

NAUTILUS

WHERE YOUR BRAIN CAME FROM
All hail the ancient sea sponge

WHY CROWDS GO MAD
The physics of mayhem

SEAHORSES IN LOVE
Lessons from the romantics of the sea



Mirror-Image Life

ONE SCIENTIST'S WILD DREAM p.22

ISSUE 52

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Because It's There

BY KEVIN BERGER

I HAD TO LINK the variety of stories in this issue under a single theme, it would be, “Because it’s there.” George’s Mallory’s famous quip about why he climbed Mount Everest speaks for the daring science on view.

The ascent begins with Chinese biochemist Ting Zhu. As you will see in “Mirror-Image Life,” Zhu is embarked on what Nobel laureate Jack Szostak calls a “hugely ambitious” adventure. Zhu’s goal is to reverse the chirality of molecules to produce a new form of life. Chirality, a Greek word for hand, refers to the fact that molecules central to life, like DNA, twist in one direction, like the threads of a screw.

Many scientists think creating mirror-image life can’t be done. “Indeed, it’s difficult and challenging, but that also makes it exciting, like climbing a high mountain,” Zhu tells *Nautilus* author Philip Ball. True, Mallory never did reach his summit; in fact, he died trying. As Ball’s fascinating article shows, Zhu is near his summit, with life and limb intact.

So much important science, which has revealed the intricacies of nature, began with scientists striking out for uncharted territory. In “Can We Stop Time in the Body?” *Nautilus* author Elena Kazamia tracks a band of biologists on a mission to create a drug that would permeate every tissue in the body and slow down its metabolic tempo to adagio. Don Ingber of Harvard, a leader in biologically inspired engineering, tells Kazamia he likes the project because it’s “so out there.”

I just love the minute obsessions of scientists. Who spends years and years studying the genes of ancient sea sponges, or the sleep habits of tiny fish in Mexican caves, or the magnetic fields of the sun? In this issue, you’ll meet them.

It’s true: science for science’s sake often turns out to have important applications. Physicist Sidney Perkowitz has written in *Nautilus* how the discovery of quantum mechanics, a theoretical quest if there ever were one, led to the computer chip and light-emitting diodes that are moving us toward a greener world. “The interplay between pure theory, and its outcomes in the everyday world, is a continuing feature of science,” he wrote.

The same is true of the science in this issue. Mirror-life molecules can improve drugs because they don’t incite immune systems to overreact and cause inflammation. Head and spinal cord injuries cause irreparable damage if aid is delayed. A biostatic drug, Kazamia writes, “delivered on the battlefield could buy time for fallen soldiers, improving their chances of survival.”

The practical side of science couldn’t be more important to our health and our planet’s. Scientific breakthroughs in medicine and technology are newsworthy, and plenty of magazines cover them admirably. But I confess, it’s the romantic pursuits, with no practical goals in sight, that most inspire my choices as an editor. And what, to reveal my bias, make *Nautilus* special.



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—Earth

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- Dona Bertarelli, Founder of Sails of Change





THE PORTHOLE

Short sharp looks at science

ZOOLOGY

A New Tarantula Is Discovered in an Unexpected Place

WHEN ALIREZA ZAMANI WAS A BOY, he wanted a pet tarantula. He liked that they were big, colorful, and easy to take care of—you can just feed a tarantula a cricket once a week and they will live for decades. But his home country of Iran didn't have the kind of pet trade that exists in the United States or Europe; in fact, scientists hadn't yet identified any species of the spider in his country. Rather than wait, he became a scientist himself—an arachnologist and taxonomist—and made tarantulas and other spiders his life's work.

Not long ago, Zamani was thrilled to get a message on his Instagram account. It contained photos of a male tarantula living in the Zagros Mountains of Northwestern Iran, a biodiversity hotspot. Zamani had been looking for such a spider for years. He suspected that the species itself was unknown to science, but immediately recognized it as belonging to the *Chaetopelma* genus, one found in Turkey and other regions in the Middle East and Lebanon. The photos had first been shared on a private WhatsApp group for exotic pet enthusiasts.

Tarantulas are a diverse family of spiders: More than 1,000 species are known around the world, and they come in many sizes, exhibit a wide variety of behaviors, and live in many different habitats, including tropical, subtropical, and desert regions. Tarantulas of the Americas are generally more docile and have less potent venom than those in Europe and the Middle East, says Zamani. Tarantulas can attack prey or disable predators either using their fangs, with which they can inject



GOLDDLOCKS The Persian Gold Tarantula was named for the wooly golden hairs on its back and legs.

venom that paralyzes, or by shooting thousands of poisonous hairs from their abdomens. If these hairs get into the airways of smaller mammals, such as rodents, the hairs can kill them.

Tarantulas and other spiders are among the most important bio-controllers of insect populations, says Zamani, consuming some 400 to 800 million tons of insects each year around the globe. In this way, they help to control the spread of disease. They also can serve as prey for certain large birds. Given the way insect populations are crashing, it may come as no surprise that spider populations around the globe are declining as well.



NOT SO ITSY BITSY Some of the biggest spiders in the world are tarantulas, which average 5 inches long. The Persian Gold's leg-span is 3.5 inches wide.

To be certain of his identification of the species in the photo, Zamani needed a specimen, so he linked the naturalist who had originally snapped the photos of the spider, Mehdi Gavahyan, with another naturalist friend of his from Tehran. Together the two of them found a female in a silk burrow in the same mountainous area and sent it along to the scientist.



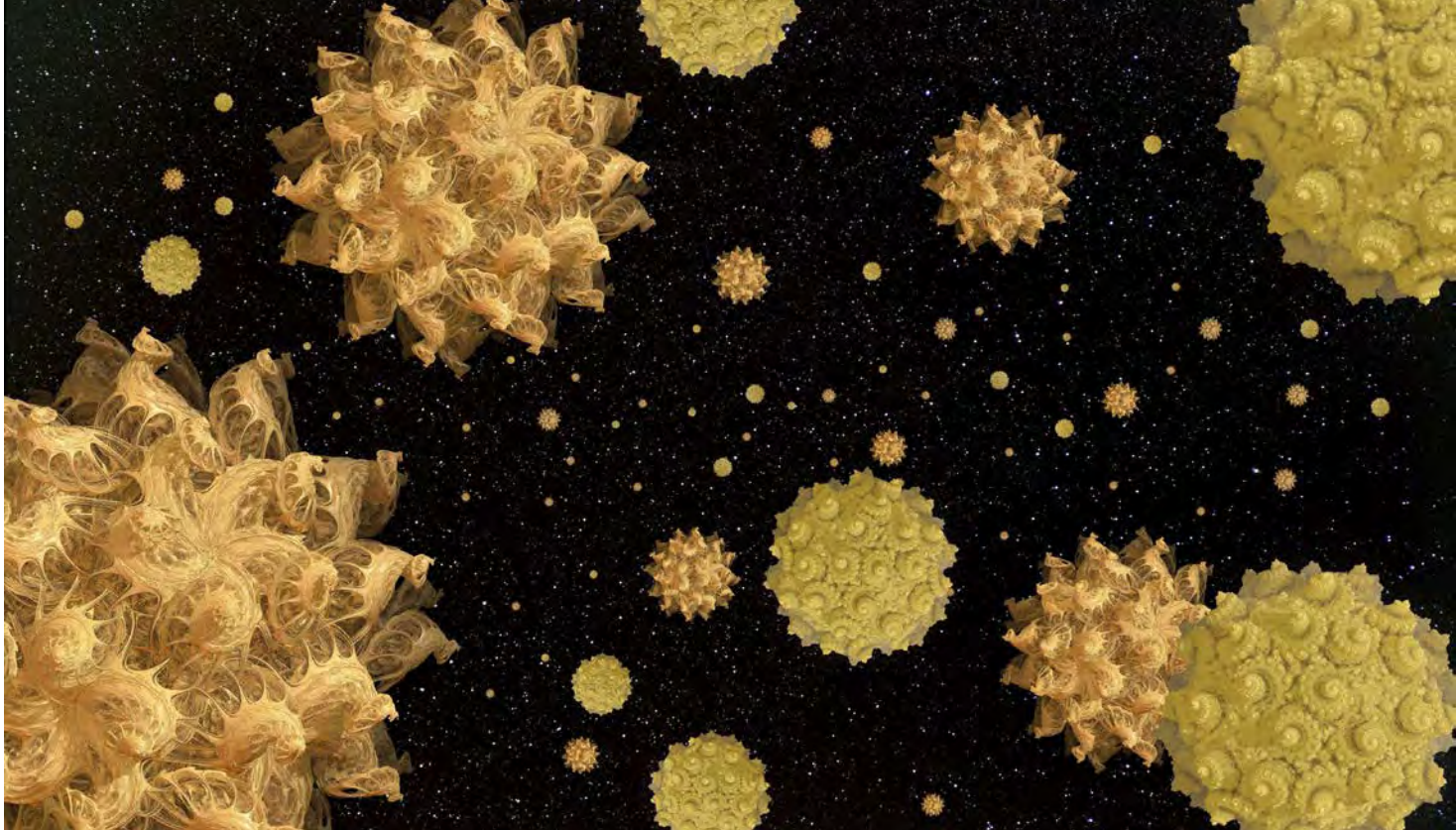
The spider measured about 3.5 inches long in leg-span—equal to the width of the average male human hand—and sported wooly golden hairs on its back. But Zamani says he was most interested in the spider's sex organs, the primary feature by which tarantulas are identified. In this case, the organs were much more elongated than those of other *Chaetopelma* species. He instantly knew he had been correct to suspect the tarantula was a distinct species.

Zamani named the spider the Persian Gold Tarantula after its golden hairs and the country where it lives (Iran is also known as Persia). It marks the first record of *Chaetopelma* in Iran—the easternmost record of the genus within its entire known range—and only the third known species of tarantulas in the country. The closest recording until then of *Chaetopelma* had occurred over 200 miles westward. Zamani published his findings, together with a colleague, in the journal *ZooKeys*.

Zamani and his co-author are hoping to work toward a full taxonomy of the genus. They note in their paper that one species that has been included in the *Chaetopelma* genus, from Cameroon, likely does not belong. Zamani himself would also like to identify more tarantula species in Iran. No doubt they would make the next edition of his first book, *Spiders and Scorpions of Iran*, the first field guide devoted to the arachnids of the Middle East.

—Kristen French

PANIC ATTACK When tarantulas feel threatened, they stand with their forelegs in the air, an aggressive stance signaling they are about to attack.



ASTRONOMY

This Molecule May Have Seeded Earth Life

FLOATING IN THE MIDDLE of our galaxy, near the center of the Milky Way, inside a cloud of gas that swirls at the temperature of 100 Kelvin or -279.67 Fahrenheit, a molecule essential to life on Earth has just been discovered. It sounds inconceivable that such a level of cosmic cold could harbor anything remotely related to a living organism—and yet it does. In fact, without this molecule, humans—and all other breathing, growing things on the planet—would not be possible.

The molecule, which scientists have been trying to detect in space for decades, is carbonic acid, a precursor to amino acids, the basic building blocks of proteins. Its chemical formula is H_2CO_3 . Hardly a household name, carbonic acid nonetheless is key to our capacity to breathe: It ferrets carbon dioxide from our blood into our lungs, where it can be exhaled into the atmosphere. It also plays important roles in various geological processes on Earth. An excess of the molecule in the oceans can lead to ocean acidification. “So while

it’s important to life itself, it’s even more important in several atmospheric and geological processes,” says Miguel Sanz-Novo at the Spanish Astrobiology Centre in Madrid. Sanz-Novo’s team confirmed the presence of carbonic acid in space for the first time, publishing their findings this summer in *The Astrophysical Journal*.

The findings bolster Panspermia, the theory that life on Earth takes its origin from space and that our planet was “seeded” by various cosmic molecules that took a ride on meteors and meteorites, which later gave rise to organisms.

“The discovery of carbonic acid in space certainly tells us that the chemical ingredients for life are present out there, in the gas that will form new stars and planetary systems,” says Víctor Rivilla, the primary investigator on the project. “So yes, they could have been incorporated into solar system objects such as comets and asteroids, which could have transported them to the early Earth, thus helping to cook the life recipe.”



Carbonic acid belongs to a larger group of carboxylic acids. Its close cousins formic acid and acetic acid were first spotted in space in 1971 and 1997, respectively. Scientists suspect that H_2CO_3 exists in various astronomical environments such as the Galilean icy moons, Mercury's north polar regions, or even on the surface or atmosphere of Mars—but its presence in space was harder to pinpoint. “This molecule was thought to exist in space somewhere, and now our investigation showed that it is in fact there,” says Sanz-Novó—in the gas from which new stars and planets will eventually form. Moreover, it seems to be quite abundant, Sanz-Novó adds.

Floating inside a cloud named G+0.693-0.027 about 100,000 light-years away from Earth, carbonic acid molecules weren't easy to discern (researchers used spectroscopy to identify them). Inside that cloud, the molecule exists in a high-energy state, which allows it to do things that it could never do on Earth: For example, as it spins in this high-energy state, it emits photons—massless particles that comprise waves of electromagnetic radiation—with a set frequency. That frequency becomes its

Our planet may have been “seeded” by various cosmic molecules.

spectral fingerprint or a mugshot, explains Sanz-Novó. Detected by two telescopes, at IRAM and Yebes observatories in Spain, and printed on paper, the fingerprint looks almost like a QR code.

Even here on Earth, H_2CO_3 is not easy to study because in ambient settings of temperature and pressure it easily breaks apart into carbon dioxide and water. To obtain a spectral fingerprint of the molecule in the lab to compare to the telescope's data, the team also had to get the molecule to a high-energy state so it would start spitting out photons.

The findings aren't only interesting from the perspective of where life came from, Rivilla adds. They also hint that we may have cosmic neighbors—the comets and asteroids most certainly took the molecules to other planets where they could develop into other life forms. “We all want to know how life could have appeared on our planet—and also if it is or is not a unique event,” he says.

The findings add another piece to the puzzle of whether we are alone in the universe—or not.

—Lina Zeldovich

ENVIRONMENT

The Invisible Impacts of Calamities

CYCLONES, TSUNAMIS, FLOODS, AND TORNADOES are devastating for humans, animals, plants, and buildings, leaving destruction and often death in their wake. But what we don't often consider is how such disasters impact microbial communities and what that can mean for the ecosystems they inhabit. As extreme storms, wildfires, and other natural disasters become more common with climate change, how they will disturb the vast, nearly invisible universe of fungi, bacteria, archaea, and other microorganisms in our midst is still largely unknown.

In a paper published in August, Johns Hopkins University infectious disease researchers Arturo Casadevall and Daniel Smith proposed a new field of

study, “disaster microbiology,” to look at the impacts that both natural and human-made calamities have on microbes. Casadevall and Smith adapted the idea from a 2022 colloquium report on climate and climate microbes from the American Society for Microbiology.

Why is “disaster microbiology” needed now?

Smith: Disasters have always happened, so it's always been relevant, but as climate change increases the pace of disasters, the need for a subfield devoted to disaster microbiology becomes more urgent. We need to better understand how microbes are changed by disasters, and then start to implement solutions so that we can mitigate the issues as they arise more frequently.

Microbes can be aerosolized by fire and survive in the smoke.



While researchers have for decades studied how flooding or windstorms can lead to changes in microbial communities that lead to infectious disease, consolidating all of this research under one subfield helps bring everybody to the same table, people from fields like engineering, modeling, microbial ecology, and infectious disease research. Together, we can analyze this data and make a plan for the future to prevent infections.

Is infectious disease the most significant concern?

Smith: Well, we are infectious disease experts, so that's our bias, but animal health and plant health and general ecosystem well-being are also important. Microbes that are beneficial for certain ecosystems could be impacted in detrimental ways.

How does knowing how microbes change following a disaster help us?

Casadevall: You can imagine that if you're going to do bioremediation—the use of microorganisms or other life to break down environmental pollutants—you can't just bioremediate by bringing in the animals and the plants, you've got to bring the microbes. You need to be able to repair those communities.

Do we know anything yet about how the fires in Maui might impact the microbiome there?

Smith: We wouldn't have data from that yet, but a lot of people study wildfire-associated microbiology both in the soil and wildfire smoke. Microbes can be aerosolized by fire and survive in the smoke that circulates far from the origin point.

How might microbes change the way they relate to mammals as they adapt to climate change and related disasters?

Smith: Microbes evolve more rapidly than mammals because their lifespans are so short. So microbes might quickly adapt to higher temperatures or reduced access to water or fewer nutrients, and those types of adaptations might make them better suited to survive inside of mammals. This is the concern with fungi, for example. They can't currently survive at human body temperature, but if they're driven to adapt to higher temperatures, that might allow them to survive and cause disease within mammals, which have a relatively high body temperature.

What do you hope disaster microbiologists will learn in the next couple of years?

Smith: Better surveillance of emerging pathogens, especially following disasters, to know what microbes are emerging, and could then be spread by the next disaster.

But on a positive note, we might gather some information about bioremediation. In some of these areas, like an oil spill, there's an enrichment of microbes that could help break down the oil. In the 1990s, for example, *Geobacter sulfurreducens*, also known as the "electric microbe," were discovered in a ditch in Oklahoma that was contaminated with oil. From there, it was found that these bacteria can help bioremediate uranium and heavy metals in groundwater. So it's possible studying the microbiomes of disasters will help with future bioremediation efforts.

—Kristen French



ZOOLOGY

How to Learn Without a Brain

THE TINY BOX JELLYFISH lives in warm coastal waters all over the world, including the murky waters of the mangrove forests of the Caribbean. Barely the size of a fingernail, they swiftly navigate a dark underwater maze of tangled roots scouting for their prey—water fleas.

The bell-shaped bodies of these jellyfish (*Tripedalia cystophora*) are so small and simple that they lack a brain. Yet, despite that seeming obstacle, they are exceedingly fast learners, scientists report in a recent study in the journal *Current Biology*. They can quickly form and retain memories about sensory information they receive from the environment and can adapt their behavior in response. The findings suggest that a “brain” is not as essential to learning as we thought.

In many ways, *T. cystophora* are unique creatures. They have far more sophisticated vision systems than other types of jellyfish, possessing four specialized visual sensory centers called rhopalia. Each rhopalia holds six eyes—for a total of 24—and contains around 1,000 neurons, so the jelly has a total of 4,000. (By comparison, a fruit fly has 200,000 neurons.) The rhopalia

generate electric signals that govern how fast the jellyfish pulsates through the water. Its pulsing motion quickens when the animal chases a flea or swerves to avoid crashing into tree roots.

While many other types of jellyfish can only detect light—sensing the direction it is coming from and following it—*T. cystophora* can also discern the contrast between dark and light, which means it can form images. “Two of their eye-structures are camera-type eyes which are basically built like yours and mine,” says senior author Anders Lydik Garm, associate professor of marine biology of the University of Copenhagen, Denmark.

Garm and study co-author Jan Bielecki, who studies neurobiology at the Kiel University in Germany wanted to know whether the jellies’ behavior—swerving between dark and light—was hardwired, or whether the jellies could learn new behavior. In their natural habitat, the jellies use their visual sense of contrast to distinguish the dark tree roots from the brighter water to avoid bumping into the tangles of protruding roots. “They use the contrast, because contrast is the



Even without a brain, jellyfish can learn from experience.

difference between how dark the root is and how bright the water is,” explains Garm. “That contrast is how they evaluate distance.” But could they learn to avoid obstacles that look different from the ones in their natural environment?

Garm and Bielecki set up an experiment. They outfitted a fish tank with a bunch of gray and white plastic strips, which were meant to mimic the tree roots and light streaming through. The trick was that to the jellyfish, the light gray color looked like a root that was simply far away. “In reality it wasn’t far away. It just seemed far away because we painted it gray,” Garm explains. Initially, the jellies perceived the gray “roots” as being remote—and bumped into them. But after a few bumps, they would learn to avoid the gray strips. “They get the mechanical sensory input telling them, *OK, this root was much closer than it originally appeared,*” says Garm—and they start changing their behavior.

Less than 10 minutes into the experiment, the jellies quadrupled the number of successful pivots to avoid collision, scientists found. “They learned that in this

condition, low contrast still means that the ‘root’ is close by, and then within three to five errors of bumping into the root they learn to turn earlier and not bump into it,” Garm says. “We were surprised at how quickly they learned.” This form of learning is called associative learning: The jellies learn to associate sensory stimuli—such as images of the gray strips—with bumps, to remember this association and then adapt future behavior.

The findings suggest that even without a brain, jellyfish can learn from experience through visual and mechanical stimuli, researchers say. But if the jellyfish doesn’t have a brain, where are these memories stored? Garm says that this learning may happen within the cells of the distributed nervous system, particularly the neurons in the rhopalia. These neurons form a memory of sensory stimulation, which then becomes associated with a particular behavior: The image of the root, plus the bump, leads to avoidance.

“Our study suggests—due to the unique evolutionary position of jellyfish—that learning is an integral function of the neuron, or at least a small neuronal circuit,” says Bielecki. If a neuron or neuronal circuit is all that is required for memory and learning, he says, then perhaps we need to rethink how we define the term “brain.” It seems you can be a bit “brainy” without one—at least, if you’re a box jellyfish.

—Lina Zeldovich

MICROBIOLOGY

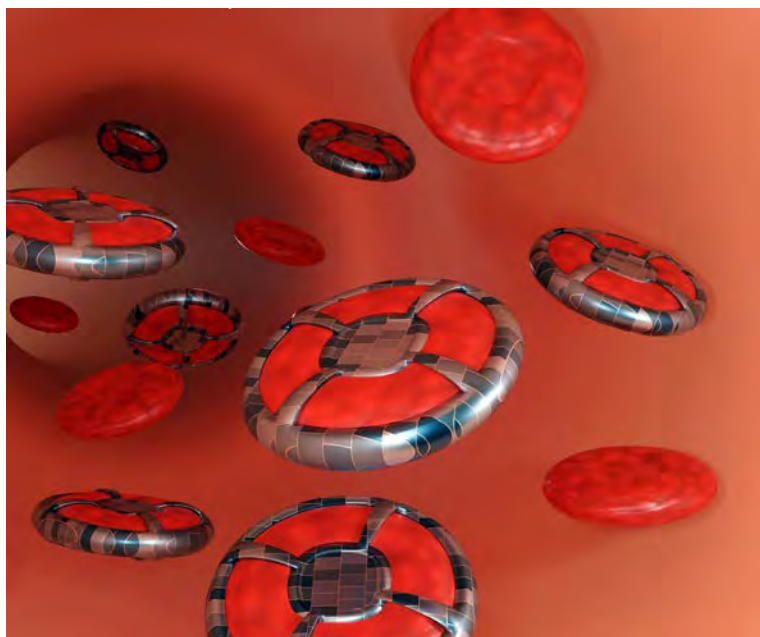
A New Way to Make Cells from Scratch

YOU ARE A MARVELOUS MENAGERIE of cells, the building blocks of life. Some 30 trillion or so of these cells compose the human body, each of them operated by a walled-off command center—the central nucleus stowing DNA—along with smaller bits of machinery surrounding it that work like little organs. These organelles are responsible for specific tasks like generating energy, making proteins, and disposing waste.

For decades, scientists have been trying to match nature’s virtuosity, tinkering with different methods

and types of materials to piece together an artificial cell that mimics what living cells can do. The effort to overcome this challenge is aimed not just at solving the origin of life, but also increasingly at biotechnology applications. Scientists have shown that such artificial cells can be integrated into living systems and complex genetic circuitry and can perform specific tasks, such as biosensing, drug delivery, anti-cancer therapeutics, and artificial photosynthesis.

One of the main engineering challenges for artificial cell design has been building the spaces where



Imagine an artificial cell that can sense cancer, produce a drug, and release it inside the body.

the little organs can reside. “The cells in your body are more complex than a bacterium, because they have this really complex spatial arrangement of things inside of them,” says Yuval Elani, a biophysicist at Imperial College London.

Recently Elani’s team made an important advance on this front: They demonstrated a new way of producing these compartments that allowed them to easily insert multiple synthetic organelles with different functions in a single cell. For example, they were able to introduce magnetic particles (a rarity in nature) into their artificial cells. This let the researchers move the cell in any direction with a magnet. Another synthetic organelle they added enabled the cell to perform certain functions in response to temperature changes. The researchers published their new results in the *Proceedings of the National Academy of Sciences*.

The findings mark a significant step in the effort to build life-like artificial cells—ones that are able to do things like move around, sense their environment, release cargo, and communicate. Elani and his team used a material called hydrogel, made from a carbohydrate called alginate, to build the cells’ internal environment, which could be likened to the chassis, or base frame, of a car. Hydrogel is an increasingly popular material for scientists engineering synthetic cells because of its versatile chemistry.

Before now, researchers had not endowed hydrogel-based artificial cells with multiple organelles at the same time, Elani says. This creates the potential for, among other things, much more advanced drug-

delivery systems. You can imagine injecting someone with an artificial cell that lies dormant for years, and then when it senses a cancerous environment, the cell produces and releases a drug inside the body. “That kills the cancer cells, the cell senses the threat’s been eliminated, and shuts back down,” Elani says.

The researchers also show in their paper how it’s possible, using a technique called microfluidics, to reliably and quickly make the cells a consistent size and shape (around 125 micrometers in diameter). That’s crucial for use in industrial or clinical settings, Elani says. Regulators “really want to know that you have full control over every aspect of that synthetic cell.”

Since they’re so short-lived, synthetic cells won’t be coming to market any time soon. “Once you make them, you have a day or two to use them,” Elani says. This is because they can’t harvest energy and materials from the environment like biological cells—yet. Elani’s team is working on this. “We’re engineering them to photosynthesize just like plant cells,” he says.

Will Elani eventually engineer artificial cells that can replicate like a biological cell can? Sure, in perhaps 15 to 20 years. “It’s a very optimistic guess,” he says. “At the moment there’s no danger.”

—Brian Gallagher

TECHNOLOGY

The Wisdom of a Brainless Robot

THINK OF A PAIR OF TANGO DANCERS, gliding across the floor, picking up subtle physical cues from one another. They move together effortlessly, like water, through a maze of carefully choreographed steps. The intelligence they possess is not just in their heads but in the muscles, tissues, and skin of the body. It's physical.

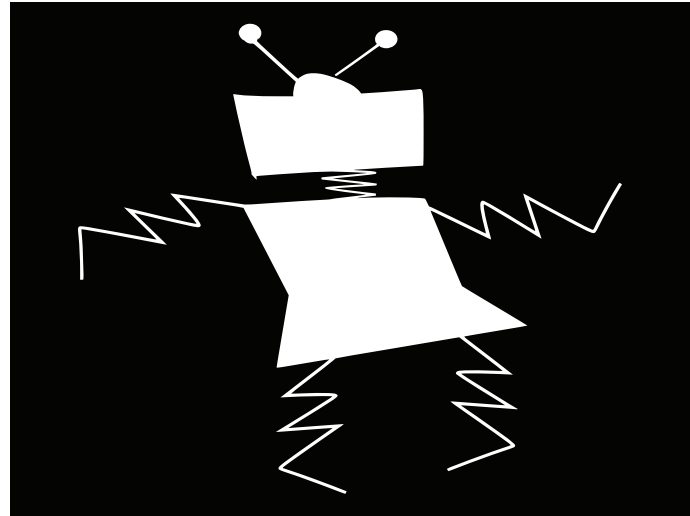
Scientists are increasingly working to build this kind of physical intelligence into robots. For machines to achieve the kind of intelligence possessed by humans and other biological creatures, they ultimately need not just brain-like computational power, but also bodily smarts—the ability to pick up sensory cues from the environment and use that information to learn and make decisions.

Recently, scientists from North Carolina State University achieved a breakthrough: They created a robot that is powered by physical intelligence alone. This “brainless” robot is the first that can navigate complex mazes without any need for computer or human guidance.

“We wanted to make a robot that could solve a maze by itself,” says Jie Yin, co-corresponding author of the paper and an associate professor of mechanical and aerospace engineering at North Carolina State University. Before now, robots could only navigate mazes within multi-walled spaces if they contained built-in electronics-based controllers and sensors, says Yin, or if they were manipulated by external sources of light or magnets.

