Why We're Superstitious P.26 | World's Tiniest Satellites Ready for Launch P.70

SCIENCE FOR THE CURIOUS

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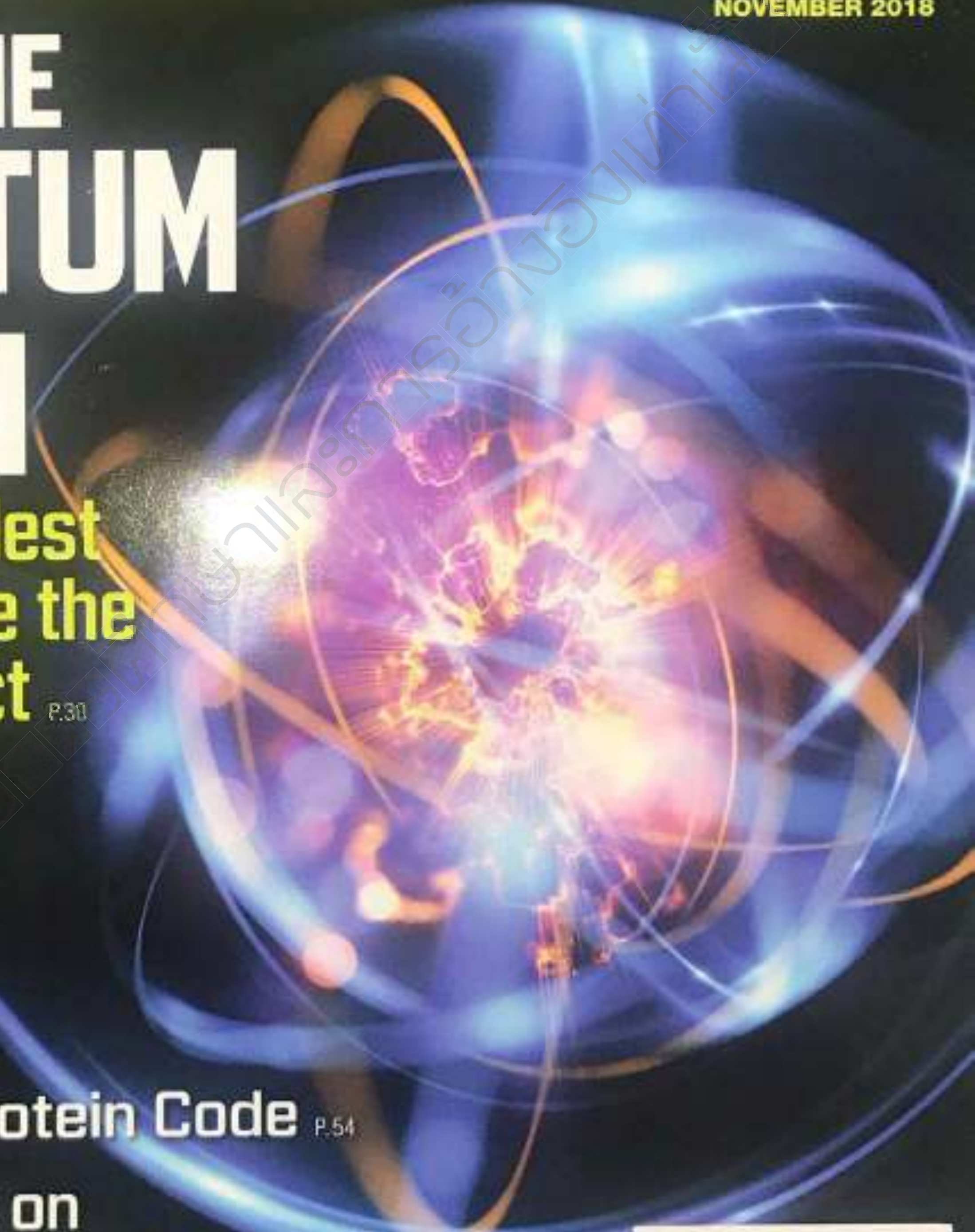
NOVEMBER 2018

LIFE IN THE QUANTUM REALM

How the Smallest Particles Make the Biggest Impact P.30



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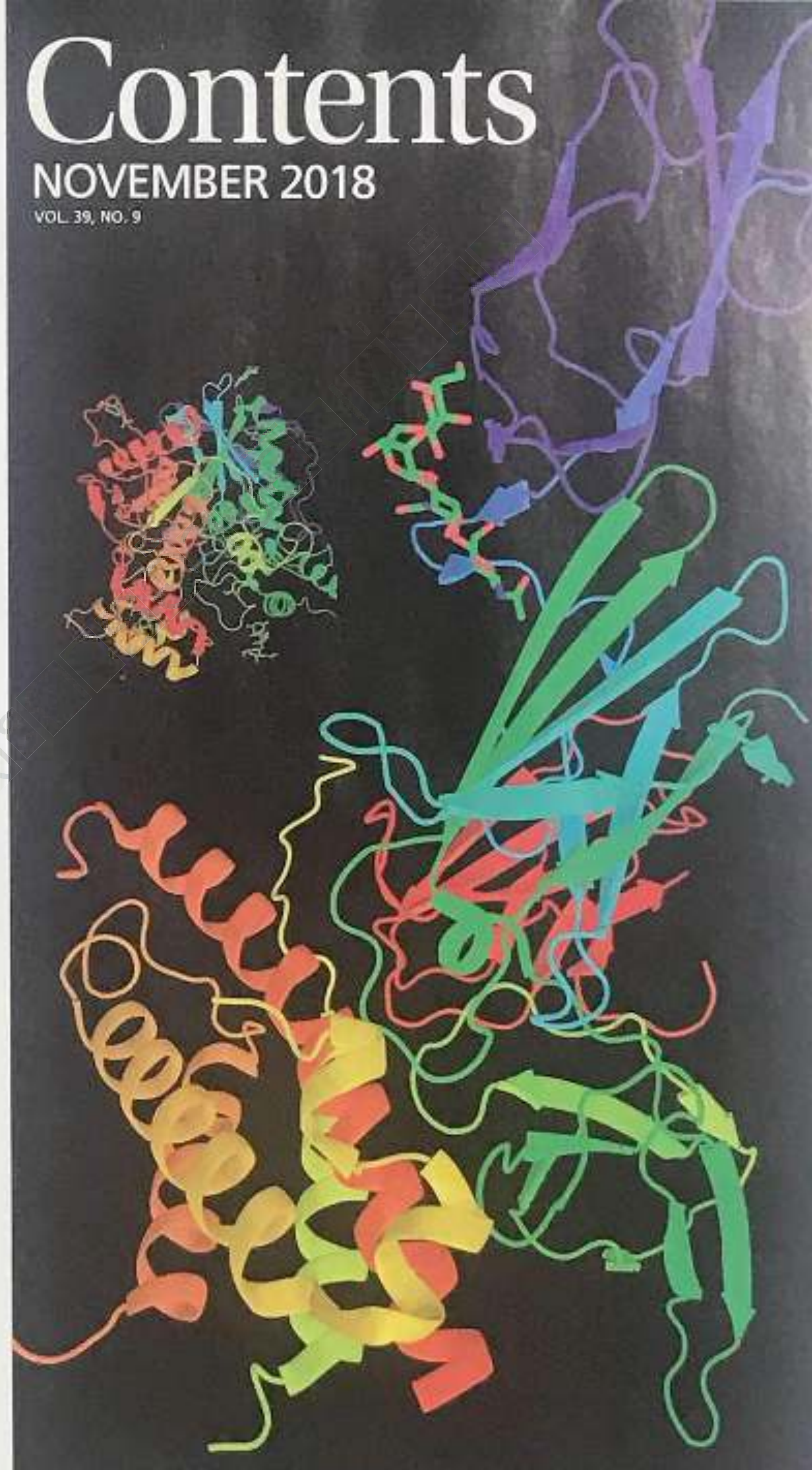

Biochemist David Baker is unravelling the mystery of proteins, crucial to building life. Read more on *page 54*.

FEATURES

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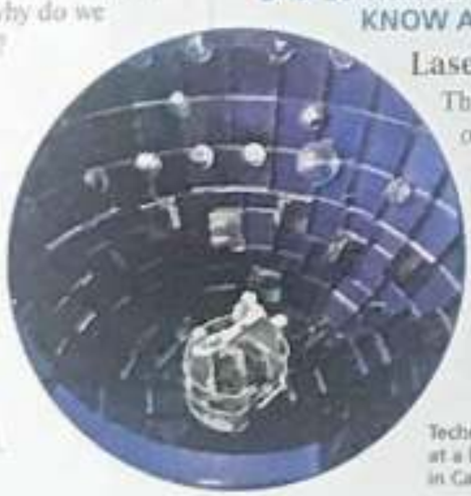
COLUMNS & DEPARTMENTS

Why do some people cling to superstition? Find out on *page 26*.



Technicians at a laser facility in California

ON THE COVER

COVER: Dmitriy Rybin/Shutterstock

Editor's Note

Perceiving Reality

I'm still a relative newbie to motorcycling. It took about a year of being on the back of my husband's BMW before I was itching to be on my own bike.

So, when I swing a leg over my Suzuki V-Strom, I'm hyper-tuned to everything — the smell of the dry autumn air, the sound of the wind sliding around my helmet and the feel of the bike as it picks up speed in second gear. And I'm constantly assessing risk and tweaking my behavior.

When you're new to riding, your perception of reality is in overdrive. Maybe it's like when we're little kids, our senses lighting up as we explore a new space. As adults, our reality is so established, we take it for granted. We expect things in our everyday world to behave in a certain way: coffee is our kick-starter, the garden's roses offer up their perfume each year and that bench will support us as we sit.

While our perception of reality underlies our behavior as we move through the world, in the super-small realm of quantum mechanics, it's the opposite. The behavior of these teeny-tiny particles lies at the bedrock of our perception. And their behavior can be pretty weird. An electron, for example, can exist as a particle and a wave at the same time. A photon can be in two places at once — and just maybe our eyes can see both.

In this issue's cover story, Contributing Editor Tim Folger takes us through the wacky world of the quantum, and how it's embedded into our lives, without us even realizing it.

Those unseen mechanics will be rolling around at the back of my brain on the two-wheeled commute to work.

Becky Lang

Feel free to send comments and questions to **editorial@discovermagazine.com**

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Inbox

PRINT FEEDBACK

An Unappetizing Illustration

("A New Animal Farm," July/August 2018)

I have been reading a lot of articles about insect consumption as a good source of protein, and your article was a welcome addition to my growing knowledge. However, you're not furthering the concept of insect consumption by saying, "But for an entire culture shift to occur, Ashour [one of the Aspire Food Group's founders] wants to change how we talk about entomophagy," and then including a full-page illustration of a fork filled with a living, squirmy mealworm and a cricket. How are we to get past the idea of eating insects if the visual is counter to the message?

Patricia Dittor
Conroe, Texas

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An Electric Issue

("Everything Worth Knowing," July/August 2018)

The latest "Everything Worth Knowing" issue was a fantastic edition! For next year, I would love to see a section on Earth's magnetic field — how it's generated by our molten core, the magnetic field's composition and its numerous benefits, of course.

Steve Brooks
Seattle

MULTIMEDIA FEEDBACK

A Little Personality

("Everything Worth Knowing: Personality," July/August 2018)

From theories to tests, we took you through the essentials of the psychology of personality. Here's what some Facebook readers had to say in response:

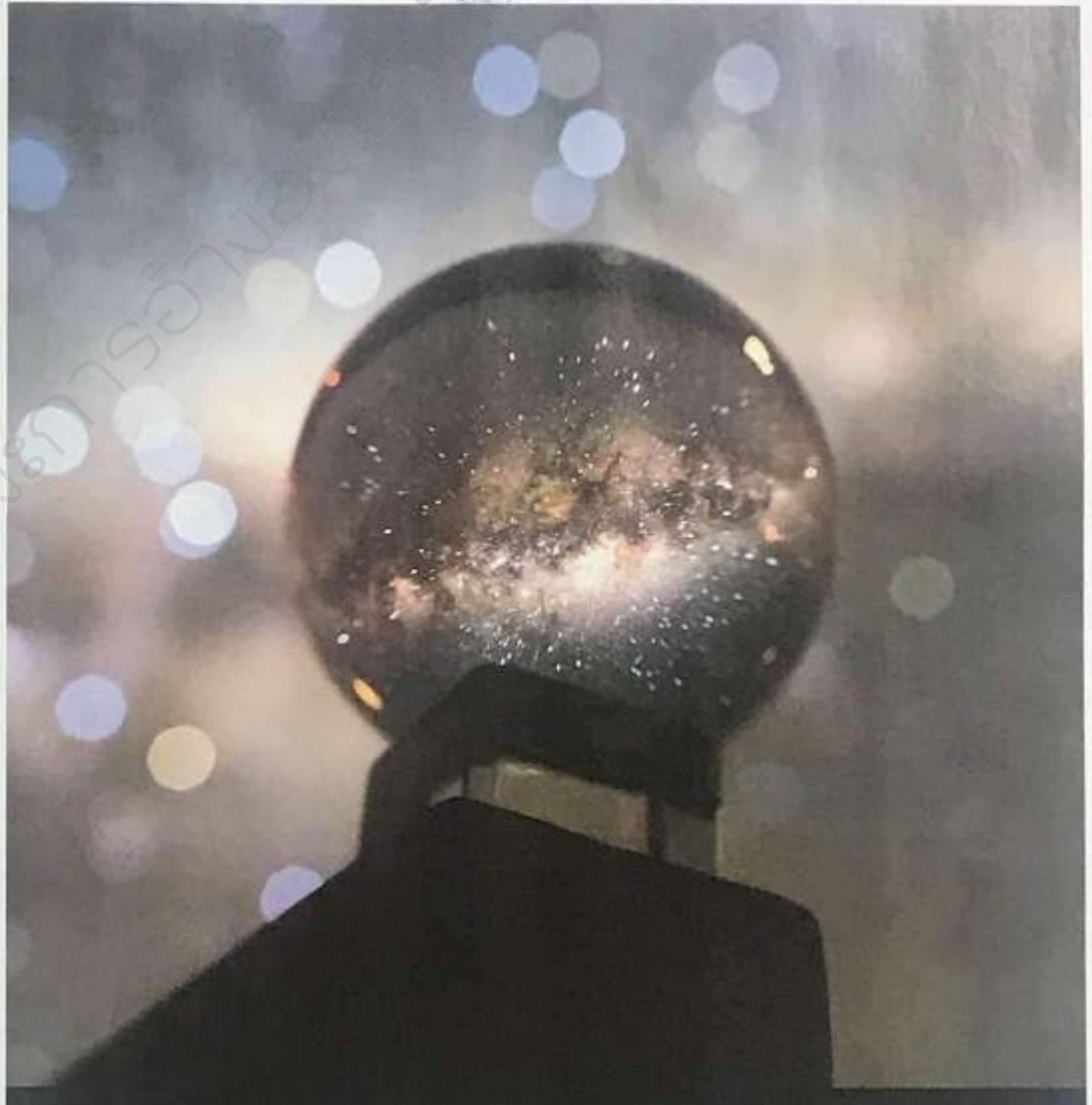
Fino Menezes: It seems to me a great injustice that while a growing number of people can boast "multiple" personalities, there are others, less fortunate, who have been left with none at all. This is the plight of the charismatically challenged in today's two-tier society.

