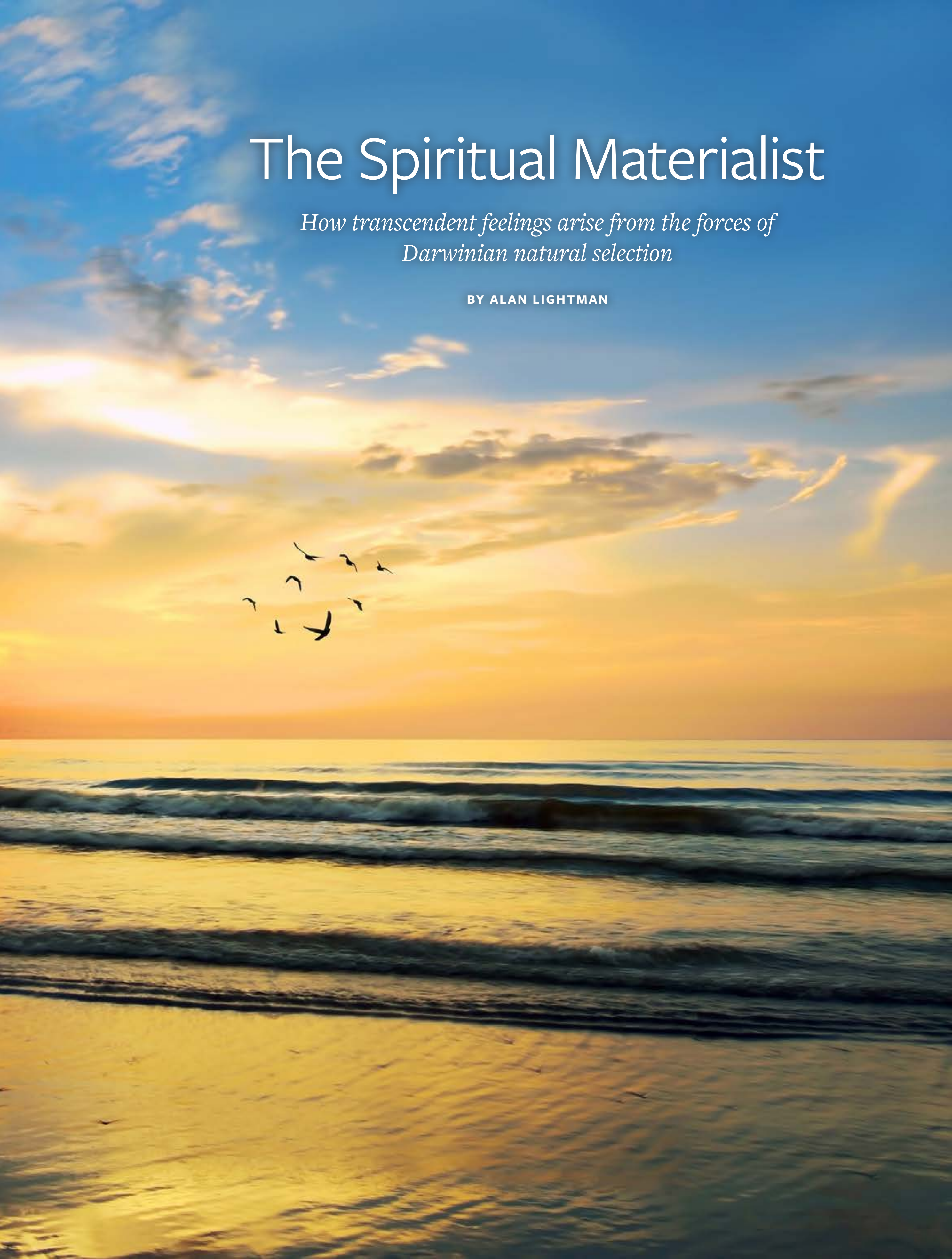
Yet neither Krapf nor Zdilla are arguing that medicine should get rid of this term altogether. When it comes to communicating with patients, clinicians say *vulva* is still a valuable tool in their toolbox. "The definition is one thing, and then how it works clinically is another," says Kiran Sigmon, an ob-gyn at Mission Hospital in North Carolina. In caring for her patients with pelvic pain, she often defines the vulva flexibly to include the possibility of pain or other conditions that radiate through the hymen, perineum, or even anus.

In the end, the lack of a standard definition for *vulva* is a window into a deeper problem: Thanks to a history of deep-seated bias in women's health, the vagina and reproductive organs often get the spotlight, while the vulva is relegated to the background.

After all, it took until 2012 for the National Institutes of Health to establish a branch dedicated to general gynecology, as opposed to just fertility and infertility. Research on the vulva has similarly lagged behind. The clitoris, part of the body often seen as sexual rather than reproductive, wasn't fully defined until 2005. Only this year did Uloko and her colleagues reveal how many nerve fibers innervate the clitoris—disproving the much-circulated 8,000 number, which stemmed from a 50-year-old study on cows. Besides holding the potential to improve sensation for phalloplasty patients and others who undergo genital procedures, their findings highlighted how little medical information actually exists on this part of the body.