The robot Yin and his team designed does not look anything like the robot of popular imagination: It has a soft body, kind of like that of an octopus, made of ribbon-like liquid crystal elastomers and shaped like a piece of fusilli or rotini pasta. It moves by rolling, drawing energy from hot surfaces (131 degrees Fahrenheit at a minimum)—the hotter the surface, the faster it moves. Having no hard, rigid materials, edges, or structures allows it to navigate tight spaces and makes it safer for humans who want to interact with it.

The researchers had already experimented with similar robots in a previous experiment, but these would get



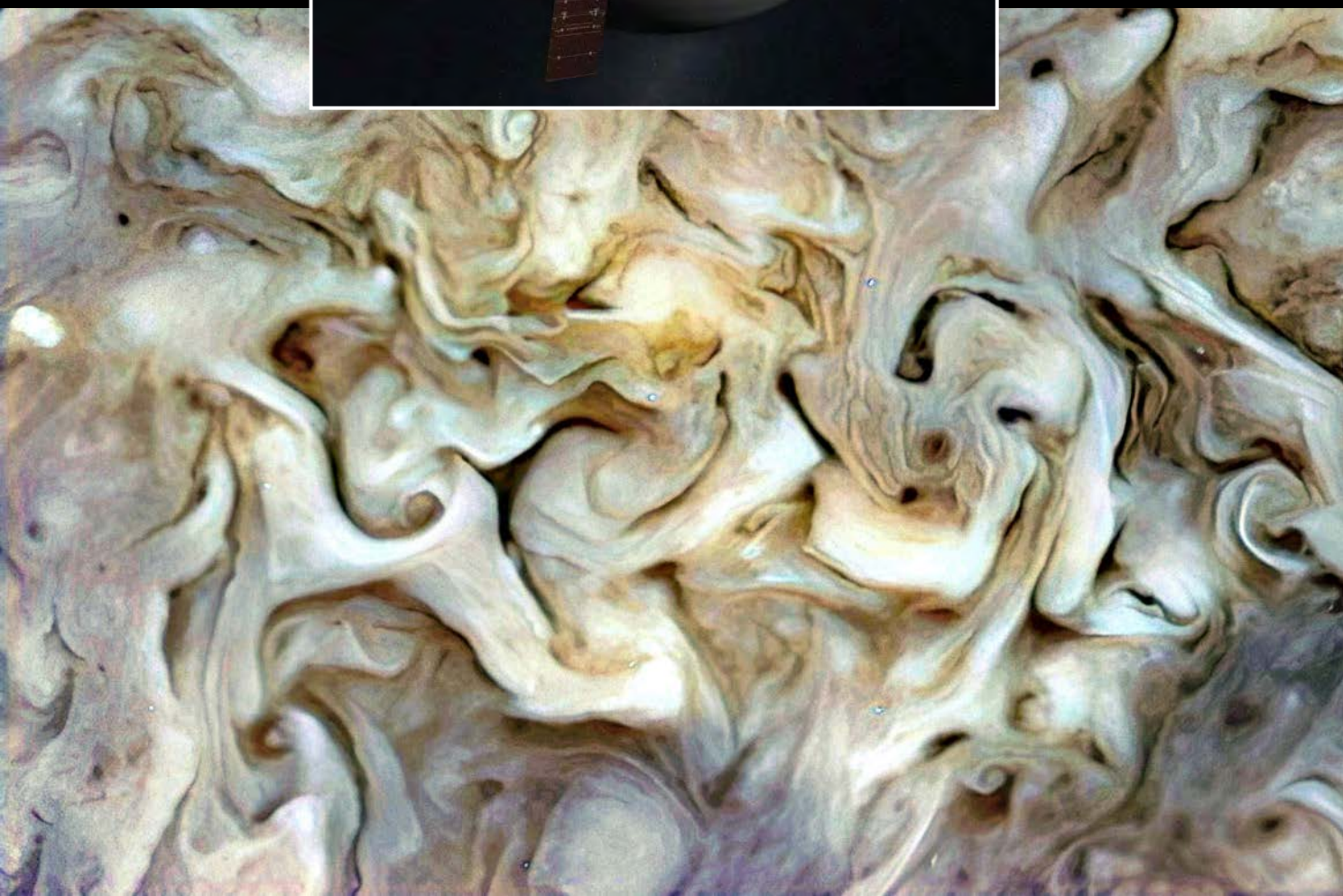
We wanted to make a robot that could solve a maze by itself.

stuck in the maze between parallel objects. This time, they also made the design of the robot asymmetrical, which allows it to move in arcs and quickly get unstuck. “It can bend in any direction, change shape, and squeeze into a space that is smaller than the robot body itself,” says Yin. Think of a cup with a wide mouth and narrow base—it rolls along a circular rather than straight path.

If this robot were outfitted with sensors and cameras, says Yin, it would be ideal for collecting data from a desert-like environment that is too hot for humans to navigate, or to assess the quality of roads, which also tend to store a lot of heat—even to complete missions on the moon, where temperatures can soar to almost 400 degrees Fahrenheit.

Yin’s robots may look more like pasta than people, but they possess a kind of intelligence that ChatGPT could only dream of.

—Kristen French

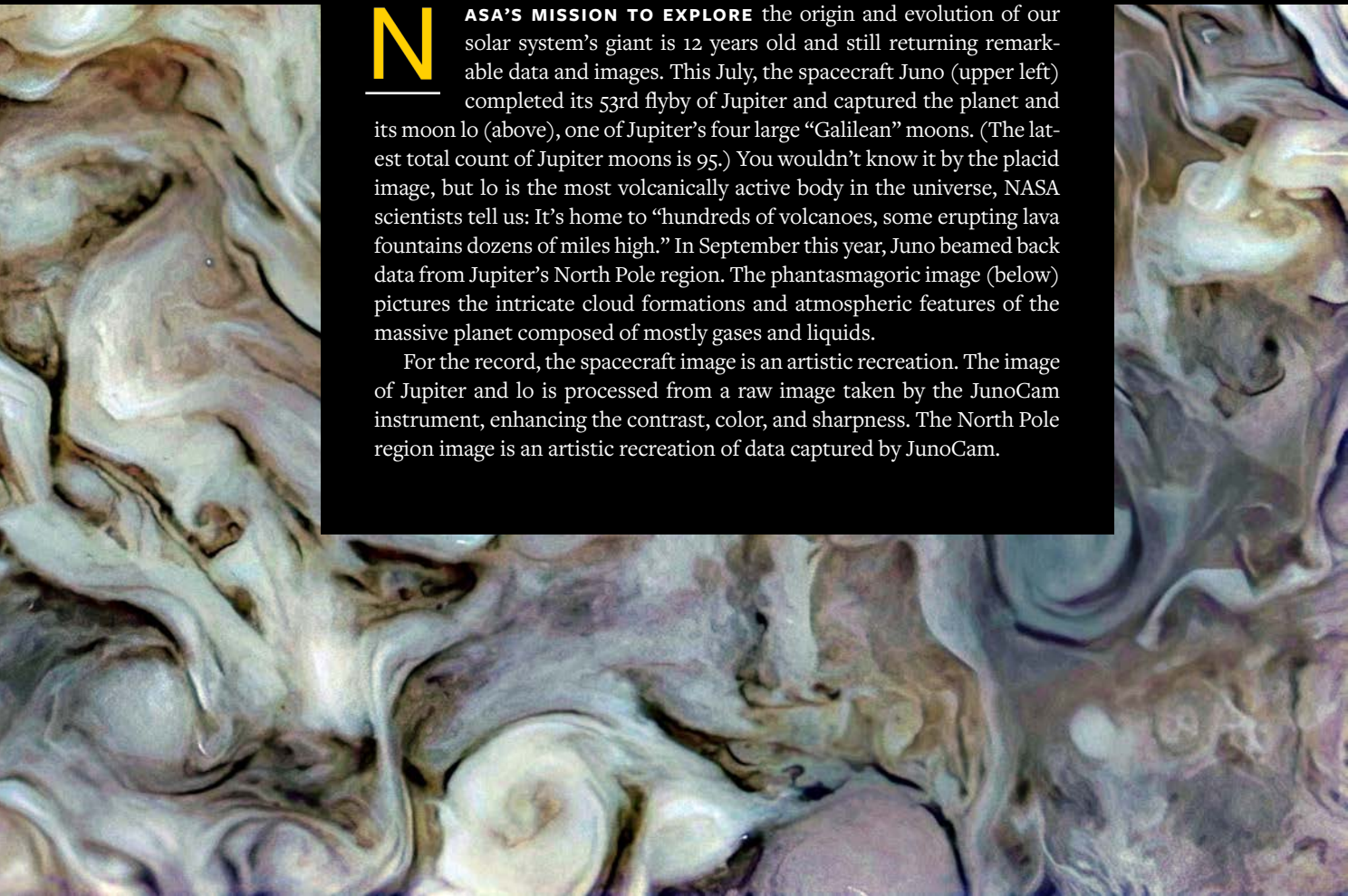


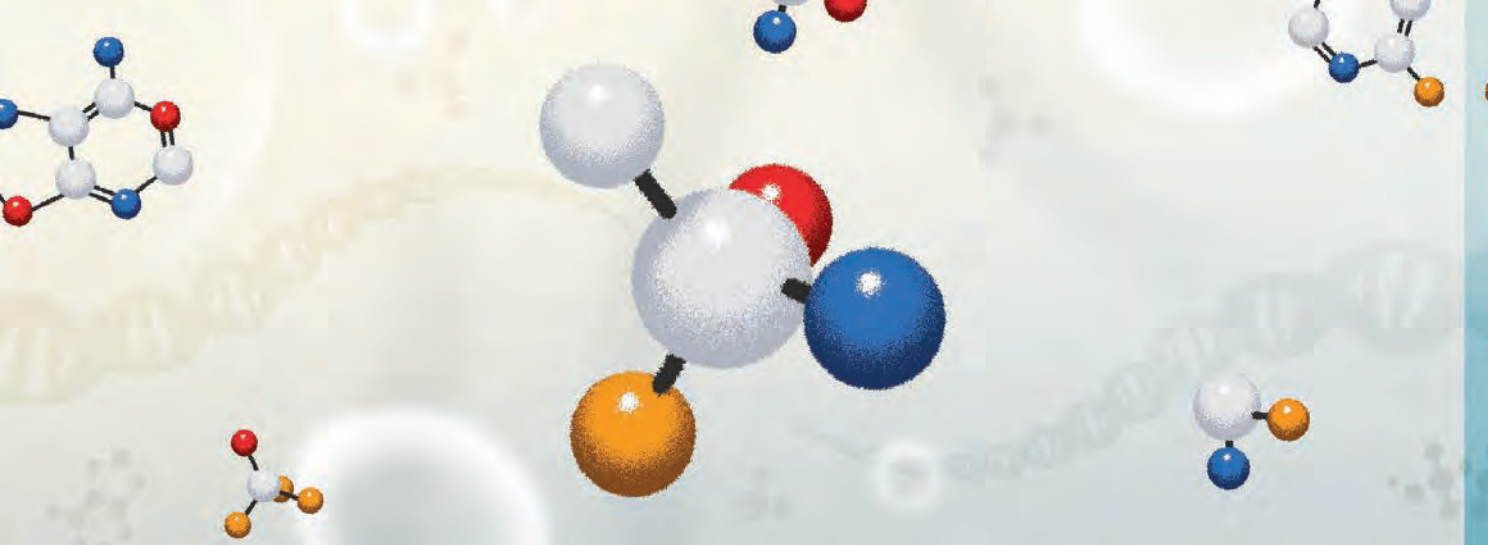


Hello, Jupiter!

NASA'S MISSION TO EXPLORE the origin and evolution of our solar system's giant is 12 years old and still returning remarkable data and images. This July, the spacecraft Juno (upper left) completed its 53rd flyby of Jupiter and captured the planet and its moon Io (above), one of Jupiter's four large "Galilean" moons. (The latest total count of Jupiter moons is 95.) You wouldn't know it by the placid image, but Io is the most volcanically active body in the universe, NASA scientists tell us: It's home to "hundreds of volcanoes, some erupting lava fountains dozens of miles high." In September this year, Juno beamed back data from Jupiter's North Pole region. The phantasmagoric image (below) pictures the intricate cloud formations and atmospheric features of the massive planet composed of mostly gases and liquids.

For the record, the spacecraft image is an artistic recreation. The image of Jupiter and Io is processed from a raw image taken by the JunoCam instrument, enhancing the contrast, color, and sharpness. The North Pole region image is an artistic recreation of data captured by JunoCam.



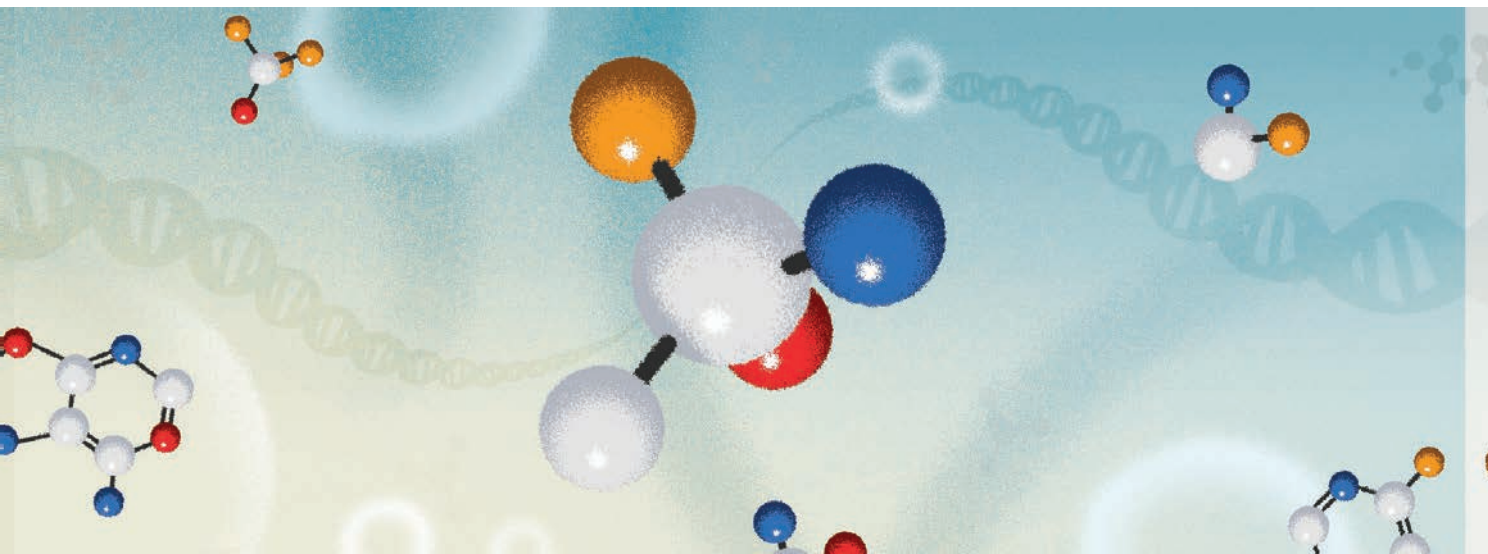


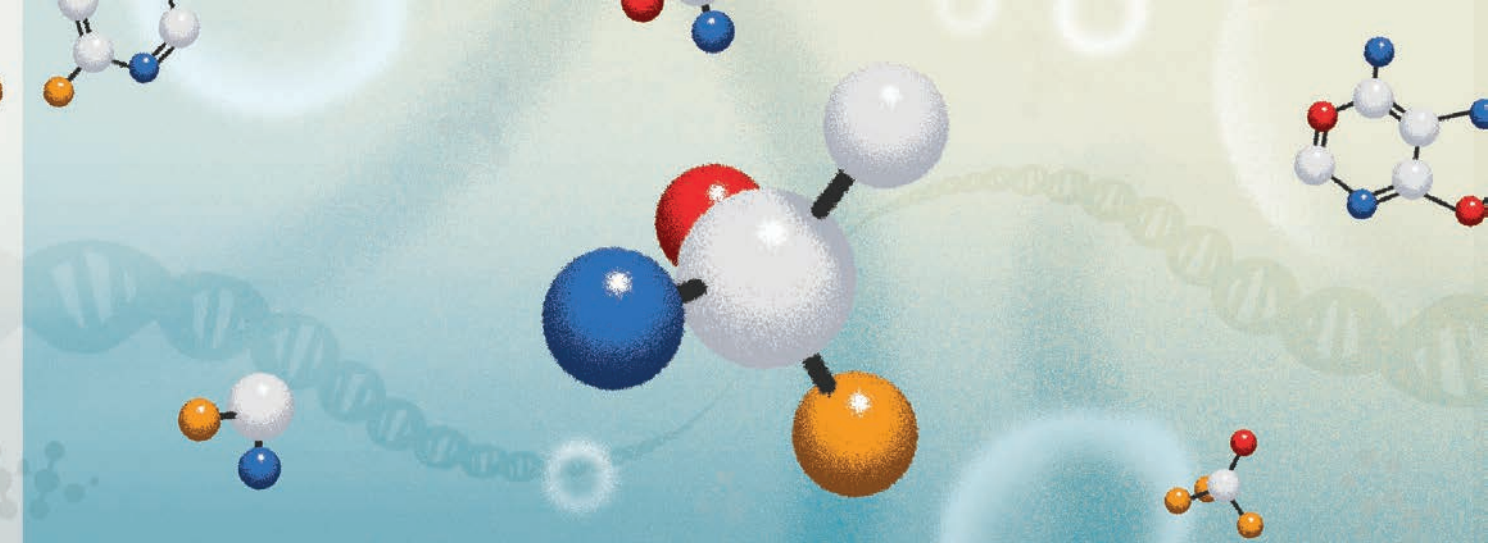
Mirror-Image Life

This biochemist is determined to create a new life form by reversing the shape of molecules

BY PHILIP BALL

ILLUSTRATIONS BY MARK BELAN

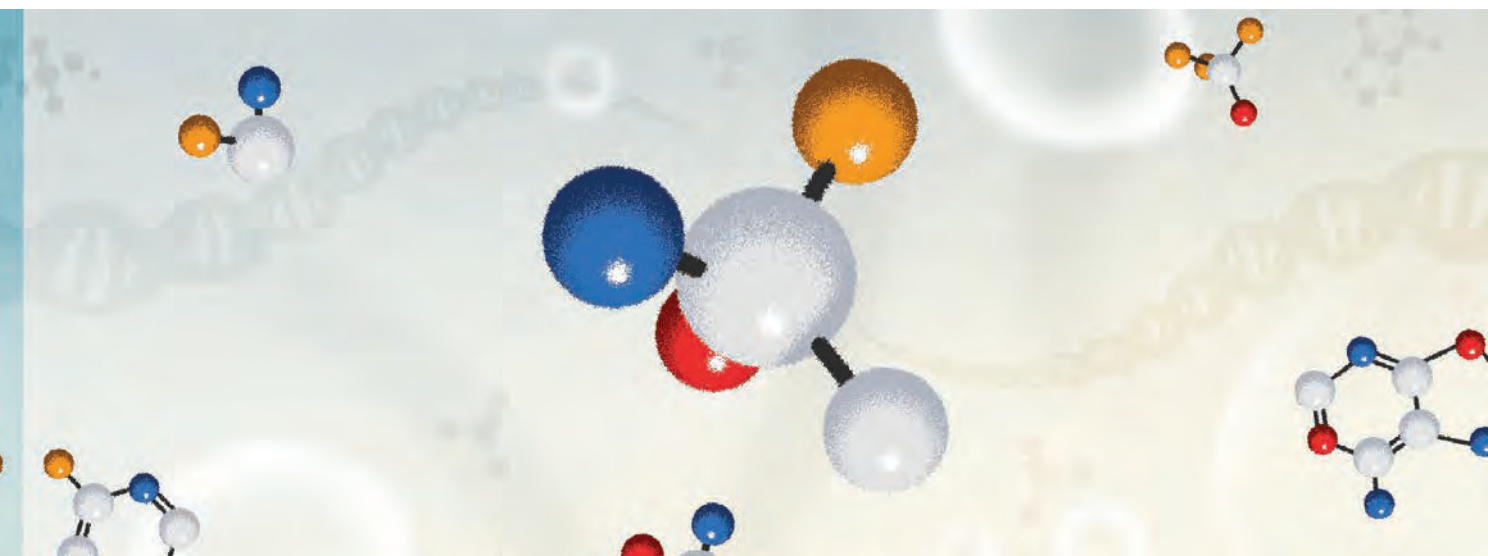


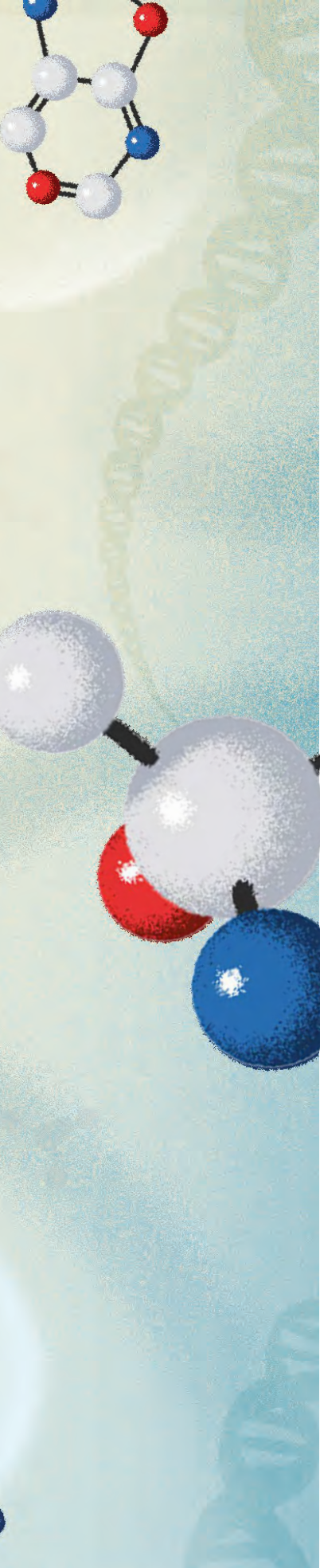


YOU'RE TWISTED. SORRY, BUT WE ALL ARE. The molecules most central to life twist one way or the other. Your most famous molecule, DNA, a spiraling helix like the thread of a screw, is right-handed. The molecules encoded by your DNA, proteins, are left-handed. Even humble sugars like glucose have a twist to their shape.

Why does this handedness, called *chirality* after the Greek word for hand, feature in the molecules (clusters of atoms) from which all life on Earth is constructed? How and when was the left-or-right chiral twist of life's components decided? No one knows—even though the chirality of life has been recognized for more than a century and a half.

But we do know that living organisms are exquisitely sensitive to this handedness. Feed bacteria with left-handed amino acids, and they'll incorporate them into their proteins. Feed them right-handed amino acids, and they are likely to ignore them, even though these are the same molecules but inverted as though in a mirror.





Maybe we just need to accept this is how life is. It exists on one side of the looking glass. But some researchers think there could be equivalent life-forms on the other side too—if only we could make them. They are already making mirror-image versions of proteins and nucleic acids like DNA. These molecules could be valuable drugs—all the more effective because their looking-glass structure should allow them to operate out of sight of the body's usual defense mechanisms for breaking apart foreign molecules.

But biochemist Ting Zhu of Westlake University in Hangzhou, China, is determined to go much further than that. He's made it his mission to create mirror-image versions of the key molecular ingredients of life. In principle, it might be possible to assemble those components into synthetic cell-like entities that can replicate and metabolize: a kind of primitive form of life, but inverted relative to every known organism, and therefore the first truly non-natural life form.

"I believe there are many alternative possibilities for life," says Zhu. "But among all of these, there is one that we know for sure would work, and that's the exact mirror-image version of ourselves." No one knows how such mirror-image cells would get along with ordinary ones—maybe they'd ignore each other, or compete? Might our planet have already conducted a version of that experiment in the wild, billions of years ago when life began?

Over the past several years, Zhu and his colleagues have performed the monumental task of making, from their constituent molecular parts, mirror-image versions of the key biomolecules in living cells: DNA, its sibling RNA, and the enzymes for replicating them and translating their sequences into proteins. He hasn't got the full set yet, but he is getting very close. Only a few components are still to be added to the basic biomolecular toolkit needed by stripped-down, minimal versions of mirror-image life.

"Ting's work is really impressive," says biochemist and Nobel laureate Jack Szostak at Harvard University, who was Zhu's Ph.D. advisor. "Making a mirror-image cell with a complete mirror-image protein synthesis system is a hugely ambitious goal. But I think it's worth trying, just to see what the hardest problems are."

"This could be the beginning of a new form of life," says Zhu. A lot of people think it can't be done—but he is determined to try, just to see if it's possible. "Indeed, it's difficult and challenging, but that also makes it exciting, like climbing a high mountain."

THE HAND(S) OF LIFE

Mirror-image life was first imagined by the man who discovered the chirality of life's molecules: French chemist Louis Pasteur. In 1848, Pasteur deduced that a byproduct of winemaking called tartaric acid may crystallize in two mirror-image crystal shapes because their constituent molecules have opposite chirality. After carefully separating the two types of crystal by hand, Pasteur dissolved them separately in water and found that when

polarized light passed through the solutions, the plane of polarization was rotated in opposite directions: to the left and to the right. Mirror-image molecular structures are called enantiomers, and are distinguished by the prefixes D and L, for the Latin words for right (*dextera*) and left (*laeva*). They are distinguished by the way their component atoms are arranged in space.

Pasteur became convinced that molecular chirality was a fundamental feature of living things: what distinguished them from the non-living world. He was wrong about that but correct that chirality is omnipresent in biomolecules. Pasteur wondered if chirality was induced by forces such as magnetism, electricity, or light, and in the 1850s he conducted a series of experiments that from today's vantage point might look borderline cranky: crystallizing compounds in magnetic fields, growing plants in sunlight with its polarization inverted with mirrors. Those efforts never led anywhere, although recently researchers at Harvard University have proposed that magnetism in minerals might indeed have played a role in giving the earliest life its particular chirality.

But Pasteur also examined the chirality of some natural molecules and showed that the amino acid asparagine, isolated from plants (the name comes from its discovery in asparagus juice), is present in just the L-form. In 1886 the Italian chemist Arnaldo Piutti discovered the D-form of asparagine and found that, while L-asparagine is tasteless, D-asparagine is sweet. In other words, mere mirror-image inversion is enough to produce different biological effects. Such distinctions became tragically apparent when it was found in the early 1960s that the two enantiomers of the drug thalidomide, prescribed for anxiety and for morning sickness in pregnant mothers, have very different effects: One is a sedative, the other can cause serious birth defects.