Evelyn Haskins: But far better to have no personality than multiple horrible ones. ☺

Feedback is edited for space and clarity.

THE CRUX

THE LATEST SCIENCE NEWS AND NOTES



GLASS GALAXY

A plain crystal ball at a Santiago flea market recently caught the eye of astronomer Juan Carlos Muñoz-Mateos, who studies galaxy formation from the Paranal Observatory in Chile. He works with the world's most advanced telescopes, and he saw the common glass sphere's potential as a different kind of astrophotography lens. A few nights later, he placed it on a handrail outside the observatory, focused his camera on the ball and made this 30-second-exposure photo, trapping the Milky Way in a cosmic marble against its own backdrop. —ERNIE MASTROIANNI; PHOTOGRAPH BY JUAN CARLOS MUÑOZ-MATEOS

BIG IDEA

The Web, Worldwide

Half of humans still lack dedicated internet access.

DESPITE THE NAME, THE WORLD WIDE WEB ... ISN'T. Some 52 percent of the world — roughly 4 billion people, mostly women — don't have access to the open web.

This has sparked something like a new space race, featuring satellites, high-altitude balloons, drones, even lasers. The rush of startups and tech companies, including SpaceX, Google and Facebook, make it only a matter of time before most humans are online.

The benefits are already clear. Getting online is financially advantageous for folks in low-income regions, especially Africa and Asia, where lack of connectivity is highest. Connectedness also promotes greater participation in politics and society.

"If people have access to faster internet speeds, then you will also see improvements in economic growth," says Dhanaraj Thakur, a researcher at the Alliance for Affordable Internet, a group aiming to lower broadband costs. "There are specific benefits in different sectors: health, education and so on."

The International Telecommunication Union has nailed down a few main reasons why online access remains elusive: insufficient infrastructure, lack of digital literacy and irrelevant content, such as English webpages when your native language is Amharic.

But one of the biggest hitches? Cost. A survey of 58 low- and middle-income countries found just 19 boast affordable internet, defined as 2 percent or less of average monthly income for one gigabyte of mobile data. Across Africa, the 2015 average cost was more than 17.5 percent of monthly income.

That's prompted interest from tech companies. It can seem altruistic, but these endeavors are also driven by the urge to find more customers, which concerns outside groups worried about privacy, data collection and free speech.

"It's not enough simply to bring the internet to a country," says Cynthia Wong, the senior internet researcher at Human Rights Watch. "It's what kind of internet do you bring, how is it going to be regulated, and how much meaningful control and choice do people have over their experience."

Ellery Biddle is advocacy director for Global Voices, which focuses on technology and human rights. She agrees the issue isn't just "connecting" countries. It's about quality. "Today, it's a matter of who has access to and benefits from that internet infrastructure," she says.

> "It's not enough to simply bring the internet to a country."

Companies have gotten creative to overcome the technological hurdles, with mixed success. In June, Facebook shuttered Project Aquila, its program of massive solar-powered drones that would've beamed the internet via lasers and then relayed it down to places without dedicated access. The much-hyped project ran just two test flights — during the first, a drone faced with high winds crashed, leading to a federal investigation. After that, Facebook decided building aircraft was too difficult — and irrelevant, with so many other companies developing autonomous Wi-Fi hotspots.

Facebook closed their lab, and they've partnered with Airbus on their drones. Now, they're testing plane-mounted lasers like Aquila's. They're also working on OpenCellular, an open-source, low-powered base station that Facebook hopes will connect billions more using cellular networks.

Facebook wasn't the only tech agency to crash and burn. Back in 2014, Google's X division moved in ahead of Facebook and purchased Titan Aerospace, which made personal solar-powered drones. During Titan's only test flight, both wings snapped off and the aircraft was destroyed on impact. The company was shut down in January 2017.

X has now switched focus to Project Loon — a balloon flotilla that bobs 12 miles above Earth, beaming 4G LTE like a cell tower. Loon was deployed last year after Peru's deadly floods and again after Hurricane Maria hit Puerto Rico. They've (temporarily) connected more than 300,000 people, the company says. And now they're eyeing rural Africa.

Meanwhile, others are focusing their efforts on making satellite internet cheaper. By year's end, startup OneWeb aims to launch the first of a constellation of 900 little, low-orbit satellites beaming high-speed internet. SpaceX wants to launch around 4,000 satellites for the same purpose; its prototypes are doing well.

Other companies, big and small, are edging in on the action. But despite these many projects, there are more roadblocks than just logging on. Biddle says Facebook and other companies often overlook government presence — and things like balloons and drones can distract leadership from building infrastructure.

"Some of the riskier 'moonshot' investments will fail, and some will find a place alongside more mature access technologies," says Nathan Kundtz, CEO of Kymeta, whose flat-panel satellite antennas came on the market last year. "Ultimately, I expect that the expansion of internet access into developing countries will continue, and that it will be a force for positive economic and social development." — TROY FARAH

Q&A

Focusing on the Small

Zoom in on four decades of microscopy advances.

HIGH SCHOOL SENIOR THOMAS DEERINCK didn't expect his life to change when he walked into his science class one day in the mid-1970s. Local research scientist Betty Barbour had come to share her stunning images of the microscopic world. She was hoping to recruit students for her electron microscopy training program, eager for new helping hands. Deerinck promptly enrolled.

Forty years later, his award-winning photos have appeared on the covers of scientific journals. He's also one of the most senior researchers at the National Center for Microscopy and Imaging Research in La Jolla, California, where he and his colleagues expand the boundaries of what a microscope can see and do.

But as his subjects have gotten smaller over the years, the large streams of data the photos produce need heavy-duty processing.

Recent images of slices of a mouse brain require a supercomputer to assemble them into a 3D model of individual neurons and synapses. The image files are big, and the 3D models are even larger, so managing data is key. Deerinck has learned that when the microscopes can see individual atoms, his small world becomes almost impossibly huge.

Q When you started in 1978, what was the state of microscopy?

A Techniques and instruments were similar to those used for decades. We shot everything on film since there were few computers and no digital cameras.

Q What have been the some of the breakthroughs in the last four decades?

A In the mid-'80s, a special tool called a laser scanning confocal microscope revolutionized light microscopy by allowing us to image thick biological samples without out-of-focus blur. In the '90s came green fluorescent protein, which makes different parts of living cells visible. We could do time-lapse imaging and see cell components interacting over time and in three dimensions. The next advance was electron tomography, where we use a high-energy beam of electrons to image a specimen from different vantage points to produce a 3D representation. It's like a CT scan, but with thousands of times better resolution.

Q What sort of microscopy challenges are you working on now?

A To improve our ability to image the mesoscale — the middle scale between macro and micro — where you can photograph the structure of an organ, such as the brain, all the way down to the individual protein molecules. Currently, there's no way to continuously image that entire range.

Q So how will you get there?

A It's going to be a combination of robotics, deep-learning computer algorithms and just improvements in the actual microscopes. We try to bring all these things together: how you prepare your specimen, choosing the right platform to image it, optimizing the platform itself and then how you deal with the deluge of data.

Q How do you make such technical photos that are also aesthetically appealing?

A I have been married to an artist for 30 years, and she is always looking at my images and saying that I should come at it from a nature photography perspective. There should be an up and there should be a down, paying attention to color, contrast and composition. Many people don't realize that the amazing beauty of nature extends to the microscopic world. — STORY AND PHOTO BY ERNIE MASTROIANNI

Thomas Deerinck's microscopic photo subjects include (from top) the synthetic bacteria *Mycoplasma mycoides*, the jagged surface of a kidney stone and a human tongue (purple) with surface bacteria (green).

REDISCOVER

A Mindset for Mars

Space agencies are still figuring out the best personalities for a trek to the Red Planet.

CAN WE GO TO MARS without going crazy? In May 2001, *Discover's* cover story asked exactly that, exploring unanswered questions about the psychological perils of humans crammed together and flung through space.

At the time, scientists didn't have much data to predict how people would handle the six-month journey. Researchers realized interpersonal skills and camaraderie would be critical to success.

We're still not sure how things would go. But growing interest in the mental risks of space travel — which NASA lists as one of the biggest threats to astronauts — has spawned a wave of new research and technology.

Experts are developing stress-management systems, including virtual reality programs and robotic companions, to help interplanetary travelers cope on their trip. And projects that simulate long-term space travel are giving researchers insights into how we'll deal. Participants endure months in cramped confines in analog missions at NASA's facilities in Houston, as well as remote places like Antarctica, the floor of the Atlantic Ocean and atop a Hawaiian volcano. The European Space Agency's CAVES program, started in 2011, sends participants into unmapped Italian caverns to test and train their cooperative exploration skills. Then there's the final run of Mars-500, another international Martian analog, where six men from four countries simulated an entire mission to the Red Planet over 17 months, from 2010 to 2011, in a tiny Moscow facility — the closest we've gotten to the real thing.

Those projects suggest space agencies are taking the psychology of astronauts more seriously than it did in 2001, says David Dinges, a professor of psychiatry at the University of Pennsylvania Perelman School of Medicine. Good thing, too, since Dinges — who was featured in our 2001 article — and colleagues published a study in 2014 reporting two Mars-500 crew members accounted for 85 percent of the mission's reported conflicts.

Clearly, selecting voyagers with the right psychological profile is critical to mission success. Though we still don't know what that profile looks like, it's becoming easier to see what won't work. "Having six Type A personalities on a long, boring voyage may not be the best combination," says psychologist Gary Strangman, who works with the Translational Research Institute for Space Health, a collaboration between NASA and a consortium led by the Baylor College of Medicine in Houston.

Jack Stuster, a cultural anthropologist who has studied journals kept by both astronauts and earthbound explorers, says behavioral issues are a surmountable challenge. Enthusiasm for putting the first footprints on Mars, he thinks, will inspire resilience: "Humans will endure almost anything to be among the first."

—STEPHEN ORNES

Missions like this one on the Mauna Loa volcano in Hawaii help astronauts train for Mars-like conditions.

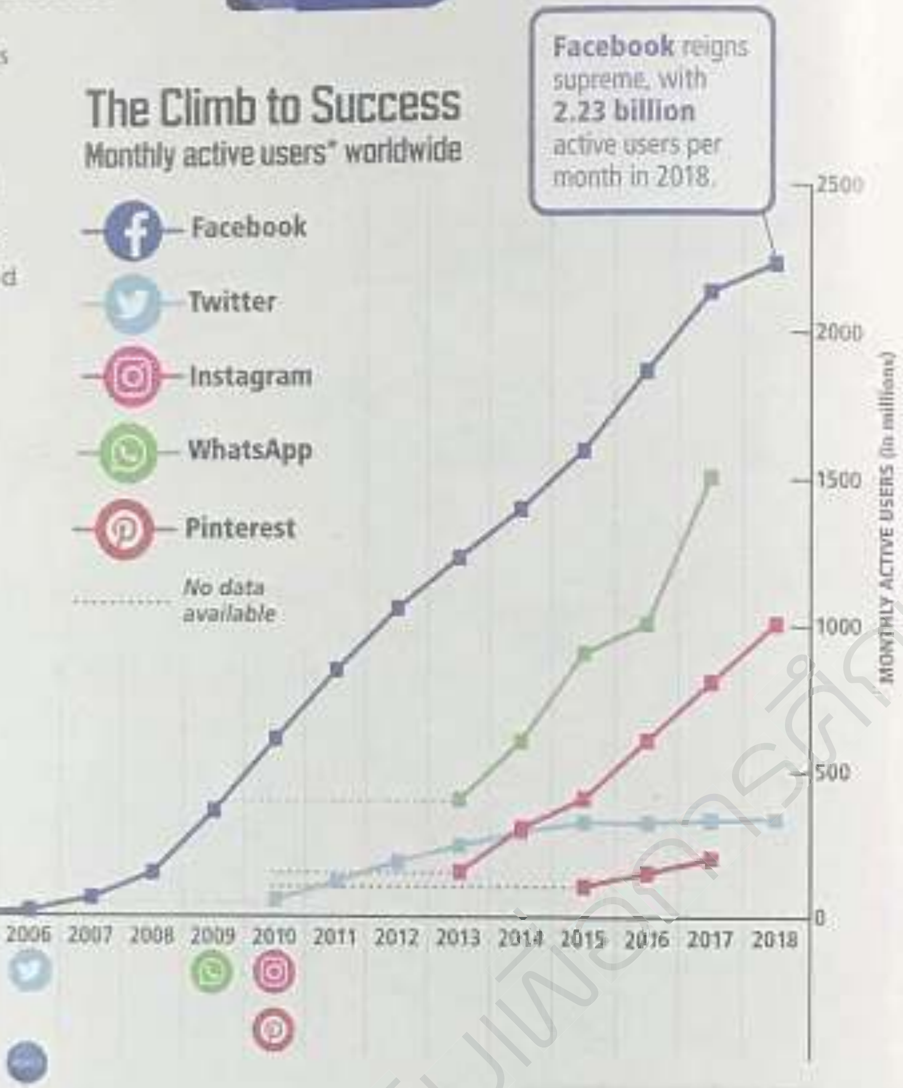
INFOART

The Life & Death of Social Media

WE'RE MORE CONNECTED THAN EVER, thanks to social media. Despite thousands of miles of distance, we can still stay in touch with friends and family. We can even make new friends and start social movements at the drop of a #hashtag. But the websites that helped make this all possible had to start somewhere. And despite their strong starts, some sites didn't last to see the interconnected world we live in today. — LACY SCHLEY

The Climb to Success

Monthly active users* worldwide



Ghosts of Social Sites Past

Eons: Site geared toward baby boomers and users age 40 and older. **2006-2012 (Users as of 2011: roughly 800,000)**

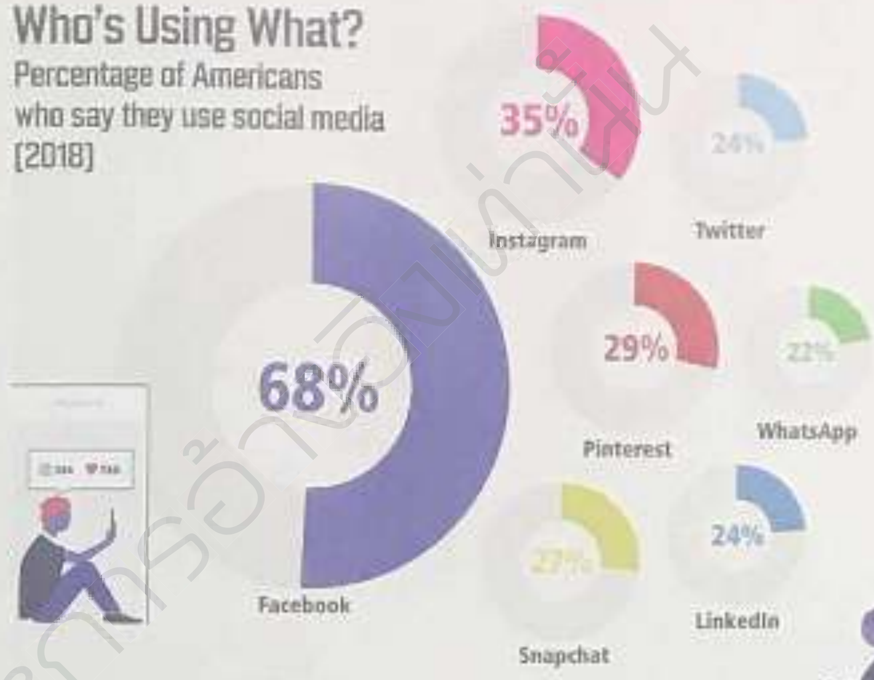
*Snapchat and LinkedIn measure users by different metrics and so are excluded from the above graph.