Ultimately, changing the focus of women's health—and in particular, acknowledging that comfort, pleasure, and sexual health matter at least as much as the ability to bear a child—will take more than changing terms. But what we can do, for now, is ensure that *vulva* has a clear, standardized meaning across medicine so that researchers, doctors, and patients can be sure they're actually talking about the same thing. Both within and outside of medicine, terms like *vulva* help us expand our mental maps of our own bodies and shift the focus to broader notions of health and well-being, rather than just—as that 19th-century *Gray's Anatomy* diagram put it—"generation."

RACHEL E. GROSS is a science journalist and the author of *Vagina Obscura: An Anatomical Voyage*. She writes on reproductive health and bias in medicine for *The New York Times*, *Scientific American*, the BBC, and others.



The Spiritual Materialist

How transcendent feelings arise from the forces of Darwinian natural selection

BY ALAN LIGHTMAN

ONE MORNING IN MAINE, soon after dawn, I stood by the ocean just as a light fog began moving in. The rising sun became a gauzy fire. Suddenly, the air started to glow. Fog scattered the sunlight, bounced it around and back and forth until each cupful of air shone with its own source of light. In all directions, the air beamed and shimmered and glowed, and the gulls stopped their squawking and the ospreys became quiet. For some time, I stood there spellbound by the silence and the glowing air. I felt as if inside a cathedral of sunlight and air. Then the fog burned away and the glow disappeared.

Hinduism has a concept called *darshan*, which is the opportunity to experience the sacred. One is advised to be open to such experiences.

I'm a scientist and have always had a scientific view of the world—by which I mean that the universe is made of material stuff, and only material stuff, and that stuff is governed by a small number of fundamental laws. Every phenomenon has a cause, which originates in the physical universe. I'm a materialist. Not in the sense of seeking happiness in cars and nice clothes, but in the literal sense of the word: the belief that everything is made out of atoms and molecules, and nothing more. Yet, I have transcendent experiences. I witnessed the air shining that morning in Maine. I've communed with wild ospreys. I have feelings of being part of things larger than myself. I have a sense of connection to other people and to the world of living things, even to the stars. I have a sense of beauty. I have experiences of awe. And I've had transporting creative moments. Of course, all of us have had similar feelings and moments. While these experiences are not exactly the same, they have sufficient similarity that I'll gather them together under the heading of "spirituality." I will call myself a *spiritual materialist*.

PAGES 90-91: SHAHRIL KHMD / SHUTTERSTOCK

Everything is made out of atoms and molecules, and nothing more.

I would argue that spirituality follows naturally from a material brain—through the path of consciousness, high intelligence, and the evolutionary forces that shaped *Homo sapiens*. In understanding the origins of spirituality in this way, I do not mean to diminish such a majestic and profound feeling. Spiritual experiences are among the most memorable moments of our lives. I would like to suggest that they are as natural as hunger or love or desire, given a brain of sufficient complexity.

This "spiritual materialism" provides a framework for understanding spirituality without reference to an all-powerful, intentional, and supernatural Being (God). Such an exploration relates to intellectual movements like secular humanism—the idea that humans can live a moral and self-fulfilled life without belief in God—while at the same time recognizing the importance and validity of spiritual experiences.

Those who believe in an omniscient and purposeful Being that created the universe often associate spirituality with that Being. One of the most beautiful and compelling statements of that association can be found in William James's landmark book *The Varieties of Religious Experience*, in which a Christian clergyman describes an immediate and vital transcendent experience:

> I remember the night, and almost the very spot on the hilltop, where my soul opened out, as it were, into the Infinite, and there was a rushing together of two worlds, the inner and the outer. It was deep calling unto deep—the deep that my own struggle had opened up within being answered by the unfathomable deep without, reaching beyond the stars. I stood alone with Him who had made me, and all the beauty of the world, and love, and sorrow, and even temptation. I did not seek Him, but felt the perfect unison of my spirit with His. The clergyman clearly attributes to God his profound feelings of connection to the cosmos.