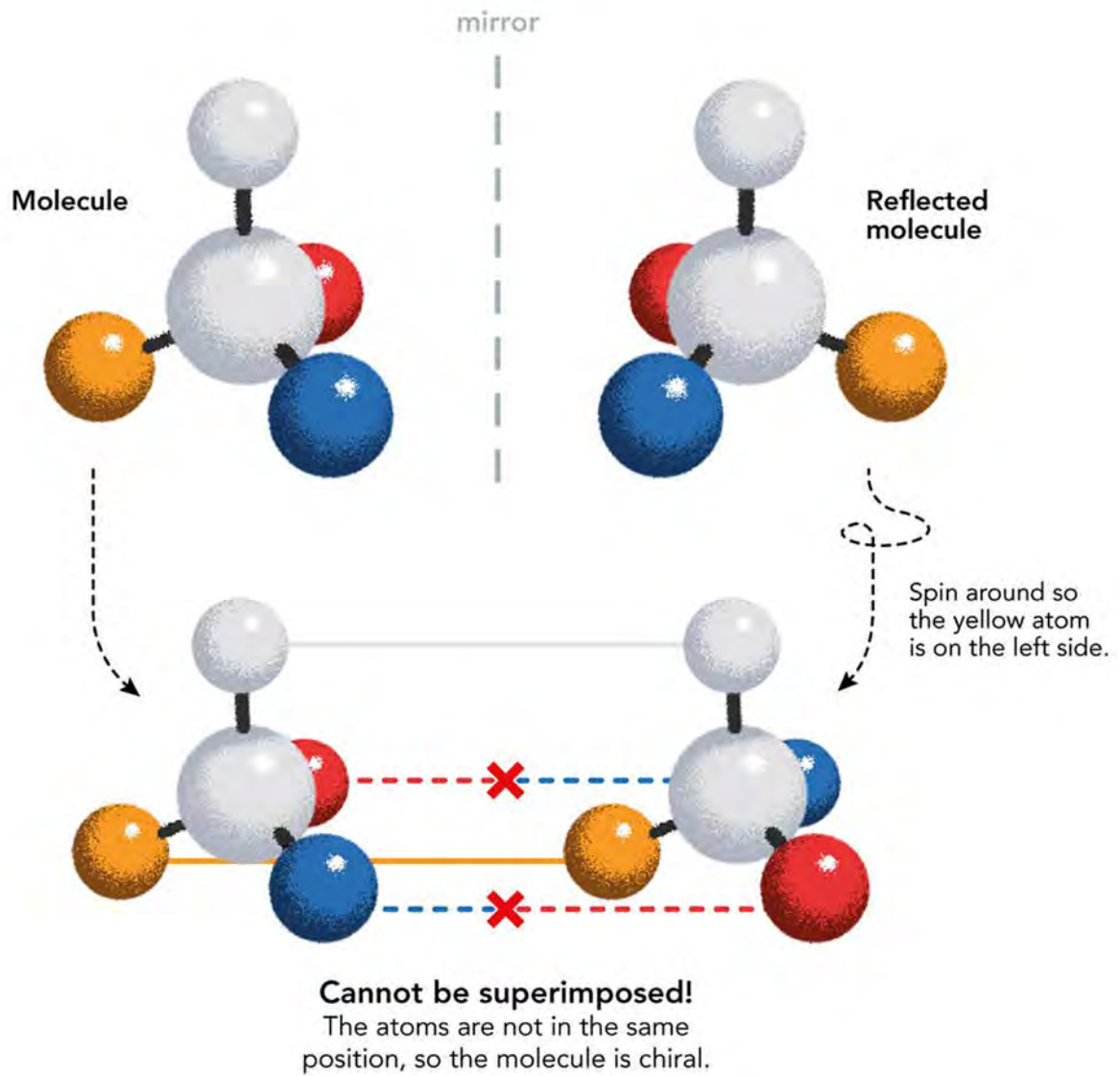
MIRROR DRUGS

We now know that all natural amino acids in proteins are L-enantiomers. But protein-like molecules made from D-amino acids by chemical synthesis have been investigated for several decades as potential drugs.

The creation of mirror-image proteins was pioneered several decades ago by chemist Stephen Kent of the University of Chicago and his co-workers. In the early 1990s, Kent and colleagues were able to chemically synthesize the enzyme HIV-1 protease, which the HIV virus uses to degrade other proteins. This allowed researchers to obtain the first crystal structure of the enzyme, assisting the development of drugs that combat AIDS by blocking the enzyme from working. Having acquired that facility for building proteins from scratch, in 1992 Kent's team made a mirror-image version of HIV protease just to see what it would do. They found that the molecule would cut up only peptides also made from D-amino acids, while ignoring those made from natural L-versions.

MOUNTAIN CLIMBER Chinese biochemist Ting Zhu is determined to create a new form of life by reversing the shape of key molecules. He agrees it's incredibly challenging, "but that also makes it exciting, like climbing a high mountain," he says.





*We just need to accept this is how life is.
It exists on one side of the looking glass.*

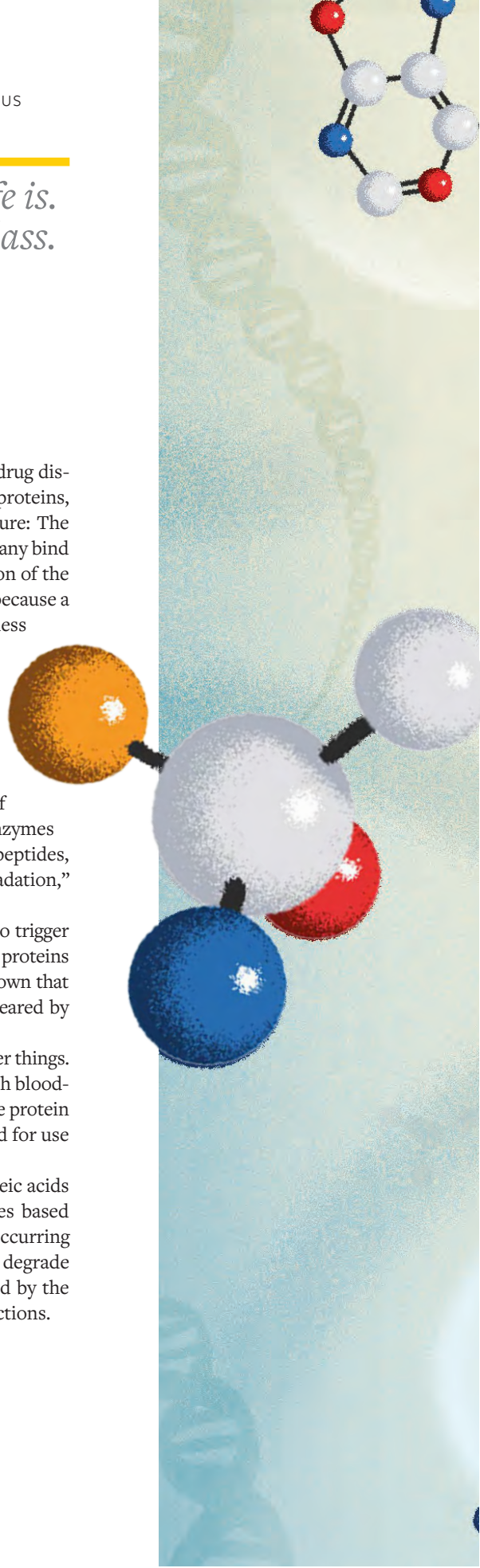
Kent realized that such reversed proteins could be useful for drug discovery. Many drugs aim to bind to and block the action of natural proteins, and such compounds are typically found by a screening procedure: The protein target is exposed to a wide variety of compounds to see if any bind to it. Many such compounds are chiral, and a mirror-image version of the target protein could double the chances of finding a good match, because a candidate in the screening library could have the correct handedness to stick only to the mirror-image form. If so, the other enantiomer, once chemically synthesized, should stick to the natural target.

D-proteins (and small fragments of them called peptides) could also be useful as drugs, for example by binding to and blocking the activity of natural proteins that are therapeutic targets. Around 80 or so normal L-peptides that do this are already on the market, but D-peptides have a distinct advantage. One of the obstacles for protein-based drugs is that natural protease enzymes quickly break them apart. But those enzymes don't work on D-peptides, and so they "are expected to be largely invisible to metabolic degradation," says Kent.

What's more, D-proteins wouldn't cause the immune system to trigger an inflammatory response, because this only happens once foreign proteins are chopped into fragments by proteases. Studies in mice have shown that D-proteins can pass harmlessly through the body before being cleared by filtration in the kidneys.

D-proteins are being explored for cancer treatment, among other things. For example, Kent's group has explored one that can interfere with blood-vessel formation in tumors. But it's still early days for mirror-image protein drugs. "To the best of my knowledge, none has yet been approved for use as a therapeutic," says Kent.

Biochemist Sven Klussmann is hoping that mirror-image nucleic acids too will find uses as drugs, and he has launched two companies based in Germany to develop them. As with D-peptides, naturally occurring enzymes that degrade nucleic acids, called nucleases, cannot degrade mirror-image nucleic acids, and they are not so easily recognized by the immune response and so are less apt to trigger inflammatory reactions.



“I believe there are many alternative possibilities for life—and one will work for sure.”

LIFE'S ESSENTIAL MACHINES

While Pasteur was conducting his weird experiments on molecular chirality with magnets and light in the 1850s, he admitted, “One had to be a little mad to undertake what I am trying to do now.” That’s a sentiment Zhu might well sympathize with. His determination to build mirror-image versions of life’s key molecules from scratch, assembling their long chains piece by piece with meticulous, painstaking chemistry, goes way beyond earlier efforts to make right-handed proteins. When he began in the early 2010s, his goal must have looked crazily ambitious. But many are astonished at the progress he has made. The work “is fascinating, pushing the limits,” says Klussmann.

A bare-bones form of mirror-image life would need just a few key molecular ingredients—a little biology primer will help to explain what those are.

In cells, the enzyme DNA polymerase makes copies of DNA molecules as the cell prepares to replicate, while RNA polymerase creates so-called messenger RNA (mRNA) molecules that carry the information for making proteins. In both cases, the sequence of nucleotides made by the polymerase is determined by that in the DNA “template” strand on which the enzyme puts together the new nucleic acid. DNA nucleotides come in four varieties, distinguished by the molecules called nucleotide bases they contain: adenine (A), cytosine (C), thymine (T), and guanine (G). Each base is attached to a sugar molecule called deoxyribose and a phosphate group, which together form the backbone of the double helix on which the bases hang. Deoxyribose is a chiral molecule, and in natural DNA it is always the D-enantiomer, which is what makes the helix twist in a right-handed fashion.

The nucleotide bases can stick to one another in pairs via weak chemical bonds called hydrogen bonds. These pairs have distinct preferences because of the way the bases fit together: A sticks to T, and C to G. So the twin strands of DNA are zipped up by hydrogen bonds, and they have complementary sequences: where one has an A, the other has a T, and so on. Crudely speaking, some DNA sequences—those of the regions corresponding to genes—encode the structures of proteins, which are crumpled-up chains of amino acids. Each triplet of DNA bases, called a codon, encodes a single amino acid: This correspondence is called the genetic code.

Base pairing allows a new DNA strand to be put together on an existing one, once that part of the double helix is unzipped. The complementary pairing means that the new strand has a sequence complementary to that of the template strand: The information encoded in the sequence is preserved. All the DNA polymerase enzyme needs to do is to join together the backbone segments of new nucleotides as they dock onto the template strand.

The assembly of an RNA molecule on a DNA template strand, catalyzed by RNA polymerase, relies on the same rules of base pairing except that in RNA a base called uracil substitutes for DNA’s thymine. Once a protein-coding gene (which might typically be a few hundred bases long) has been transcribed into mRNA, the RNA molecule floats free from the DNA template strand and is translated into a protein by a large cluster of proteins and RNA



molecules called the ribosome. Amino acids are brought to the ribosome attached to small RNAs called transfer RNA (tRNA), which dock onto the mRNA so that the amino acids get linked into the corresponding sequence.

The processes of information transfer involved in DNA replication, transcription, and translation comprise the so-called Central Dogma of molecular biology adduced in 1957 by British biologist Francis Crick, co-discoverer of DNA's double-helical structure. Information goes from DNA to DNA during replication, said Crick, and from DNA to RNA to protein during transcription and translation. He also allowed for the possibility that it could pass from RNA back to DNA—a suggestion validated in the 1970s when researchers discovered that viruses that encode their genes in RNA (examples now include HIV and SARS-CoV-2) could insert them into the host DNA. This “reverse transcription” is orchestrated by a polymerase called reverse transcriptase, which itself is encoded in the viral genome.

REVERSING THE PARTS

Zhu's aim is to create mirror-image versions of all the components involved in enacting the Central Dogma. Then he can progress from DNA to proteins in this looking-glass world, as well as enabling DNA replication. This would give him the minimal set of biomolecules needed for putting together an inverted life form.

His first target, attained in 2016 while he was based at Tsinghua University in Beijing, was an inverted DNA polymerase. Wisely, he chose to synthesize the smallest such protein known, called African swine fever virus polymerase X. To make the inverted enzyme, Zhu's team used now well-established chemical methods for joining amino acids one by one, although it was challenging to apply them to such a long chain. A mechanical engineer by training, Zhu learned his chemical craft under the expert guidance of Szostak, who has long pursued the challenge of making rudimentary synthetic living entities called protocells from scratch.

Once Zhu's team had put the enzyme together, they verified that it was able to complete a 12-base strand of L-DNA on an 18-base template strand, filling in the remaining six nucleotides. The enzyme did that job rather slowly compared with natural polymerases, however, taking about four hours: Because the African swine fever virus polymerase X is so small, it isn't terribly efficient. Given even longer—a day and a half—the enzyme was able to extend such a 12-base “primer” strand all the way along a 56-nucleotide template. Better still, the mirror-image polymerase worked for making RNA too, transcribing L-RNA on an L-DNA template.

It would be useful to use such a mirror-image DNA polymerase to *amplify* strands of L-DNA—that is, to make copies from which it can make further copies, boosting the number of strands exponentially. That's what happens in the process called the polymerase chain reaction (PCR), ubiquitous in genetic biotechnology for making lots of DNA from tiny samples. (It's the process used in the PCR test for COVID-19, where tiny amounts of viral genome in swab samples are amplified so that they can be identified.) To conduct PCR, the double-strands made by a DNA polymerase are separated so that each strand can act as a template for further replication, and the cycle is repeated many times. The strands are separated by warming them up, which unzips the hydrogen bonds holding them together. This heating is apt to destroy most polymerase enzymes, but standard PCR uses one taken from a thermophilic (“heat-loving”) bacterium that lives in hot thermal springs, which is more resistant to heat.

As his next target for mirror-image biochemistry, Zhu chose a DNA polymerase called Dpo-4 from a heat-tolerant microbe, *Sulfolobus solfataricus*. The researchers made it in 2017 and showed that indeed it could be used for looking-glass PCR. In 2019, Zhu's team made a mutant form of the polymerase that could not only transcribe L-RNA from L-DNA but also reverse-transcribe it, writing an RNA sequence back into DNA: another link of the information-transfer network in the Central Dogma.

“The devil is in the details,” he says cautiously, “and there are a lot of devils.”

In 2022, Zhu and colleagues synthesized the mirror-image form of the massive 883-amino-acid protein RNA polymerase used by the T7 bacterial virus, a widely used enzyme for transcription because of its efficiency and accuracy. This achievement, says chemical biologist Richard Payne of the University of Sydney, “represents a monumental feat of total chemical synthesis and a pivotal breakthrough on the journey toward mirror-image life.”

With nucleic-acid polymerization under his belt, Zhu moved on to the biggest challenge for a mirror-image Central Dogma: a reversed ribosome capable of translating L-RNA into D-proteins. The ribosome is not a single enzyme but a huge piece of biochemical machinery, with many component parts. In the ribosomes used by the common gut bacterium *Escherichia coli*, for example, there are around 55 proteins and three ribosomal RNAs.

Zhu began working toward this goal in 2019, and the following year his group at Tsinghua reported that they had synthesized mirror-image versions of three key ribosomal proteins. They used their polymerases also to make a mirror-image ribosomal RNA molecule and showed that the three proteins would assemble spontaneously with this RNA into the complex found in the ribosome.

Now Zhu says that he and his team at Hangzhou have made nearly all the molecular components of the ribosome, although they have not yet published this work. How close is he? “The devil is in the details,” he says cautiously, “and there are a lot of devils.”

There might be a dark biosphere—a whole ecosystem of mirror-image life forms.

LIFE, INVERTED?

If Zhu succeeds in making a mirror-image ribosome, it could be a huge boost for D-protein therapeutics, because then such proteins could be made simply by producing the corresponding mirror-image DNA—a simpler task—and transcribing and translating it.

“A working synthetic ribosomal system for making mirror-image proteins would be a practical demonstration of the power of chemical synthesis applied to enzyme protein molecules,” Kent says. “It would show that we do in fact understand the key aspects of how proteins are biosynthesized.”

Yet Zhu’s ultimate goal is not drugs but life itself: making a mirror-image protocell with all that it needs to replicate and to use its genome to generate the enzymes it needs to function and metabolize. That would arguably constitute the first genuinely artificial life form. Goodness knows what such a thing might be used for, but Kent attests this curiosity-driven work—what he calls “ambitious and excellent science”—is its own justification. “Good research does not need to be justified by practical applications,” he says.

Can such mirror-image life ever be made in the lab? A minimal protocell that can transcribe and translate its genome into functional proteins need only have the basic molecular ingredients encapsulated within a lipid membrane. A more ambitious goal would be an entire mirror-image bacterium, with all its nucleic acids, proteins, and sugars inverted. If such an organism is ever made, it should look and act no different from a normal bacterium. Only by zooming in on the individual molecules would the looking-glass difference become apparent.

Right now, though, all this is still fantasy. Zhu points out that no one has yet made a replicating synthetic protocell even using the normal biomolecular machinery. He thinks it makes sense to wait until that is done before trying to do it with mirror-image molecules.

Mirror-image life might also help to explore “one of the biggest mysteries surrounding the origin of life on Earth,” says Zhu—its “homochirality,” or why it uses only D-nucleic acids and L-proteins. Some think the choice was entirely random: Perhaps both enantiomers existed among the prebiotic building blocks, and some random fluctuation in the concentrations of one type got amplified by feedback processes and gained precedence. Others wonder if some tiny chiral bias might have been introduced by more fundamental factors, such as the left-right symmetry-breaking called parity violation, known to occur in nuclear processes involved in radioactive beta decay.

Having a mirror-image biochemistry might not answer the question of homochirality, but it could supply a new direction to probe: by putting both enantiomers of the biomolecules together in the same test tube and seeing what happens, especially if the molecules can mutate and evolve. Zhu says that in dilute solutions, mirror-image proteins and nucleic acids seem to ignore one another. But if they interact in more concentrated conditions, might just a single chirality emerge from the melee?

There is another possibility, too. “Is life on Earth really homochiral, or do we just not have the right tools to look for the other chiral version?,” Zhu asks. What if mirror-image life exists in some corners of the natural environment that we’ve overlooked because we don’t have the means to detect it? There might be a dark biosphere—a whole ecosystem of undetected mirror-image life forms. If so, a PCR system that can amplify the inverted DNA from such organisms could help to bring it to light.

Once he has made a working mirror-image ribosome, however, Zhu says he’ll probably leave the challenge of complete mirror-image proto-life to others. At that point, he’ll be ready to move on to other projects. Besides, he has another way to explore the dreams of alternative life. “Things I can do, I’ll do in the lab,” he says. “Things I cannot do yet, I’ll write them as science fiction.” ☺

PHILIP BALL is a freelance science writer based in London, and the author of many books on science and its interactions with the broader culture. His latest book is *How Life Works*.



A photograph of two fishermen in a small boat on the water at sunset. One fisherman is standing and holding a long pole, while the other is sitting. The sun is low on the horizon, creating a warm orange glow. The sky is a mix of orange, pink, and blue. The water reflects the colors of the sky and the silhouettes of the fishermen.

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Where Did the Brain Come From?

600 million years ago, the sea sponge had a dream

BY KENNETH S. KOSIK

BEFORE OUR EVOLUTIONARY ANCESTORS had a brain—before they had any organs—18 different cell types got together to make a sea sponge. Remarkably, some of these cells had many of the genes needed to make a brain, even though the sponge has neither neurons nor a brain.

In my neuroscience lab at the University of California, Santa Barbara, my colleagues and collaborators discovered this large repository of brain genes in the sponge. Ever since, we have asked ourselves why this ancient, porous blob of cells would contain a set of neural genes in the absence of a nervous system? What was evolution up to?

The sea sponge first shows up in the fossil record about 600 million years ago. They live at the bottom of the ocean and are immobile, passive feeders. In fact, early biologists thought they were plants. Often encased by a hard exterior, a row of cells borders a watery center. Each cell has a tiny cilium that gently circulates a rich flow of microorganisms on which they feed.

This seemingly simple organization belies a giant step in evolution. For the previous 3 billion years, single-celled creatures inhabited the planet. In one of evolution's most creative acts, independent cells joined together, first into a colony and later into a truly inseparable multicellular organism.

Colonies of single cells offered the first inkling that not every cell in the colony had to be identical. Cells in the interior might differ subtly from those on the periphery that are subject to the whims of the environment. Colonies offered the advantages of cooperation among many nearly identical cells.

The next evolutionary innovation, multicellularity, broke radically from the past. With multicellularity,



cells became highly specialized; they relinquished their individual identities and independence for the greater good of the organism. This innovation was one of the greatest acts of altruism in the history of life.

Although these cells were now no longer able to survive on their own, the organism gained by the collective functioning of different cell types. As organisms added specialized cells, integrated modules called organs conferred novel functions and abilities.

Nowhere have specialized cells within an organ become more diversified than in the nervous system. The evolution of the nervous system in animals was critical to the wildly successful kingdom of life. But it did not happen all at once. As ancient creatures crossed the long-vanished boundary from single-celled organisms to animals, a complex nervous system emerged.

The early evolution of animals is full of puzzles, and the origin of the nervous system lies at the core of the maze. From a common ancestor of all animals, for which no trace exists today, sprang two lineages called sister groups. The more recent sister is the sponge. The older sister is the comb jelly, which is just a few millimeters in size or as large as five feet, consisting of a jelly-like body with a layer of cells above and below that creates a cavity.

To encode a nervous system requires thousands of genes, each of them with many thousands of nucleotides, the letters of the DNA code. Acquiring this massive genetic storehouse of instructions while sustaining viability each step of the way was a daunting task. After 3 billion years of single-cell organisms that adapted to the changing climate of the early Earth, the first animals began to flicker in the dark roil of the ocean bottom, hardly recognizable as an innovation against the highly competitive world into which they were born.

From the sponge evolved the entire animal kingdom, including us. The comb jelly, although it still survives today, was an evolutionary dead end devoid of the potential from which a novel species could evolve. Curiously, the comb jelly has a nervous system, but the sponge, as noted, does not, even though it has many of the genes needed to make one.

Many questions surface from this history. Did the common ancestor of both the sponge and comb jelly already have a nervous system that was lost in the sponge? Or did the nervous system get invented twice, once in the comb jelly and then again in the evolutionary descendants of the sponge?

A deep look at the synapse offers some clues. The synapse is among the most salient features of a nervous



BRAIN PUZZLE Sea sponges (pictured here is *Amphimedon queenslandica*) whose lineage dates back hundreds of million years, contain genes for a brain, even though sponges don't have a brain themselves. This riddle has provided scientists a window on the extraordinary ways of evolution.

Why did this porous blob of cells contain neural genes? What was evolution up to?

system. This complex structure is used for communication between two neurons, or a neuron and another target cell like a muscle. It has two parts, one that sends the message, and the other that receives the message. The message sent to the receiving cell is integrated within an intricate network, designed to make a single decision—either fire or not. The instructions are packaged in chemicals released by the sending cell and read by the receiving cell.

From an engineering perspective, this design makes no sense. If you want to wire one thing to another, you wire them together directly. Neurons, with their synaptic way stations, bring an electrical signal traveling along an axon to an abrupt halt, convert it to a signal that releases chemicals across the synapse, and initiate an electrical signal on the other side of the synapse. This slows down the entire process and introduces some error when the signal is transmitted, because synapses are not 100 percent reliable. What makes the synapse so remarkable is its ability to change with experience. It can become more or less efficient in transmitting a signal depending on the input it receives. It is a built-in mini learning device, spread through the nervous system, like the tiny knots of hand-tied fishing nets.

With my students, we burrowed deep into the synapse, to the very genes that encode its proteins. The two sides of the synapse must be precisely aligned for efficient transmission of the message. This precise alignment is mediated by a protein scaffold that locks the two sides in place. Some of the hundreds of proteins that together function as a synapse, particularly the scaffold proteins, had already begun their evolutionary journey in single-celled organisms. Scaffolds suspend what is attached to them. The sponge utilized the ancient scaffold, but wiped it clean and suspended new proteins from it to build the synapse. Evolution drew upon ancient genes, as a parts list, to construct the nervous system.

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The sea sponge reveals what a partial nervous system looks like along the way toward a full-fledged one. To feed, the sponge's watery interior is lined with flagella, hairlike appendages, that maintain a coordinated beat to circulate microorganisms for ingestion. The coordination beat of the flagella suggested something akin to an inchoate neural system.

Two years ago, a remarkable set of experiments came from the lab of Detlev Arendt at the European Molecular Biology Laboratory in Heidelberg. Arendt and colleagues discovered that two different cell types in this digestive chamber can make contact, and these two cells express the specific proteins that lie on one or the other side of the synapse. These first experiments at cell-cell communication are not synapses; they lack the machinery to convert the contact to an electrical signal in a neuron. Nevertheless, nature had begun to explore neural-like communication.

History is written by the victors, so evolution only tells us about the winners—those who survived, either as modern living progeny of an ancient ancestor or encrusted in the fossil record of a once successful existence on the planet. From such rudimentary beginnings, nervous systems with synapses capable of buzzing their chatter all around the body became winners in the animal kingdom.

The nervous system evolved and radiated throughout the animal kingdom. It led to survival tactics such as mating, the color changes of octopuses, hibernation, the waggle dance of bees, and dream states while sleeping. Brains could grow as big as a VW engine in the blue whale or shrink to a speck of tissue the width of a human hair in the ragworm.

The nervous system and the enhanced fitness it offered was one likely basis for the great divide between the plant and animal kingdoms that set each on separate evolutionary paths. It provided animals with motility, while plants bypassed the entire undertaking. And animals have adapted motility in a legion of styles: the swimming of fishes, the flying of birds and bats, the crawling of insects, the slithering of snakes, the swinging arms of gibbons, and the preposterous sideways scampering of crabs.

It's easy to underestimate the complexity of motility. An animal must predict where within the obstacles of its surrounding space it will be with each motion,

The ancient, unassuming sea sponge made possible a vast variety of future lifeforms.

and the speed at which it will move. It must feel the motivation to move, whether that be the detection of danger, the sensation of hunger, the pursuit of a mate, or the restless urge to wander. You can almost see the brain in action when you approach a squirrel in the road—it hesitates for a split-second while deciding to dart toward its intended destination, with some uncertainty about what might lie there, or back to the familiar safety from where it came. With motility comes choice, whether free or not is another matter.

How astounding that within a 600-million-year-old sea sponge, a gene set lay the framework for a future that could not have been anything more than an abstract space, an intangible dream, as elusive as the space of consciousness.

This abstract space is the property of “evolvability,” built deeply within the structure of biology, to create variation among species that is heritable and increases the organism's fitness for its environment. Evolvability does not reside in any gene sequence but is a collective property through which genes are connected to the environment.

The sea sponge, with its unrealized nervous system, was oblivious to the eons that stretched out in front of it, as it silently worked out its future. That future lay in its genes, a set of instructions that can faithfully reproduce over generations and change form as they evolve. Evolution conferred the unassuming sea sponge with a genetic program that made possible a vast variety of future lifeforms. Together life intricately and beautifully melds constancy over generations and change over evolutionary time in a beautiful dance. ☺

KENNETH S. KOSIK is a neuroscientist whose research has appeared in *The New York Times*, the BBC, CNN, PBS, and *60 Minutes*.

Can We Stop Time in the Body?

Inside the “out there” quest for a drug that would help doctors save lives before it’s too late

BY ELENA KAZAMIA

THE CEREMONY TAKES PLACE on the night of the full moon in February, which the Tibetans celebrate as the coldest of the year. Buddhist monks clad in light cotton shawls climb to a rocky ledge some 15,000 feet high and go to sleep, in child’s pose, foreheads pressed against cold Himalayan rocks. In the dead of the night, temperatures plummet below freezing but the monks sleep on peacefully, without shivering.

Footage of the ritual exists from the winter of 1985 when a team of medical researchers led by Herbert Benson, a Harvard cardiologist, was allowed in as observers at a monastery just outside the town of Upper Dharamsala in northern India.¹ Benson had the blessing of the Dalai Lama, with whom he had developed a friendship; the physician was driven to understand the physiological mechanisms that allowed the monks to survive the night. Their bodies had entered a state that required years of meditative and physical practice that the Dalai Lama called miraculous. Had Benson’s research taken place today, it is very likely he would have called it “biostasis.”



SLOW LIVING Inspiration for a biostatic drug came from hibernating animals, such as Alaskan brown bears, who can shift their metabolism into a lower gear for winter.