Friendster: Social-networking-turned-social-gaming site. **2002-June 2015. (Users as of 2008: roughly 30 million)**

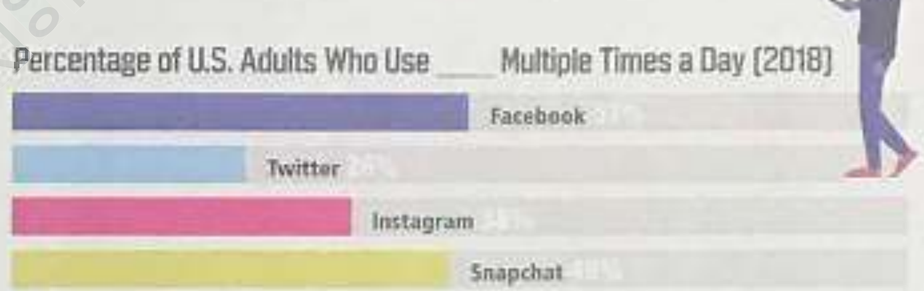
Xanga: Though this personal blogging site is technically still around, it's been under a redesign since at least 2013. **1999-2018 (Users as of 2006: 27 million)**

Who's Using What?

Percentage of Americans who say they use social media (2018)

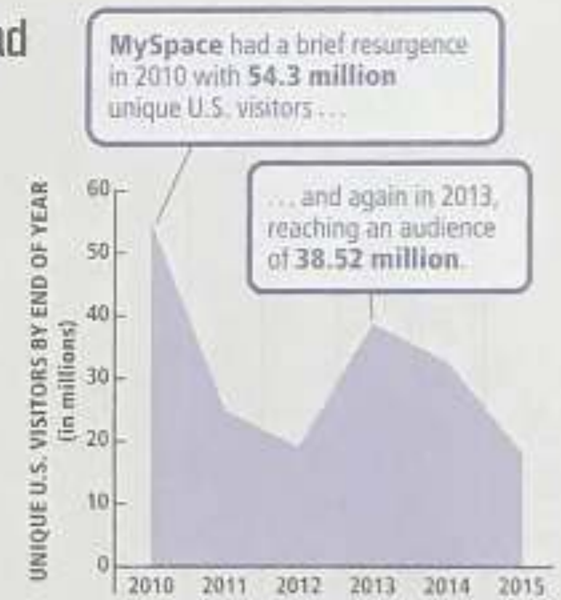


Percentage of U.S. Adults Who Use ___ Multiple Times a Day (2018)



Back From the Dead

MySpace: There was a time when MySpace was in the same boat as Xanga — essentially dead. To regain some popularity, the site went through a redesign and shifted its focus in 2010 from personal profiles to music. Then it went through another redesign in 2013. When that wasn't enough, in 2014, MySpace made a seemingly last-ditch effort with an email blast to users reminding them of all the pics they uploaded in the angst of their youth. The appeal to nostalgia worked — at least for a little while.



Visit DiscoverMagazine.com/SocialMedia for a full list of sources.

Notable Moments in Tech Media History

Mid-1990s: The internet becomes widely available with the emergence of affordable personal computers and web browsers like Netscape.

1999: Apple offers Wi-Fi compatibility in its iBook laptops, the first tech company to do so, spurring an industry-wide trend.

2006: Facebook, which originally only allowed people with .edu email addresses to join, opens up membership to anyone. The move sparks Facebook's rise through the ranks of social media sites.

2007: Apple releases the iPhone, pushing smartphones and mobile apps into the mainstream.

THE CRUX

FAR, FAR AWAY

BABY, YOU'RE A STAR

Stars are born from gas, and spiral galaxy Messier 66 (aka M66, or NGC 3627) has a lot of both. When gas gathers, it clumps into dense clouds, which can then collapse to form stars. Astronomers can find such areas of stellar birth by looking within the ultraviolet spectrum of light, since newborn stars emit more of it than older stars. Hubble's recent Legacy ExtraGalactic UV Survey (LEGUS) explored M66 and 49 other nearby star-forming galaxies, aiming to better understand how, where and when galaxies create stars. — ERIKA K. CARLSON; PHOTO BY NASA/ESA/LEGUS TEAM

TRENDING

Breast Cancer's Financial Toll

In the United States, your wallet can take a hit with any sort of health scare. For those fighting cancer, costs frequently spiral out of control. But how often do doctors talk with their patients about the financial aspects of treatment? In a recent study, researchers at the University of Michigan surveyed 845 doctors and roughly 2,500 people diagnosed with breast cancer to find out. And it seems many patients feel like their concerns aren't being heard.

AT LEAST SOMEWHAT WORRIED ABOUT FINANCES

38%

73% of this group say doctor's office didn't help deal with financial impact of diagnosis

DOLLARS AND CENTS

14% LOST more than 10 percent of household income because of missed work

17% SPENT more than 10 percent of household income on out-of-pocket expenses

WHICH DOCTORS DISCUSS FINANCIAL BURDENS WITH PATIENTS?

Medical oncologists*	50.9%
Radiation oncologists	43.2%
Surgeons	15.6%

*Use chemotherapy as well as hormonal, biological and targeted therapies

CONCERNS BY ETHNICITY

Cut food budget to help pay for treatment		Wanted to talk to providers about financial impact
45.2%	Black	31.1%
35.8%	Latina	30.3%
22.5%	Asian	25.4%
21.5%	White	15.2%

Percentage

Source: "Unmet Need for Clinician Engagement Regarding Financial Toxicity After Diagnosis of Breast Cancer," Cancer, 2018

Building Blocks

Surprise! It's a Dragon!

Researchers found a new dinosaur at the wrong place and the wrong time in China. The previously unknown species of advanced sauropod — giant, long-necked herbivores — was named *Lingwulong shenqi*, or "amazing dragon from Lingwu." The multiple fossils found in northwest China are 174 million years old, about 15 million years earlier than paleontologists thought this particular branch of the sauropod family existed. The fossils are also the first of their kind from East Asia, another surprise. Researchers had believed the region was never home to these animals. The find suggests advanced sauropods evolved much earlier and were distributed much more widely than we thought.

A Snack Fit for a Star

In a first, astronomers may have witnessed a star eating a planet — well, sort of. The star in question, RW Aur A, is about 450 light-years away, but it's been on experts' radars for decades because it has a history of dimming every so often before returning to its usual shine. Recently it's been dimming a lot more than usual. Now, data from NASA's Chandra X-ray Observatory suggest those shady periods may be due to the nearby collision of two newly formed planetary bodies. When those masses hit each other, debris likely fell into the maw of RW Aur A, resulting in dust and gas that obscured the star. Seeing this event and continuing to track what's going on could help scientists learn more about how planetary bodies form and what factors affect their survival.

A Curious Mind

Want your kids to be better at math and reading? Encourage their curiosity. A recently published study found that inquisitive children understand basic math and reading concepts better. Researchers used data from a long-term project funded by the U.S. Department of Education that's been following babies born in 2001. Surveyors checked in with the children's parents regularly over the first five years, measuring their kids' math and reading abilities as well as their curiosity in kindergarten. After analyzing the results, the study's authors saw the connection between curious minds and math and reading skills, even after controlling for things like ability to focus and control impulses — something called effortful control. The results point to another tool to help kids succeed in school, the authors say.

Olive Protection

Europe's olive trees are suffering. The culprit — *Xylella fastidiosa*, a devastating bacterium that's common in the Americas — can infect up to 350 different plant species. The pathogen made its way across the pond only recently. Farmers in Europe have to move fast to stop its spread (usually by sap-eating bugs), or else risk destruction of their crops. In response, experts have developed an aerial remote-imaging system that scans orchards to pick out infected trees before they show the telltale symptoms: withered branches and scorched leaves. The system, which uses a combination of thermal and electromagnetic imaging, can flag infected trees with over 80 percent accuracy. This thermal image shows the severity of symptoms of an orchard in southern Italy from blue (least severe) to red (most severe).

"It's a little bit like you waking up in New York ... and then deciding in the morning as you step out the front door, **'Nah, not going to work today. Today I'm going to Antarctica.'** In terms of body length, that's roughly what the **Bogong moths** are doing."

— neurobiologist Eric Warrant on the annual trans-Australia migration of Bogong moths

Pain, Motion, Repeat

Chest-tightening, world-spinning attacks leave a 25-year-old grasping for answers.

BY TONY DAJER

"It's like being electrocuted," said Alana, her body quivering. "It keeps happening. Doctors can't tell me why."

The 25-year-old had been walking with a friend on a sidewalk when everything started spinning and her body shook. Her chest tightened and she couldn't breathe. Her friend called an ambulance, which brought her to the emergency room.

Dizzying, heart-thumping experiences like this one had been happening to her every few weeks for eight months. Brain scans showed nothing amiss. A specialist had found no inner ear problem. Her neurologist suspected arrhythmia (or irregular heartbeat), but she hadn't seen a cardiologist yet to have it checked out.

Her vitals, such as blood pressure, pulse and body temperature, were all normal.

It wasn't making sense. Here was a fit, young woman who didn't drink or do drugs. She had never been hospitalized. Yet she seemed close to a complete mental breakdown.

Dizzying, heart-thumping experiences like this one had been happening to her every few weeks for eight months.

A DIZZYING SITUATION

Young professionals being seized by panic attacks is not uncommon. But Alana's condition seemed to be something else.

Her episodes might be caused by benign positional vertigo, in which people experience a spinning sensation when they move their head. Another possibility was a hyperthyroid condition, but that usually causes a fast heartbeat.

I dismissed both in part because Alana was experiencing pain throughout her body, something not usually associated with vertigo or a hyperthyroid condition.

For a moment I considered she might have an irregular heartbeat, as her neurologist thought. The condition is known to bring about dizziness, lightheadedness and shortness of breath. But Alana's electrocardiogram, which checks the electrical activity of the heart, revealed no issues.

Sometimes when I'm stumped about the cause of a patient's complaints, I think about other patients I've seen who had similar symptoms, or who had symptoms that manifest in a similar sequence.

As I examined Alana, I thought about Peggy.

A PATTERN EMERGES

Two months earlier, Peggy had arrived in the emergency department sobbing, vomiting and doubling over from stomach pain. She was in the middle of a recurring attack, she told me. It always went the same way: stomach pain, vomiting and an awful taste of sulfur in her mouth.

As we talked about her medical history, Peggy said she also sometimes had migraine headaches. This stopped me for a moment. The hallmark of what we broadly call migraines is recurrent, stereotypical attacks that eventually resolve completely. Could Peggy's attacks be migraines?

An estimated 36 million Americans suffer from migraines, which typically are severe, throbbing or pulsing headaches, often accompanied by vomiting. Scientists aren't sure of their root cause, but there appears to be a genetic component, since migraines run in families.

Peggy did not have a throbbing headache when she came in, but recurring symptoms suggested she was having a repeat migraine attack. In an odd twist of neurology, and to the diagnostic confusion of doctors, people can have migraines without headaches. Even odder, the same person can have a different series of symptoms at different times.

The trigger of the attack can also

change. For a while it might be a certain smell. Then it shifts to, say, being in a stressful situation.

Eventually we figured out that Peggy had an abdominal migraine, which is accompanied by nausea, vomiting, belly pain and, in her case, that distinctive sulfur taste. Despite multiple medical work-ups and even hospitalizations, it had gone undiagnosed since she was 8 years old.

ANOTHER KIND OF ACHE

"Have you ever had migraines?" I asked Alana as she lay on the stretcher, arms clutching her chest.

"Yes," she said. "As a teenager, the headaches were so bad, I'd have to take loads of Advil and lie in a dark room for hours."

My hunch was that Alana was in the middle of a vestibular migraine, a variant where the brain's electrical waves propagate through the cerebellum, the brain's balance center. A vestibular migraine is often not accompanied by a headache, and its symptoms mirror those of peripheral vertigo.

Vestibular migraines strike 1 in 100 people. The singer Janet Jackson is among them; her attacks have been so intense that in 2008 she had to cut short a concert tour.

Doctors have plenty of theories on migraine causes. The latest is called cortical spreading depression, which refers to a spontaneous electrical wave that travels through the brain's cortex.

Migraines, this theory holds, start when the spreading electrical wave activates the trigeminal ganglion, a cluster of neurons that sit close to the brainstem. This sets off a chemical cascade that releases inflammatory proteins along the meninges, the multi-layered outer envelope of the brain that is crammed with pain-producing sensory nerves. This produces the jackhammer headache.

But that's not the end of it. The electrical and chemical ripples can stimulate neurons throughout the brain, according to this theory. The result is "migraine aura," the non-headache barrage of symptoms that has been described in medical literature for centuries. Wavy lights are the classic manifestation, but there are many other aura symptoms.

Vestibular migraines occur when electrical waves propagate through the brain's cerebellum, shown in red.

"How do you feel?" I asked. She rewarded me with her first smile since her arrival. "It's gone," she said.

The list includes pain in the arms and legs, and sensitivity to light, noise and smells. Also possible are stomach pain and nausea, as Peggy had experienced, and chest tightness and vertigo, Alana's primary symptoms. In addition, migraine auras can cause temporary, partial or full blindness, as well as muscle weakness.

One recent patient at the emergency department was unable to speak. We'd almost treated her for a stroke, but something didn't fit. After the attack passed, she said her migraines often appear as strokes.

Migraine auras and pounding headaches are inconstant partners. An attack might precede or accompany a headache. Or it might go solo. Moreover, not all headaches come with an aura.

CALM AFTER THE STORM

Migraine treatments are tailored to the specific phases of the attack. At the first sign of a migraine aura or a throbbing headache, a person can be prescribed serotonin-like drugs of the so-called triptan class, taken by injection or pill. Introduced 25 years ago to great fanfare, the drugs work for many patients, but not all. They are most effective early in an attack. Other early phase mainstays include naproxen, caffeine and aspirin.