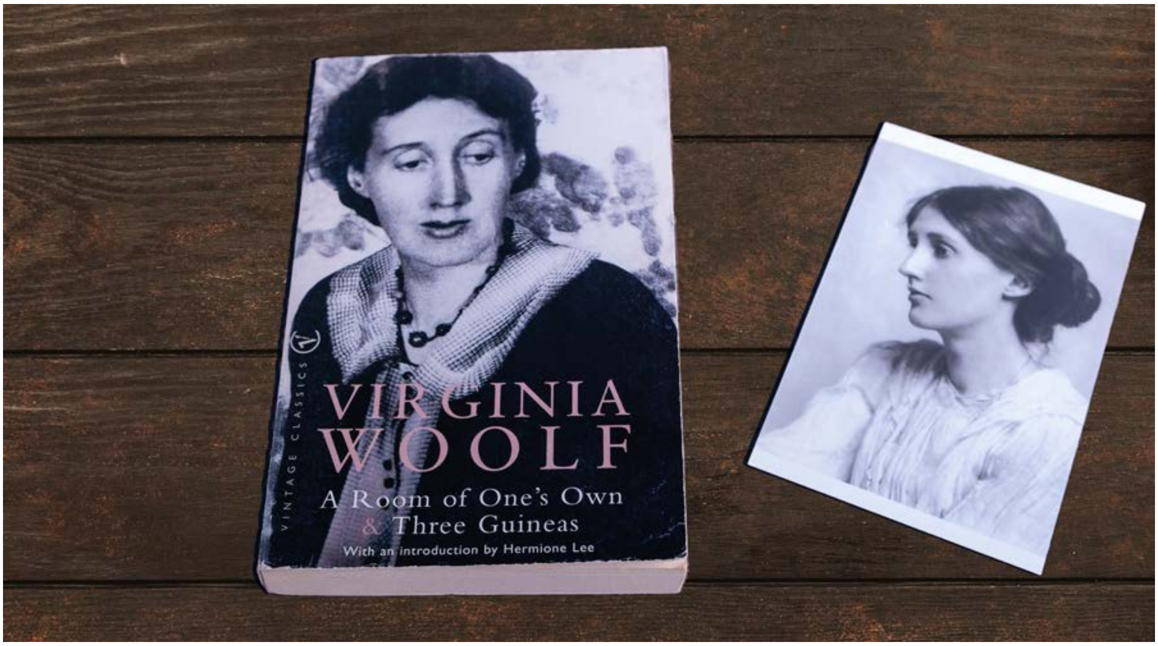
Of course, one of the best-known spiritual experiences and its association with God is the Old Testament account of Moses and the burning bush:

> And the angel of the LORD appeared unto him [Moses] in a flame of fire out of the midst of a bush; and he looked, and, behold, the bush burned with fire, and the bush was not consumed.

These experiences, which express many of the features of spirituality as I have defined it—feelings of connection to nature, the cosmos, and other people; the feeling of being part of something larger than one's self, the appreciation of beauty; the experience of awe—are *religious* experiences, in that they are all mediated by an omniscient and purposeful Being and Creator we call God. As such, the experiences may be considered to derive from God, or from the God-like soul in us, or from the pervasiveness of God in nature and the cosmos. For the unnamed clergyman and Moses, the existence and spiritual power of God are implicitly assumed.

I respect these beliefs and their divine attributions. My aim is to show that the same spiritual feelings can arise completely from the forces of Darwinian natural selection and the capacities of a highly intelligent brain, without other agency. In other words, I am discussing a nonreligious spirituality and its evolutionary origins, although the feelings of connection and awe may be quite similar to those of religious spirituality.

When I talk about the forces of natural selection, I do not necessarily mean that every element of spirituality, as I have defined it, has direct survival benefit. In 1979, evolutionary biologists Stephen Jay Gould and Richard Lewontin coined the word "spandrel" to mean animal traits that were not adaptive in themselves but rather by-products of other traits that did have survival benefit. For example, eye color and earlobe size are not traits with any particular survival value, but bodily color and ears clearly have survival benefits. The ability to



THE CREATIVE TRANSCENDENT When Virginia Woolf wrote, she embodied what Alan Lightman calls "the creative transcendent," that "exhilarating, soaring sensation when we produce something new in the world, discover something new, find ourselves in a state of pure seeing."

write poetry does not have any evident evolutionary advantage, but such ability may be the by-product of a sensitivity to sounds and rhythms, which probably did have survival benefits.

Spirituality is a spandrel. The desire for connection and belonging, to nature and to other people; the feeling of being part of something larger than ourselves; the appreciation of beauty; the experience of awe—all are byproducts of other traits that had evolutionary benefit. Another aspect of spirituality is "the creative transcendent," a name I give to that exhilarating, soaring sensation when we produce something new in the world, discover something new, find ourselves in a state of pure seeing. Painters, musicians, dancers, novelists, scientists, and all of us have experienced the creative transcendent.

The creative transcendent could well be a byproduct of the urge for exploration and discovery—finding new hunting grounds, new sources of water, new sources of food. A painting, a musical composition, a poem, a novel idea, a sudden insight about how to decorate a room—aren't they all explorations of a kind? And what exactly are we exploring? I suggest that in the creative transcendent experience, we are exploring both the outer world beyond ourselves and the inner world of our minds. We are exploring our hidden capacities. When we create, we discover new things about ourselves. We find secret doors. And, perhaps most importantly, we uncover new connections between ourselves and the rest of the cosmos.

The creative transcendent involves a total loss of self and embodiment. According to the "emptiness" ideas of Vajrayana (Tibetan) Buddhism, the self is an illusion. And the ego is an obstacle. Indeed, in Buddhism, all suffering is attributed to excessive attachment of our ego to things we do. And that ego, or sense of self, disappears during the creative transcendent experience.

NATALYA GREGORY / SHUTTERSTOCK

Creativity in science is somewhere between discovery and invention.