If the life burning within us is a symphony, then metabolism is its score.

Our bodies run a very tight ship. To keep living, we need a constant supply of oxygen, and our temperature is allowed to fluctuate within narrow limits. A fever can turn deadly, as can severe hypothermia. Healthy bodies have a steady heartbeat and a dependable oxygen consumption rate, which physicians use as a measurement of metabolism. If the life burning within us is a symphony, then metabolism is its score—the perfect sum of all the chemical reactions that take place inside our cells, carefully orchestrated.

Until recently, at least from the perspective of Western medicine, life's tempo was considered non-negotiable. The change in outlook has come from an unusual initiative, a program led by the Defense Advanced Research Projects Agency (DARPA), which supports the United States military. Over the past five years, DARPA has funded research into biostasis, which aims to bring the metabolic symphony to a halt, before resuming the score some indefinite time later, exactly where it left off.

One promise of the DARPA biostasis research is a state of suspended animation or physiological stability, delivered in the form of a drug, rather than through years of meditative practice. This would differ from anesthesia by acting on all human tissues equally, rather than suspending only consciousness and pain. Biostasis aims to snap-freeze the whole body, without the cooling.

With biostasis, DARPA planted a flag in uncharted medical territory,

asking researchers to reach beyond normal health. Tristan McClure-Begley, a former program manager at DARPA, who founded the biostasis project, explained its key impetus was extending the “golden hour”—the period immediately after a severe injury when medical and surgical treatment could prevent death. With head and spinal cord traumas in particular, irreparable damage accrues if aid is delayed. A biostatic delivered on the battlefield could buy time for fallen soldiers, improving their chances of survival.

DARPA issued a call to fund researchers to develop a biostasis drug, and the Wyss Institute for Biologically Inspired Engineering at Harvard University is one of the teams that answered. “This DARPA call was fun because it was so out there,” said Don Ingber, founding director of the Institute and a chaired professor at Harvard’s medical and engineering schools. “There was no place to start, no drug target or screen to implement,” he added. It is remarkable that in the absence of academic precedent or a history of research to draw on, the first successful biostasis drug was proposed earlier this year.²

SNC80, the name that the small-molecule drug is known by, was first tested on *Xenopus* tadpoles. The cold-blooded amphibian embryos are easy to manipulate in the lab and are useful models for approximating human nervous and immune systems. They have a large bulbous head with a brain and spinal cord and a tail for swimming. The tadpoles have a beating heart, gills, and intestines.

What did the scientist think of the monks who slowed their own metabolism?

The core organs are important as indicators for what may happen to an equivalent human organ, whereas the tadpoles' swimming ability sets up a quick and easy screen for biostasis.

A minute dose of the chemical, which permeated the translucent skin of the tadpoles, slowed down their swimming, halved their heart rate, and brought their oxygen consumption—the gold standard for measuring metabolic rate—to one third of baseline. Most importantly, the effects were reversible. Within an hour of the drug being drained, the tadpoles went back to briskly swimming around petri dishes. To the best of the researchers' knowledge, no core organs of the tadpoles were adversely affected by the drug.

Megan Sperry, a postdoctoral fellow at the Wyss Institute who led the tadpole research, explained that molecules of SNC80 were able to penetrate all tadpole tissues, including their guts, gills, and skeletal muscles. Here was a drug that impacted the whole organism, likely tinkering with something critically central to biology, which acted to arrest all biological processes indiscriminately. It was later found that SNC80 works to slow down mitochondria, the power houses of all cells, arresting metabolic processes without killing tissues. Importantly, Sperry said, the drug did not “induce toxicities.”

Reversibly shutting down metabolism is not unheard of in nature. Much of the bio-inspiration came from digging deep into ecological studies of hibernating animals. Species such as brown bears living in Alaska can actively shift their metabolism into a lower gear for winter, slowing their heart rate to four beats per minute and dropping their body temperature to below 40 degrees Fahrenheit. The visually unassuming wood frog *Rana sylvatica* can go as far as completely freezing solid to skip the Arctic winter season.

Perhaps the most impressive feat of biostasis, which has not escaped DARPA's attention, is performed by the spiny desert mouse. With rounded ears, dark oil-slick eyes, and a golden coat, it has capabilities worthy of DC superheroes. Not only is the spiny desert mouse the only mammal known to be capable of tissue regeneration, growing back skin, sweat glands, fur, and even cartilage with little to no scarring when a predator takes off a bite, in times of extreme need it can go into full body torpor for six to seven hours at a time. It can do this in the heat of the African desert, a rare example of torpor as a response to hot rather than cold temperatures.

The greatest challenge with developing a biostasis drug for humans is finding a chemical that can act on the whole body, affecting a variety of tissues

and organs gently but profoundly. The Harvard team tested the impact of SNC8o on “organs-on chips,” microchip devices with tiny channels lined with living human organ cells. They also tested its impact on select human tissue cultures, including the gut and the liver, as well as on whole pig organs and limbs. The effects were remarkable—a viable pig heart could be preserved for twice as long as it could using traditional preservation techniques that rely on mechanical cooling. “And a pig heart is almost as big as a human heart,” Ingber said. “So that’s probably the most impressive thing we’ve done.”

The perfect biostasis drug would be something that doesn’t affect the harmonies of metabolic processes, and the complex wiring that integrates different tissues of a body into a single whole. Ingber admits SNC8o is not that perfect drug. But as is often the case with drug development, the experiments have been a good start. SNC8o is the “first step toward compounds that reversibly slow down metabolism,” Ingber said. “And we have already identified new versions of the molecule that are more potent. This one works at the level of tissues and individual organs.” The next step would be to get the drug to work on the whole person.

Herbert was able to convince the Tibetan monks he had observed in the remote Rumtek Monastery to participate in a medical study.³ Sitting cross-legged in a large unheated ceremonial room, the monks consented to wearing special face masks during their daily meditation, connected to a respirometer. This allowed the physicians to collect small quantities of expired air during their breathing, which they analyzed for oxygen content. Strikingly, they found that during several different meditative practices, resting metabolism “could be both raised (up to 61 percent) and lowered ([by] 64 percent),” the latter of which is on par with the effects of SNC8o on *Xenopus* tadpoles.

I asked Ingber what he thought about the monks, who showed that metabolism in the whole human body could be slowed. “At some high level, you’re probably right that there’s a nervous system involvement in all this,” he said. “But oxygen utilization is only one part of metabolism. A Tibetan monk will be awakened if you tap on him. So it’s not exactly a torpor state, but it’s certainly the first step toward slowing metabolism, which can be done for short times.”

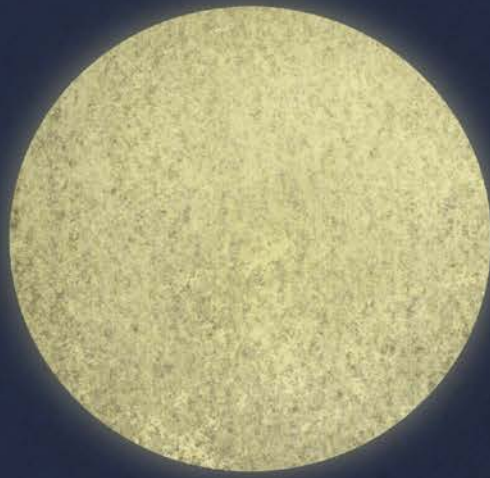
The initial goal of biostasis research—a state of suspended animation that can last as long as it takes to reach distant planets or survive beyond the “golden hour” after catastrophic injury—remains out of reach. But not entirely. We are, after all, animals ourselves. “The way I see it,” Ingber said, “is that animals like the Alaskan ground squirrel can go into torpor and don’t need to eat for extended times. Bears can hibernate. I was just thinking this summer about hummingbirds and butterflies. They go into torpor every evening.”

As scientists continue to work on a therapy to induce humans into a full-body torpor, maybe they should take another close look at the ceremony of Tibetan monks, meditating in the winter cold. They look as peaceful and content as butterflies. ☺

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What We Can Learn From an Insomniac Fish

When sleep doesn't come on time

BY KATHERINE HARMON COURAGE



ON THE SURFACE, sleep seems obvious, essential. It comes in long, languid, predictable waves, washing over humans and elephants, birds and fish and beetles. It comes bearing restoration, repair, learning. It follows an ancestral rhythm played deep within our cells, cued by the movement of our planet around our star.

Perhaps we could believe this nice, simple fantasy, were it not for an irksome little eyeless fish.



More than a decade ago, this fish—the Mexican tetra (*Astyanax mexicanus*)—caught the eye of a graduate student at New York University. It was not new to science—it had been the subject of fascination for aquarists and researchers for decades, who marveled at its ghostly appearance and the splash of skin where its eyes should have been. But other quirks of the fish turned out to be even more mysterious.

In Manhattan, the fish were far from their place of origin: a collection of unassuming caves strung through northeastern Mexico. Inside these caves, it is pitch dark, always cool, quiet, and rather boring. A seemingly perfect place to sleep.

So Erik Duboué, the observant graduate student, decided to test if these fish showed any unusual sleep

habits. One night in 2009, he made a 2 a.m. visit to the lab and noticed something strange about these sightless fish: They seemed wide awake. On further investigation, he found that despite their soporific native environs, they actually hardly sleep at all. In fact, he discovered, they doze just about three and a half hours out of each 24-hour period. And their bouts of sleep seem to come on entirely randomly and only in brief spurts.

Curiously, these eyeless cavefish seem to have been flourishing on this quiescence interruptus for hundreds of thousands of years. “What you have is a fish that is completely healthy—it just doesn’t need to sleep,” says Duboué, who is now a molecular geneticist at Florida Atlantic University.



Since then, Duboué and others have been studying the strange sleep of these wakeful creatures—prodding them in the lab to rouse them from their occasional slumber and plumb their DNA. Combined with investigations into other animals, as well as some peculiar experiments that have sent humans to sleep in caves, scientists are uncovering new, closely guarded truths about sleep that have eluded us in our bright, rhythmic world.

IN THE PANOPLY OF EVOLUTION'S CREATIONS, plenty of animals actually appear to do just fine on little sleep. Frigatebirds in the Galapagos go on weeks- (and sometimes months-) long hunting trips over the ocean, drifting off to sleep—mid-flight—for up to several minutes at a time and for just about 40 minutes total each night—less than a tenth of their usual daily rest. Even the sagacious African elephant seems to sleep only a couple fragmented hours a night in the wild—while living into their 60s and 70s and maintaining astonishing cognitive, social, linguistic, and recollective capabilities. These and other extreme examples have thrown into question our long-held assumptions about the primacy of sleep.

But the Mexican blind cavefish piqued Duboué's interest because their sleeplessness was particularly unexpected. Members of the very same species, *A. mexicanus*, also live and thrive just outside the caves—darting through glinting, sunlit rivers. These fishes are decorated to match their environment, have two perfectly functional eyes, and catch a healthy 13 hours of Zs.

The differences between the populations—surface- and cave-dwelling—had made the fishes a quiet darling of biologists¹. They offered a real-life way to probe the work of evolution. But scientists had largely focused on the fishes' striking physical differences. These adaptations made some sense. No need to throw energy into growing eyes or creating pigments if they were perfectly useless in the pitch dark.

Until Duboué came along, though, no one had taken much notice of the way the fishes sleep. "Sleep seemed like a reasonable thing to study in a fish that had spent 1 million years—depending on who you ask—in perpetual darkness," he says.

He built his first sleep-tracking experiment with cameras to track the fishes' movements. But he couldn't

Inside these caves, it is a seemingly perfect place to sleep.

resist checking on the fish. So he let himself into the lab on W. 4th Street in the middle of the night. Immediately he could tell these cavefish populations were not sleeping at all like the surface-dwelling ones.

The beauty of the eyeless cavefish, from a scientific perspective, is that they show the same sleeplessness across a range of different populations—from caves in Tamaulipas to San Luis Potosí—even though each population was stranded inside its particular cave separately.

Some 800,000 to 1 million years ago, during the Calabrian, surface water flowed across that part of the continent, making much of the area a connected habitat throughout which the fish could swim—up and down waterways, in and out of caves, basking in the sunlight, and presumably sleeping a regular, circadian-guided sleep at night. But then, the water receded. The caves were cut off from the main water channels, and the fish inside them were trapped.

And this happened again, hundreds of thousands of years later—as recently as 200,000 years ago—this time stranding new surface Mexican tetras in caves, those that had continued to evolve, as species are wont to do, over the hundreds of thousands of years.

Nevertheless, across the long-isolated caves, the fish populations seem to have converged on the same end-less, sleepless nights—offering a rare view into sleep evolution that was a scientific first.²

Many of these adaptations—from eyelessness to sleeplessness—scientists discovered, seem to have occurred through different genetic pathways. But fish from both waves of cave strandings show changes in genes that control a neurotransmitter called hypocretin. Hypocretin is, as Duboué explains it, "a wake-promoting system." And in their lab studies, they found that all of the Mexican blind cavefish did, indeed, have an overabundance of cells that produce hypocretin.



ZERO WINKS In populations that have long been isolated in caves, the Mexican tetra (*Astyanax mexicanus*) morphed into an eyeless, colorless, and nearly sleepless version of its surface-dwelling cousins. Just why it lost its sleep—and nearly all detectable circadian rhythms—is still a subject of scientific investigation.

Hypocretin is not just for fish. It plays the same wakeful role in animals of all stripes, including humans. A disruption in the hypocretin pathway causes narcolepsy in humans—and in dogs, where it was originally discovered.

“That’s a really interesting thing,” Duboué says, that this same system helps to control sleep and wakefulness “whether you’re a human or whether you’re a mouse or whether you’re a fish.” Even one that only sleeps a few eyeless winks here and there.

Because there are two things we usually think of controlling sleep: the circadian cycle and the external cues that keep that cycle playing in tune.

IN ALMOST ALL ANIMALS, sleep is presumed to be under the control of circadian rhythms, which are, in turn, organized by external cues known as zeitgebers (“time-givers”). A zeitgeber is a powerful whisper from without, an environmental lullaby—*go to sleep*—and nature’s alarm clock—*time to wake*. Circadian cycles were once thought to be entrained only by sunlight, but researchers have since found all sorts of environmental forces that nudge it: temperature, moon cycles, even food availability. For example, in a world without light, deep sea mussels living by hydrothermal vents in the midnight zone of the oceans keep time with the tides.

The Mexican blind cavefish, though, seem to live in deafening zeitgeber silence. No temperature variation,

no light changes, not even the pull from the moon on their small pools. Some researchers posited perhaps bats flying in and out of some of the caves, depositing guano into the water at particular intervals after feeding, could be an adopted zeitgeber. But scientists have found no evidence that the bats’ rhythms affect the fishes’ sleep. Could it be that this total absence of zeitgebers made their circadian orchestra play so out of tune with the rhythms of their surface-dwelling peers?

When Duboué and other researchers went looking, though, they found the circadian orchestra’s pit quiet. Many animals that live away from light have an underlying circadian cycle that can activate if they are exposed to regular light patterns. Not these fish. “They have lost their entrainable rhythms, for one reason or another,” Duboué says.

How, then, do the fish know when to sleep, and when to wake? That, he says, is still an open question.

“We know that sleep and circadian rhythms are related to one another,” Duboué says. But studying these and other subterranean animals has revealed that, “the evolutionary forces that drive circadian rhythms and sleep need are likely different from one another.”

Many subterranean species have short sleep durations but still have functioning circadian clocks—including other cavefish species Duboué has studied in Laos and Thailand—even though they have lived without light to sync them for potentially hundreds of thousands of

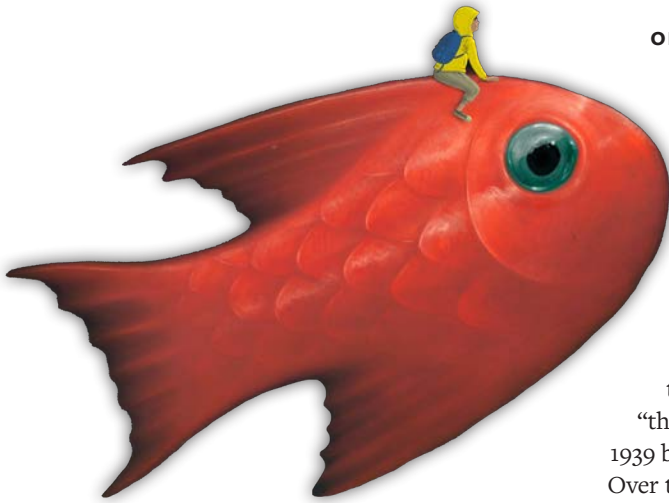
The African elephant seems to sleep only a couple fragmented hours a night in the wild.

generations. (Somalian cavefish have lost circadian rhythms that can follow light cues but have, so far, kept ones that sync with feeding.) Genetic studies have revealed that species of cavefish that have been isolated in caves more recently, evolutionarily speaking, are much more likely to retain active circadian cycles, despite falling off of a 24-hour rhythm of sleep.

Although this dislodging of sleep from the circadian cycle might sound strange, it makes some logical sense. Plenty of organisms maintain circadian cycles for things like feeding and reproduction, but don't necessarily participate in sleep as we would recognize it: bacteria, plants, fungi. Scientists have also found repression of or changes to circadian cycles in strange places³: baby honeybees, Arctic reindeer, some species of mole rats. It also takes energy to maintain any kind of system, including circadian rhythms, and cave environments tend to have a scarcity of food. So perhaps if circadian rhythms weren't needed, they simply went the way of the fishes' eyes, kicked to the evolutionary scrap heap?

"We usually hear 'trait' and think of morphology," says Markus Friedrich, who is chair of the biology department at Wayne State University and has studied sleep rhythms—and lack thereof—in other cave-dwelling species. Like one of Darwin's finches: Change the environment, and the beak changes as well. So, too, could it be with the incredibly complex behavior of sleep? The precise evolutionary dynamics for how this might work are still being sorted out. "The circadian clock is most likely just one of a number of regulatory processes that affect sleep," Friedrich says.

Sleep, he points out, is a trait just like any other in animals. And "the trait sleep is moldable."



ON JUNE 4, 1938, Nathaniel Kleitman, a psychology professor at the University of Chicago, and graduate student Bruce Richardson entered a grand hall-like cavern deep in Mammoth Cave in Kentucky to see if an extreme environment, devoid of routine zeitgebers, would alter their own sleep rhythms.

They packed lanterns and thermometers and rat traps (so as not to be disturbed). And no clocks. Beds, nice linens, and randomly timed meals were provided by the nearby Mammoth Cave Hotel. They spent 32 days underground, where the temperature was always 54 degrees Fahrenheit, and "the silence was also complete," Kleitman wrote in his 1939 book *Sleep and Wakefulness*.

Over the course of their month-long stay, the two scientists fell into a 28-hour-day, sleeping for about 9 hours and keeping busy for the next 19. This at once seemed to validate Kleitman's assertion that "there is no foundation for assuming that some cosmic forces determine the 24-hour rhythm"—but also suggested that there were underlying, internal forces keeping human sleep organized into singular, daily, rhythmic bouts.

PROFESSOR SANDMAN

Nathaniel Kleitman, a psychology professor, volunteered himself and a graduate student to descend into a cave for a month in 1938 to see what happened to their sleep rhythms when they were away from typical zeitgebers. The pair, pictured mid-experiment here, tracked sleep and wake times as well as body temperature and other physiological fluctuations during their stay.



Other human cave sleep experiments since then have entailed even longer underground stays—removing people from familiar zeitgebers for upward of a year, as in the case of Italian sociologist Maurizio Montalbini. Montalbini undertook numerous record-breaking cave stays—often solo—including one subterranean sojourn starting in 1993 that lasted for 366 days (which he thought had been just 219 days). In other studies of groups of people voluntarily isolated underground or in hyper-controlled bunkers, some people settled into rhythms of 14-hour sleep followed by 34 hours of activity, another created a day that was 58 hours long. But by and large, most people stayed on a close-to-24-hour cycle, underscoring the drive circadian rhythms have in our bodies, even when isolated from standard cues, over the course of a small fraction of a lifetime.⁴

“What we learned from these experiments is that we are actually pretty similar to fruit flies in that the circadian clock is the dominant force in regulating sleep activity,” says Friedrich, who has studied the sleep of subterranean beetles that live in the same vast cave system to which Kleitman and Richardson retreated.

Friedrich points out that fruit flies actually tend to wake before the sun rises, perhaps readying themselves for prime foraging times. Humans and other animals likewise have probably been entrained by predictable day-night cycles for wakefulness in preparation for the best times to find food—and to avoid becoming it. In that way, Friedrich says, “animals are predictors

of future events.” But for cavefish, in an environment devoid of these fluctuations, the future is more or less just the same as the present: All times are equally optimal for feeding just as they are for rest or wakefulness.

The early zeitgeber-deprivation experiments in humans paved the way for a forceful drive to center sleep—and other bodily functions, such as hormone release and the immune system—on circadian cycles. Their critical role in organizing biology was increasingly recognized over the following decades—and in 2017, the Nobel Prize in Physiology or Medicine was awarded to three researchers who had uncovered the molecular underpinnings of the circadian cycle. Kleitman’s cave observations were a “key event in the history of human circadian rhythm research,” wrote Jerome Siegel, director of the Center for Sleep Research at the University of California, Los Angeles Semel Institute for Neuroscience and Human Behavior, in a 2001 tribute to Kleitman. But could this powerful force behind human sleep also be nudged off its post?

IN HIS 1930S CAVE STAY, one of Kleitman’s goals was “to determine how easily man can break away from the 24-hour habit,” a newspaper clipping from the time wrote. More than half a century later, Montalbini explained that he embarked on his lengthy zeitgeberless stays underground in part to better understand what might happen to humans when they lived away from Earth’s rhythms for long stretches at a time.

Sleep is a terribly disadvantageous state to be in.

Thirty-two days or even 366, it turned out, was hardly enough time to turn any of these scientists into entirely arrhythmic sleepers, but neither did it steal away their eyes, of course.

So what might happen if we, too, were to leave, for many more generations, the comfortable rhythms of our Earth's surface, to set up residence on a planet or moon with a vastly different solar day, or in a space colony or underground metropolis with none? Would our species, too, diverge from an eight-hour, organized sleep pattern?

Friedrich posits a resounding "yes." "We are evolving and highly adaptive," he says. And there is reason to think a new sleep pattern adapted to our new environment would prevail, given enough time.

This possibility is supported by research into the ways that human sleep already varies with different zeitgebers. Siegel, whose own work found that it was a lack of hypocretin cells—those that are so overabundant in the Mexican blind cavefish—that caused the sleep disorder narcolepsy in humans, has long sought to better understand sleep, and what brings it on and keeps it away.

"There are a lot of myths about human sleep," Siegel says. "Even my colleagues in the field of sleep science argue about them." One running myth is that we're meant to be sleeping when it is dark and awake when it is light—with sleep cycles as long as 12 hours—and that industrialization mucked this up with its artificial lights. Not so, says Siegel.

In some of his recent research, he has probed the power of zeitgebers to organize human sleep. He's done this not by isolating people from them as in cave studies, but by trying to find people living with our ancestral cues in their most natural state. Siegel has spent years studying the sleep patterns of hunter-gatherer and traditionally agrarian groups in Africa, South America, and the South Pacific. This work has led him to home in on the power of an often-overlooked zeitgeber that seems to tune sleep for humans: not light, but temperature.⁵

His research has tracked sleep in communities in Namibia, for example, where temperatures range from freezing to over 100 degrees Fahrenheit over the year, with considerable variation during the day. In a classic, lab-based sleep study, this variation would have been considered too messy. He thinks of it differently. "That's not a contamination, that's the normal way that sleep evolved," says Siegel, who also contributed to the research tracking the surprisingly scant sleep of wild African elephants. Studies in labs—and the unnatural experiment of widespread climate control—have severely muted this ancient, important zeitgeber, he suggests, with at times dramatic impacts on human sleep. A steady day-to-night temperature, as many people in climate-controlled environments experience, might be a large factor in insomnia rates, he posits. This condition afflicts some 10-30 percent



of people in industrial and post-industrial societies, versus about 1 to 2 percent in contemporary hunter-gatherer and agrarian groups, he says—including those who can switch on a light at any time.

Unlike the cavefish, though, most humans have only been living in contemporary zeitgeber environments—where some signals, like temperature ebbs and flows, are muted, and others, like light exposure, thrown into cacophony—for several generations. Our classically entrained circadian conductor is still trying to stay in control. There is no way to know how many generations of humans it might take to find more sleep harmony again.

Sleep diversity and flexibility, however, lurks in most species. The cavefish cousins in Mexico, sighted and blind, simply provide the most extreme example of this—dramatically different manifestations of sleep behavior in the same species. As Duboué points out, though, among humans, individual sleep patterns already range considerably, from five to 10 hours. And increasingly researchers have found natural variation in preferred sleep onset and wake times.

As Duboué argues, studying sleep in all of its wild, natural variation is essential to better understand its vast potentials. Most of what we know about sleep is based on studies of model organisms—bred over decades to be as uniform as possible and kept through generations in highly controlled environments. So to truly understand sleep, scientists need to put on their wellies and go back out into the messiness of nature.

In his research on beetles in dark and twilight zones in Mammoth Cave, Friedrich and his colleagues found even a single individual bug could switch its sleep patterns depending on the environment—a finding that harmonizes with decades of research in the lab testing animal sleep responses to odd patterns of light and dark. “You could call it sleep plasticity,” Friedrich says. “We now realize that sleep duration and patterns are just one of many outcomes.”

“One of the things I’ve taken away from this is just how fast sleep can evolve,” Duboué says. “Sleep is probably one of the fastest evolving traits.” If the Mexican tetras who found themselves stuck in a cave dispatched with regular, consolidated sleep so (relatively) quickly, over just hundreds of thousands years, it begs the question: How important, truly, is a long, uninterrupted

slumber? Sleep, as Duboué points out, is a terribly disadvantageous state to be in: It’s not conducive to eating, mating, or self-defense.⁶ “From an evolutionary perspective, sleep actually doesn’t make a lot of sense—and yet it has persisted in the animal kingdom.”

And so these fish and the other curiously sleepless animals have opened a rather maddening can of worms: Do we even really know what sleep is for? It turns out that theories abound, but firm answers are elusive.

Nor have we yet been able to read the fine print of the bargain—Faustian or not—that these and other wakeful animals have struck, evolutionarily, to wriggle out of what seems like such a hard and fast requirement for animal life.

For his part, Duboué will continue to ponder these questions in his own quiet dark of the night. “I’ve never slept well,” he says. “I’m a complete, terrible insomniac.” So he will have lots of time to make his way through the next difficult problems in the strange land of sleep. 🌀

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The Faulty Weathermen of the Mind

Could a theory from the science of perception help crack the mysteries of psychosis?

BY SHRUTI RAVINDRAN

W

HEN PETER K. CHADWICK WAS A BOY, his mother accused him of being the Devil. She had her own demons—childhood abuse, cheating husband, family betrayals, poverty, cancer. She told Peter he was a “no good,” a “rotter,” and a “bloody Chadwick.” Don’t trust a soul, she told him, and harangued him whenever he began to develop affection for anyone.

Peter grew callous and paranoid, which didn’t earn him any friends. He was bullied at school. Classmates gossiped, slandered, and ridiculed him. After he walked out on his mother when she was on her deathbed, he was overcome with guilt, and took it as proof that he was everything his mother and classmates accused him of being.

Determined to assert his own identity against the world and his mother, Chadwick became a psychology professor. In the summer of 1979, when he was in his early 30s, it all fell apart. Chadwick lost his job as a professor and was eking out a penniless existence in Hackney, London. He was certain he was a target of a campaign of persecution, and began to suspect he was, in fact, the Devil.



If we have never felt a mild earthquake before, we may briefly mistake it for a dizzy spell.

While sitting on a bench in Hackney, Chadwick heard a little girl ask her mother, “Is that man possessed by the Devil, Mummy?” The mother looked at Chadwick and replied, “Yes, dear.” Chadwick took the coincidental remark as final confirmation. He was now convinced an organization of technological experts, enemies, neighbors, and newspaper personnel were monitoring his thoughts and sending him replies through the radio. Were they trying to manage his fate, Chadwick asked himself, cure him of his evil?