By the time patients get to the emergency room, their migraines are usually peaking. In those cases, our go-to intravenous drugs include anti-inflammatories like Toradol and anti-dopamine agents like Reglan, which we gave Alana.

Thirty minutes later, I peeked into her room. She was curled up sleeping. I shooed out two of her visiting friends, left the room and closed the door.

I checked on her two hours later. She looked clear-eyed and refreshed.

"How do you feel?" I asked.

She rewarded me with her first smile since her arrival. "It's gone," she said.

Alana's neurologist placed her on migraine preventatives — daily magnesium supplements and vitamin B_2. She was given sumatriptan, now one of the more widely used migraine medicines, to take at the first sign of trouble.

Months later, I asked her neurologist how Alana was doing. She hadn't had any migraine episodes, he said.

The storm had blown offshore, but Alana would still need to guard against incoming waves. ◼

Tony Dajer is director of the emergency department at New York-Presbyterian/Lower Manhattan Hospital. The cases described in Vital Signs are real, but names and certain details have been changed.

Knock on Wood

Why we latch on to superstitious behaviors, and how to give them up.

BY GALADRIEL WATSON

Last March, it snowed. And snowed and snowed. It was so heavy that roofs around my town were caving in, trapping pets and trucks and leaving people homeless. My own roof had several feet piled on. One night, flakes perpetually pelting down, I couldn't sleep. I listened for the creaks of soon-to-collapse timbers. I imagined the porch overhang ripping away from the kitchen. I stared into the dark.

Did I eventually haul myself out of bed to shovel the roof? No. My fear of falling from such a height was too great — as was my love of a warm bed.

Instead, I knocked on wood. Repeatedly. My bedside table is wood, and my knuckles rapped it with each new terrifying thought. A wooden necklace hangs at the head of my bed. I tapped that, too.

This wasn't a one-time, snowstorm-of-the-century deal. No matter the season or situation, knocking on wood is how I ward off the dangers in life.

LEARNED YOUNG

I'm not alone. "Superstitions and magical thinking aren't really special," says Jane Risen, a professor of behavioral science at the University of Chicago. "They're just part of the way we think about things."

Don't open an umbrella indoors. Avoid black cats. Be wary of Friday the 13th. Superstitions like these abound. In 2015, a poll by *60 Minutes* and *Vanity Fair* found that 60 percent of respondents admitted to knocking on wood.

Don't open an umbrella indoors. Avoid black cats. Be wary of Friday the 13th. Superstitions like these abound.

These beliefs begin in childhood. "Kids have to learn about these things first," says Jacqueline Woolley, a professor of psychology at the University of Texas at Austin and an expert on childhood superstitions. "They're picking up the superstitions of their particular culture."

But soon after this childhood belief peaks, it starts falling. Take the concept of luck. By age 4, children are starting to hear about it. A couple of years later, they believe in it pretty strongly. "But then the skepticism kicks in pretty quickly after that," says Woolley.

She and her team witnessed this transition during a study published in 2017 in the *Psychonomic Bulletin & Review*. When told an improbable story — for example, one in which a severely injured dog heals without medical care — most children tried to find a natural explanation. But 5- and 6-year-olds also often credited miracles or luck. These supernatural explanations started to drop with 7- and 8-year-olds. And 9-year-olds were much more likely to say that events were caused by skill or effort, not luck.

I can't remember when my knocking-on-wood habit kicked in. I do, however, remember avoiding stepping on sidewalk cracks (or I'd break my mother's back). I also remember that habit quickly dying, since it was impractical and simply hadn't proven true.

KNOWING BETTER

Despite this childhood rise and fall in superstitious beliefs, some persist into adulthood, even for people (like me) who don't truly believe. Will knocking on wood really save my roof? No. Yet I do it anyway.

In a study published in 2008 in the *Journal of Personality and Social Psychology*, Risen found that participants believed it was bad luck to tempt fate — even when they didn't believe in fate.

She further examined this contradiction in a 2016 study published in the *Psychological Review*. "We see people maintaining these beliefs that they themselves acknowledge are irrational," she tells me. "They'll say, 'I know it's crazy, but I'm going to do this.' We have [these beliefs] because they're the output of pretty basic cognitive processes."

We have two ways of thinking, she

explains. One is intuitive: fast, efficient and quick to jump to conclusions. This can provide a seeming rationale for those crazy beliefs. Did my roof collapse? No. Therefore, my knocking on wood must have been effective — I'll do it again next time.

Then we have a slower, more deliberate way of thinking. It may jump in to point out my faulty reasoning and recognize that my knocking has nothing to do with whether or not the roof caves in. But, Risen says, "detecting an error in your intuitive belief doesn't necessarily lead you to correcting it. It seems that some intuitions are just very difficult to shake."

People also like to feel a sense of control. I may not have been shoveling on the roof, but at least I was doing *something*. And it may have given me enough peace of mind to allow me

to (eventually) sleep. "These beliefs and behaviors actually do end up regulating your emotions," says Risen. "When you knock on wood, you may worry about this less."

And it never hurts to hedge your bets — usually. Woolley provides her own example of owning a "parking angel" that once hung from her rearview mirror. If she were alone and desperate for parking, she might rub the angel and recite its attached poem. But if she had company in the car, "I might look like a fool, so I'm not going to do it," she says.

Woolley explains that, once a superstition is established, we do a cost-benefit analysis that can make it seem like not performing the ritual poses a risk. Skipping it can even give some people anxiety. So if no one is around to think the superstitious ritual is crazy — and add a cost to performing it — we are more likely to complete it out of a "better safe than sorry" mindset, indicating we must believe in it at least a little bit.

I also wonder if parenthood has anything to do with the strength of my beliefs. I don't only knock on wood to save my roof, but to save my children. Is my son at a party? Please bring him home safe. Is my daughter on a road trip? Please keep the roads clear.

And while my kids have never been gravely ill (knock on wood), superstitions have helped other parents in that terrifying situation. During a 2017 study in the neonatal unit at Santa Lucia General University Hospital in Cartagena, Spain, researchers discovered that about 40 percent of parents said they believed in magical concepts like the evil eye, and protective amulets were placed by more than 26 percent of the children.

THE MYTH OF OLD WIVES' TALES

So am I relegated to this superstitious life forever? No, according to Nadia Brashier, a postdoctoral fellow at Harvard University specializing in memory and judgment. She and her team published a 2017 study in *Psychology and Aging* on magical thinking in adults. They found that older adults, whose average age was about 70, were less superstitious than young adults averaging about 19 years old.

The key seems to be an accumulation of life experience. My mother never got hurt when I stepped on sidewalk cracks. I own a black cat that has never (as far as I know) caused problems. Although I used to fly on airplanes with a lucky teddy bear, the one time I forgot him, the plane didn't crash. Once older adults have accumulated some evidence that those beliefs don't work, "they kind of update" their beliefs about cause and effect, says Brashier.

"You may be very well practiced at completely ignoring black cats," Risen tells me. But to kick harder superstitious habits, I should break the reinforcing cycle. Instead of knocking on wood, noticing the positive results and concluding I should do it again next time, I should dare not to knock on wood. "Assuming that it goes OK, you have to remember and note that experience," she says. "Then the next time will be a little bit easier because you'll realize, 'Oh wait, things were fine last time.'" By keeping track of these outcomes over time, I can build up data that my slower side of thinking can grasp and use to shake my superstitious beliefs, Risen says.

So a couple of days ago, when my son stayed out late, I held back my hands. I avoided wood. I even managed to sleep. And guess what? He came home just fine.

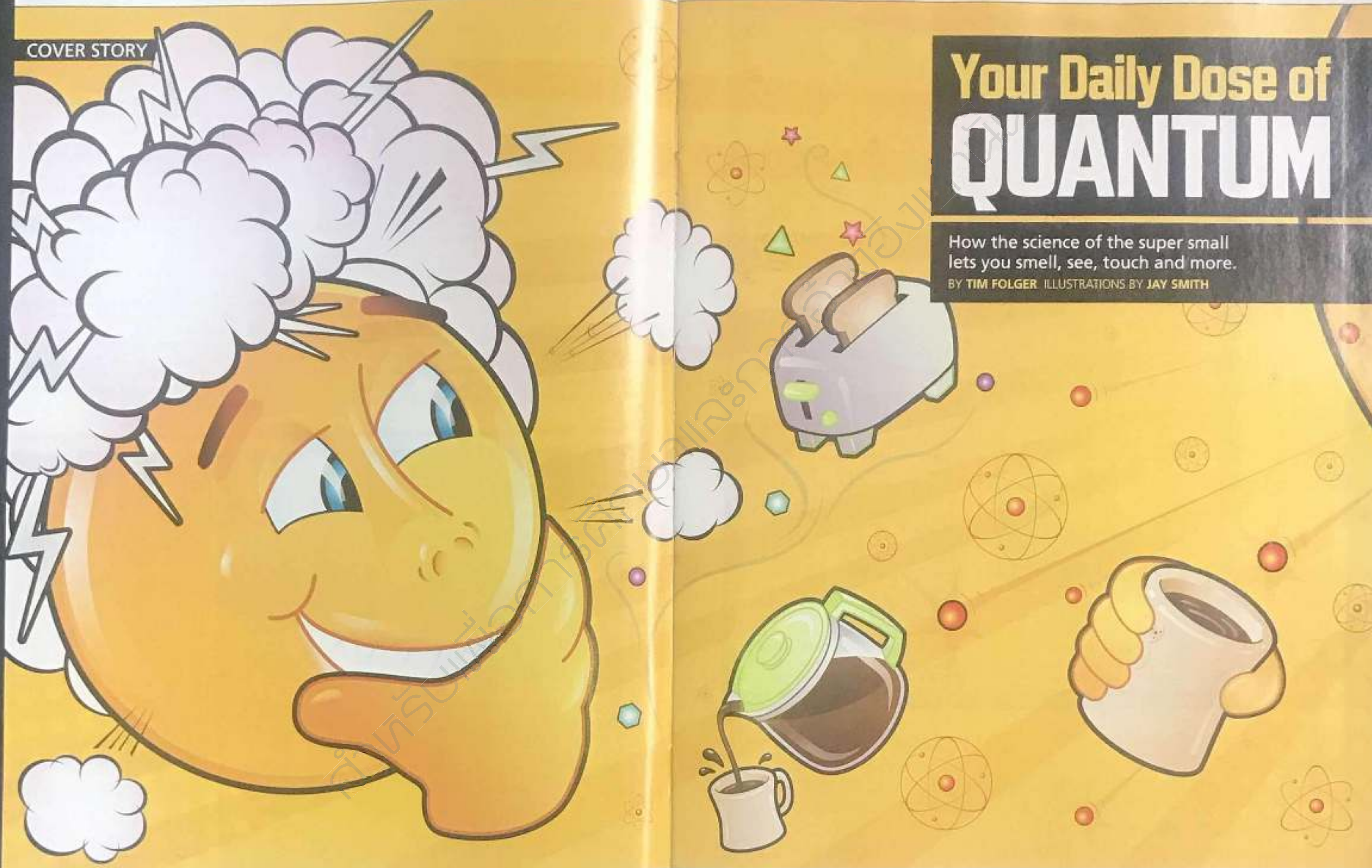
This winter, I'll try it with my roof. ■

***Galadriel Watson**'s upcoming book for kids highlights impressive human abilities and the science behind them.*

Your Daily Dose of QUANTUM

How the science of the super small lets you smell, see, touch and more.

BY **TIM FOLGER** ILLUSTRATIONS BY **JAY SMITH**



If Max Planck hadn't ignored some bad advice, he would never have started a revolution. The pivotal moment happened in 1878, when young Planck asked one of his professors whether to continue pursuing a career in physics. Herr Professor Philipp von Jolly told Planck to find another line of work.

All the important discoveries in physics had already been made, the professor assured his young protégé. As Planck later recalled, von Jolly told him, "[Physics] may yet keep going in one corner or another, scrutinizing or putting in order a jot here and a tittle there, but the system as a whole is secured, and theoretical physics is noticeably approaching its completion."

Putting one of those jots in order, it turned out, eventually won Planck a Nobel Prize — and led to the birth of quantum mechanics. The troublesome trifle concerned a very ordinary phenomenon: Why do objects glow the way they do when heated? All materials, no matter what they're made of, behave the same way with increasing temperature: turning red, then yellow, then white. Yet no physicist in the 19th century could explain this seemingly simple process.

The problem came to be called the ultraviolet catastrophe, because the best theorem of the day predicted that objects heated to very high temperatures should spew infinite amounts of short-wavelength energy. Since we know a strong current *doesn't* turn light bulbs and toasters into energy-spewing death rays, 19th century physics clearly wasn't the last word.

Planck found an answer in 1900 with what amounted to a modern-day hack. He proposed (guessed, really) that energy could only be absorbed or emitted in discrete packets, or quanta. It was a radical departure from so-called classical physics, which held that energy flowed in smooth, continuous streams. At the time, Planck had no theoretical justification — but it turned out to work anyway. His quanta effectively capped the amount of energy that heated objects could release at any temperature. No more death rays.

So began the quantum revolution. It would take decades of incandescent theoretical work by Albert Einstein, Werner Heisenberg, Niels Bohr and other titans to transform Planck's inspiration into a full theory, but it all started because no one understood what happened to things when they get hot.