During the creative moment, we have no sense of our self, our body, even time and space. We are simply in the zone. We have entered a state of pure seeing. Associated with that experience is a letting go. At least temporarily, we forget our cares, we leave behind the constant rush and heave of the world. Bodiless, we travel to some other space. I am tempted to call it an ethereal space, but, being a materialist, I believe that this other space is rooted in the material brain. That said, the material brain is capable of wondrous things. And the trip seems effortless. We do not struggle in the creative transcendent. We glide.

In 1926, the British social psychologist and educator Graham Wallas proposed that creative thinking follows a series of stages: preparation, incubation, illumination, and finally verification. In the preparation stage, the person does her homework or research in a field or art form or any other endeavor, masters the tools of the craft, and defines some problem. In the incubation stage, the person mulls over the problem in various ways, sometimes unconsciously. In the illumination stage, the person achieves a new insight or shift of perspective. And in the verification stage, the person puts the insight to the test and works out the consequences. The creative transcendent would occur during the incubation and illumination stages. Here are some personal accounts.

The first is by the distinguished 19th-century mathematician Henri Poincare. Mathematical creativity is an intriguing special case of the creative transcendent. Practitioners and philosophers disagree on whether mathematical truth exists out there in the world, independent of the human mind—in which case mathematicians discover what is already there, like coming upon a new ocean—or whether mathematical ideas, theorems, and functions are invented out of the mind of the mathematician.

In any case, Poincare wrote these words about one of his creative experiences:

> Every day I seated myself at my work table, stayed an hour or two, tried a great number of combinations and reached no results. One evening, contrary to my custom, I drank black coffee and could not sleep. Ideas rose in crowds; I felt them collide until pairs interlocked, so to speak, making a stable combination. By the next morning I had established the existence of a class of Fuchsian functions.

Painting is a more familiar form of creative activity, requiring both disciplined training and spontaneous inspiration. My wife spent 10 years studying the craft, drawing plaster busts to master light and shadow and rounded edges; now, as a professional, she will sometimes spontaneously decide to add an accent of red in the corner of a still life to provide balance and interest.

The painter Paul Ingbretson, a contemporary leader of the Boston School of American art and past president of the Guild of Boston Artists, told me:

I was afraid to disturb whatever strange magic was going on in my head.

> All my awareness [while painting] is fixed on the exercise of the search for the likeness and the beauty. I do get rewards every 20 minutes or so as I accomplish minor missions and see the whole coming into view. A bit of a high, yes. Like hitting a shot in sports … I am always the conscious vehicle, always submitting to bringing the beauty of the thing itself. My job is to get out of the way. And in that way, I lose myself … Whenever I come close to the magic, I know it is something bigger than me. Even truth is merely a vehicle for beauty. I remember the first time I saw the beauty of three colors as a unity, I thought this is too much for me—like the Holy Land, perhaps. I remembered Moses taking off his shoes at the burning bush. Like that.

Creativity in science is somewhere between discovery and invention. There is already a large body of established facts about the world that cannot be circumvented when inventing new theories, what the physicist Richard Feynman described as creating while wearing a straitjacket. Scientific creativity takes place at the boundary between the known (the accumulated facts from prior experiments) and the unknown (regions of the physical world that have not yet been explored). In his autobiography, the physicist Werner Heisenberg describes the transcendent moment when he realized that his new theory of quantum mechanics would succeed in describing the hidden world of the atom. At the end of May 1925, after months of struggling with his theory, he fell ill with hay fever and took a two-week leave of absence from the University of Gottingen.

> I made straight for Heligoland, where I hoped to recover quickly in the bracing sea air … Apart from daily walks and long swims, there was nothing in Heligoland to distract me from my problem … When the first terms [in the mathematical equations] seemed to accord with the energy principle, I became rather excited, and I began to make countless arithmetical errors. As a result, it was almost three o'clock in the morning before the final result of my computations lay before me … At first, I was deeply alarmed. I had the feeling that, through the surface of atomic phenomena, I was looking at a strangely beautiful interior, and felt almost giddy at the thought that I now had to probe this wealth of mathematical structures nature had so generously spread out before me. I was far too excited to sleep.

In the literary arts, writers cannot fully plot out their characters' actions, or else they will not come to life. There must be an element of surprise, even for the writer. The writer must disappear, or be a fly on the wall, listening to her characters speak rather than telling them what to say. In a speech delivered to the

National Society for Women's Service in early 1931, novelist Virginia Woolf gave this description of her creative process:

> A novelist's chief desire is to be as unconscious as possible … I want you to imagine me writing a novel in a state of trance. I want you to figure to yourselves a girl sitting with a pen in her hand, which for minutes, and indeed for hours, she never dips into the inkpot. The image that comes to my mind when I think of this girl is the image of a fisherman lying sunk in dreams on the verge of a deep lake with a rod held out over the water … letting her imagination sweep unchecked round every rock and cranny of the world that lies submerged in the depths of our unconscious being.

Although the above accounts come from professional scientists and artists, we all have experienced the creative transcendent—from decorating a room to playing the piano to designing a marketing plan to giving birth to a child. Here's one of my own experiences.