Chadwick took a temporary office job. One day, he was ruminating on how he should end his life when a man came out of a side office and said to a manager, “So, he’s got to do it by bus, then?!” “Yes,” the manager replied. So that was it. Chadwick had to crush his skull under the wheels of a bus to save his soul. One gloomy September morning, he flung himself headlong into the path of an oncoming bus on West London’s New King’s Road. Remarkably, Chadwick survived with only minor injuries.

The events of Chadwick’s life and his attempted suicide were recounted by Chadwick himself in a 1993 paper published in the *Journal of Mental Health* titled, “The stepladder to the impossible: A first hand phenomenological account of a schizoaffective psychotic crisis.”¹ “There is a rich orchestra of forces which eventuate in the psychotic experience,” Chadwick wrote. But one key moment proved pivotal in the unfolding of his break with reality: when “real events, guilt, coincidences, and occasional misoverhearings” shifted his perception of the forces controlling his actions from “internal to external.” He had become *possessed* by his own imagination.

PSYCHOSIS—AN UMBRELLA TERM for a cluster of symptoms that mark a distinct break from “reality”—has long reigned among the biggest mysteries in psychiatry, a field beset by mysteries. Every year, about 37 million people suffer from symptoms of psychosis, which include, among other things, paranoia, trouble thinking logically, and confused speech. Many people

develop these symptoms with the onset of schizophrenia—a devastating mental illness that tends to feature socially unusual behavior, carries a high risk of suicide, and lacks a cure. But others have symptoms without ever developing that disease.

Some of the earliest accounts of psychosis come from ancient Greek and Roman literature penned in the fifth century B.C. Philosophers and scientists have



struggled since that early time to understand how it arises in the mind—and how to treat it. This is due, in part, to the diversity and idiosyncrasy of the symptoms that constitute it. Some sufferers experience visual or auditory hallucinations, but others do not, and these symptoms may or may not coincide with strange fixed beliefs. As in Chadwick's case, someone in the midst of a psychotic episode might experience delusions of reference that transform anything from the outside world, including billboards or conversations, into urgent portents intended just for them.

While the neuroscientific underpinnings of such phenomena remain elusive, scientists who study perception are beginning to develop the first compelling

framework to explain what happens when someone experiences a psychotic break. That framework is based on an increasingly popular theory of perception called predictive processing.

According to predictive processing's account of human consciousness, we are not sensorial cameras, passively taking in the sights, sounds, smells, and textures of which our reality is composed. Instead, we construct our perceptual experiences by apprehending—predicting—what all our sensory inputs mean, based on our past experiences (or “priors”). When something new emerges in our experience, something we have not encountered before or are not expecting, the brain may misinterpret the signals and make a faulty prediction about what it is sensing—if we have never felt a mild earthquake before, we may briefly mistake it for a dizzy spell, for instance, or vice versa—but as more information arrives, the brain updates and corrects its internal models of the world.

But for people who are experiencing psychosis or schizophrenia, “control” over this internal model of reality seems to give way. These individuals can end up constructing a model that leans too heavily toward prior expectations, in a way that appears to “run roughshod” over the sensory evidence flowing in, says Chris Frith, a British neuroscientist some consider the father of predictive processing. Presented with new information, the system tends to behave a bit like a stuck camera, super-imposing old images over new ones.

“It's like if someone is constantly predicting the weather wrong, you would ignore them when they tell you it's going to rain,” says Frith, who is a professor emeritus at the Wellcome Trust Centre for Neuroimaging at University College London. But people with schizophrenia keep listening to the faulty weathermen. They fail to correct their flawed models with new information. These glitches cause the alterations in perception, belief, and the self that people with psychosis experience, a growing body of research suggests, leading them to see or hear things that are not there.

SEEING SHADOWS Ketamine has been known to safely mimic both the positive and negative symptoms of schizophrenia, including hallucinations. Scientists are using it to study psychosis.



He began to suspect he was, in fact, The Devil.

ONE OF THE FIRST CLUES that schizophrenia and psychosis might result from faulty predictive processing came from research into, of all things, tickling. When healthy people try to tickle themselves, they can't. They do not experience the associated ripples of pleasurable feeling and queasy laughter, the crawling sensation of electricity riding up the skin. But this rule does not hold with patients who have schizophrenia. When they tickle themselves, they feel tickled.

In research published in 2000, neuroscientists Sarah Blakemore, Daniel Wolpert, and Frith set out to understand this unusual hallmark of the disease.² In a set of experiments, they tested two groups of people on their tickle reflexes: one was symptom-free and the other had experienced auditory hallucinations or so-called “passivity”—the switch in perception that makes people with psychosis feel like they're being acted upon by unseen forces in their environment.

The healthy group, it turned out, were only able to tickle themselves when they did so using a robot arm that had been programmed to produce a delay. Frith posited that something similar happens to people with schizophrenia. A faulty expectation and a delay in the delivery of sensory information could lead them to feel that their own actions had been initiated by some external force. “At the bottom end of the hierarchy,” Frith says, people with schizophrenia “have a weaker sense of what to expect.” This could account for their susceptibility to “delusions of control,” wherein they suspect that spies or aliens are orchestrating their actions.

In earlier theoretical work, Frith had traced such delusions of external control to a deficiency in

“self-monitoring.” Other neuroscientists have since made similar arguments.³ According to their reasoning, a process of self-monitoring, a kind of internal CCTV, or central feedback loop, allows our nervous systems to distinguish between self-generated and externally generated stimuli. But when something in this monitoring system is broken, it leads to undetected mismatches between intent and action, and self-generated stimuli are erroneously attributed to external causes. The errors in attribution of stimuli don't get corrected. Predictive processing breaks down.

PERCEPTUAL ILLUSIONS CAN AND DO occur in healthy people—they are at the root of most magic tricks, for example, which work by upending expectations. In fact, scientists say that research demonstrating the critical role expectation plays in perceptual illusions in healthy people provides further evidence that faulty predictive processing is what drives psychosis. For instance, people whose sensory inputs are cut off—if they enter a sensory deprivation tank, say, or experience sight loss—can experience florid visual hallucinations. And among patients with Charles Bonnet syndrome, diminished visual acuity gives rise to intricate phantom images of landscapes, people, and animals. Paul Fletcher, a psychiatry and neuroscience researcher at Cambridge University with a special interest in psychosis, explains that in such cases, “cutting off the sensory input leads to an excessive overweighting of prior expectations.” Deprived of the sights we're accustomed to seeing, we might repopulate our mind's eye with visions—real or imagined—we have encountered in the past.

A similar glitch in the brain's machinery occurs with a phenomenon called the "hollow mask illusion," a common visual misconception that causes most healthy people to view the concave side of a mask as though its features were convex, or sticking out in their direction. According to the predictive coding framework, this illusion occurs because we fill in the hollows with our prior expectations, accrued over a lifetime of observing and committing to memory fully convex faces.

For people with schizophrenia, oddly, the hollow mask seems to look just like a hollow mask. The reason for this is not entirely clear. But Fletcher theorizes that we have *hierarchical* sets of expectations—those that operate on a basic level, right where we receive the information from our sensory feelers, and those that develop one level deeper, where we store the blueprints for our inner world-building. "It's like a whole series of cogs interacting with each other," Fletcher explains. "And if you're not using your expectations at that lower level, then there's a lot of unexplained stuff that is percolating forward." The bigger the errors, ambiguities, and unexplained signals coming through at the bottom level, the more "noise" we have to contend with when we cobble together our models of reality.

Curiously, while people with schizophrenia don't see normal faces in the hollow mask, they do seem to have a heightened propensity to see faces and other patterns in noise more broadly. In a 2015 study, Fletcher and Christoph Teufel, a specialist in the neuroscience of vision at Cardiff University, showed a bunch of two-tone images with hidden faces in them to two groups: one comprising people at risk of developing full-blown psychosis, and especially prone to hallucinations, and a healthy control group.⁴ They then showed them the clear source image—of a face—which had been obscured in the two-tone image. This would function as their "prior expectation."

"What Christoph predicted was that people with hallucinations would actually have an advantage in doing that task, because they can take prior expectations and use them more strongly," recalls Fletcher. Though it was what he expected, he was still surprised to find it was indeed the case. The group with symptoms of early psychosis were exceptionally good at spotting the hidden image of a person, when compared to the other group.

When patients who have schizophrenia tickle themselves, they feel tickled.

Many researchers believe that psychosis actually exists on a continuum, that the general population exhibits varying levels of proneness to it, but that these manifest in ways that do not greatly disturb the healthy person's functioning. For example, hallucination-proneness might manifest as a tendency to glimpse dark forms scurrying across the floor if you've once spotted a cockroach, and delusion-proneness in being quick to suspect that peals of laughter in a cafe must be directed at you. In one experiment, Fletcher and Teufel gathered two such groups of otherwise healthy people, one prone to hallucinations and the other to delusions, and tested their performance at spotting the hidden faces lurking among abstract black-and-white images. The hallucination-prone group proved especially good at the task.

To Teufel, this finding provides evidence "that an undue reliance on prior knowledge in vision might *precede* mental illness, rather than being a consequence of it." The finding also chimes in with previous work⁵ that has found⁶ that strange visual symptoms—such as an altered perception of others' faces and bodies, changes in form or sensitivity to light, and a tendency to see the contours of things in a warped or blurry manner—illusory patterns that might result from lingering previous impressions—can powerfully predict the onset and severity of psychosis. "It is therefore possible," Teufel adds, "that this undue reliance [on priors] is one of the risk factors for the development of visual hallucinations." A subsequent study published in *Frontiers in Psychology* in 2021 by German researchers provides further support for this idea.⁷

Like visual hallucinations, auditory ones seem to derive from faulty expectations, as well, according to a 2017 study published in *Science*.⁸ Lead author Philip Corlett, an experimental psychologist at Yale, who has been studying the formation of delusional beliefs for the past



BEHIND THE MASK The “hollow mask illusion” is a common visual misconception that causes most healthy people to view the concave side of a mask as though its features were convex, or sticking out in their direction.

two decades, and his colleague A.R. Powers, together induced what they called “conditioned hallucinations” among four groups of subjects. These included one drawn from psychiatric patients who heard voices, those with similar illness who did not hear voices, another made up of self-identified psychics without a psychiatric diagnosis, who heard voices but attributed them to “metaphysical” sources, and a control group without diagnosis or voices. All four groups were trained to associate a checkerboard pattern with a barely audible sound, and reported hearing the tone when they saw the checkerboard, even when a tone was not played. “And that was particularly true with somebody who heard voices outside of the lab in their everyday life,” Corlett said.

DRUG TRIP ACCOUNTS often bear striking similarities to accounts of psychotic breaks: the strange dream-like feeling that induces you to see your surroundings in a new, heightened, and meaningful light. The occasional paranoia. The tendency to spot faces everywhere you look. So it’s fitting that researchers have used psychedelics to help them study the predictive processing account of psychosis.

One drug that offers some tantalizing clues is the dissociative ketamine, which Corlett and Fletcher have used to model psychosis, just as researchers in the ’20s and ’30s did with mescaline and LSD. “We knew from ketamine’s use as an anesthetic that it caused ‘emergence phenomena’; when people woke up from the anesthesia they resembled patients with schizophrenia in their experiences and thoughts,” Corlett explains. The drug has been known to safely mimic both the positive and negative symptoms of schizophrenia, including hallucinations, and acts on—that is, blocks—the transmission of the neurotransmitter glutamate, which is implicated in learning and the consolidation of memory.

In a 2009 study, Corlett found that, when healthy people were administered ketamine, it led to a “perturbation” in the signaling of prediction errors, which was

Perceptual illusions can and do occur in healthy people—they are at the root of most magic tricks.

“almost identical to that observed in people experiencing a first episode of psychosis.”⁹ Essentially, when prediction errors repeatedly engage a memory (or belief), they lead to its reconsolidation and strengthening, rather than its weakening (or extinction),” he adds. That persistent glitch could offer clues about the strange tenacity—and malleability—of delusions over time.

Last year, Corlett repeated his experiments that produced conditioned auditory hallucinations in people with schizophrenia. But this time he also measured participants’ levels of the neurotransmitter glutamate—whose transmission is blocked by ketamine—and struck upon something of a neurochemical smoking gun. Those who had low levels of glutamate in the anterior insula, a region associated with conscious awareness, had stronger prior beliefs about the connection between the checkerboard and the tone, predisposing them to conditioned hallucinations.

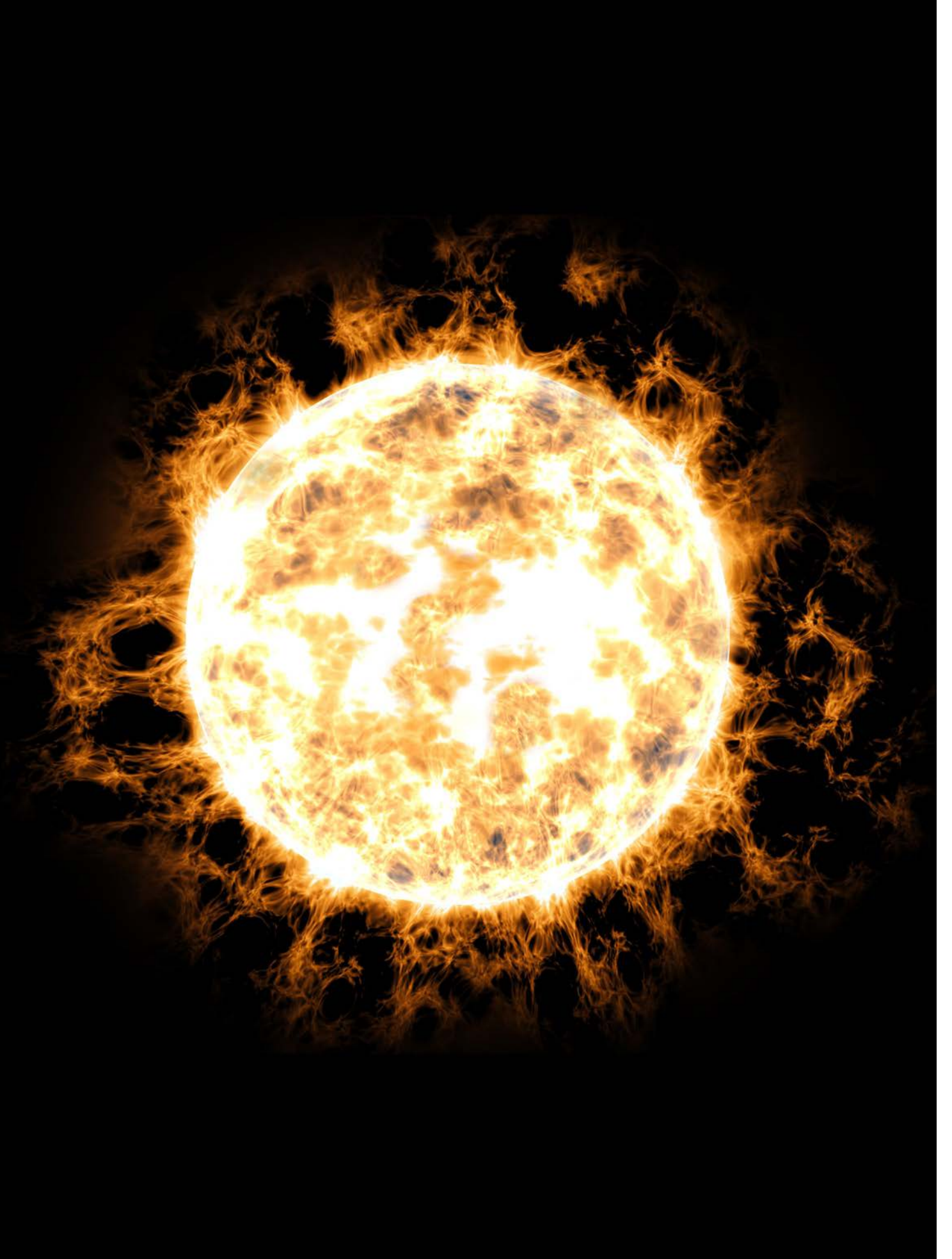
In other words, glutamate is quite likely tangled up in the overweighting of prior expectations, and could play a key role in generating hallucinations. Probing that finding further could bring scientists closer to understanding, on a neurobiological level, what was happening when Chadwick’s mind was overtaken by the “deranged poetry of thought” that made him leap in front of a bus. And possibly, even how to treat it.

And yet, as Chadwick writes in his account, drugs alone may not be sufficient for a cure. His own recovery required not just antipsychotics, but, among other things, “painful insight,” as well as “reality testing”—clarification of what was internal and external—and “thousands of hours of refreshing sprightly chatter about nothing of much meaning and importance,” to enculturate him back into society at an everyday level. He had to, in effect, retrain the faulty weathermen of his mind. ☺

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The Sneaky Force Behind Our Sun's Violent Outbursts

A strange discovery from flying close to the sun

BY PAUL M. SUTTER



ANY OF THE MYSTERIES OF OUR SUN are not buried at its core, as we might expect. They are dancing ferociously on its surface. Plasma leaps out, arcing millions of miles into space before plunging back to return to its fiery home. Massive solar flares shoot deadly X-ray radiation into the solar system. And coronal mass ejections loft chunks of the sun's own body into space, creating storms of energy that can wreak havoc on the planets in our solar system.

For millennia, astronomers marveled at the displays, puzzling over what might be causing them. But marvel was about all they could do. The shows of force could usually only be glimpsed, briefly, during a total solar eclipse, when the moon blocked the body of the sun and the sun's corona—its outermost atmosphere—and wild prominences became visible.

Now, however, scientists have sealed the wax on their proverbial wings and are flying ever-so-close to the sun, able to witness its atmosphere and study it directly in all its fiery glory.

After launching in 2018, NASA's Parker Solar Probe has been flinging itself around Venus, using the planet as a sink of gravitational energy to draw the probe closer and closer and *closer* to the sun's chaos. Joined by the ESA's Solar Orbiter, which launched in 2020, the bold pair have been beaming back astonishing evidence about what is driving the sun's high-energy fury. The results suggest that it is not plumes of combusting fire

or the violent strikes of meteors, as earlier astronomers had once suggested, but more likely a humble, unassuming, usually ignored force in the universe: magnetic fields.

As an astrophysicist, I have a soft spot for magnetic fields. They never truly get the attention they deserve. My own research has investigated the subtle role they play on the largest of cosmic scales. And I've learned over the years that when there is some process in the universe that you don't fully understand, it's worth taking a looking at magnetic fields. Because even though they're weak, they're often sneaky.

Magnetic fields are everywhere in the universe. Any time you take a collection of charged particles and accelerate them, the resulting electrical current generates the formation of an attendant magnetic field. Earth has charged particles whipping around in its molten core, and so magnetic fields wrap around our planet in a protective embrace. Clouds of forming stars

The Parker Solar Probe had to take an Icarian risk.

have turbulent flows of charged particles, and along with them tangled, knotty magnetic fields. Even entire clusters of galaxies, the largest gravitationally bound structures in the universe, are home to magnetic fields stretching millions of light-years on a side.

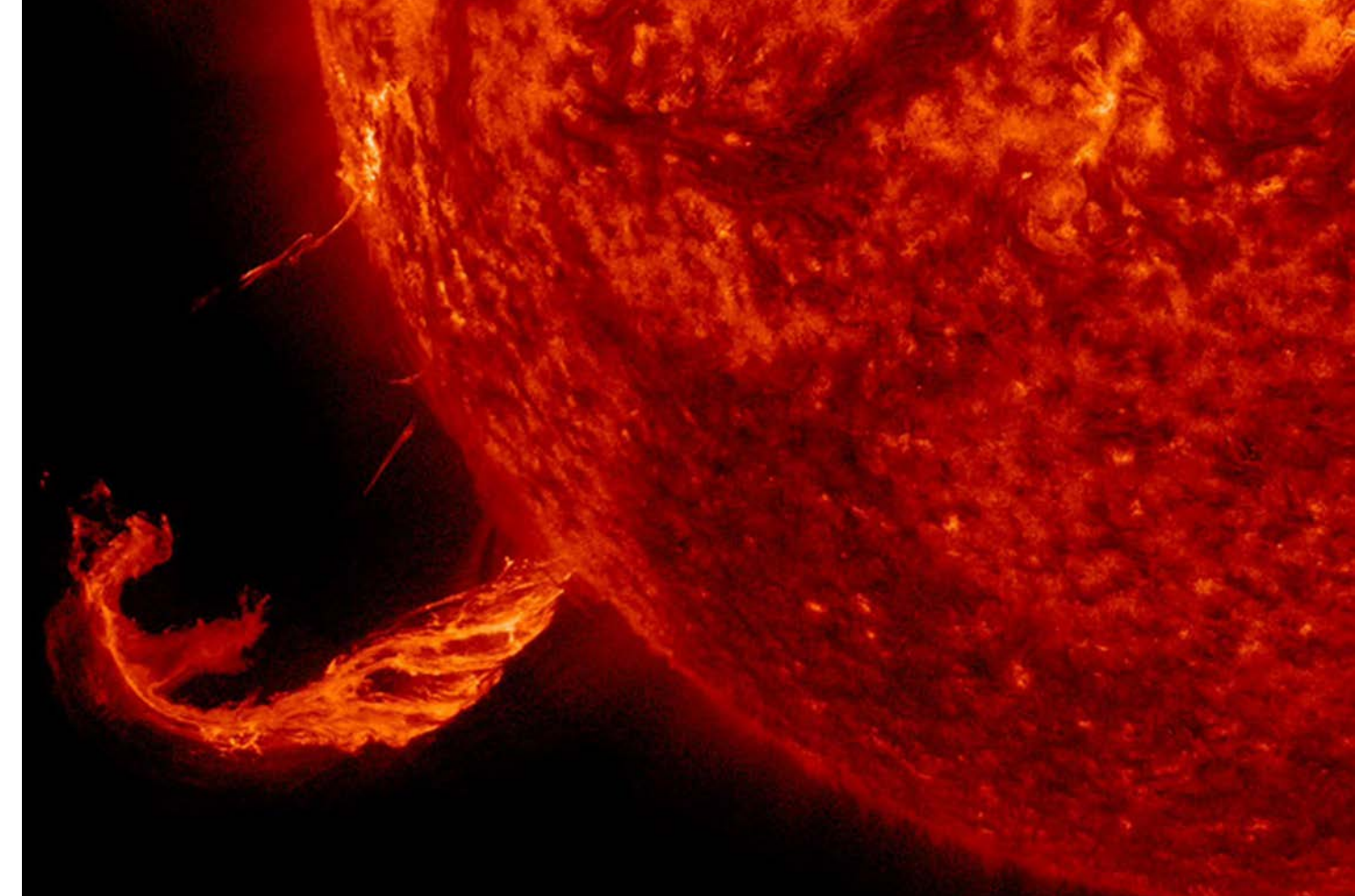
And yet for all this magnetic abundance in the universe, the fields themselves are one of the weakest phenomena in the natural world, so feeble they can almost always be ignored in any consideration of physics. They rarely play a starring role in astrophysical processes; they simply seem to exist as a happenstance.

On Earth, it takes the combined might of the entire molten core to generate a magnetic field strong enough to gently nudge a compass needle around. For any living creatures on Earth, with the exception of migratory birds and a handful of other species, if we were to lose our magnetic field, we wouldn't really notice it in the day-to-day. The same holds true for the vast majority of astrophysical cases: The magnetic fields are *there*, winding throughout the universe, but are relegated to the role of non-speaking background actors, not one of the main cast.

Our sun, being a giant ball of plasma, naturally has a magnetic field of its own. It's not particularly strong, however, only roughly twice as strong as Earth's, and less than a quarter the strength of Jupiter's. And, honestly, even though magnetic fields are approximately everywhere in the universe, they don't seem, usually, to do much of anything.

But for decades, some bold astrophysicists, like the pioneering Eugene Parker, for whom the Parker Solar Probe was named, suspected that magnetic fields might play an outsized role in the radical dynamics of the sun. And so, the Probe, along with the Solar Orbiter, were launched with instruments specifically designed to measure the strength and scope of the sun's ever-changing magnetic fields. Combined with more traditional instruments, like heat-resistant telescope optics and particle detectors, the teams behind the missions hoped that the probes might alight on some strange, intricate connection between the sun's magnetic fields and its awesome displays of raw power.

To accomplish this, the Parker Solar Probe had to take an Icarian risk. In April 2021, NASA's Parker Solar Probe became the first instrument ever devised by human hands to "touch the sun," sailing into its inferno of a corona, where temperatures soar to 2 million degrees Fahrenheit (200 times hotter than the surface of the sun itself). Whipping around our home star at a speed of more than 90 miles per second—also setting a record for the fastest spacecraft in history—Parker approached within about 6.5 million miles of the solar surface. Spending only a short time at that close distance on that pass, the Probe collected as much data as possible: mapping the solar surface, measuring the stream of high-energy particles traveling through the corona, and measuring the magnetic fields as they twist and wrap throughout the sun's environment.



From this extreme front line, Parker has been beaming floods of data back to Earth, where scientists are still processing and analyzing them. What is becoming clear is that the sun's magnetic fields are operating with an unusual superpower—one that enables them to leap from the background to become a major player on the stage of the sun. To speak and have strong opinions of their own. To transform and shape the worlds around them.

We are learning that when it comes to the surface and atmosphere of the sun, magnetic fields are usually quiet. But when they speak their minds, we can't ignore them.

The superpower is this: Magnetic fields, though typically humble on their own, under the right conditions can twist and bundle themselves together, transforming from weak threads to powerful cables. These knotted, self-wrapped twines snake in and out of the solar surface, threading deep into the plasma heart of the sun and far out into the corona. Once in place, they become far stronger than average, no longer responding to the motions of the plasma around them, but instead directing their own flows.¹

We see this most clearly during the eruptions of solar prominences. When we observe the great arches of plasma reaching out and back into the sun, we are witnessing the flow of superheated electrically charged plasma forced to follow the bundles of magnetic field lines.

INVISIBLE THREADS

New data from extreme solar missions are finding that typically weak magnetic forces might bundle together to drive the massive jets of plasma that leap from our sun's surface.



Magnetic fields can twist and bundle themselves together, transforming from weak threads to powerful cables.

The tangled mass of twisting magnetic field lines can, however, reach a critical breaking point. If the fields become too tightly woven, too constricted, then plasma piles up at either end. This drives the magnetic fields even tighter together, and eventually, if the pressure becomes too great, they snap. This snapping of the magnetic field releases an enormous amount of pent-up energy.² First in the form of X-ray radiation—the solar flares. And if the magnetic bundles go deep enough into the bulk of the sun, it can lead to the launching of material along the broken lines of magnetism in the form of a coronal mass ejection, like the one Parker flew through last fall, described in a new paper.³

With the Parker and Solar Orbiter, scientists have been able to watch these processes play out in real time. The collection of magnetic fields, the bundling together into thick ropes, the channeling of plasma, the storing of energy, and the ultimate release of the sun's magnetic fury. Scientists have now been able to watch—close up—as kinks in the magnetic field lines zip up and down, in and out, transporting energy from the surface of the sun to the corona, heating it up.⁴ As the interior of the corona heats, the outer layers energize and detach completely, becoming the solar wind.⁵

These aren't just abstract explorations of some distant astronomical target. This is our sun—the source of all light and warmth here on Earth, as well as a source of potential danger. When solar flares erupt, the resulting X-rays bombard our planet. When coronal mass ejections race outward, they can fly in our direction.

INTO THE FIRE A new paper describes the Parker Solar Probe's safe passage through a coronal mass ejection event—captured in this series of images in a burst of plasma from below.

Space weather forecasts are essential to protecting our satellite infrastructure and electricity grids.