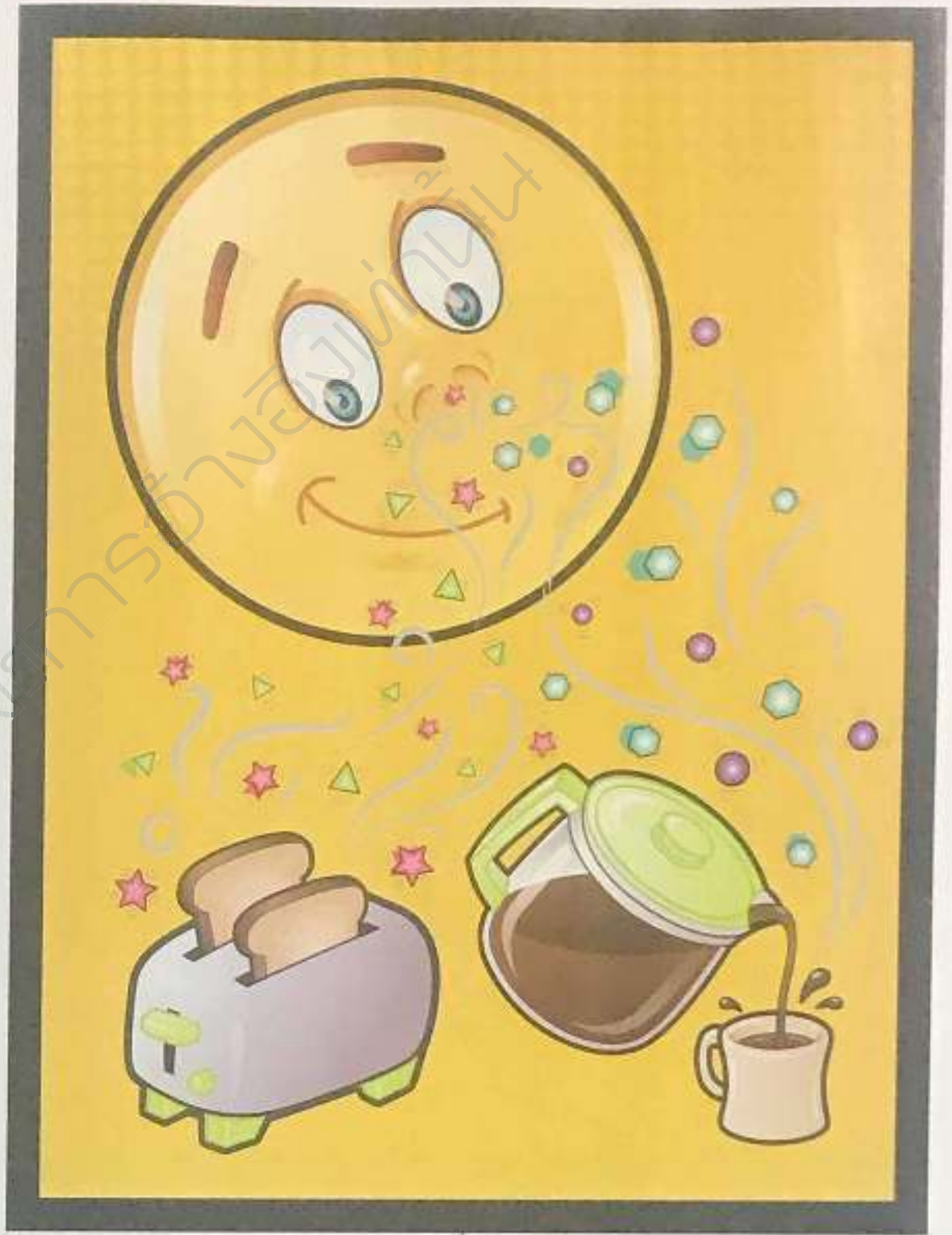
The resulting theory, quantum mechanics, deals with particles and blips of energy in the realm of the ultra-small, divorced from our everyday experience, and all but invisible to our clumsy mammalian sensory apparatuses. Well, not completely invisible. Some quantum effects are hiding in plain sight, blatantly and beautifully obvious, like the sun's rays and the twinkling of the stars — something else that couldn't be fully explained before the advent of quantum mechanics.

How much of the quantum world can we experience in our daily lives? And what sort of information can our senses glean about the true nature of reality? After all, as the origin of the theory itself makes clear, quantum phenomena can lie just under our noses. In fact, they may be taking place right *inside* our noses.

THE QUANTUM SCHNOZZ

What's going on in your nose when you wake up and smell the coffee, or the slice of bread browning in your non-lethal toaster? For such an in-your-face sensory organ, the nose is poorly understood. No less a luminary than Enrico Fermi, who built the world's first nuclear reactor, once remarked to a friend while frying onions that it would be nice to understand how our sense of smell works.

So you're lying in bed, and someone has thoughtfully brewed some freshly ground Sumatran dark roast. Molecules from the elixir waft through the air. Your inhalations draw some of these molecules into a cavity between your eyes just above the roof of your mouth. The molecules stick to a layer of mucus on the upper surface of the cavity, embedded with olfactory neurons. Dangling from the brain like the tentacles of a jellyfish, olfactory neurons are the only part of the central nervous system constantly exposed to the outside world.



If the biophysicist is right, and we do smell vibrations in addition to shapes, how do our noses manage the feat? He speculates that a quantum effect called tunneling might be involved.

What happens next isn't quite clear. We know the molecules bind to some of the 400 different receptors on the surface of the olfactory neurons; we don't know exactly how that contact creates our sense of smell. Why is smell such a difficult sense to understand?

"In part, it's the difficulty of setting up experiments to probe what's going on inside the olfactory receptors of the nose," says Andrew Horsfield, a materials scientist at Imperial College London.

The conventional explanation for how smell works seems straightforward: The receptors accept very specific shapes of molecules. They're like locks, which can be opened only by the right keys. Each of the molecules escaping from your cup of joe, according to this model, fits into a particular set of receptors in your nose.

> Some 93 million miles separate the sun and Earth, and it takes photons just over eight minutes to cover that distance. But the bulk of their journey occurs inside the sun, where a typical photon spends a million years trying to escape.

The brain interprets the unique combination of receptors activated by their bound molecules as the smell of coffee. In other words, we smell the shapes of molecules.

But there's a fundamental problem with the lock-and-key model. "You can have molecules of wildly different shape and composition, which all give you the same odor perception," says Horsfield. It seems that something more than shape must be involved, but what?

A controversial alternative to the lock-and-key model suggests our sense of smell arises not just from the shape of molecules, but also from the manner in which those molecules vibrate. All molecules constantly jiggle with distinct tempos, based on their structure. Could our noses somehow detect differences in those vibrational frequencies? Luca Turin, a biophysicist at the Alexander Fleming Biomedical Sciences Research Center in Greece, believes they can.

Turin, who also happens to be one of the world's leading perfume experts, was inspired by a vibrational theory of smell first proposed by chemist Malcolm Dyson in 1938. After Turin first caught scent of Dyson's idea in the 1990s, he started looking for molecules that would allow him to test the theory. He hit upon sulfur compounds, which have a unique odor and a characteristic molecular vibration. Turin then needed to identify a completely unrelated compound — one with a different molecular shape than sulfur but possessing the same vibrational frequency — to see if it would smell anything like sulfur. Eventually, he found one, a molecule containing boron. And sure enough, it reeked of sulfur. "That's when the penny dropped," he says. "I thought, 'This cannot be a coincidence.'"

Since that odoriferous eureka moment, Turin has been gathering experimental evidence to support the idea, collaborating with Horsfield to work out the theoretical details. Five years ago, when Turin and colleagues designed an experiment in which some of the hydrogen molecules in a musk-scented fragrance were replaced with deuterium — a variety of hydrogen containing an extra neutron — they found that people could smell the difference. Since hydrogen and deuterium have identical shapes but different vibrational frequencies, the results again suggested that our noses could indeed detect vibrations. Similar experiments with fruit flies complemented those results.

Turin's idea remains contentious — his experimental data have divided the interdisciplinary community of olfactory researchers. But if he is right, and we do smell vibrations in addition to shapes, how do our noses manage the feat? Turin speculates that a quantum effect called tunneling might be involved.

In quantum mechanics, electrons and all other particles possess a dual nature; each is both a particle and a wave. This sometimes allows electrons to spread out and travel, or tunnel, through materials in ways that would be forbidden to particles under the rules of classical physics. The molecular vibrations of a scent molecule might provide the right jump down in energy that electrons need to tunnel from one part of an odor receptor to another. The tunneling rate would change with different molecules, triggering nerve impulses that create the perceptions of different smells in the brain.

Tucked away in our noses, then, might be a sophisticated electronic detector. How could our noses have evolved to take advantage of such quantum strangeness? "I think we underestimate the technology, so to speak, of life by a couple of orders of magnitude," says Turin. "Four billion years of R&D with unlimited funding is a long time. And I don't think this is the most amazing thing that life does."

SIGHT UNSEEN

OK, so you're quaffing your coffee, nearly awake. Your eyelids are gearing up for daytime mode, blinking, letting in a bit of the light that's streaming through the window. As you sip your brew, ponder this: The particles of light warming your face and entering your eyes originated a million years ago in the center of the sun, around the time our not-quite-human ancestors started to use fire. The sun wouldn't even be sending out those particles, named photons, if not for the same phenomenon that might underlie our sense of smell — quantum tunneling.

Some 93 million miles separate the sun and Earth, and it takes photons just over eight minutes to cover that distance. But the bulk of their journey occurs inside the sun, where a typical photon spends a million years trying to escape. Matter is so tightly packed at the center of our star — the hydrogen there is about 13 times denser than lead — that photons can travel only an infinitesimal fraction of a second before being absorbed by a hydrogen ion, which then spits the photon out for another soon-to-be-interrupted journey, ad infinitum. After about a billion trillion such interactions, a photon finally emerges from the surface of the sun, having zigged and zagged randomly for a thousand millennia.

But the photons never would have been born, and the sun wouldn't shine, were it not for quantum tunneling. The sun and all other stars generate light by nuclear fusion, smashing hydrogen ions together to form helium, a process that releases energy. Every second, the sun converts about 4 million tons of matter into energy. But hydrogen ions, single protons, have positive electric charges and naturally repel each other. So how can they possibly fuse?

With quantum tunneling, the wave nature of protons allows them to overlap ever so slightly, like ripples merging on the surface of a pond. That overlap brings the proton waves close enough so that another force — the strong nuclear force, which kicks in only at extremely small distances — can overcome the particles' electrical repulsion. The protons fuse and release a single photon.

Our eyes have evolved to be exquisitely sensitive to these photons. Some recent experiments have shown that we can even detect *single* photons, which raises an intriguing possibility: Could humans be used to test some of the weird features of quantum mechanics? That is, could a person — like a photon or an electron or Schrödinger's hapless cat, dead and alive at the same time — directly engage with the quantum world? What might such an experience be like?

"We don't know because no one has tried it," says Rebecca Holmes, a physicist at Los Alamos National Laboratory in New Mexico. Three years ago, when she was a graduate student at the University of Illinois at Urbana-Champaign, Holmes was part of a team led by Paul Kwiat that showed people could detect short bursts of light consisting of just three photons. In 2016, a competing group of researchers, led by physicist Alipasha Vaziri at Rockefeller University in New York, found that humans can indeed see single photons. Seeing, though, might not accurately describe the experience. Vaziri, who tried out the photon-glimpsing himself, told the journal *Nature*, "It's not like seeing light. It's almost a feeling, at the threshold of imagination."

In the near future, Holmes and Vaziri expect experiments that will test what people perceive when photons are put into strange quantum states. For example, physicists can coax a single photon into what they call a superposition, where it exists in two different places simultaneously. Holmes and her colleagues have proposed an experiment involving two scenarios to test whether people might directly perceive a superposition of photons. In the first, ho-hum scenario, a single photon would go into either the left or right side of a person's retina, and the person would note on which side of the retina they sensed the photon. But in the other scenario, a photon would be placed in a quantum superposition that would allow it to do the seemingly impossible: travel to both the right and left sides of the retina simultaneously.

Would the person then sense light on both sides of the retina? Or would the interaction of the photon with the eye cause the superposition to "collapse," as physicists say, into one position or the other — and if so, would it happen equally on the right and left side, as theory suggests?

"Based on standard quantum mechanics, the photon in the superposition probably wouldn't look any different to them than actually randomly sending a photon to the left or the right," says Holmes. If it turns out that someone participating in the experiment did indeed perceive the photon in both places simultaneously, would that mean the person herself was in a quantum state? "You could say the observer was in a quantum superposition for some vanishingly small amount of time," says Holmes. "But no one has tried this, so truly, we don't know. That's reason enough to do the experiment."

FEELING YOUR WAY

Now back to that cup of coffee. The cup feels substantial, a solid chunk of matter firmly in contact with the skin of your hand. But that's an illusion: We never really touch anything, at least not in the sense of two solid slabs of matter coming together. More than 99.9999999999 percent of an atom consists of empty space, with nearly all its stuff concentrated in the nucleus.

When you exert pressure against the cup with your hand, the seeming solidity comes from the resistance of electrons in the cup. Electrons themselves don't have any volume at all — they're just fleeting, zero-dimensional flecks of negative electric charge that surround atoms and molecules like clouds. And the laws of quantum mechanics limit them to specific energy levels around atoms and molecules. As your hand grasps the cup, it forces electrons from one level to another, and that requires energy from the hand's muscles, which the brain interprets as touching something solid.

Our sense of touch, then, arises from an exceedingly complex interaction between electrons around the molecules of our bodies and those of the objects we encounter. From that information, our brain creates the illusion that we possess solid bodies moving through a world filled with other solid objects. Touch doesn't give us an accurate sense of reality. And it may be that *none* of our perceptions match what's really out there. Donald Hoffman, a cognitive neuroscientist at the University of California, Irvine, believes that our senses and brain evolved to *hide* the true nature of reality, not to reveal it.

"My idea is that reality, whatever it is, is too complicated and would take us too much time and energy [to process]," he says.

More than 99.9999999999 percent of an atom consists of empty space, with nearly all its stuff concentrated in the nucleus. When you exert pressure against a cup with your hand, the seeming solidity comes from the resistance of electrons in the cup.

Hoffman likens the picture our brain constructs of the world to the graphical interface on a computer screen. All the colorful icons on the screen — the trash can, the mouse pointer, the file folders — bear no resemblance at all to what's really going on inside the computer. They're abstractions, simplifications that allow us to interact with complex electronics.

In Hoffman's view, evolution has shaped our brains to operate in much the same way, as a graphical interface that doesn't reproduce the world with any sort of fidelity. Evolution doesn't favor the development of accurate perceptions; it rewards ones that enhance survival. Or as Hoffman puts it, "Fitness beats truth."