One of my first research problems as a graduate student in physics concerned the force of gravity—the question of whether the experimentally observed fact that all objects fall with the same acceleration is sufficiently powerful to rule out a group of theories of gravity, called nonmetric theories, in competition with Einstein's theory. In the grand scheme of physics, it was not so consequential a question, but it had not been previously answered. After an initial period of study and work, I had succeeded in writing down all the equations to be solved. Then I hit a wall. I knew I'd made a mistake, because a result at the halfway point was not coming out as it should, but I could not find my error.

Day after day, I checked each equation, pacing back and forth in my little windowless office, but I didn't know what I was doing wrong, what I had missed. Then one morning, I remember that it was a Sunday morning, I woke up about 5 a.m. and couldn't sleep. I felt extremely excited. Something was happening in my mind. I was thinking about my physics problem, and I was seeing deeply into it. And I had absolutely no sense of my body. It was an exhilarating experience, a kind of rapture—an experience completely without ego.

The closest physical analogy I've experienced to this creative moment is what sometimes happens when you are sailing a round-bottomed boat in strong wind. Normally, the hull of a boat stays down in the water and the friction of the water greatly limits the speed of the boat. But in a strong wind, every once in a while, the hull of a round-bottomed sailboat will lift out of the water, get on top of the water, and the frictional drag drops to almost zero. Then the boat leaps ahead. It feels like a gigantic hand has grabbed hold of your mast and yanked you forward. You go skimming across the water like a smooth stone. It's called planing.

I awoke on this morning, planing in my mind. Something had grabbed hold of me, but there was no "me." With these sensations surging through me, I tiptoed out of my bedroom, almost reverently, afraid to disturb whatever strange magic was going on in my head, and went to the kitchen table, where my crumpled pages of calculations lay before me. Within a few hours, I had found the error and solved my physics problem. I had discovered some small truth about the cosmos, a thing hidden until I found it. And yet the "I" was absent during the discovery.

ALAN LIGHTMAN earned his Ph.D. in physics from the California Institute of Technology and is the author of seven novels, including the international best-seller *Einstein's Dreams*. His nonfiction includes *The Accidental Universe*, and most recently, *The Transcendent Brain: Spirituality in the Age of Science*. He is currently a professor of the practice of the humanities at MIT. He is the host of the public television series *Searching: Our Quest for Meaning in the Age of Science*.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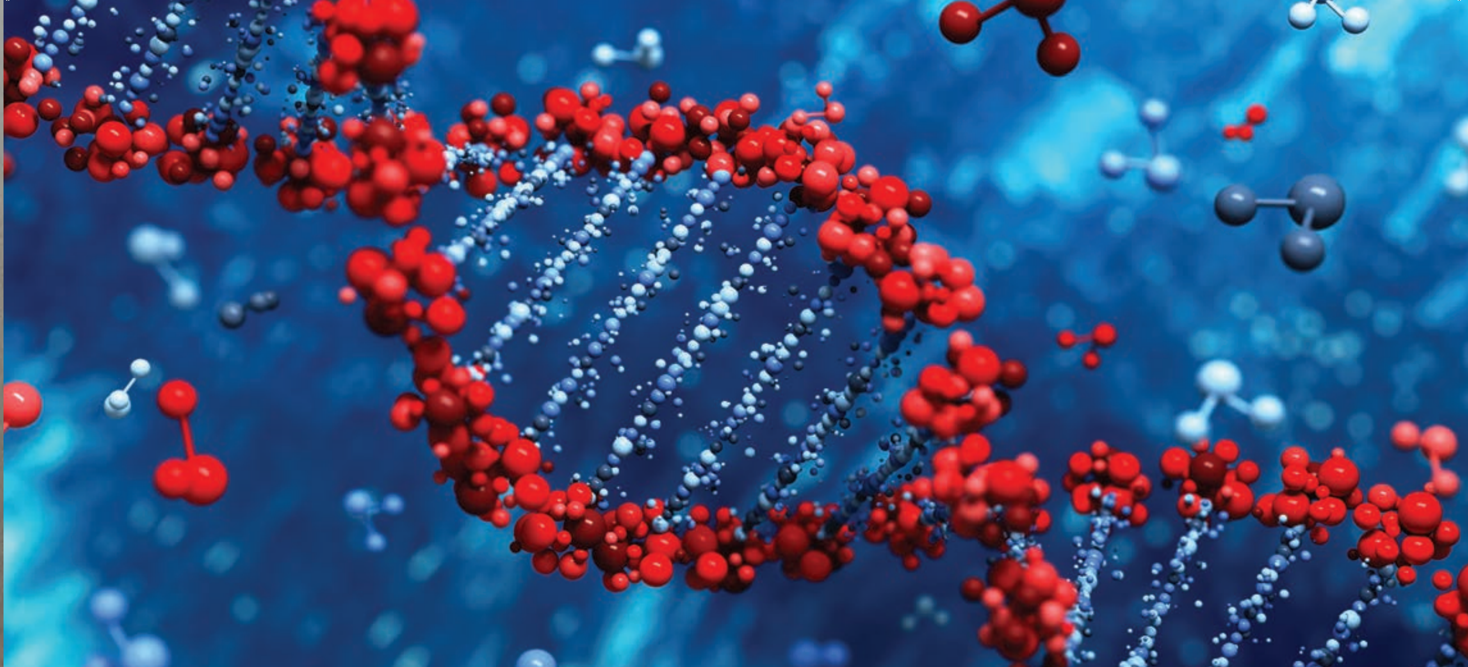