Understanding the dynamics of the sun, especially the critical role that tangled magnetic fields play, can help us make better space weather forecasts. These forecasts are essential to protecting our satellite infrastructure—and even our Earth-based electricity grids and radio communications, whose weaknesses were evident during the especially strong solar storm in 1989. Right now, solar storm forecasts rely on constant observations of the sun’s activity, waiting for a burst to happen and sending out an alert. But often, we only know a storm is approaching after it’s already been launched from the sun, giving us just several minutes’ lead time. Understanding the role of magnetic fields can help us spot the precursors to a storm as it’s building, leading to longer warning times and a better sense of a particular storm’s anticipated severity.

But even with this newly emerging picture of the sun’s temperamental and powerful magnetic forces—and our increasing vulnerability to their whims—there is much more work to be done.

The Parker Solar Probe and Solar Orbiter will continue their dangerous missions for the next few years, observing carefully with each new eruption, each new storm, for the delicate lines of magnetic fields to conspire. As the Solar Orbiter continues to circle the sun from a comparably cool 26 million miles’ distance, the Parker will keep hurling itself around Venus to get closer and closer to the sun. By the time it sails its final pass, anticipated in December 2025, it is expected to travel within 4 million miles of the sun’s surface before running out of fuel. From all of these flybys, data will be mounting for scientists to sift through and make sense of over years—and likely decades—to come.

Next year, the ESA hopes to launch Proba-3, an experimental mission to test a new kind of multi-satellite formation that could deliver even more details about the sun’s tumultuous outer layers. Combined with dedicated ground-based observatories, astronomers hope to continuously monitor the sun in as many ways as possible, to further elucidate the complex and ever-changing relationship between magnetic fields and the solar plasma that births them and can then be controlled by them.

Far from any mechanical forces envisioned by early astronomers, the driving forces of the sun’s powerful displays are typically so quiet that they eluded suspicion for centuries. And hopefully, with even more daring missions in the future, humanity will continue to unravel more mysteries of the unseen power of magnetism in our universe. ☺

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Dr. Doom on the Hottest Summer (So Far)

Why we should respect worst-case scenarios

BY KATHERINE HARMON COURAGE



JUNE, JULY, AND AUGUST of this year were the hottest on record for planet Earth. This Fourth of July is reported as likely the warmest day on Earth in some 125,000 years. The second-hottest was July 3. In the United States, more than 6,500 local heat records were shattered this summer. Based on the unprecedented and relentless milestones, in September, the United Nations Secretary General António Guterres declared that “climate breakdown has begun.”

Scientists have been warning about this possibility for decades. And in recent years, the mounting climate-related disasters—extreme storms, droughts, floods—have pointed toward an accelerating rush into the relative unknown of climate catastrophe.

Action as a citizen is far more powerful than action as a consumer.

But Guterres himself is not a climate scientist (though he did study physics and taught systems theory at university). So we wanted to know: What should we make of this ominous proclamation?

We called Luke Kemp, who is a research affiliate at the Centre for the Study of Existential Risk at the University of Cambridge and currently a visiting faculty fellow at the Notre Dame Institute for Advanced Studies.

Kemp lives in the intellectual world of the unlikely-but-calamitous. While most people are fretting over a change in storm surges along the Eastern Seaboard, he is swimming around in a not-too-distant possible future where the East Coast begins miles farther west.

The scientific community has focused attention on limiting warming to 1.5 to 2 degrees Celsius above pre-industrial levels, aiming to avert too much disruption to civilization as we know it. But we are most likely to see warming of at least 2.7 degrees—and possibly up to 8.6 degrees—by 2100. (It's worth noting that, save for a dip during the first year of the COVID-19 pandemic, global emissions are still climbing annually.) Kemp argues that scientists have done a terrible job considering and communicating what these more severe outcomes would mean for us, as a species.

"Prudent risk management requires consideration of bad-to-worst-case scenarios," he and his colleagues wrote in a PNAS paper last year. "There are ample reasons to suspect that climate change could result in a global catastrophe," they wrote. But "at present, this is a dangerously underexplored topic." Research has found, for example, at a 6- to 9-degrees Celsius warming (well within the realm of possibility in the next 75 years), the East Antarctic ice sheet would be doomed, possibly sending sea levels up more than 130 feet. At even just 2 degrees warming, the West Antarctic ice

sheet will likely begin an irreversible demise, eventually raising sea levels by 10 feet—even if the warming trend was quickly reversed.

And these risks, he and his colleagues argue, are not singular, but are likely to compound and interact with one another. It wouldn't just be a rise in sea levels, but also simultaneous economic crises, political conflict, famine, and mass illness.

Kemp explains what's in a word like "breakdown," how we can turn overwhelming complexity into stark simplicity, why he doesn't really care if his students leave the lights on, what we can learn from the Bronze Age, and why people should keep inviting him to parties.

When the United Nations Secretary General António Guterres used the term "climate breakdown," it sounded like a pretty serious proclamation. As someone who thinks a lot about these things, what does that phrasing mean to you?

"Breakdown" has never had an official consensus definition. What it means varies by the person. These are, of course, very concerning and dramatic proclamations. But scientifically, they don't mean much by themselves.

To me, it means that there is a threat of transgressing the major planetary boundaries and stable systems. And this could trigger several tipping points in the Earth system that could push us toward a state in which it is no longer suitable for human habitation, for human prosperity.

As a journalist, I think a lot about how these different phrases—*climate change*, *climate crisis*, or the trusty old *global warming*—might have different impacts. In your work, how do you think about these different terms and their impacts?

I've tried to develop a much more refined and sharp lexicon and terms that we can use. The terms we use are important. There are no innocent terms, and your choice of words can either obscure or elucidate meaning. In terms of "breakdown," it's really about the idea that the changes we're experiencing are unprecedented and could have a large-scale disruption to our socioeconomic systems globally. And that can lead to mass mortality and morbidity.

What term do you use most often these days?

It depends on the audience and what I'm talking about. For instance, the term "existential threat" is very poorly defined and ambiguous. However, when speaking to a public audience, it usually gets the point across more or less that it's a very big, scary threat that could threaten industrial civilization—or the future of the human species.

In your paper from last year, you refer to "catastrophic climate change scenarios" and argue that we've actually done a really terrible job considering them. I feel like, as a species, we're pretty good at worrying. Why do you think we've turned such a blind eye to these possible outcomes?

There are several possible explanations for this. The goals of the Paris Climate Agreement simply divert our attention toward 1.5 and 2 degrees Celsius, and away from high-temperature scenarios.

Additionally, thinking about complex risks, knock-on effects, and thinking about high-temperature scenarios, it's just harder, it's more difficult to model.

On top of that, there's also the influence of the fossil fuel industry and the merchants of doubt, who have made it incredibly difficult to talk about any kind of catastrophic or extreme climate risk without automatically being labeled alarmist. There is the pressure, as Michael Oppenheimer put it, for climate scientists to "err on the side of least drama."

How do we try to wrap our heads around such extreme outcomes and such complex factors?

When we think about catastrophe, about risks or threats, we almost always tend to think about one hazard by itself. It's important to get away from this simplistic way of thinking, where one often asks: Is climate change an existential risk?

Of course, that's a silly question to ask. It depends on a whole bunch of other outside factors. Three degrees of warming in a world marked by equality, trust in public institutions, good adaptive technology and governance, and multilateral cooperation, we could navigate that. Three degrees of warming in a world marked by multilateral conflict, war, dangerous new technologies, polarization, and inequality—that becomes a much more calamitous prospect.



NO OSTRICH While most of the scientific community zeros in on the implications of a small amount of warming for the planet—an absolute best-case scenario—Luke Kemp advocates for a deep exploration of what will happen with substantially higher amounts of warming.

It's a very big, scary threat that could threaten industrial civilization—or the future of the human species.

When we think about breakdown, when we think about risk, we need to think about the overall scenario. And the politics which we find ourselves in are going to impact the overall level of risk. That's probably sounding pretty nerdy, but it's important.

No, that's really helpful. It was also a helpful reminder in your paper about how so many of these tipping points are interconnected—as you pointed out with COVID or the financial crisis—how these things that seem very separate in our lives now could easily fall, kind of like a web of dominoes.

Yes. And it's important to keep in mind that we don't need to be overwhelmed or paralyzed by complexity.

Underlying that complexity is a very simple picture. When we look at the production of risk, things become dramatically and profoundly simplified. There's almost always a small number of companies and countries who are pushing us toward ecological catastrophe. If you're looking at global emissions, it's roughly the top 10 percent of emitters who are responsible for about three-quarters of cumulative global emissions. Roughly a quarter comes from one country: the U.S. If you're looking at companies, it's pretty much just the fossil fuel industry that is the big one to blame. About 71 percent of industrial emissions come from 100 companies. And the same goes for a whole bunch of other areas. There's a really interesting study looking at the finances of deforestation in the Amazon, and you can pick out a couple of key financiers—in particular BlackRock—who are essentially funding much of the wholesale destruction of the Amazonian Basin.

I think there's a real need to think about this politically and to think about: Who are the actors and the

networks in the political economy that are causing global risk and climate breakdown? Then we actually have a startlingly simple and easy picture to deal with.

That feels like a refreshing way to look at it.

Refreshing, yes. It's potentially also disturbing in that these are usually actors and players who are incredibly powerful, right? And that's probably why we don't talk about them so much. It's much easier to blame people and everyday citizens than to blame the U.S. military or BP.

Yeah, I suppose that does make it feel a bit futile when it's not just up to us and whether or not we're carrying our own reusable straws.

This is something I used to say to my students back in Australia. If everyone paid attention to turning off their lights, it would barely make a dent in Australia's emissions. Even if they took a whole bunch of other wholesale behavioral change measures. And if you're operating under a carbon pricing system, it wouldn't matter, as the reductions get traded anyway.

But if everyone in Australia changed the way they voted, then suddenly you could have a target of net zero carbon emissions by 2040 or 2050. Action as a citizen is far more powerful than action as a consumer.

You also study the collapse of past civilizations. Is there one that comes to mind that you think is the most relevant for us to think about currently?

One problem we have when we look at past societies is we almost always look at small, individual states. For instance, in Jared Diamond's book *Collapse*, he has five case studies, and only one of them is actually a

We don't need to be overwhelmed or paralyzed by complexity.

larger-scale one, and that's the Maya, who aren't actually a single state. They're actually a kind of cultural zone with different city states.

Personally, I think the most elucidating and useful parallel is probably the collapse of the late Bronze Age, which involved roughly nine different large-scale polities. The interesting and important thing here is that they were deeply economically and politically connected. Some archeologists have even gone so far as to say that this Mediterranean structure of the Bronze Age was globalized in its own way.

I'm a very big fan of historian Eric Cline's work on this and how he suggests that what happened in the late Bronze Age was a combination not just of certain threats—like drought, climatic variation, migration, displacement—as well as certain vulnerabilities—rebellion, for instance, and inequality. But also the very structure of the system. In work I did with Eric, we suggest that the interconnectedness of that world actually made them more vulnerable in some ways. Once a sufficient number of city states and trading hubs went down, that created a kind of amplifying feedback, which destabilized the system and made it more likely for more cities and trading hubs to crash, and the entire system basically spiraled out of control.

And that is potentially my biggest fear going forward: I think our homogenized, interconnected world is very good at buffering against small shocks. But it's much more likely to amplify a sufficiently large shock into a system-wide crisis.

Has studying these kinds of looming potential disasters changed anything in the way you live your own life?

If anything, it has made me much more aware of and cognizant of issues of justice. I think some of the best evidence we have suggests that what really builds resilience in societies is a high level of democracy and participation. It makes for a more flexible society that is much more willing to respond to crises and problems. So, strangely enough, my studies of global catastrophe

have made me a much bigger fan of democratization. It's changed my politics in many ways.

That's interesting. Your background is in international relations and economics, and then you found yourself in the field of disasters. I mean, your main post is at a place called the Centre for the Study of Existential Risk. Do these things keep you awake at night?

Surprisingly, it's not as distracting or as perturbing as you might think. I certainly had a period of my life, when I was in Copenhagen for the climate negotiations and I had just finished reading *Six Degrees*. That was a moment which was really fracturing for me—realizing the realpolitik of the world and how incapable we were of actually reaching shared solutions globally, and also just the sheer severity of the problem.

But you develop a certain kind of emotional distance from the problem. And I find, personally, that, like all humans, risks seem much worse and disasters are much worse, when they have a human face on them. I find it much more difficult to read about things like genocide, political violence, and gendered violence, for instance, than I do when I think about 6 degrees of warming—even though 6 degrees, just in the sheer number of fatalities and the sheer amount of suffering, could be far, far worse. But it lacks that human element to clearly connect with.

But what does impact me tends to be the knowledge that these risks are being produced by a small number of powerful actors, usually at the expense of the rest of us.

Are you fun at parties? Or are people like, *Oh no, here comes the apocalypse guy*?

I'd be flattered if they said, *Hey, here comes Dr. Doom!* I like to think that I'm usually quite a cheerful, jubilant Australian. ☺

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

Seahorse Love Works in Mysterious Ways

Seahorses don't care if there's plenty other fish in the sea

BY TILL HEIN

SEAHORSE ILLUSTRATIONS BY ROGER HALL

HUMAN COUPLES COULD LEARN a lot from seahorses. The marine marvels spend only quality time together. They flirt, swim together, and mate. The rest of time they go their own way, drifting in ocean currents, leisurely eating their fill. But they do look forward to getting together again.

Right after sunrise, male and female seahorses approach one another, gently rubbing their noses together and then begin to circle each other. Many of them make seductive clicking noises. The partners gracefully rock back and forth, as though to the beat of underwater music. They dance and cuddle together dreamily, as though they've lost track of time.

However, love can be dangerous for seahorses. During partner dancing, hormones are released that can make their camouflage fade. This causes changes in color, so their bodies begin to glow, and the contrasts in the patterns of their skin become more pronounced. Researchers hypothesize this is how seahorses signal their willingness to mate.





The partner dances also serve as a means of seduction. Before mating, courtship can take many hours. Finally, the female signals that she's ready.

She swims up toward the water surface, pointing her snout toward the sky, and stretches her body out straight as a stick—a pose that is irresistible to the male. The stallion of the sea presses his chin against his chest and makes his prehensile tail open and close like a switchblade. This enables him to pump water into his brood pouch to show his beloved mare of the sea how roomy it is.

Soon afterward, the mare and stallion of the sea snuggle up together closely and let themselves drift upward. They press their bodies together so that their snouts and abdomens are touching. On account of the curves in their body posture, the space between them looks like the shape of a heart. Then, something amazing takes place. A tubular rod called the ovipositor, which looks a little like a penis, appears in the middle of the female seahorse's belly. At the climax of the love scene, both partners lift their heads as though in ecstasy, curving their backs, and the female seahorse transfers her eggs into the male's brood pouch, while her partner fertilizes them with his sperm.

Shortly afterward, the loving couple separates. The colors and patterns of their bodies fade again. The male shakes himself to ensure that the fertilized eggs slide into a favorable position in his pouch. His partner usually swims away to go hunting and feeding. However, for the expectant father, the difficult time of pregnancy now begins.

Scientists have long been trying to determine why it's the males that become pregnant in the realm of seahorses. Only recently have the first explanations come to light.

In 2001, Tony Wilson, professor of evolutionary biology at Brooklyn College, and his colleagues, were able to prove that expectant male seahorses provide nutrition for the embryos in their pouch. In the meantime, it has become more evident how closely the male seahorse pregnancy resembles that of female mammals. For example, the male seahorse's immune system protects the embryos from infections. Scientists at the GEOMAR Helmholtz Centre for Ocean Research Kiel are currently studying the microbiome of the male's pouch (the symbiotic



bacteria) involved in seahorse pregnancy. The expectant father transfers his microbiome to the embryos via his pouch, fortifying his offsprings' immune systems.

Furthermore, the embryos' waste materials are discharged by the pregnant male, and nutritious, high-energy fats are provided for them. A gaseous exchange enables the embryos to breathe.

The question remains, though, of how the female's eggs get fertilized by the male. Biologists had assumed the males fertilized the eggs directly in their brood pouch. Yet researchers have discovered a curiosity, at least in the case of the yellow, common, or spotted seahorse (*Hippocampus kuda*). The males cannot deposit their sperm in their brood pouch because their sperm tube ends outside of it. The long-snouted seahorse (*Hippocampus guttulatus*) and short-snouted seahorse (*Hippocampus hippocampus*) cannot fertilize the eggs in their pouch either; it would be anatomically impossible. So how does the sperm reach the eggs?

British professor of zoology William Holt of the University of Sheffield is an expert on seahorse reproduction. He explains that in the case of yellow seahorses, the male's semen is emitted while mating, but the opening of the brood pouch is around 4 millimeters from the end of the sperm duct. "Hard to imagine how the sperm could swim that far without getting lost in the sea, simply because they're much too slow," says Holt. "In the meantime, we presume that while the female is transferring her eggs to the male's pouch with her ovipositor, she also collects the sperm from the seawater, so it enters the pouch along with the eggs." Holt considers it very likely that fertilization in other seahorse species takes place in the same complicated manner.

"Collecting" sperm in the water? Very bizarre. Why would seahorses spend so much energy on courtship and mating? Why couldn't female seahorses simply spawn in the water, like practically all other female fish, and let the males fertilize their eggs in the water by themselves? The reproductive behavior of the yellow seahorse seems illogical and absurd—as though a hunter were to load a rifle, only to throw it at a stag instead of shooting it.

Axel Meyer, professor of evolutionary biology at the University of Konstanz in Germany, smiles. Not all processes in nature are perfectly efficient, he says. "Evolution doesn't begin with a blank page; instead, it makes do with whatever's already there." Evolution is not like "an engineer—rather, it proceeds via trial and error." Organisms have to function in each and every generation, meaning that the evolutionary process is founded on serendipity. "That's why there are random mutations in the genome, which are passed on as preconditions." Some things can only change very slowly, and others not at all. There are still quite a few "misconstructions" in nature, says Meyer. Albatrosses have a wingspan of

The
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spend
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together.

The couples get together daily to greet each other and dance.

up to 11 feet, meaning they are so heavy that when they land, they sometimes break their necks. “Even the design of human beings isn’t failsafe,” says the evolutionary biologist. “The close connection between our airway and our esophagus leads to the risk of choking to death.”

Darwin wrote about the “survival of the fittest” in 1869, a term he adopted from British philosopher and sociologist Herbert Spencer. “Darwin applies this principle to specimens of the same species,” explains Meyer. “And you shouldn’t let the word ‘fittest’ make you think of a fitness studio.” In nature, the deciding factor is how many offspring a specimen has, in comparison to the reproductive success of its contemporaries. “Fitness is measured as the relative chance of survival and reproductive success of the specimen’s genome in comparison to its competition in the given population.”

Evolutionary scientists, such as Meyer, consider the fact that the opening of a male seahorse’s semen duct is not well positioned as proof that male pregnancy evolved in small steps—and wasn’t planned on the drafting table.

An even greater mystery is posed by the seahorses’ monogamy. Only 3 percent of all mammals have lasting partnerships, and even fewer amphibians, reptiles, and fish do. However, most seahorses are model couples that are never unfaithful to each other. Not only do they have a loving courtship, but they also invest a great deal in their relationship, spending a lot of time together in common activities.



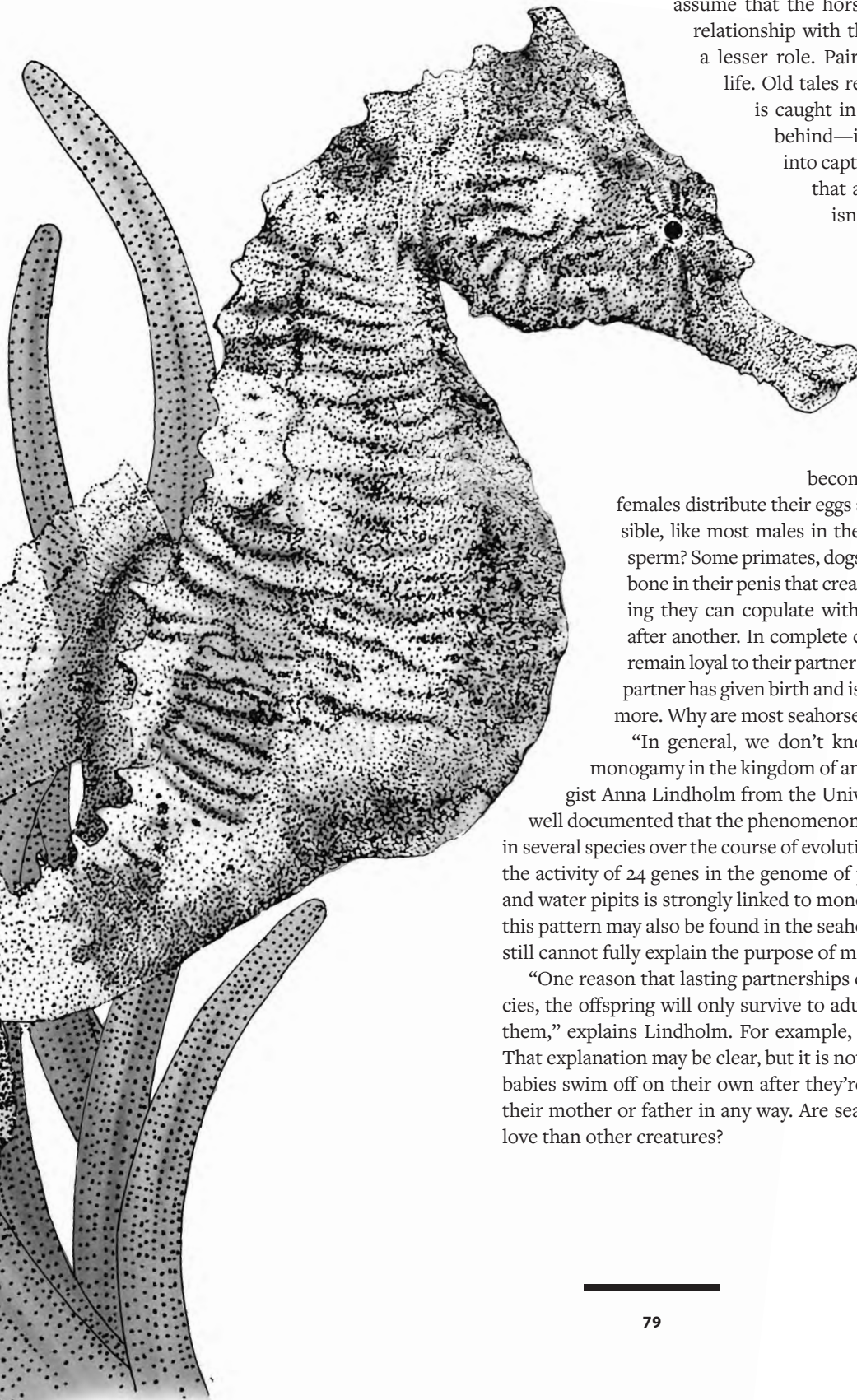
In many seahorse species, the couples get together daily to greet each other and dance. Behavioral scientists assume that the horses of the sea strengthen their relationship with these rituals, whereby sex plays a lesser role. Pairs usually remain together for life. Old tales relate that if one of the partners is caught in a net, the other won't leave it behind—instead voluntarily following it into captivity. Aquarium keepers recount that after the death of a seahorse, it isn't rare for the remaining partner to also perish within the next few days. Is it grief that robs the remaining widow or widower of the will to live?

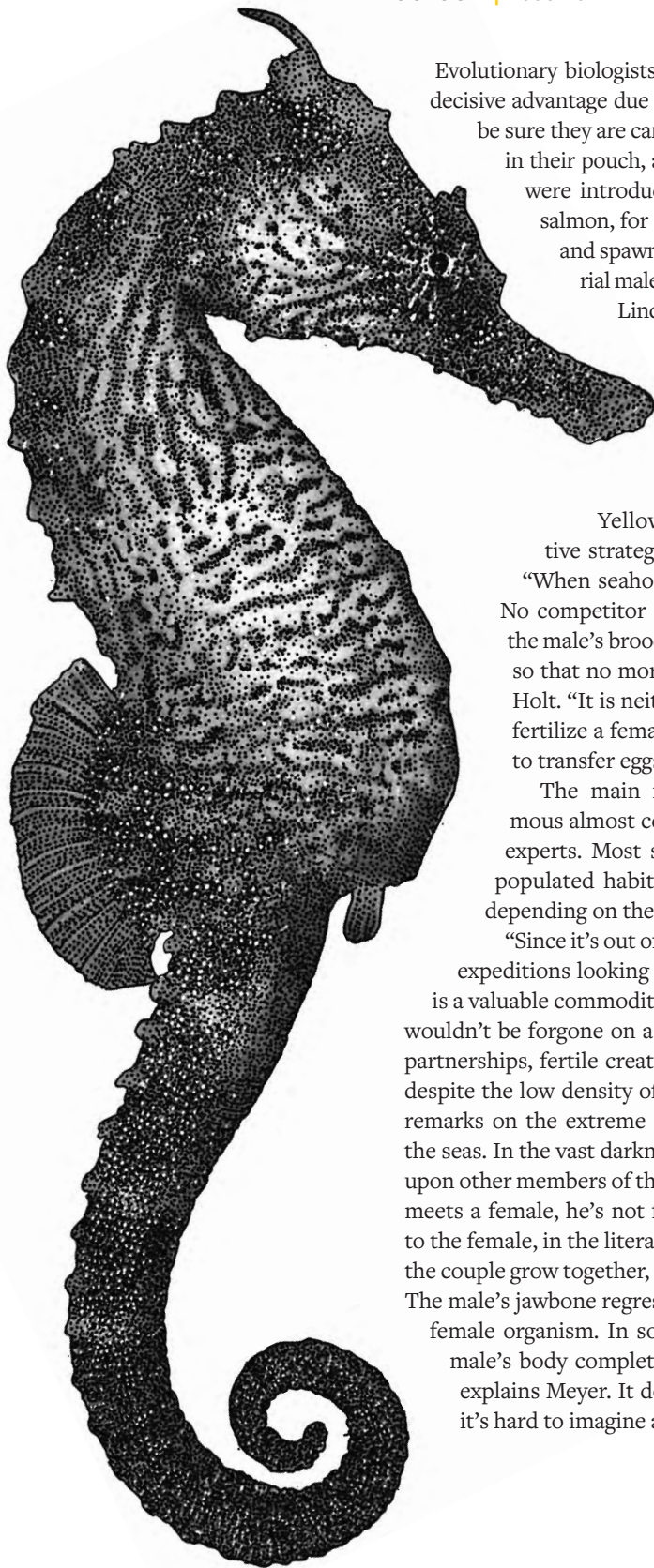
Seahorses' uncommon reproduction presents another question:

It's the male seahorses that become pregnant, so why don't the females distribute their eggs among as many partners as possible, like most males in the animal kingdom do with their sperm? Some primates, dogs, and whales even have a kind of bone in their penis that creates a permanent erection, meaning they can copulate with several different partners one after another. In complete contrast, most female seahorses remain loyal to their partner and do not mate again until their partner has given birth and is ready to become pregnant once more. Why are most seahorses loyal till death?

"In general, we don't know a lot about the genesis of monogamy in the kingdom of animals," says evolutionary biologist Anna Lindholm from the University of Zurich. However, it is well documented that the phenomenon independently came into being in several species over the course of evolution. A 2019 study has shown that the activity of 24 genes in the genome of prairie voles, poison dart frogs, and water pipits is strongly linked to monogamous behavior. Presumably, this pattern may also be found in the seahorse genome. Yet this discovery still cannot fully explain the purpose of monogamy.

"One reason that lasting partnerships can pay off is that, in some species, the offspring will only survive to adulthood if both parents care for them," explains Lindholm. For example, in storks, wolves, and beavers. That explanation may be clear, but it is not valid for seahorses, since their babies swim off on their own after they're born and aren't supported by their mother or father in any way. Are seahorses simply more capable of love than other creatures?





Evolutionary biologists doubt that. Yet seahorses do have one decisive advantage due to their monogamy. Pregnant males can be sure they are carrying only their own biological offspring in their pouch, and not any so-called cuckoo's eggs that were introduced by the competition. In the case of salmon, for example, a second male often flashes by and spawns in the female's "nest," after the territorial male, or "official father," has done so, explains Lindholm. Yet how great is the certainty of a biological pregnancy in male seahorses, if their sperm—at least in the case of yellow seahorses—isn't deposited directly into their brood pouch?