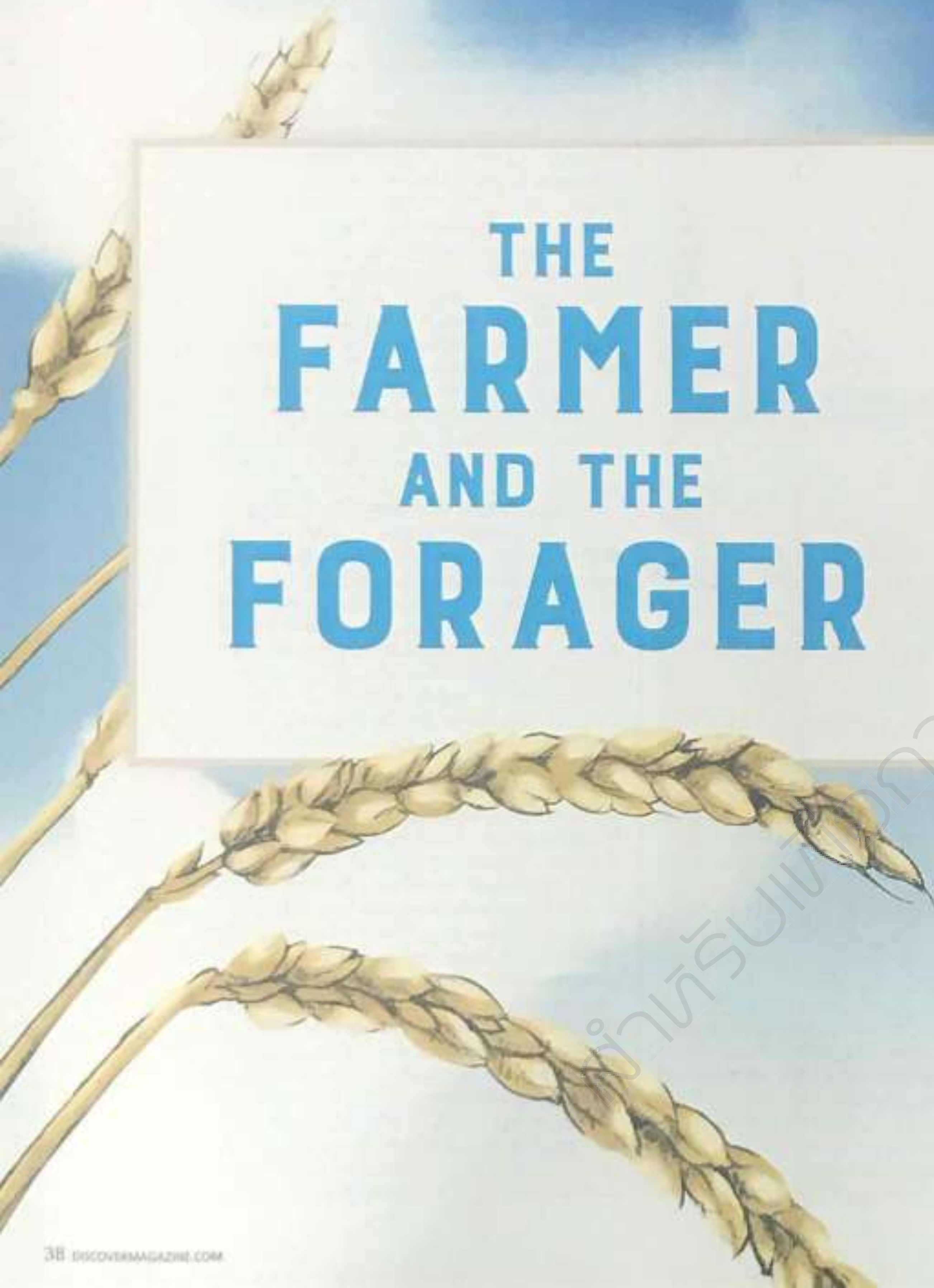
Hoffman and his graduate students have run hundreds of thousands of computer models in recent years to test his ideas. In the simulations, artificial life-forms compete for limited resources. And in every case, the organisms programmed to emphasize fitness outcompete the various ones primed for accurate perceptions. For example, if one organism is tuned to accurately perceive, say, the *total* amount of water present in an environment, it will lose out to an organism that's tuned to perceive something simpler: the optimal amount of water needed to stay alive.

So while one organism might construct a more accurate representation of reality, that representation doesn't enhance its survivability. Hoffman's studies have led him to a remarkable conclusion: "To the extent that we're tuned to fitness, we will not be tuned to reality. You can't do both."

His ideas align with what some physicists believe to be a central message of quantum theory: Reality is not completely objective — we cannot separate ourselves from the world we observe. Hoffman fully embraces that view. "Space is just a data structure," he says, "and physical objects are themselves also data structures that we create on the fly. When I look at that hill over there, I create that data structure. Then I look away and I've trashed that data structure because I don't need it anymore."

As Hoffman's work shows, we haven't yet come to grips with the full meaning of quantum theory and what it says about the nature of reality. Planck himself struggled for most of his life to understand the theory he helped launch, and always believed in an objective universe that exists independently of us. He once wrote about why he decided to go into physics against the advice of his mentor: "The outside world is something independent from man, something absolute, and the quest for the laws which apply to this absolute appeared to me as the most sublime scientific pursuit in life." Maybe it will take another century, and another revolution, to prove whether he was right, or as mistaken as Professor von Jolly. ■

Tim Folger is a contributing editor to Discover and series editor of The Best American Science and Nature Writing, an annual anthology. He lives in New Mexico.

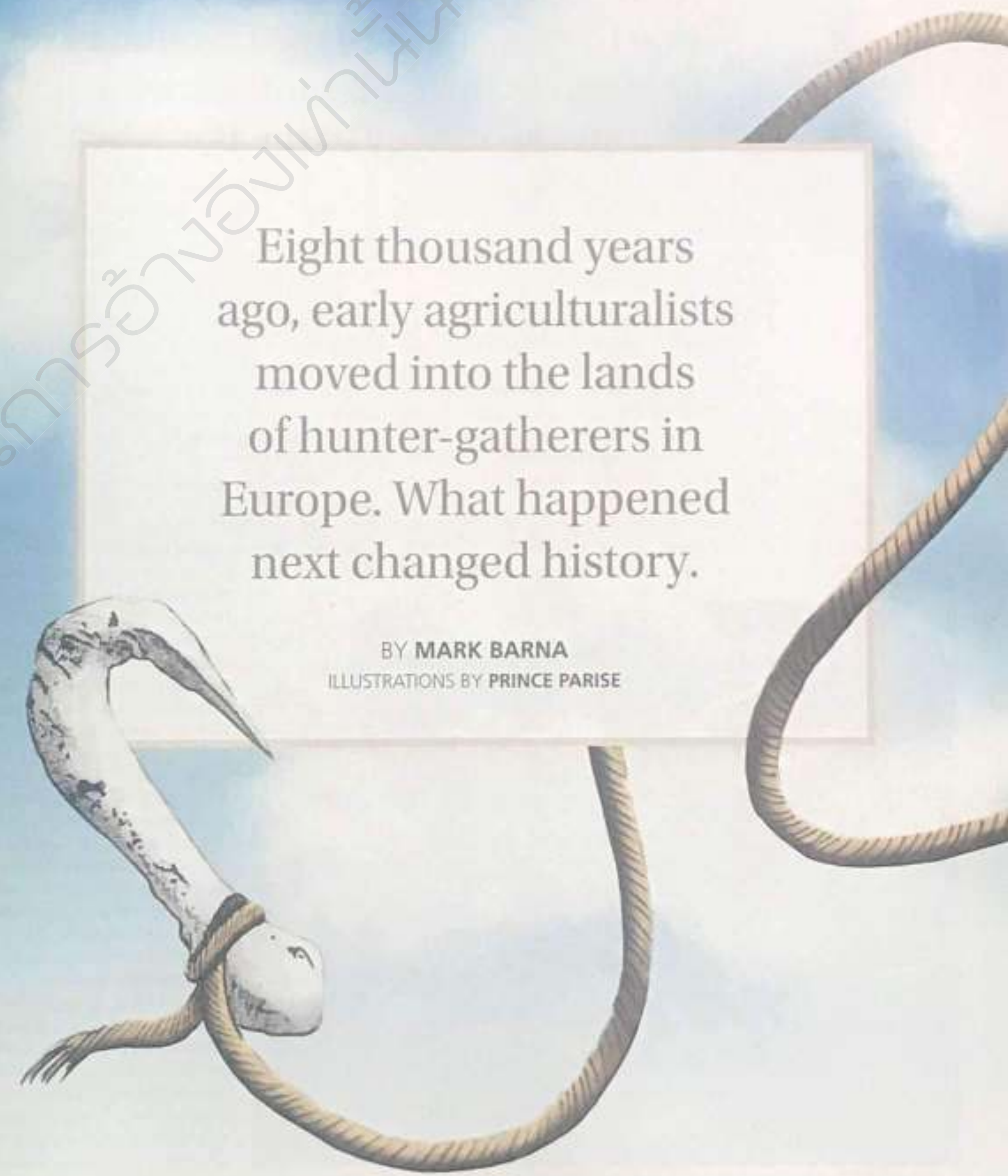


THE FARMER AND THE FORAGER

Eight thousand years ago, early agriculturalists moved into the lands of hunter-gatherers in Europe. What happened next changed history.

BY **MARK BARNA**

ILLUSTRATIONS BY **PRINCE PARISE**



The barrel-chested man is known to us only as Burial 7/I. His 8,000-year-old remains were found at a fishing camp that hugs a curve in the Danube River as it winds through southeastern Europe, on its way to the Black Sea.

For most of his life, he stalked red deer in dense forests and wrestled sturgeon from whirlpools in the churning river. But later in life, he seemed to turn away from the hunter-gatherer life of his ancestors and toward that of a settled agriculturalist.

Burial 7/I, according to some of the archaeologists who have studied him, was born a hunter and died a farmer — though other researchers dispute that. It's just one of the questions that linger over this stretch of the Danube, where archaeological finds are revealing details of an unprecedented encounter between traditional European hunter-gatherers and early farmers moving into the area from the south.

Since the 1960s, at these sites where the Danube forms the border between Serbia and Romania, archaeologists have turned up artifacts and human remains that are 7,900 to 8,200 years old. The sites here represent the oldest examples in Europe of interaction between farmers and foragers during the region's Neolithic transition, when the semi-nomadic hunter-gatherer lifestyle that had persisted for millennia was replaced with agricultural communities. That transition, which occurred at different times in different places, changed the course of humanity.

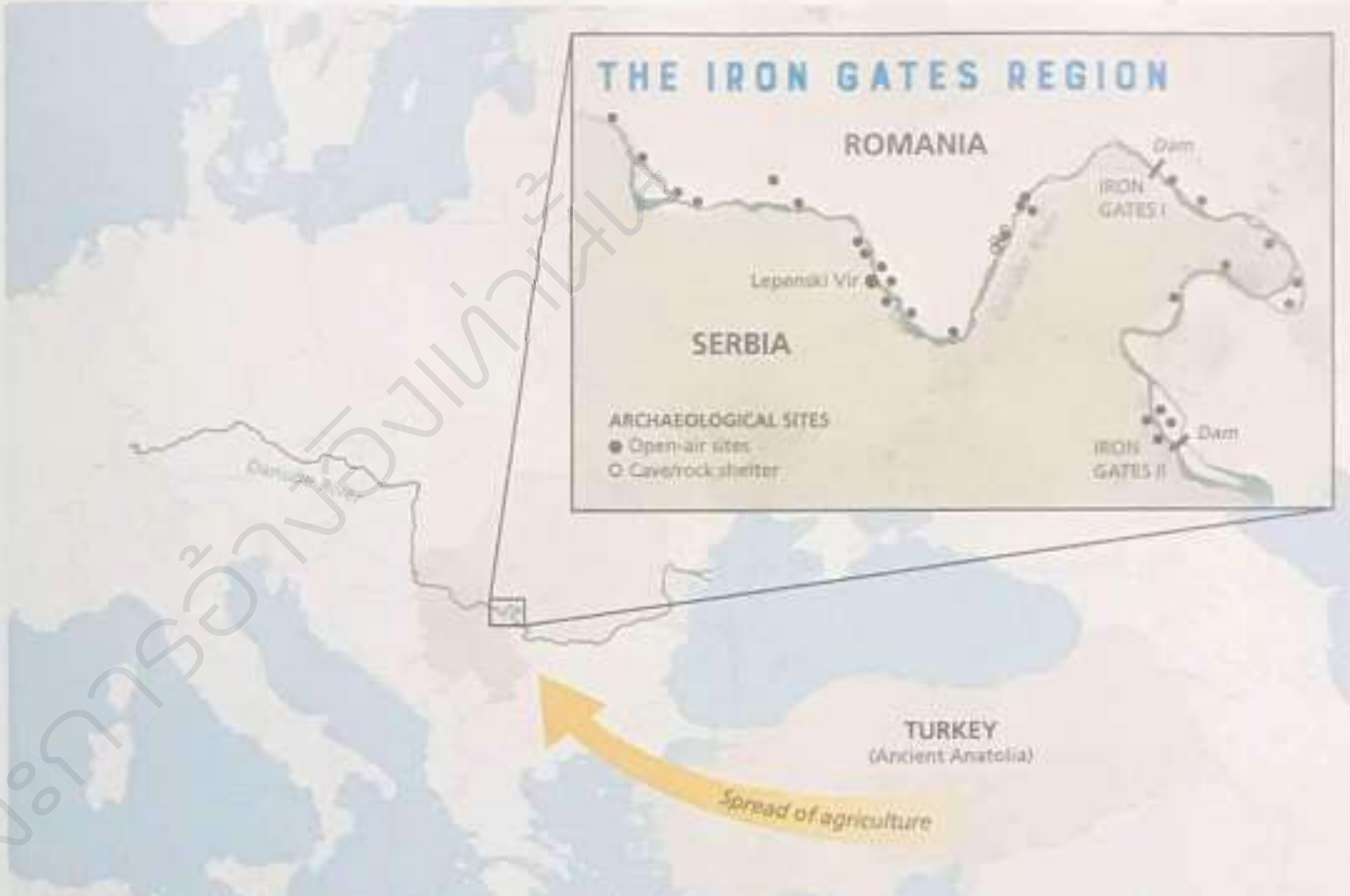
"It is probably the most exciting period in history that I am aware of," says Joachim Burger, an archaeologist and population geneticist at Mainz University in Germany.

The sites offer a glimpse of the everyday life of people living at this time of momentous transition. And thanks to analysis of Burial 7/I and other remains through ancient DNA sequencing and other methods, researchers are uncovering more details — and more mysteries — about the individuals who called this bend in the river home.

Ancient DNA analysis has established that the arriving farmers were most closely related to people living in northwestern Anatolia, or the Asian part of modern Turkey. Agriculture had been a way of life for them for thousands of years. It had spread from the Fertile Crescent in the southeast, a region that today includes Iran and Iraq.

The Anatolians arriving at the Danube's banks to farm were not the first to get their hands dirty in European fields. Hundreds of miles to the south, by the Aegean Sea in southern Greece, agriculturalists were reaping and sowing 500 years before the Anatolians showed up. But there is scant evidence that those earlier farmers interacted with local hunter-gatherers.

▼ The skeleton known to archaeologists as Burial 7/I was interred 8,000 years ago along the Danube River with an additional human skull, as well as the skull of an auroch (a type of wild cattle).



Source: "Radiocarbon and Stable Isotope Evidence of Dietary Change from the Mesolithic to the Middle Ages in the Iron Gates: New Results From Lepenski Vir," Radiocarbon, 2004

▲ Neolithic farmers migrating out of Anatolia brought their way of life to a corner of southeastern Europe. The region, rich in archaeological sites, is now known as the Iron Gates, named after Cold War-era dams erected along the Danube River there.

Before the fifth millennium B.C., or 7,000 years ago, farmers and foragers rarely crossed paths; examination of burial remains shows genetic separation, says Burger. "They probably saw each other from a distance occasionally and just stared at each other, thinking, 'Oh, those strange people.'"

Whether farmers or foragers, groups were small and scattered, dwarfed by the limitless European landscape. In addition, they sought different environments, says Stephen Shennan, an archaeologist at the University College London and author of the book *The First Farmers of Europe*. Foragers opted for forests and mountains full of game, or rivers and coasts teeming with fish. Farmers chose flatland with fertile soil in temperate climates.

And yet, against all odds, here along the Danube, contact happened. "It is something very special and doesn't represent the norm at all," says Shennan.