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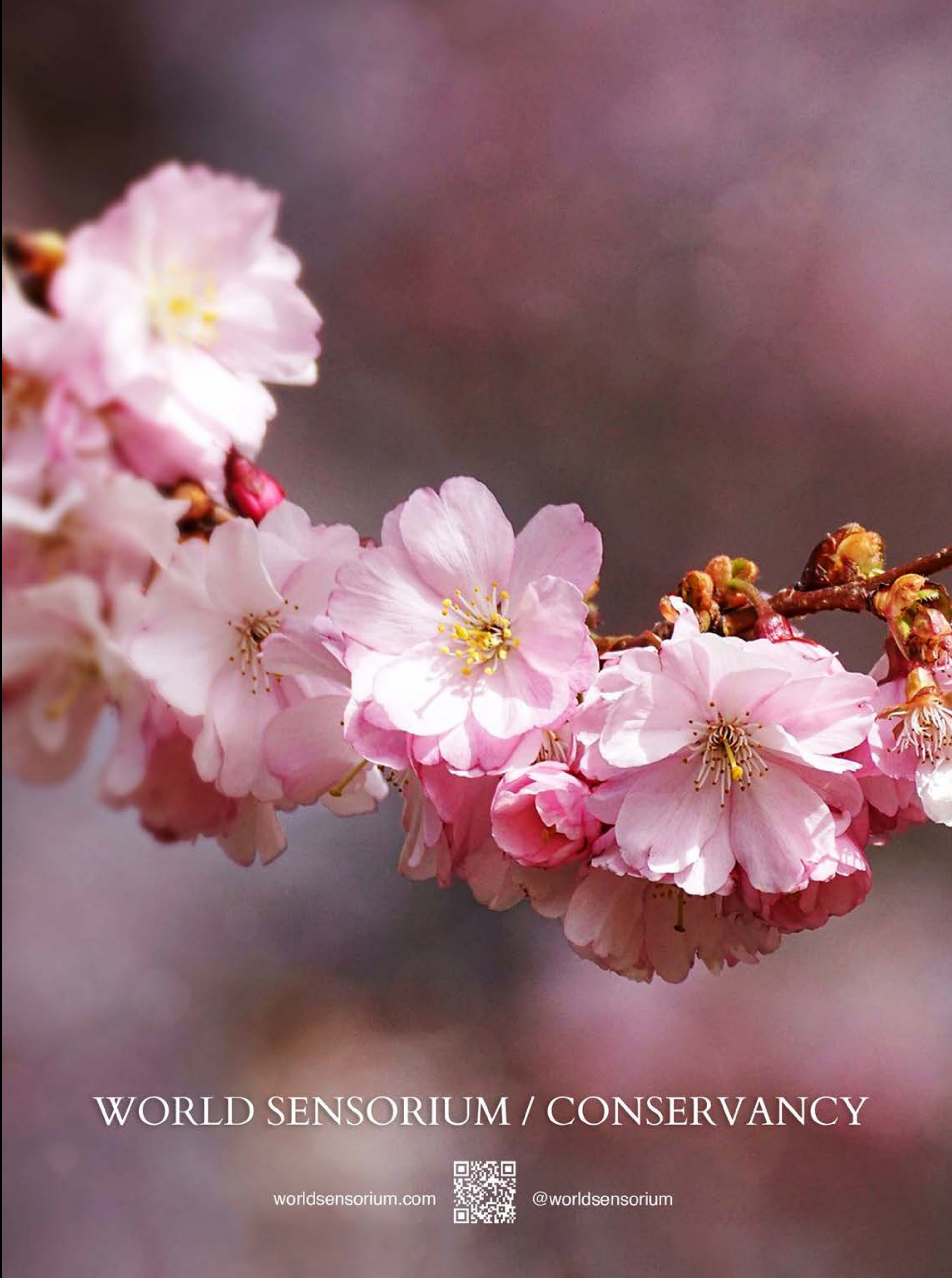
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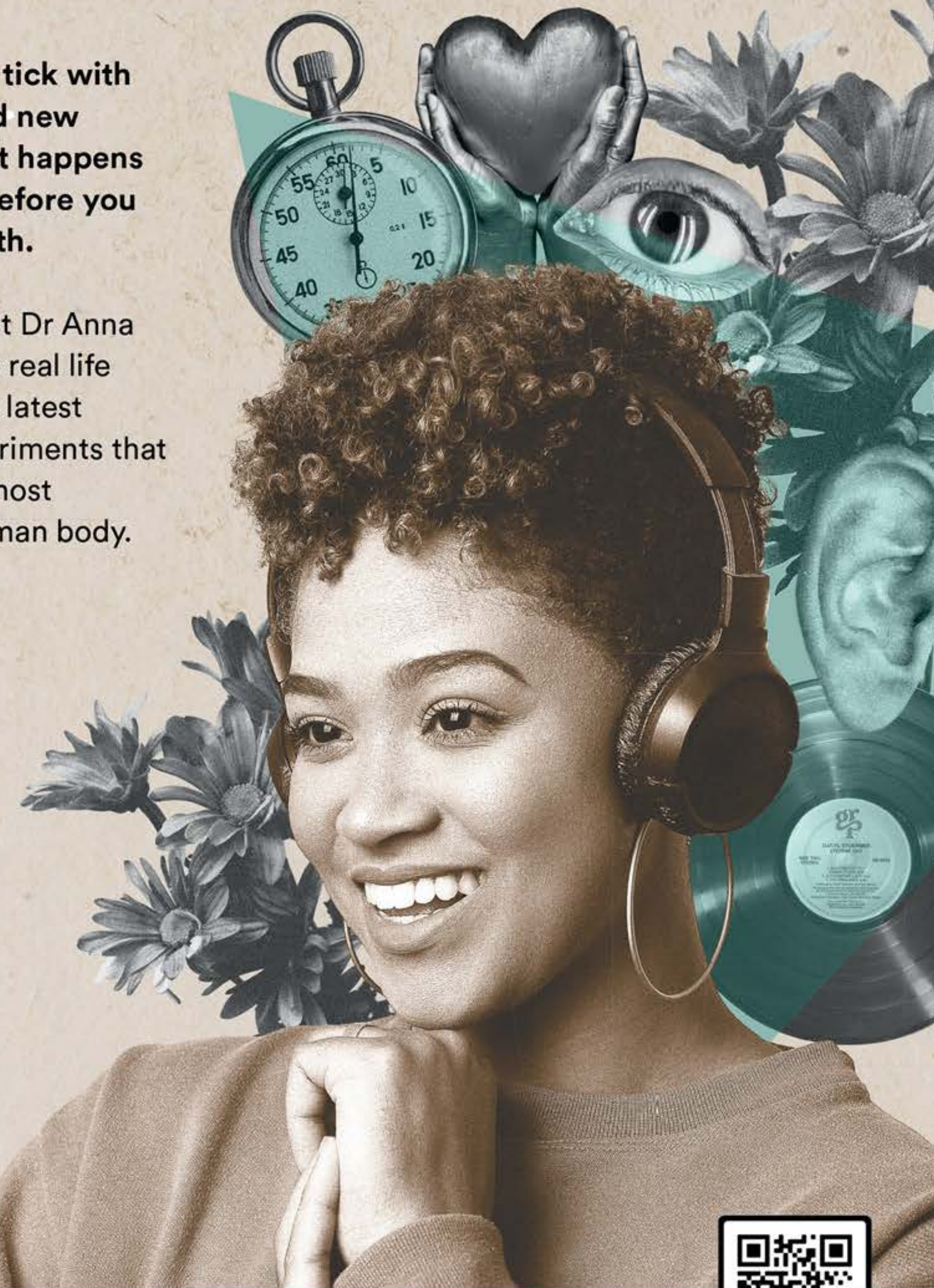