Could other male seahorses also add their semen? Holt dismisses this.

Yellow seahorses' complicated reproductive strategy does give them a degree of certainty. "When seahorses mate, they're very close together." No competitor can come between them. "In addition, the male's brood pouch closes again after a few seconds, so that no more eggs can be transferred," emphasizes Holt. "It is neither possible for more than one male to fertilize a female's eggs, nor for more than one female to transfer eggs to his pouch." It's a fair deal.

The main reason many seahorses are monogamous almost certainly lies elsewhere, according to the experts. Most seahorse species live in large, sparsely populated habitats, yet they are slow swimmers and, depending on the species, some of them are very rare.

"Since it's out of the question for seahorses to go on long expeditions looking for a mate, any available sexual partner is a valuable commodity, for both the male and the female, and wouldn't be forgone on a whim," says Meyer. "Thanks to lasting partnerships, fertile creatures can efficiently pass on their genes despite the low density of members of the same species." Meyer remarks on the extreme case of the anglerfish in the depths of the seas. In the vast darkness, it is very rare for creatures to come upon other members of their species. If a male deep-sea anglerfish meets a female, he's not fussy. He immediately attaches himself to the female, in the literal sense of the word. At first, the skins of the couple grow together, and later even their circulatory systems. The male's jawbone regresses—and eventually it merges with the female organism. In some species of deep-sea anglerfish, the male's body completely disintegrates, except for the testes, explains Meyer. It doesn't sound like a dream wedding, but it's hard to imagine a closer and more intimate relationship.

Are seahorses simply more capable of love than other creatures?

For love-bound seahorses, “married couples” practice their partner dancing routines daily—as well as their longer wedding dances—ensuring the technically precise delivery of the female’s eggs into the male’s pouch. Experts surmise this also enables them to adjust their reproductive cycles, which are driven by sexual hormones. The female’s next batch of eggs therefore ripens just after her “husband” has finished giving birth to the last brood.

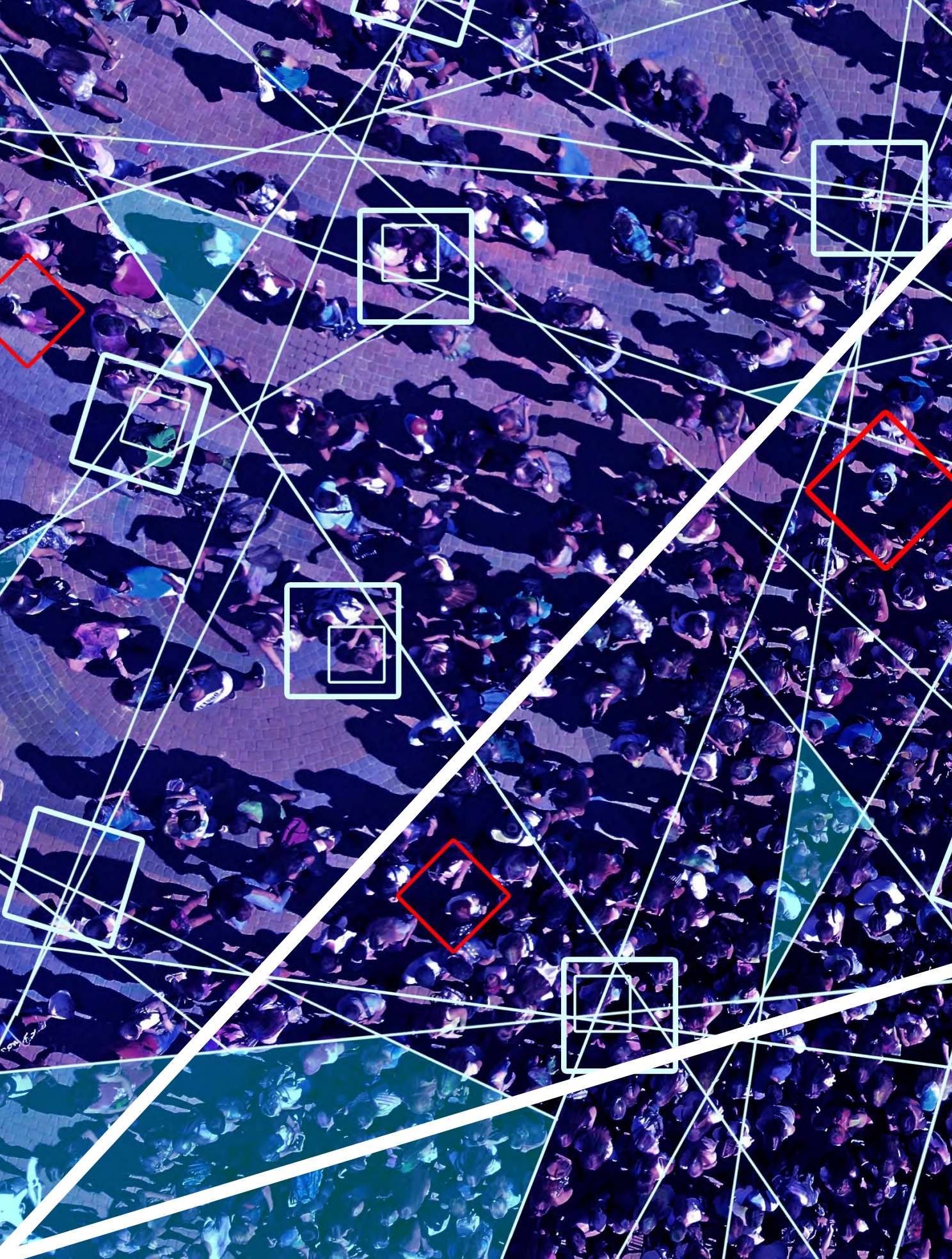
As the saying goes, all roads lead to Rome—or to successful reproduction. In fact, not all seahorses are loyal. A restless female Denise’s pygmy seahorse (*Hippocampus denise*) proved that she was always on the go. Scientists observed that this tiny seahorse was two-timing her partners. She danced wedding dances with both of them and mated with both. The biological advantage was that she halved the risk of losing a mate and all her offspring. This calculating seahorse followed the strategy favored by stock market speculators and didn’t put all her eggs in one basket!

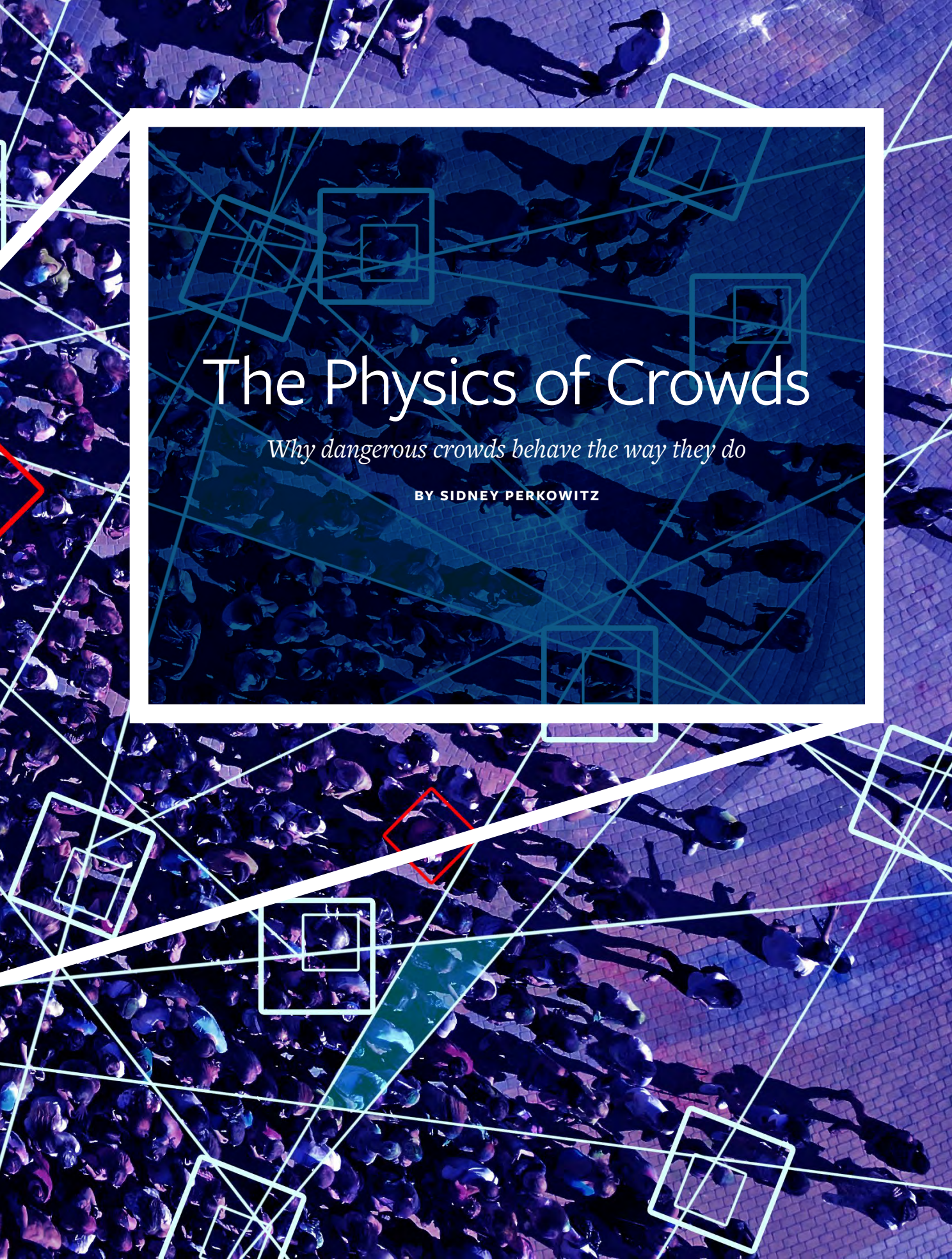
Some stallions of the sea are even more promiscuous. Big-belly seahorses (*Hippocampus abdominalis*), at home in Australia and New Zealand, do not seek lasting partnerships. Instead, they mate with almost any female at hand. That fits in well with the “loyalty due to scarcity” theory of the biologists, since big-belly seahorses live together in a smaller area than most other species.

Many other species of seahorses—romantic wedding dances or not—have a bit on the side in the tumult of an aquarium. If there were sufficient partners available, some male seahorses would mate with up to 25 different females a day. Perhaps a *bon mot* of *Homo sapiens*, “morality means lack of opportunity,” also applies to seahorses. ☺

TILL HEIN studied history, German, and Russian before becoming an editor and a science journalist. He is a great friend of fish and has written profiles of finned creatures for over 10 years, from hagfish to gray sharks to seahorses. He lives in Berlin.

Adapted with permission of the publisher from *The Curious World of Seahorses: The Life and More of a Marine Marvel*, written by Till Hein and translated by Renée von Paschen. Published by Greystone Books in October 2023. Available wherever books are sold.



An aerial photograph of a large crowd of people on a paved surface, overlaid with a complex network of white and red geometric lines and squares. The lines form a web-like pattern across the entire image, with some squares highlighting specific areas of the crowd. The overall color palette is dominated by deep blues and purples, with a bright red line cutting across the lower left.

The Physics of Crowds

Why dangerous crowds behave the way they do

BY SIDNEY PERKOWITZ

IN OCTOBER 2022, 159 people died as crowd pressure caused a human pile-up in the Itaewon district of Seoul, South Korea. The victims were among an estimated 100,000 people celebrating Halloween in an area known for its active nightlife and narrow streets. With a tightly packed crowd, it would have taken only a single incident, such as a person stumbling, to initiate instability. The resulting wave of pressure quickly spread in a sloping alley some 12 feet wide, and people were crushed by the unrelenting force of others in the crowd.

This catastrophe was a national tragedy in South Korea, but it is not the largest such event. Documented fatal crushes stretch back through history. In 1896, a rush during a festival celebrating the coronation of Russian emperor Nicholas II killed more than 1,280 people. And in 2015, a crowd crush among 2 million Muslims attending the annual *hajj* to Mecca in Saudi Arabia left more than 2,000 people dead. In these cases, people panicked as they were squeezed by the crowd and could not escape. Though rare, these events are devastating and seem like they should be preventable—especially today.

The complex field of crowd science has long been working to understand how throngs can turn dangerous. It has borrowed from psychology and epidemiology, and now is also incorporating complex systems theory, physics, and physiology, combined with plentiful empirical data coupled with computer modeling. Scientists have even started turning their eyes toward the dangerous dynamics of virtual crowds.

We all have something to gain from this gathering field of science, because whether at a sports match, show, busy market, rush-hour metro, or in an online community, most of us find ourselves, at times, in a crowd.

In physics, the closer two electrons get, the more strongly they repel each other—a phenomenon known as a repulsive force. With this force in play, they can never collide. Similarly, in most circumstances, people operate with a “social force,” avoiding collision with one another, for example, on a busy sidewalk.

Unlike electrons, people also react intelligently to their neighbors’ actions, and these reactions can result in collective crowd behavior. A team of United States-based researchers studied videos of moving crowds and confirmed, in a 2014 paper, perhaps unsurprisingly, that people alter their paths to avoid collisions over a range of walking speeds.¹ But that data led to a new empirical and universal law of repulsion between two people, which stated that people altered their paths based not on distance—like electrons—but instead on time until collision. When this law was applied to computer-simulated crowds, it predicted actual behavior. For instance, crowd members heading toward different exits in a stadium minimize disruptive interactions by spontaneously forming themselves into unidirectional lanes.

These lanes are an example of an emergent property, when a group of interacting entities shows behavior that its separate



components do not exhibit. In 2021, a team of researchers based in Japan confirmed that the anticipation of future outcomes is important for how a crowd organizes itself.² The researchers set in motion two crowds of 27 members each to meet while walking in opposite directions. In repeated trials, each group neatly formed itself into unidirectional lanes. That intelligent organization changed, however, when just three members of one group were given mobile phones and told to type on them to solve math problems while walking. The distraction disrupted the formation of lanes for both crowds, with higher probabilities of colliding. This shows how even minor disturbances can alter crowd behavior and underlines the tight link between individual behavior and the physical actions of a crowd.

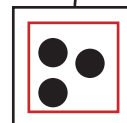
And when a disruption is coupled with high density, the results can quickly turn deadly.

Keith Still, a crowd scientist at the University of Suffolk in the United Kingdom, defines his work as the study of crowd densities above about one person per square meter (11 square feet). Below that value, pedestrians can freely move to avoid collisions or adjust to changing conditions. At two people per square meter, walking speeds are reduced. At four people per square meter, involuntary contact occurs; at six to seven people per square meter (the equivalent of 1,600 to 1,800 people crammed onto a tennis court), the close contact makes motion difficult; and at 10 people per square meter, movement is virtually impossible. In a playful video clip, Still illustrates how just six men—held within a rope loop of one square meter—overlap and lurch forward only awkwardly, even as they calmly try to synchronize their steps. At these critically high densities, an uncoordinated crowd in motion can hardly proceed and begins piling up; in a static crowd, one person in distress can cause a crush.

Knowing what level of crowd density is dangerous helps authorities handle large-scale public events. Still's work was employed, for example, to assess crowd safety in planning for the U.K.'s royal wedding of Prince William and Kate Middleton in 2011. In real-time, public safety organizations can also now use this sort of information to monitor crowds with video cameras backed up by computer or AI analysis to identify areas of developing concern. And researchers can gather video, along with digital data from smartphones and Wi-Fi networks, to better understand crowd dynamics post hoc—even when things go well.

The study of how crowds move has long borrowed from physical theory, in particular from fluid dynamics, viewing a dense mass of people as a continuous medium. The behavior of a continuous fluid medium—a liquid or gas—depends on the properties and interactions of the individual particles that make it up. In water, the basic particles are H₂O molecules; in a crowd, the “particles” are people, whose interactions determine overall crowd behavior.

But when the density becomes very high and individual motion is highly restricted, a crowd can behave more like so-called “soft matter.” This is any “squishable” material, such as butter or Silly Putty, that can be easily



deformed and displays both solid and liquid characteristics. Soft matter research is a developing area in physics and is providing a new physical tool to study crowds in the dangerous realm of extremely high densities. Knowing that an ultra-dense crowd does not flow freely like water but moves more like kneaded clay helps explain the special conditions that individual crowd members would experience.

That could well have been the case in the Seoul tragedy. We do not know the precise density the crowd reached before its internal pressure became lethal, but the devastation seen in the aftermath shows that the density was far into the danger zone defined by Still. This would have utterly precluded any free motion or “social force” avoidance maneuvers based on physical repulsive forces and fluid dynamics. Instead, the crowd likely behaved according to the physical laws of soft matter and developed strong internal forces that tragically crushed individuals caught up within its pressure points. With more data, the conditions that produced those forces could have been better understood to help in future crowd control.

But crowd behavior isn’t just about physics. There are myriad psychological phenomena at work—especially when things start to go wrong.

A flow of sentiment becomes a powerful force in dictating a crowd’s behavior, as Gustave Le Bon proposed in 1896 in *The Crowd: A Study of the Popular Mind*. Le Bon introduced the idea that emotional states (and cognitive ones) can be infectious, giving rise to the concept of emotional contagion. In this process, a person takes in an emotion expressed by someone else, then expresses that feeling, which affects others. This soon generates a common emotional state such as fear or anger that grips a crowd.

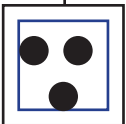
In 2015, Funda Durupinar at Bilkent University in Turkey and colleagues introduced a useful model for this transference in a crowd. They took an epidemiological

When a disruption is coupled with high density, the results can quickly turn deadly.

approach where, like the germs from an infectious disease, people received doses of emotion from those already infected, and became themselves infected if the total dose exceeds a certain threshold (as determined by typical psychological profiles).³

Building on that work, an international team of researchers, in 2021, considered the psychological, physical, and physiological factors involved as people panic when they become aware of a threat, then try to move away from it.⁴ The researchers used known theory and data to simulate on a computer the relevant characteristics of the members of a crowd fleeing the scene of a threat. The first step was to determine the bodily effort as each person ran, based on typical body weights and speeds. From the physiological energy expended, the researchers calculated the heart rate, which measures the degree of fear and the continuing emotional contagion triggered by the person running away. Combining all these effects, the researchers were able to calculate the trajectory and position for each person, spreading more panic as they fled.

As this computer simulation unfolded, it gave realistic results. A virtual person near the danger zone soon panics and tries to get away as quickly as they can. As emotional contagion spreads, those farther away also become fearful and try to escape. The researchers then compared the simulation to videos of experiments where real people reacted to simulated dangers, and to videos of real crowds responding to real emergencies: a





NO WAY OUT This narrow alley in Seoul was where a crowd of revelers celebrating Halloween in October 2022 suddenly transformed from a flowing throng into a dangerous “soft matter” mass, ultimately killing 159 people in a panic-fueled crush.

suspected bomb in the Shanghai subway system and a shooting outside the British Parliament. In all cases, the model results were reasonably similar to the observed behaviors, more so than other models that did not include all three factors of the psychological, physical, and physiological, underscoring the complex, interdisciplinary, and ever-evolving nature of crowd science.

Results like these are beginning to elucidate how physical crowds operate in daily life, or under panic conditions. But today, many interactions occur not in real-world crowds but in virtual ones. Although the dynamics are different than in a physical crowd, scientists are still finding lessons from physics to try to better understand the risks to individuals from these virtual mobs.

It turns out that masses of physically separated people have displayed their power for centuries, as Charles Mackay wrote in his 1852 *Extraordinary Popular Delusions and the Madness of Crowds*. He detailed how dispersed throngs of people can get swept toward a common idea, such as the speculative tulip mania in the 1630s, or toward a common action, as in the Crusades of the Middle Ages. Now, online connections enable the

rapid transfer of feelings, opinions, and information—whether true or false—among the members of virtual crowds, vastly accelerating crowd dynamics in the ether and sometimes producing very real effects in real life.

Virtual crowds may draw individuals toward a black hole of extreme political and social opinions. Studies show that the rhetoric of these groups can boil over from online discourse to encourage real-world violence, and the interconnections they provide can support the organization of group actions like the deadly riot at the U.S. Capitol on Jan. 6, 2021. The risk that online-fomented events like these will continue to threaten people and political stability in the real world make it important to discover how online crowds perpetuate extreme opinions that may have outsized impacts.

One early analysis shows the central importance of connectivity in encouraging the growth of extremism within virtual crowds. The work was published in 2015 by researchers in the U.S., Brazil, and Israel.⁵ Assessing public opinion across the globe about religion, politics, climate change, abortion, and other hot-button issues, they noted a decrease in moderate voices with “the rising of extreme opinions ... the opinion or attitude of an



UNSUSPECTING EXTREMISTS Scientists have found that, like shockwaves traveling through a physical medium, extreme opinions can ripple rapidly through online crowds, turning a majority toward a new dangerous perspective.

initially small group could become the rule.” To study this premise, the researchers examined many hundreds of recent surveys in various countries asking about these divisive issues.

The survey responses were sorted either as extremely in favor or against an opinion—or moderately in favor or against it. Tabulating the proportion of people with extreme views, the researchers found a surprise. In many of the surveys, across a range of issues, the fraction of respondents with extreme views was in a small minority and proportional to the total number of responders. But for most surveys where the fraction of extreme views exceeded 20 percent of respondents, the number of extremists was found to be up to five times larger than a linear relationship would predict. This nonlinear behavior means that above 20 percent extremism, extremists may disproportionately influence groups—and in unexpected ways.

Why would a relatively small nucleus of extremists lead to intensely extreme groups? The answer comes from statistical physics, where the onset of nonlinear behavior is a sign of interactions among separate units that produce a major change; for instance, when H_2O molecules become correlated at zero degrees Celsius, causing liquid water to turn into solid ice. Similarly, the

researchers found that to successfully reproduce their empirical observation of a 20 percent tipping point for extremism, they had to use a mathematical model that included interactions among the survey respondents. The researchers characterized these interactions as occurring across social networks where “new opinions can take form and existing ones can be either strengthened or weakened”—exactly what online virtual crowds efficiently facilitate.

This field, fueled by increasing urgency, is gaining speed. In 2023, physicist Pedro Manrique and colleagues at George Washington University published a new general theory describing the dynamics of online crowds that spread hate or extreme views.⁶ In their work, they explain, “Society is struggling with online anti-X hate and extremism, where ‘X’ can nowadays be any topic, e.g., religion, race, ethnicity.” Such communities, up to millions strong, spread harmful content on platforms like Facebook and its Russian counterpart, VK. The groups grow quickly and seemingly out of nowhere, note the researchers, as individuals and similar groups fuse with them within a platform and across different platforms. Then the supermassive anti-X groups also often abruptly fission and die off when platform moderators notice them and shut them down.

Since early writing about crowds in the 19th century, crowd science has evolved to where it can now make quantitative predictions about both actual and virtual crowds. But the essential step to preventing future disasters is to continue pulling from a vast array of scientific fields to better understand the dynamics that portend danger. In addition to saving the lives of the unlucky few, the field can be a model for dealing with other complex problems facing all of humanity, such as climate change, future pandemics, and artificial intelligence. And with any luck, it could help us overcome at least some of the madness of human crowds. ☺

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My Brain Doesn't Picture Things

I can't imagine sights, smells, or sounds. What's wrong with me?

BY MARCO GIANCOTTI

I'M LYING DOWN in a white cylinder barely wider than my body, surrounded on all sides by a mass of sophisticated machinery the size of a small camper van. It's an fMRI machine, one of the technological marvels of modern neuroscience. Two small inflatable cushions squeeze my temples, keeping my head still.

"We are ready to begin the next batch of exercises," I hear Dr. Horikawa's gentle voice saying. We're underground, in one of the laboratories of Tokyo University's Faculty of Medicine, Hongo Campus. "Do you feel like proceeding?"

"Yes, let's go," I answer.

The machine sets in motion again. A powerful current grows inside the cryogenically cooled wires that coil around me, showering my head with radio waves, knocking the hydrogen atoms inside my head off their original spin axis, and measuring the rate at which the axis recovers afterward. To the sensors around me, I'm now as transparent as a glass of water. Every tiny change of blood flow anywhere inside my brain is being watched and recorded in 3-D.

Understanding aphantasia means learning something more about what it means to be human.

A few seconds pass, then a synthetic female voice speaks into my ears over the electronic clamor: “top hat.” I close my eyes and I imagine a top hat. A few seconds later a beep tells me I should rate the quality of my mental picture, which I do with a controller in my hand. The voice speaks again: “fire extinguisher,” and I repeat the routine. Next is “butterfly,” then “camel,” then “snowmobile,” and so on, for about 10 minutes, while the system monitors the activation of my brain synapses.

For most people, this should be a rather simple exercise, perhaps even satisfying. For me, it’s a considerable strain, because I don’t “see” any of those things.

For each and every one of the prompts, I rate my mental image “o” on a 0 to 5 scale, because as soon as I close my eyes, what I see are not everyday objects, animals, and vehicles, but the dark underside of my eyelids. I can’t willingly form the faintest of images in my mind. And, although it isn’t the subject of the current experiment, I also can’t conjure sounds, smells, or any other kind of sensory stimulation inside my head.

I have what is called “aphantasia,” the absence of voluntary imagination of the senses. I *know* what a top hat is. I can describe its main characteristics. I can even draw an above-average impression of one on a piece of paper for you. But I can’t visualize it mentally. What’s wrong with me?

MY WHOLE LIFE, I’ve been aware—sometimes painfully so—of my own peculiarities, strengths, and weaknesses: A terrible memory, a good sense of direction, and what I felt was a lack of “visual creativity,” among others. I always thought these were just random, disconnected traits, and didn’t think much about them. Who doesn’t have their quirks?

Then, some time in 2021 (not coincidentally, I forget exactly where or when) I read about aphantasia for the

first time, and it hit me hard: When people say “picture this scene in your head,” they aren’t speaking metaphorically! *People can actually invoke shapes and colors in their minds.* The shock of this realization was followed by a piecing together of many of those little idiosyncrasies of mine into a single, coherent phenomenon that fit with the scientific description of the condition. By the time my formal diagnosis came, I was already quite sure I was aphantasic.

I share this trait with many people. Occasional reports of people claiming to be without a “mind’s eye” go back to the 1800s, with several cases briefly mentioned in the scientific literature throughout the 20th century. Yet these cases were ignored by the broader scientific community, relegated to the fringes of the field as outliers or misunderstandings.

It was only in the 2010s that the topic began to attract attention. A man approached Adam Zeman, professor of cognitive and behavioral neurology at the University of Exeter, in the United Kingdom, claiming to have lost his mind’s eye following a heart surgery. In 2010, Zeman published a study showing that the man had different brain activation patterns from other subjects when trying to imagine things.¹

This was an interesting case study on its own, but something more surprising followed the publication of Zeman’s paper: Several people contacted him claiming to have had that same condition for as long as they could remember. Zeman and his collaborators assessed their claims using the Vividness of Visual Imagery Questionnaire (VVIQ), a popular measure of internal visualization quality, and found that these individuals indeed seemed to have little to no ability to visualize at will. The researchers published these findings in 2015, and proposed to call the condition “aphantasia”—literally “the absence of images” in Greek.²



With this new label, word about aphantasia finally started to spread within the neuroscience community and the broader public. More groups of researchers around the world began studying it, and every year a larger number of papers on the topic reaches scientific journals. We now know that roughly 1 out of 25 people are “aphantasics” (or “aphants,” in internet slang)—a rare condition, but common enough that each of us must know several people in the category.

For those equipped with a trusty inner eye, hearing about aphantasia can be a puzzling experience. How can someone even function as a human being without the ability to imagine pictures and sounds?