THIS COULD HAVE ENDED BADLY, GIVEN OTHER OUTCOMES IN HUMAN HISTORY.

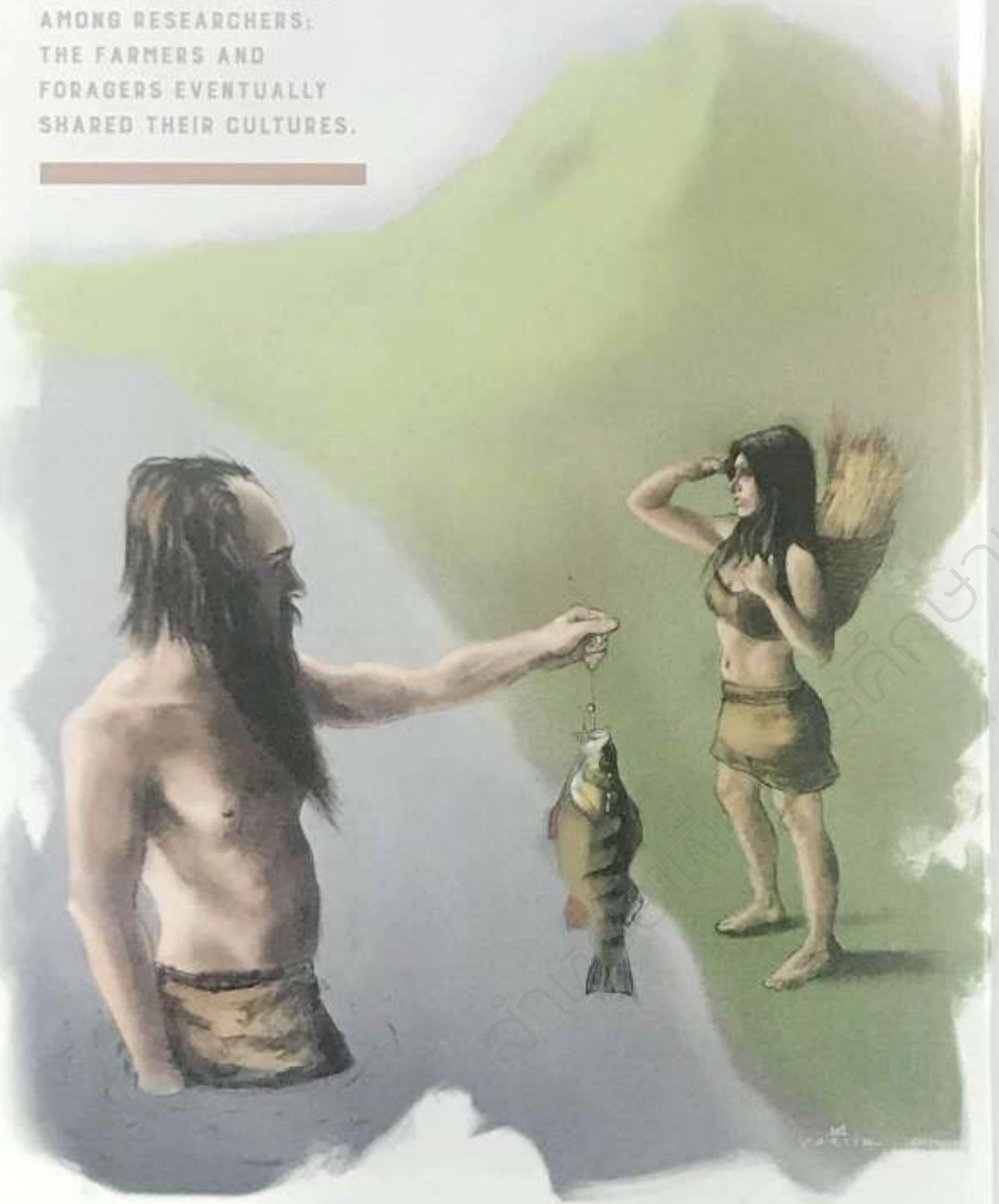
FISHERMEN FORAGERS

Home to scores of prehistoric settlement sites, this nearly 100-mile stretch of river is known as the Iron Gates region, named after two dams built decades ago. Just as the Danube is a resource for modern populations, it sustained the hunter-gatherer bands that lived there more than 8,000 years in the past.

While many forager groups in other parts of the world moved with the seasons, hunting game and gathering plants, Iron Gates bands stuck close to the river valley. Excavations of their encampments reveal large amounts of fish bones; dietary clues preserved in the foragers' bones showed heavy fish consumption.

Their favorite catch was apparently sturgeon, some specimens longer than a man, as they swam upriver in spring from the Black Sea to breed and spawn. The activity required planning, and it was a group effort: Parties would have used boats, nets, harpoons and stone mallets for clubbing, says Columbia University archaeologist Dušan Borić, who has excavated Iron Gates sites.

ONE FACT NOT DISPUTED AMONG RESEARCHERS: THE FARMERS AND FORAGERS EVENTUALLY SHARED THEIR CULTURES.



▲ Lepenski Vir, a key site for Neolithic foragers and farmers, was relocated in 1971 during dam construction to avoid being flooded; it's now protected from the elements on a hillside above the whirlpool for which it was named.

Favorite fishing spots would have been the river's whirlpools, where the currents confused the animals and made them easy prey — and a protein-rich staple.

Sofija Stefanovic, an anthropologist at the University of Belgrade, says that based on her bone analyses of many Mesolithic remains at Iron Gates, the foragers were healthy with no signs of malnutrition. "Their diet in the Mesolithic was actually perfect," she says. "In many cases, they lived quite long, 50 to 60 years."

FIRST CONTACT

Besides eating a diet of mostly fish, the foragers looked physically different from the farmers. Remains from Iron Gates reveal the male hunter-gatherers, on average, were more muscular and about a head taller than the male farmers, though women from both cultures were about the same height.

The farmers likely traveled from Anatolia along the Black Sea coast to the Danube peninsula, where they turned upriver and into the heart of southeastern Europe. Upon arrival, they probably aimed to befriend the locals, a common practice of migrants entering an inhabited territory, says University of Kansas archaeologist Ivana Radovanović, who studies Iron Gates. They'd want to be on good terms to pick the foragers' brains about the region.

This could have ended badly, given other outcomes in human history. In the 1500s, the arriving Spanish in Mexico wiped out the Aztec and Incan empires. The Pilgrims in New England were friends with Native Americans, until they weren't.

But at Iron Gates, farmers and foragers got along. Human remains unearthed at the numerous sites have no battle wounds or other injuries consistent with full-scale conflict. "The evidence shows that these two populations were relatively peaceful in their interactions, rather than killing each other or [attacking] each other," says Borić. "I would not exclude the possibility of outbursts of violence, but there is no systematic violence of one population on the other."

There are a number of reasons why the hunter-gatherers may have been friendly toward the new arrivals. For example, they might not have viewed the migrants as a threat. At least initially, the foragers outnumbered the migrants. A 2015 paper in *Archaeological and Anthropological Sciences* placed the river valley's hunter-gatherer population in the hundreds. No warrior invasion here. And the migrants' interest was agriculture, not muscling a netted sturgeon out of a whirlpool. So territorial conflicts were unlikely.

Still, the foragers' receptiveness also could have been something else entirely: They were already aware of the farming way, to some extent.

Vast trade networks linked the foragers with regions perhaps as far away as Greece, as

▲ A broad bend in the Danube River, seen here from the Serbian side looking into Romania, is home to Lepenski Vir (at far left) and several other archaeological sites dating back more than 8,000 years and charting the arrival of agriculture.

indicated by exotic items found at Iron Gates: seashell beads from the Black Sea and tools made of volcanic obsidian mined from an island in the Aegean Sea. In fact, hunter-gatherers of the era were no strangers to networking. "Their trade connections were massive and probably still underestimated," says Burger.

Crops may have been among the items traded. According to a paper published in 2016 in the journal *PNAS*, Iron Gates hunter-gatherers were eating domesticated wheat and barley as early as 8,600 years ago, more than 400 years before the Anatolian farmers arrived. Researchers discovered starch granules in the tooth plaque of some of the foragers. The starch, they contend, came from domesticated grains not grown in the region.

Trading for crops before embracing agriculture is common. North American foragers traded for domesticated maize for hundreds of years prior to cultivating it themselves, the paper points out. Still, some scientists want to see more evidence. Mirjana Roksandic, a University of Winnipeg anthropologist who has excavated at Iron Gates, isn't convinced that wild and domesticated starch grains can be distinguished from each other in tooth plaque.

One fact not disputed among researchers: The farmers and foragers eventually shared their cultures. Both groups saw benefits to it, says Burger. The foragers had a generous food supply, which intrigued the farmers. And the foragers were open to learning about food production. Within a few generations, ancient DNA shows, the two groups were having sex and raising families. "For people to marry into another population, there must be a high economic attraction underlying this process," says Burger. "Otherwise, you wouldn't do it. It's not like you fall in love and it's a romantic story. You are attracted because you think you can have a better life."

A CULTURAL POTPOURRI

Among the Iron Gates settlements is Lepenski Vir, named after the whirlpool at its doorstep. (Vir means "whirlpool" in Serbian.) Perhaps only a few dozen people occupied it at any one time, according to the paper in *Archaeological and Anthropological Sciences*. But many people were buried there: Nearly 200 human remains have been recovered, some beneath buildings.

From about 9,500 years ago, when only hunter-gatherers lived in the area, to about 7,500 years ago, when Iron Gates was the sole domain of farmers, Lepenski Vir was variously a fishing camp, a social destination, a settlement, a burial site and perhaps a spiritual center. It might have been all or a combination during some periods. The river site offers a wealth of evidence for cultural exchange during the transition.

Consider how the bodies were buried. In southeastern Europe, hunter-gatherers buried their dead on their backs with hands usually placed on the stomach and legs straight. Anatolian farmers buried their dead on their sides in a curled position.

BURIAL POSITIONS

▲ Two different styles of burial at Lepenski Vir and other sites in the region reflect the disparate cultures merging into one. Foragers native to the area buried their dead on their backs, but farmers arriving from Anatolia laid them to rest on their sides, knees pulled toward elbows.

This all gets jumbled at Lepenski. Several people with DNA matching Anatolian farmers were buried in the hunter-gatherer manner; curled burials appeared at the tail end of the transition, about 8,000 years ago.

The decorative items the two groups wore also became mixed up. Foragers adorned themselves with disk-shaped beads like those worn by Anatolians, while forager beads made from mollusks vanished from the archaeological record. Other evidence shows that farmers brought with them more than just agriculture. Shards of pottery, the first found in the area, and bones of domesticated animals — including goats, cattle and pigs — have been recovered.

The foragers also changed their diet. Bone collagen analysis reveals they were consuming less fish and more grains and meat, like the farmers in Anatolia.

HERE WAS THE NEOLITHIC TRANSITION EMBODIED IN ONE PERSON.

THE LAST FORAGER

Ancient DNA and artifacts aren't the only means to tell the story of Iron Gates. Scientists can determine migration patterns by measuring strontium isotope ratios in tooth enamel, which forms in early childhood. Unlike genetic material, tooth enamel is generally impervious to degradation after death. Strontium comes from weathering rocks, and it ends up in water and food, seeping into tooth enamel layers. The molecular particles are a signature of a geographic region and indicate where someone lived in youth. If someone were born in northern Greece or Anatolia, the strontium signal would be different from that of Iron Gates natives.

Scientists have long suspected that Danube foragers and their farming neighbors gathered at Lepenski Vir to exchange stories and ideas, and probably to find mates. The strontium analysis, published in a 2013 *PNAS* paper, supports this idea. Of the 45 remains tested, 10 belonged to women who came from Anatolia, presumably as part of the farming communities — a head-turning number in what is essentially a forager settlement. Adding to the mystery, three of those women were buried in the hunter-gatherer manner.

The discovery suggests the casual manner in which farming spread, says Borić, co-author of the paper. "It is very likely that Neolithic women coming into the forager settlements spread [farming] skills," he says.

Lepenski Vir's most intriguing human burial is that of 7/I — the large-framed man, likely in his 50s, that some researchers believe was born a hunter and died a farmer. He was laid to rest beneath a building's plaster floor, with the detached skull of another individual placed over his left shoulder.

Researchers examined collagen from the man's right femur and a rib, according to a study published in 2015 in *Radiocarbon*. The femur, which stops replacing collagen usually in early adulthood, suggested a diet primarily of fish, typical of Iron Gates foragers. The rib, however, indicated a farmer's grain and meat-heavy diet. Collagen in a rib is continually replaced, so it suggests a person's diet in their final years, says Clive Bonsall, lead author and an archaeologist at the University of Edinburgh.

▲ From left: Limestone beads found in an Iron Gates grave, statues that may depict fishlike gods, a reconstructed house at the Lepenski Vir site and perforated shell beads all provide clues to how farmers and foragers interacted 8,000 years ago.

Rather than feasting on, say, a plate of catfish in the years before his death, Burial 7/I might have spooned up calorie-rich porridge, a mix of cereals and goat's milk. Here was the Neolithic transition embodied in one person.

Despite the dietary turn, the ways of his ancestors didn't completely escape him: The man was laid to rest on his back, body straight, palms on his belly.

The conclusions in the *Radiocarbon* study are controversial. Originally excavated in the 1960s, Burial 7/I's remains have been moved to different storage locations and sometimes mishandled, says Roksandic, who examined the skeleton in the late 1990s and is the paper's co-author. Contamination is possible, she acknowledges. But Bonsall says bone collagen is relatively resistant to postmortem alteration. He hopes that future analysis of the skeleton's DNA and teeth will answer questions raised by colleagues.

By the time the man died, about 8,000 years ago, hunter-gatherer culture was in its twilight at Iron Gates. "It takes not more than 300 years, and the whole area is full of farmers," says Burger. "The hunter-gatherers have been replaced."

FARMER BOOM

Before the foragers were fully absorbed into the farming communities, however, Lepenski Vir appears to have been the region's first multicultural nexus. "That might have contributed to the creativity we see at the site, and what makes the site so important," says Borić.

Within hundreds of years of first contact in Iron Gates, complex agricultural societies sprang up in southeastern Europe, along with other advances, such as intricate metalwork.

Meanwhile, agriculture was also spreading outside southeastern Europe. By the middle of the sixth millennium B.C., some 400 years after Burial 7/I, farming was in central Europe and on the Iberian Peninsula, according to a paper published in *Nature* in February. By the end of that millennium, agriculture had reached Eastern Europe, which included farming settlements in the Ukraine of hundreds of people.