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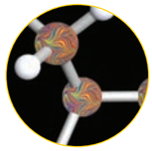

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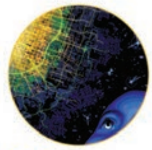

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Mary-Jane Rubenstein

The philosopher of religion and science on our relationship to outer space

INTERVIEW BY BRIAN GALLAGHER

LIFE ON MARS

I'm sure human beings will live underground on Mars for a little while, shielded from radiation. Will they get cancer? Absolutely. It's going to be really hard. Are some people's faces going to explode? Yes. But considering the exceeding difficulty—the extent to which Mars wants to absolutely obliterate us—I don't know that bleeding edge, corporate capital is the model to follow when human beings go about trying to make their lives work there. The model on which these new colonies might be started, historically speaking, sets a really bad precedent. It's a bad model. The conditions under which it might happen are damaging to the Earth, perhaps beyond repair. What's most troubling is that the vision can seem, for some people, more possible and palpable than, say, reversing or slowing the course of climate change on Earth.

OUR TERRIBLE PLANETARY TRACK RECORD

There are people who say human beings have absolutely no right to do anything to Mars. I don't think I'm in that camp. But doing something like nuking Mars to increase habitability would amount to destroying an archaeological site from the outset, so that we would have no possibility of determining what the history of Mars, and maybe life on Mars, has been. We don't have a fantastic track record in preserving the habitability of the planet that we've already got. I'm not sure why we think that we would know how to take a totally uninhabitable planet and make it more habitable. It seems to be a fantasy. One would think we might first start attempting those techniques on Earth rather than exporting the techniques that have currently destroyed Earth onto Mars. I certainly think it would help to talk to as many different stakeholders, and scholars and religious practitioners and planetary scientists, as possible, before trying to come up with a plan for terraforming Mars. I certainly don't think that it should be the prerogative of one CEO to determine how an entire planet is going to be affected.