The biggest source of confusion with aphantasia comes from the assumption that “imagination” and “forming mental images” are one and the same thing. This is, of course, incorrect. I’m able to imagine anything, except it is all devoid of sensory representations. The imagined objects exist in my mind as interconnected concepts, like bullet lists of facts about things. For example, when I reread the scene in Ernest Hemingway’s *The Old Man and the Sea* where the protagonist battles a giant marlin, I’m able to take in a large amount of information: We’re on his skiff, bobbing on the waves of the deep waters of the Gulf of Mexico, the sun hammering mercilessly on the poor man while he pulls on the line for hours on end. I can reason about the situation, try to predict what could happen next, and relate with the character’s plight.

None of this requires having a picture of the scene in my head. This way of imagining is, perhaps, more abstract than what most people are used to, but not significantly less useful.



A surprising aspect of this is that, for me, the physical “bullet-list concepts” don’t just float haphazardly in nothingness, but are embodied in coherent three-dimensional structures that I can manipulate in my mind. In the scene of the old fisherman, I can imagine moving around the small boat, sitting down next to Santiago, and I can “feel” the monstrous mass of the fish floating near the vessel. This spatial awareness might be what allows me to find my way around my bedroom in darkness: I know where the furniture is and the rough distances between things even without seeing

them. The science is still unclear as to why someone like me can form spatial thoughts without the accompanying imagery, but some speculate that it might have something to do with a separation of these functions in and around the visual cortex.

For non-aphants, it’s also hard to imagine how those of us without this sensory mind’s eye remember events if we can’t call to mind images, smells, or sounds. Scientists have begun trying to untangle this difficult question about the brain as well. In a 2015 paper, a group of researchers from the University of Toronto led by psychologist Daniela Palombo identified a new syndrome they called “Severely Deficient Autobiographical Memory,” or SDAM for short.³ People with SDAM lack the ability to relive past experiences in their minds. While this condition is rare among the general population, a preliminary survey hints at a link with aphantasia, with as many as 51 percent of a sample of 2,000 SDAM individuals also having aphantasia.

My own experience is similar. Past episodes of my life—when I can recall them at all—feel distant and non-sensory. SDAM is a new discovery, still unknown to most practicing psychiatrists, so people like me have to rely on self-diagnosis for the time being. But the symptoms described by the researchers match with what I’ve always taken for granted. I would describe my recollections as summaries of key facts rather than first-person “mind movies.” When asked, out of the blue, about an experience I’ve surely had—say, any childhood birthday party—my mind first responds by drawing a blank. It feels as if my episodic memories were filed into a “mental cabinet” without an index. Many memories are in there, somewhere, but retrieving them is a daunting task unless I’m provided with very

IN THE MOMENT The author enjoying the passing sensation of an *ashi-yu*, or “foot bath,” at the foot of Sakurajima, an active volcano in southern Japan whose name means “Cherry Blossom Island.” Images and sensations from this moment will soon scatter from his mind, like petals on the breeze, but that doesn’t much bother Giancotti.

specific prompts. With some groping work of deduction (where did I live at the time? Who did I hang out with?) I can gather enough hints to bring out some locations and non-visual facts: I had a big party in our countryside garden when I was 11 or 12; there was cake; a lot of kids running around and ... that’s about it.

HOW DOES ALL OF THIS affect my life? The surprising answer is that it doesn’t, at least not in any debilitating way. To my great relief, people rarely ask me what happened at parties held decades ago. But even when there is a need to describe scenes or people visually, I usually have enough “verbal facts” and eloquence to give a satisfying answer, without the need to replicate the actual pictures in my head.

Among researchers, the consensus seems to be that aphantasia doesn’t meet the criteria to be called a disability, and that aphantasic individuals, in general, are fully functional and just as successful at living their lives and performing in their careers as the rest of the population. This seems to be further supported by a new paper published by two researchers at Sorbonne University.⁴ They presented their participants, including many aphantasics, with a series of tasks involving the comparison of shapes, colors, words, faces, and spatial relations in one’s head. Aphantasics were as accurate as the other participants in all the tests, although they took longer to solve the imagery-based tasks, presumably because they used different, less-direct strategies to complete them.



Yet, some of those who discover they have aphantasia despair at the news. I’ve seen people make claims like “my whole life was a lie” and “this must be what ruined my marriage.” While I’m not quite as pessimistic, I can relate with that minority of fellow aphants. Sure, aphantasia and SDAM may not be causing major problems in our daily lives, but wouldn’t their subtle effects compound over time? And could they not be the cause of many of our other more embarrassing weaknesses and shortcomings?

For many of us, the aftermath of learning about one’s aphantasia leads to some sort of self-consciousness crisis. Suddenly, your performance in every other aspect of life comes under scrutiny, and blaming your congenital aphantasia for it is almost irresistible. Is drawing without a reference so difficult because of my



aphantasia? Could SDAM be why I'm so bad at keeping in touch with people? Would I be less socially awkward without it? Very few of these supposed connections have been tested yet, let alone confirmed by solid scientific studies. Yet almost every aphantasic I've talked to does this. But everyone seems to focus their self-doubt on whatever they don't like about themselves, scapegoating different shortcomings.

I have learned to embrace the diversity of aphantasia, and I hope to spread the word about it. And so does Junichi Takahashi, the first researcher I talked to about my condition. Takahashi is a psychologist at Fukushima University and was one of the first scientists to pay attention to aphantasia in Japan, where I've lived since 2011. He set up a website with the VVIQ survey, which is what led me to confirm my suspicions of having aphantasia. I got in touch with him directly and began to learn more about the science behind mental visualization and its absence.

Rather than studying aphantasia as a single phenomenon, Takahashi is trying to bring clarity to its diversity. In July 2023, he and several co-authors published a paper examining subtypes of aphantasia.⁵ While most previous studies relied solely on the VVIQ questionnaire to identify aphantasic individuals, Takahashi and his team administered a battery of additional

psychological question-sets to the same subjects and analyzed their correlations.

One of these questionnaires probed the vividness of multi-sensory mental imagery, including the sense of hearing, smell, and so on. Can aphantasics mentally replay their parents' voices or the unique taste of cheesecake? Another questionnaire tested the tendency toward verbally oriented (relying more on words to figure out things) or visually oriented (relying more on images) thinking styles. Yet another one was used to detect "face blindness," the inability to recognize faces.

Their statistical analysis revealed that all of these factors are somewhat correlated, but none fully. For instance, many of their aphantasic subjects lacked all of their "mind senses," but some did have the ability to imagine sounds, flavors, or other non-visual sensations. The paper also found that face blindness did occur more often among people with aphantasia (40 percent) than in the control group (20 percent), but is far from being a universal aphantasic trait.

But all this talk of questionnaires and self-reports brings us to the age-old question: How do we know that aphantasia really exists, as opposed to being a form of psychological denial or simply a different interpretation of the same inner experience?

When aphantasia was first formally proposed, some researchers wondered whether the purported lack of visualization ability might in many cases be, not a congenital trait, but a psychopathological issue, such as neurosis or a defensive response against trauma. A kind of “philosophical language barrier” further complicates the issue: We might be talking about the same thing with different words and, language being the only medium we have to compare inner experiences, we have (or, rather, had) no way of confirming that. Even Ludwig Wittgenstein, one of the great philosophers of the 20th century, wondered about this very scenario more than 60 years before aphantasia got its name: If a person claimed they can’t imagine a picture but is still able to draw one, he asked, should we believe that something different is really going on in their head?

Scientists are now finding ways to answer these questions with hard, objective data. “Even before aphantasia became a thing, researchers tried separating people with low VVIQ from those with high VVIQ, and found that the performance at certain tasks is different between the two groups,” Takahashi explained to me. “There is also a lot of research showing a good correlation between VVIQ scores and fMRI scans.” The way the questions are posed in the questionnaire seems to work well enough to pick out individuals with demonstrably different visualization abilities.

Of the groups working on this front, Joel Pearson’s is one of the most active. His team at the University of New South Wales, in Australia, has been researching mental imagery since long before aphantasia became widely known. In 2022, his team even found a measurable physical characteristic of aphantasics.⁶ They discovered that, while the pupils of typical people involuntarily contracted when imagining bright shapes, no such response happened to the aphantasic group. In other words, Pearson’s team showed the first physiological difference confirming the reports of people claiming to have aphantasia. It looks like, at least in most cases, *something* different is happening inside our heads.

And some are trying to go even further. That’s why I periodically get into the fMRI machine in Dr. Horikawa’s lab to get my brain scanned. A researcher at NTT Communication Science Laboratories in Japan, Tomoyasu Horikawa specializes in using AI to decipher the contents of the human visual cortex. He has recently turned his attention to aphantasia. I connected with him in April 2023, when Takahashi suggested I join Horikawa’s new research project. Horikawa is still collecting data from me and several other people, but preliminary, unpublished analysis indeed



Aphantasia is turning out to be a little cornucopia of scientific insights.



shows a quantitative difference in brain activity when aphantasic and typical subjects imagine things. When measuring the “distinctness” of brain activation patterns—how accurately the same patterns are repeated in a subject’s brain when imagining the same object, and how reliably different when imagining different objects—aphantasic subjects seem to score a bit lower. But he says that much more data is necessary to definitely tell. That may turn out to be the best proof of the neural differences between people with and without the condition.

ALL THINGS CONSIDERED, learning about my aphantasia made me doubly optimistic, both at the collective and personal levels.

In terms of social impact, aphantasia is turning out to be a little cornucopia of scientific insights. Already scientists are working with aphantasics not only to understand the condition itself, but also to shed light on the intricate workings of the human brain in general.

Rebecca Keogh, a cognitive neuroscientist at Macquarie University, in Australia, for example, has looked into the mechanisms of PTSD by comparing the occurrence of intrusive thoughts between aphantasics and people

who can visualize. For Horikawa, aphantasia is a way to isolate the precise neural processes that create mental imagery in the general population. And researchers from the universities of Calgary and Radboud in the Netherlands recently published an article in *Nature Reviews Psychology* arguing for the use of aphantasia to resolve long-running debates about “embodied cognition”—a theory that treats thinking as a process involving mental simulations of one’s body and sensations, as opposed to only abstract concepts and symbols. The absence of something—like the lack of “inner senses” in aphantasics—can teach us much about the presence of it. This might be the biggest reason why I participate in these experiments: Understanding aphantasia means learning something more about what it means to be human.

In a sense, discovering aphantasia as a scientific topic is a bit like landing on a beach on an unknown continent. We know it’s new, but we have no idea of its geography and size. The binary division between “aphantasic” and “everyone else” might be a short-lived one. The subtype studies of Takahashi and others may lead to a more detailed map of the myriad ways a lack of visualization manifests in people and how they work around it. The brain seems to always have more surprises in store for us, more facets and inter-connections where we previously expected simplicity. We now have an even more interesting landscape to explore.

And as this additional diversity comes into focus, it is easier for us to marvel at the paradox of human cooperation. What would seem like fundamental differences in the way we think—some with pictures, others without—do not lead to fundamental barriers in the way we talk to, connect with, and love each other. We are able to form societies and, through struggle and errors, build thriving communities despite these cognitive differences, and maybe because of them.

On the personal level, my “self-consciousness crisis” is eclipsed by a more powerful “self-knowledge renaissance.” Learning that I have aphantasia gave me the habit of carefully observing my inner experience. It led, among other things, to realizing that I may also have SDAM and mild synesthesia, something that I

I would not want to remove the aphantasia even if it were possible.

had never paid any attention to before. It also honed my ability to explain to others what goes on inside me. Armed with these new skills, I can say that I am better at managing myself and at picking the battles that I am best at. I feel like I have gained much and lost nothing.

Some people ask me if my aphantasia can be cured. The easy answer is no, because you can't cure what isn't a disease, and anyway we don't know enough about it yet to influence it. The more sincere answer is that I would not want to remove the aphantasia even if it were possible. Temporary visualization tools? Sure. But not permanent changes to my brain. Whatever compounding effects it had on me over the decades, it helped produce the person I am today. I'm glad it did, even counting all the flaws. The question I started with—what's wrong with me?—was both rhetorical and itself wrong. The better question is one we all ask ourselves at some point: "What makes me who I am?" 🌀

MARCO GIANCOTTI is a freelance writer, product manager, and aphant living in Japan. He has graduate degrees in astrophysics and aerospace engineering—both of which happen to rely on equations more than on mental pictures. He is working on an accessible reframing of key science insights on his website, Plankton Valhalla (which, yes, does contain lots of visualizations). Follow him on Twitter @marco_giancotti.

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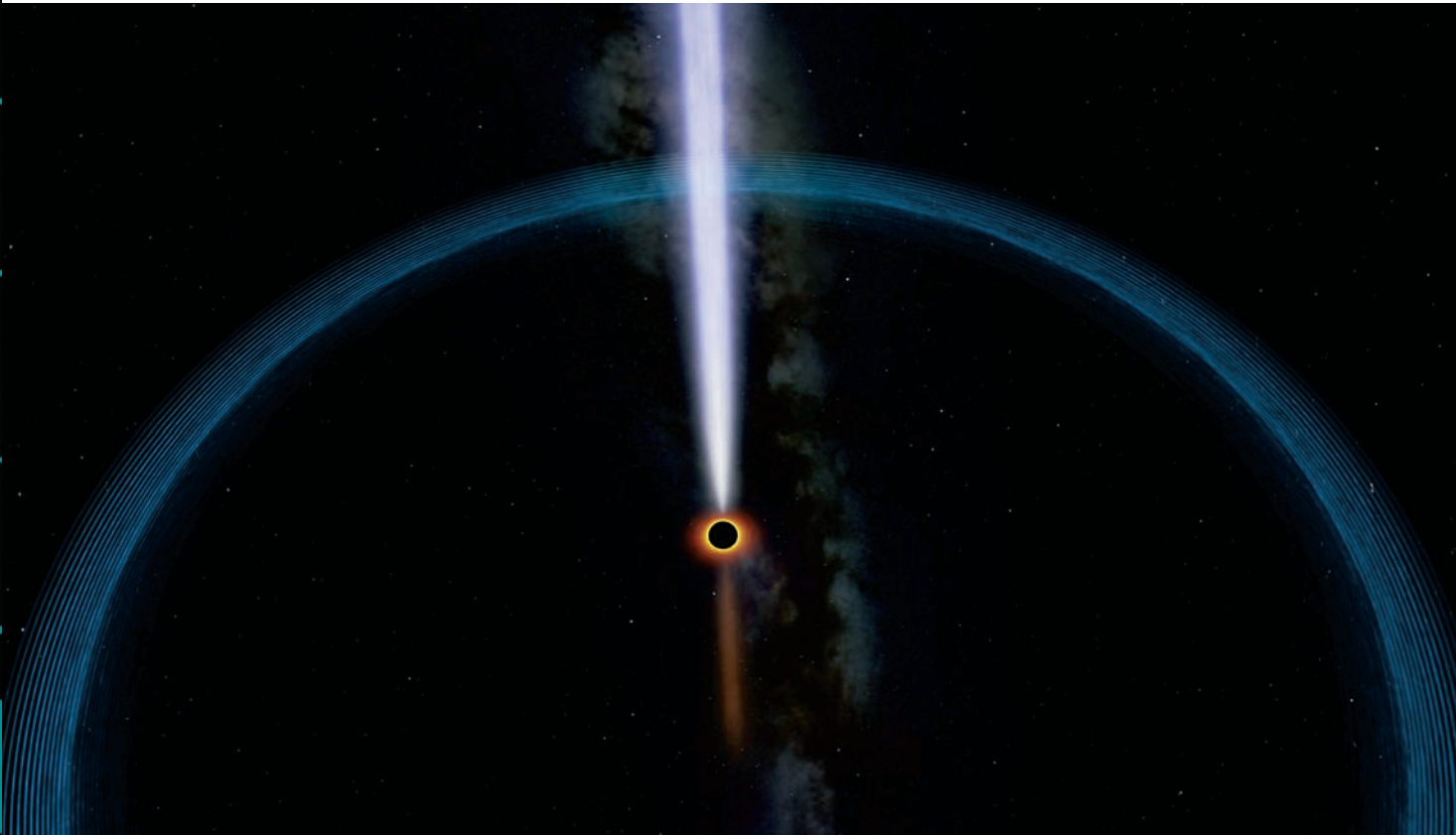
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Sunday, November 5, 2023, 3 p.m. – 4 p.m.

This immersive new production from the Museum of Science, Boston, and Multiverse Concert Series, in collaboration with the Harvard-Smithsonian Center for Astrophysics and Black Hole Initiative, takes you on a symphonic journey through spacetime, performed by a chamber orchestra accompanied by stunning, immersive visuals by the Museum of Science, Boston's Charles Hayden Planetarium animators. Score by David Ibbett.

The concert is presented in memory of NAS member Eugene Roberts (1920-2016) Ph.D., F.A.I.C.

National Academy of Sciences
Fred Kavli Auditorium
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Washington, D.C.

Details and free tickets are available at
<https://blackholesymphony.eventbrite.com>

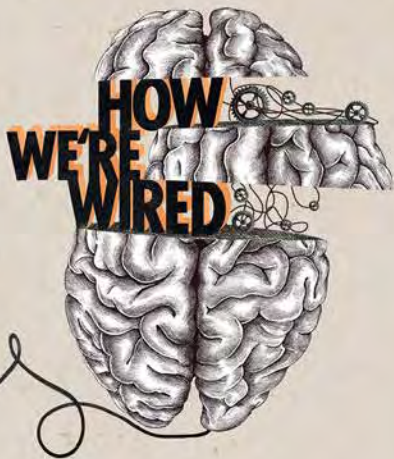
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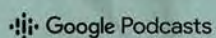
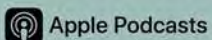
Presented by anthropologist Dr Anna Machin, this series features real life stories, expert analysis, the latest research and at-home experiments that will open your eyes to the most fascinating organ in the human body.



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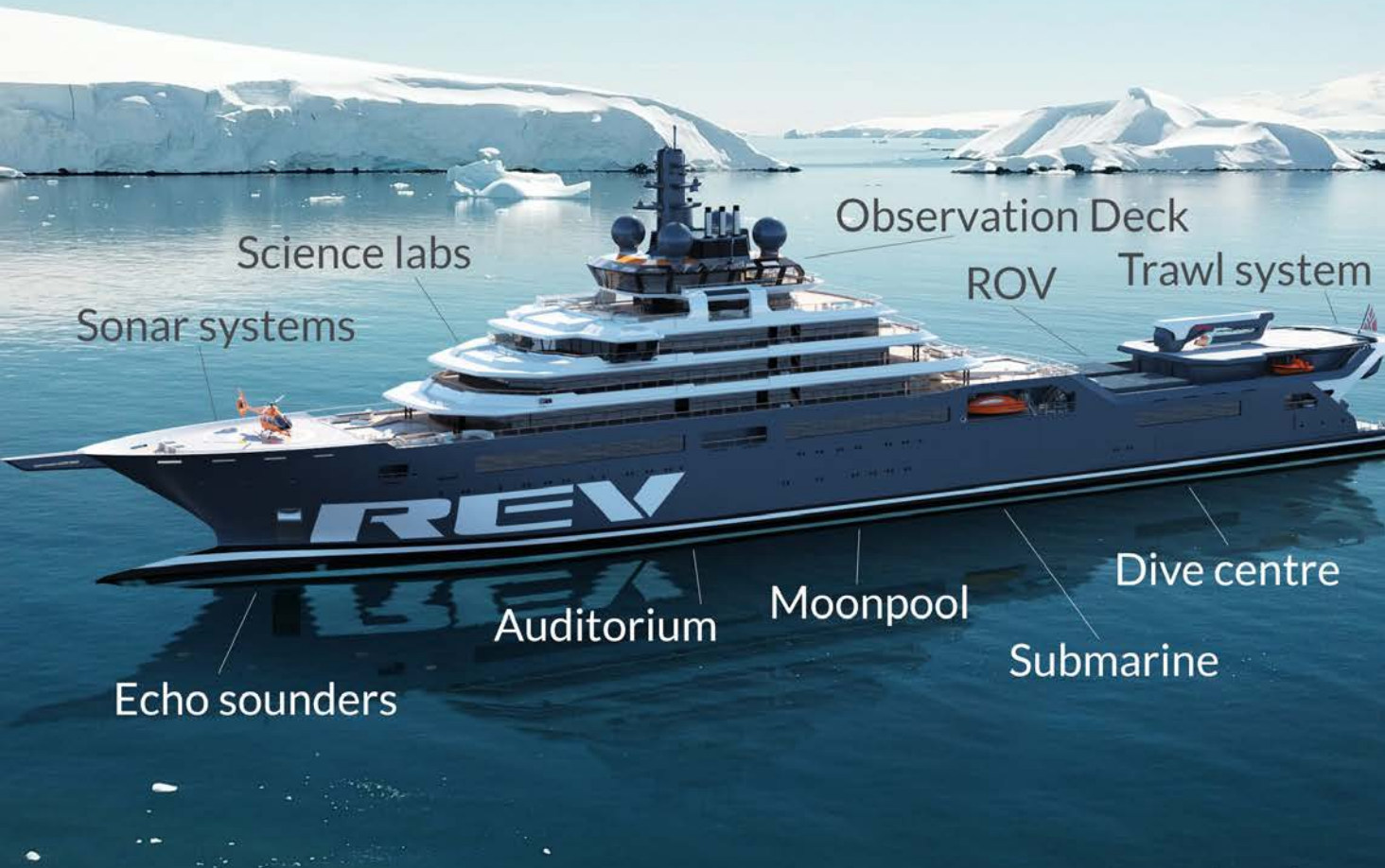
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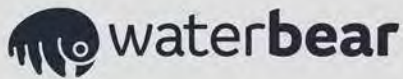
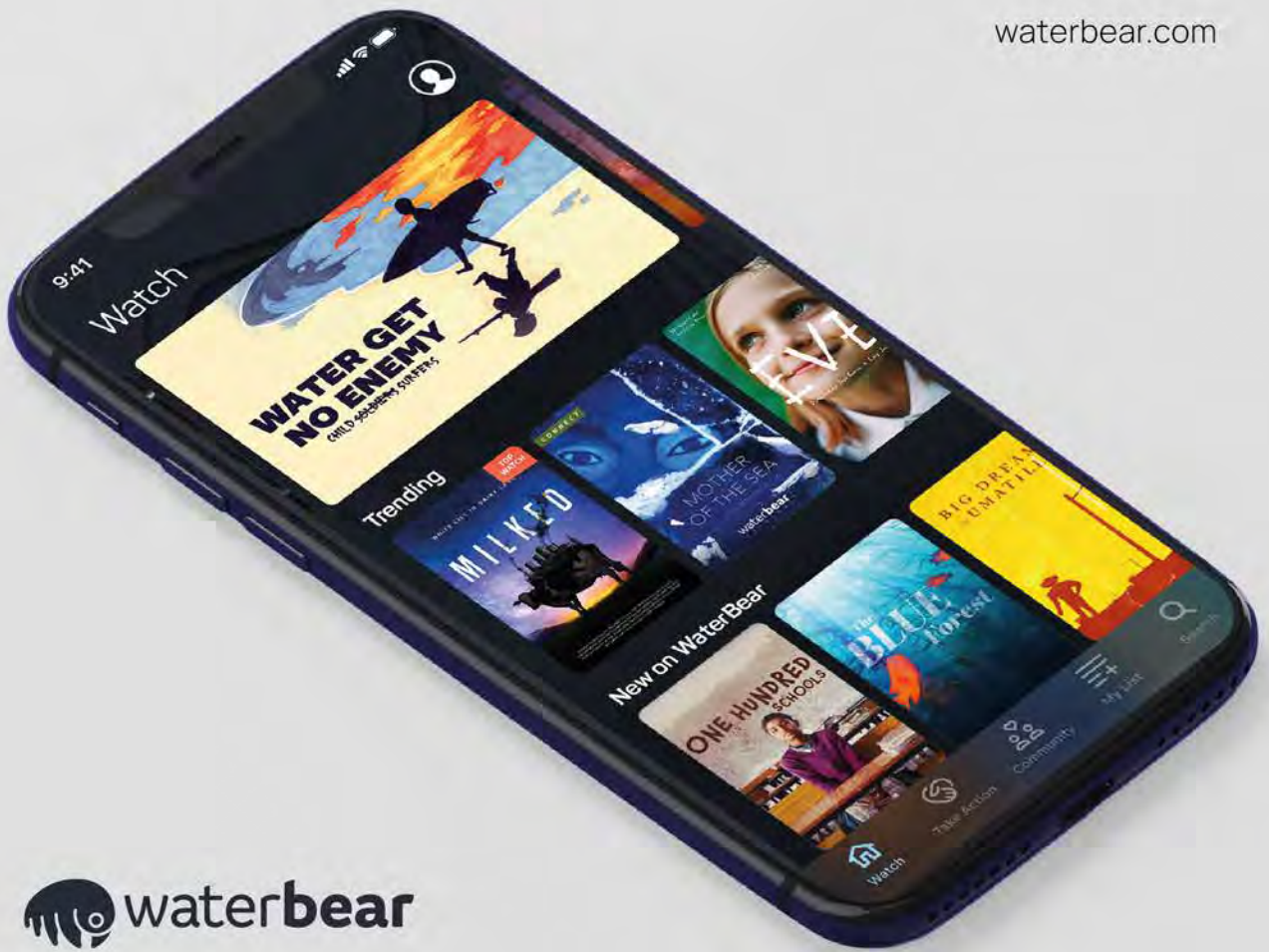
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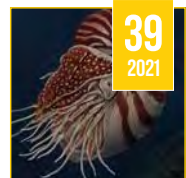
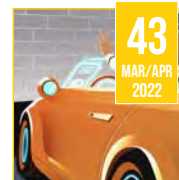
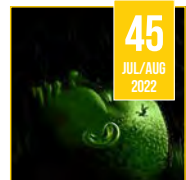
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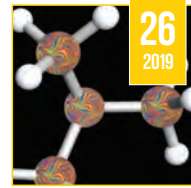
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Eugenia Cheng

The mathematician on the value of stupid questions

INTERVIEW BY ELIZABETH LANDAU

STUPID QUESTIONS

A few years ago, a high school girl did a TikTok asking a lot of questions about math, like how do we know it's right. There was a big social media pile-on. A lot of people called her the dumbest person ever. But I wrote a reply to each of her questions that just took off, and then a series of radio interviews. Loads of people wrote to me from around the world telling me they were so moved that they cried, that they had to stop their cars by the side of the road. These were fully grown men telling me they never felt validated about all those questions they'd wanted to ask. They'd spent their whole lives accepting that they were stupid in this way. That's why I wrote this book, *Is Math Real?: How Simple Questions Lead Us to Mathematics' Deepest Truths*. There really are no stupid questions in math. If something is genuinely baffling you, that's a good sign. Research mathematicians feel confused all the time and use that as an urge to keep asking questions rather than to run away.

WE ARE ALL MATH PEOPLE

Humans have a very strong propensity for spotting patterns. It's something we have done across all cultures and civilizations because we want to understand what's going on around us. On the internet, people will say, "Oh, if you call that math, then everyone's doing math." As if that's a bad thing. But I'm like, "Yeah, everyone is doing math." That doesn't mean that

you're doing mental arithmetic and trigonometry all the time. But discovering connections and patterns, which is at the core of math, is a deeply human urge.

IS MATH REAL?

Sometimes people think math is just made up. And they say that to denigrate it. But what does real even mean? And if it's not real, so what? Fiction and feature films are not *real* stories, but they still teach us things about our lives. Some of the power of math lies in the very fact that it's made up. It's in our imagination, and so it has fewer constraints.

THE POWER OF PLAY

I don't know if we can get rid of standardized testing, because people are so invested in it. But I think the idea that we have to teach certain content to students, such as timetables, is really harmful, because we don't pay enough attention to how they feel about it. I've seen the consequences of that with my art students. They deliberately forget it as fast as possible when they leave school and might even run away from math for the rest of their lives.

In kindergarten, there's typically a very playful approach to math. It's not serious. You count with blocks, you play with objects. When I've helped with math in kindergarten, the children scream with excitement. The fear hasn't set in yet. But in the higher grades, they have to answer questions correctly, and get told how good they are. By the time students get to college, they're horrified. Of course, if you make it all the way through school, and go to grad school for math, and you start your research, you get to play around again. I wish we could maintain play all the way through and let children discover things for themselves. ☺



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