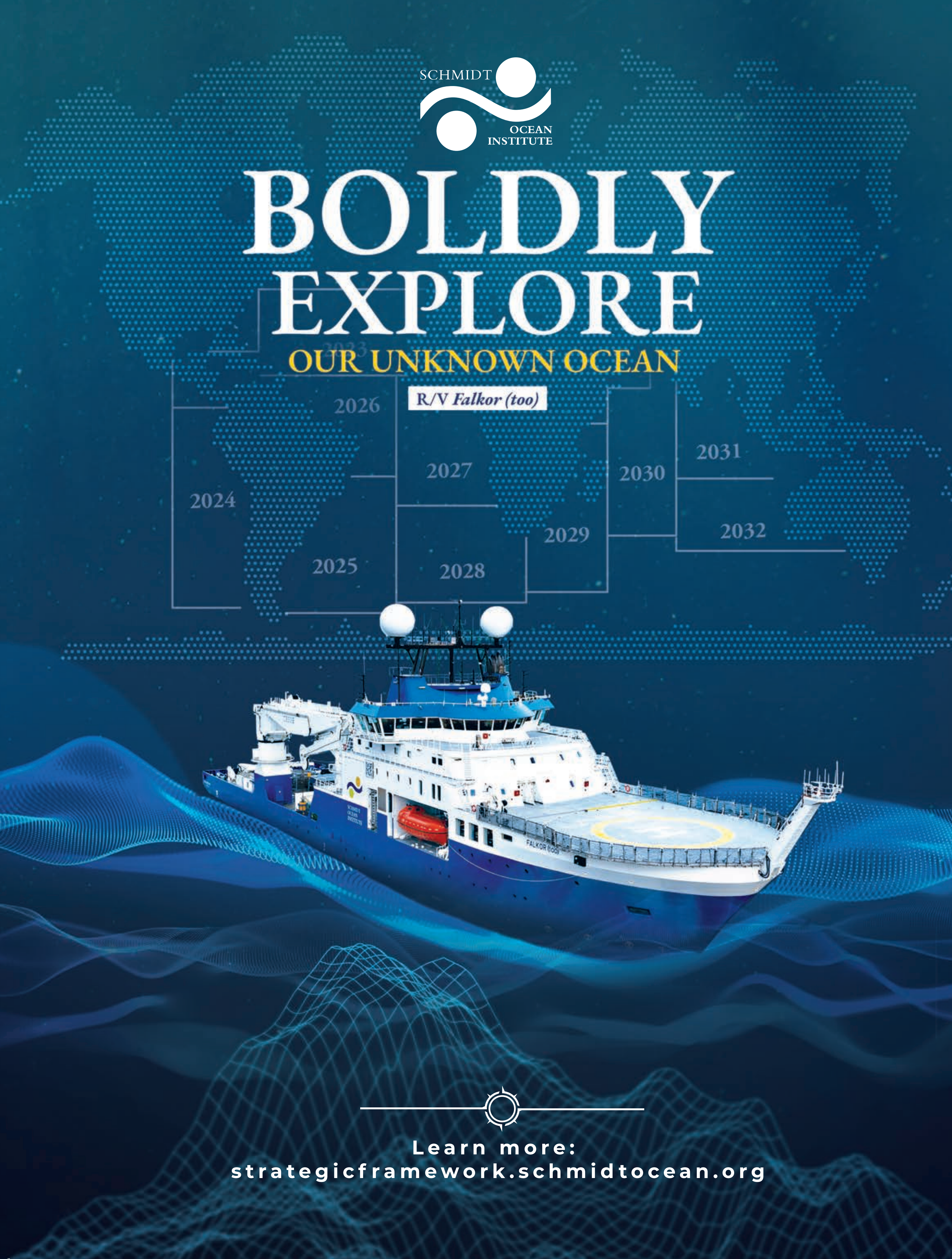
THE MOON "FOR ALL MANKIND"

When NASA leased land from the Navajo to test their rockets in the late '60s, a Navajo poet said, "Could you deliver a message to the moon people, please?" And NASA executives were like, "Sure, we'll deliver a message to the moon people." And the message the Navajo folks wanted to send was, "Watch out for these white guys." Because they're going to destroy the moon people in the same way they destroy the Earth. The Navajo speaker did not feel included in the walk on the moon. He was feeling like this was going to be an extension of the same thing that displaced his people. I don't know how you would measure comparative benefits, but it's not immediately clear that Neil Armstrong and Buzz Aldrin's walk on the moon has done anything for poor and oppressed folks as a net good, if you can even speak that way.

"PANTHEISTIC MYSTICISM" AS A SPACE ETHOS

Robert Zubrin, president of the Mars Society, accused some advisors to NASA of taking "pantheistic mysticism" too seriously. The idea is that the planets might be sacred, for example, or the rocks might have some kind of agency. Rivers might be alive. My cheeky reply is, "I don't know, the opposite of pantheistic mysticism, which is to say scientific instrumentalism, has been really devastating for Earth. It might not be a great system to export somewhere else." A regard for the more-than-human world as important in its own right and worthy of respect maybe would be a better basis to start from.

RACHEL LUI PHOTOGRAPHY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