The swiftness of the agricultural revolution makes the interaction at Iron Gates all the more interesting. An ancient subsistence strategy was starting to vanish. A cultural watershed, perhaps the most significant in human history, was underway. Change was happening on an unprecedented level. But from the viewpoint of an individual living through it, the transition was pretty casual — manifesting, on occasion, as foragers and farmers talking shop above the thrum of a river. ◼

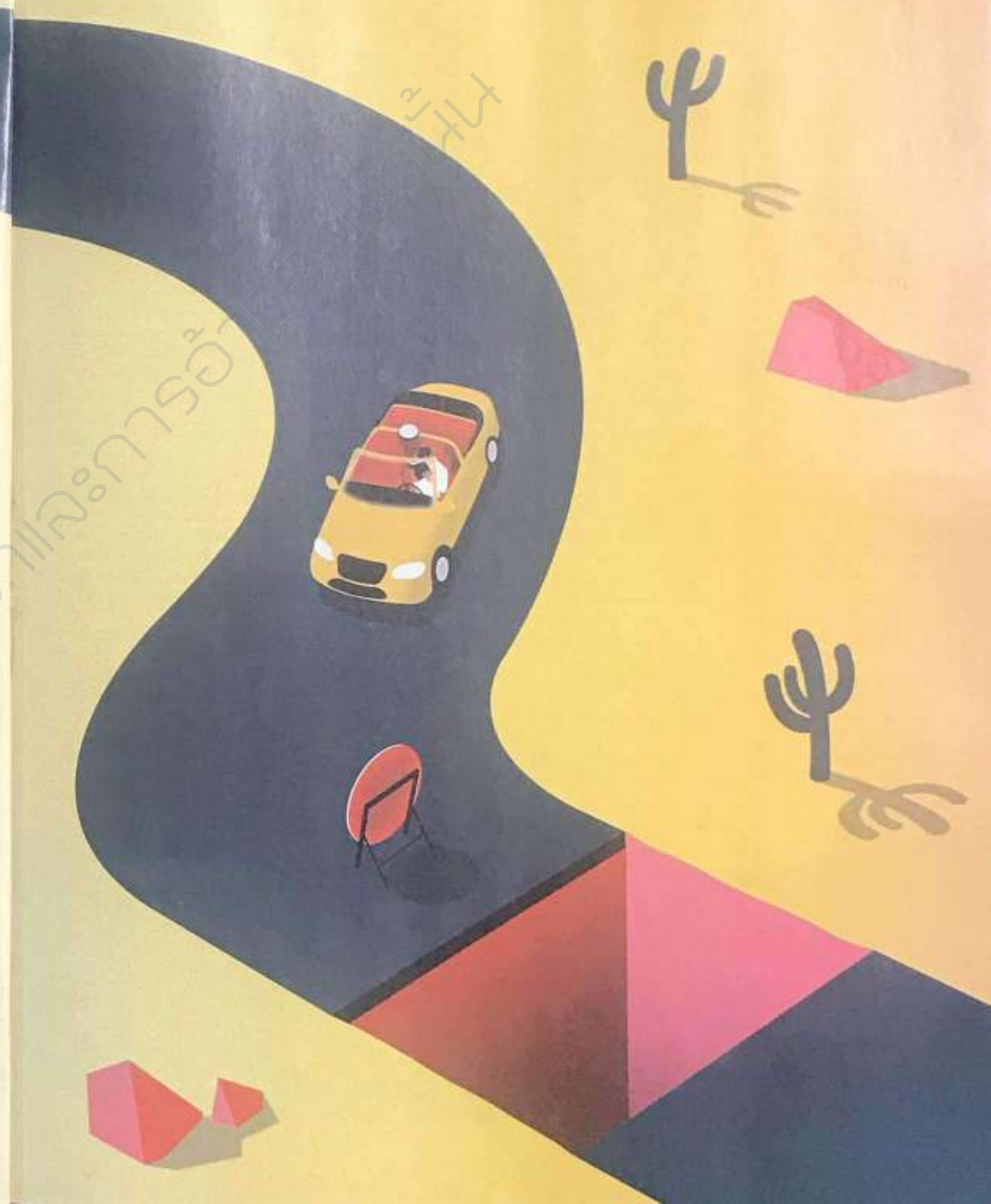
Mark Barna *is an associate editor at* Discover.

BABY, CAN YOU DRIVE MY CAR

AUTOMAKERS ARE REVVING UP FOR A **VERY NEAR FUTURE** OF ***FULLY AUTONOMOUS VEHICLES.***

CAUTION: SPEED BUMPS AHEAD.

BY **HANNAH FRY**
ILLUSTRATIONS BY **NEIL WEBB**



The sun was barely above the horizon on March 13, 2004, but the Slash X saloon bar, in the middle of the Mojave Desert, was already thronging with people.

The bar is on the outskirts of Barstow, a California town between Los Angeles and Las Vegas. It's a place popular with cowboys and off-roaders, but on that spring day it had drawn the attention of another kind of crowd. A makeshift stadium that had been built was packed with engineers, excited spectators and foolhardy petrol heads who all shared a similar dream: to be the first people on Earth to witness a driverless car win a race.

The race had been organized by the U.S. Defense Advanced Research Projects Agency, or DARPA (nicknamed the Pentagon's "mad science" division). The agency had been interested in unmanned vehicles for a while, and with good reason: Roadside bombs and targeted attacks on military vehicles were a major cause of death on the battlefield. Earlier that year, DARPA had announced its intention to make one-third of U.S. ground military forces vehicles autonomous by 2015.

Up to that point, progress had been slow and expensive. DARPA had spent around half a billion dollars over two decades funding research at universities and companies in the hope of achieving its ambition. But then came an ingenious idea: Why not create a competition? The agency would invite anyone in the country to design their own driverless car and race them against each other on a long-distance track, with a prize of $1 million for the winner. It would be a quick and cheap way to give DARPA a head start in pursuing its goal.

On the morning of the 132-mile race, a ramshackle lineup of cars gathered at Slash X, along with a few thousand spectators. Things didn't quite go as planned. One car flipped upside down in the starting area and had to be withdrawn. A self-driving motorbike barely cleared the start line before it rolled onto its side and was declared out of the race. One car hit a concrete wall 50 yards in. Another got tangled in a barbwire fence. The scene around the saloon bar began to look like a robot graveyard.

The top-scoring vehicle, an entry by Carnegie Mellon University, managed an impressive 7 miles before misjudging a hill — at which point the tires started spinning and, without a human to help, carried on spinning until they caught fire. It was over by late morning. A DARPA organizer climbed into a helicopter and flew over to the finish line to inform the waiting journalists that none of the cars would be getting that far.

The race had been oily, dusty, noisy and destructive — and had ended without a winner. All those teams of people had worked for a year on a creation that had lasted, at best, a few minutes.

But the competition was anything but a disaster. The rivalry had led to an explosion of new ideas, and by the next DARPA Grand Challenge in 2005, the technology was vastly improved. An astonishing five driverless cars completed the race without any human intervention.

Now, more than a decade later, it's widely accepted that the future of transportation is driverless. In late 2017, Philip Hammond, the British Chancellor of the Exchequer, announced the government's intention to have fully driverless cars — without a safety attendant on board — on British roads by 2021. Daimler, a Germany-based auto manufacturer, has promised driverless cars by 2020, and Ford by 2021. Other manufacturers have made similar forecasts for their driverless vehicles.

On the surface, building a driverless car sounds as if it should be relatively easy. Most humans manage to master the requisite skills to drive. Plus, there are only two possible outputs: speed and direction. It's a question of how much gas to apply and how much to turn the wheel. How hard can it be?

But, as the first DARPA Grand Challenge demonstrated, building an autonomous vehicle is a lot trickier than it looks. Things quickly get complicated when you're trying to get an algorithm to control a great big hunk of metal traveling at 60 mph.

BEYOND THE RULES OF THE ROAD

Imagine you've got two vehicles approaching each other at speed, traveling in different directions down a gently curved county highway.

A human driver will be perfectly comfortable in that scenario, knowing the other car will stick to its own lane and pass safely a few feet to the side. "But for the longest time, it does look like you're going to hit each other," explains Paul Newman, professor of robotics at the University of Oxford and founder of Oxbotica, a company that builds driverless cars.

How do you teach a driverless car not to panic in that situation? You don't want the vehicle to drive off the side of the road trying to avoid a collision that was never going to happen, says Newman. But, equally, you don't want it to be complacent if you really do find yourself on the verge of a head-on crash. Remember, too, these cars are only ever making educated guesses about what to do.

How do you get it to guess right every single time? That, says Newman, "is a hard, hard problem."

It's a problem that puzzled experts for a long time, but it does have a solution. The trick is to build in a model for how other — sane — drivers will behave. Unfortunately, the same can't be said of other nuanced driving scenarios.

HOW DO YOU TEACH A SELF-DRIVING ALGORITHM TO UNDERSTAND THAT YOU NEED TO BE EXTRA CAUTIOUS WHEN PASSING A GROUP OF KIDS PLAYING WITH A BALL ON THE SIDEWALK?

"What's hard is all the problems with driving that have nothing to do with driving," says Newman.

For instance, how do you teach a self-driving algorithm to understand that you need to be extra cautious upon hearing the tunes of an ice cream truck, or when passing a group of kids playing with a ball on the sidewalk?

Even harder, how do you teach a car that it should sometimes break the rules of the road? What if an ambulance with its lights on is trying to get past on a narrow street and you need to drive up on the sidewalk to let it through? Or if an oil tanker has jackknifed across a country lane and you need to get out of there by any means possible?

"None of these are in the [U.K.] Highway Code," Newman points out. And yet a truly autonomous car needs to know how to deal with all of these scenarios if it's to exist without *ever* having any human intervention. Even in emergencies.

That's not to say these are insurmountable problems. "I don't believe there's any level of intelligence that we won't be able to get a machine to do," says Newman. "The only question is when."

Unfortunately, the answer to that question is probably not anytime soon. That driverless dream we're all waiting for might be a lot further away than we think. That's because there's another layer of difficulty to contend with when trying to build that sci-fi fantasy of a go-anywhere, do-anything, steering-wheel-free driverless car, and it's one that goes well beyond the technical challenge.

THE PEOPLE FACTOR

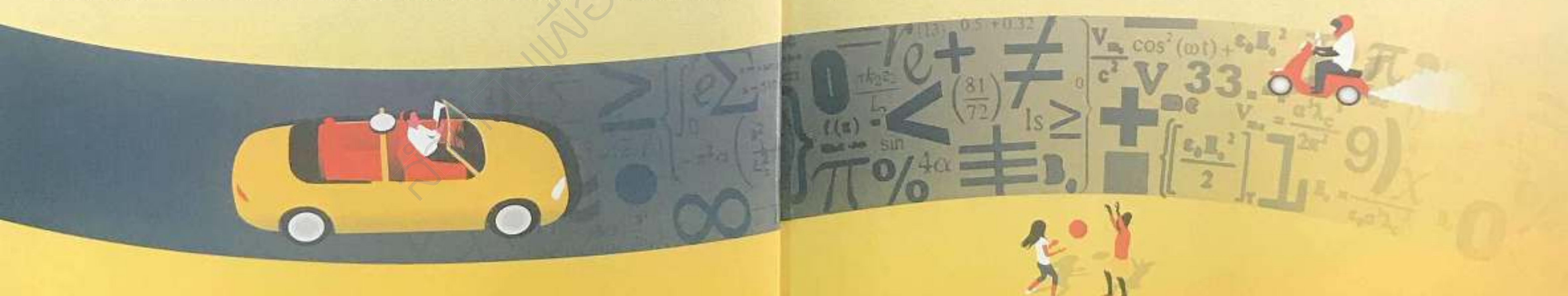
A fully autonomous car will also have to deal with the tricky problem of people. "People are mischievous," says Jack Stilgoe, a sociologist at the University College London who studies the social impact of technology. "They're active agents, not just passive parts of the scenery."

Imagine a world where truly, perfectly autonomous vehicles exist. The No. 1 rule in their onboard algorithms will be to avoid collisions wherever possible. And that changes the dynamics of the road. If you stand in front of a driverless car, it has to stop. If you pull out in front of one at a junction, it has to behave submissively.

"People who've been relatively powerless on roads up till now, like cyclists, may start cycling very slowly in front of self-driving cars knowing that there is never going to be any aggression," says Stilgoe.

Getting around this problem might mean bringing in stricter rules to deal with people who abuse their position as cyclists or pedestrians. It's been done before, of course: Think of jaywalking. Or it could mean forcing everything else off the roads, as happened with the introduction of the automobile. That's why you don't see bicycles, horses, carts, carriages or pedestrians on an expressway.

If we want fully autonomous cars, we'll almost certainly have to do something similar again and limit the number of aggressive drivers, ice cream trucks, kids playing in the road, roadwork signs, difficult pedestrians, emergency vehicles, cyclists, mobility scooters and everything else that makes the



problem of autonomy so difficult. That's fine, but it's a little different from the way the idea is currently being sold to us.

"The rhetoric of autonomy and transport is all about *not* changing the world," says Stilgoe. "It's about keeping the world as it is but making and allowing a robot to just be as good as and then better than a human at navigating it. And I think that's stupid."

But hang on, some of you may be thinking. Hasn't this problem already been cracked? Hasn't Waymo, Google's autonomous car, driven millions of miles already? Aren't Waymo's fully autonomous cars (or at least, close-to-fully-autonomous cars) currently driving around the roads of Phoenix?

Well, yes. But not every mile of road is created equally. Most miles are so easy to drive, you can do it while daydreaming. Others are far more challenging.

At the time of writing, Waymo cars aren't allowed to go just anywhere: They're "geo-fenced" into a small, predetermined area. So, too, are the driverless cars Daimler and Ford propose to have on the roads by 2020 and 2021, respectively. They're confined to a pre-decided go-zone. And that does make the problem of autonomy simpler.

Newman says the future of driverless cars will involve these types of go-zones.

"They'll come out working in an area that's very well known, where their owners are extremely confident that they'll work," says Newman. "So it could be part of a city, not in the middle of a place with unusual roads or where cows could wander into the path. Maybe they'll work at certain times of day and in certain weather situations. They're going to be operated as a transport service."

STAYING FOCUSED

Lisanne Bainbridge, a psychologist at the University College London, published a seminal essay in 1983 called "Ironies of Automation," on the hidden dangers of relying too heavily on automated systems. A machine built to improve human performance, she explained, will lead — ironically — to a reduction in human ability.

UNTIL WE GET TO FULL AUTONOMY, THE CAR WILL STILL SOMETIMES UNEXPECTEDLY HAND BACK CONTROL TO THE DRIVER. WILL WE BE ABLE TO REMEMBER INSTINCTIVELY WHAT TO DO?

By now, we've all borne witness to this in some small way. It's why people can't remember phone numbers anymore, why many of us struggle to read our own handwriting and why lots of us can't navigate anywhere without GPS. With technology to do it all for us, there's little opportunity to practice our skills.

There is some concern that this might happen with self-driving cars — where the stakes are a lot higher than with handwriting. Until we get to full autonomy, the car will still sometimes unexpectedly hand back control to the driver. Will we be able to remember instinctively what to do? And will teenage drivers of the future ever have the chance to master requisite driving skills in the first place?

But even if all drivers manage to stay competent, there's another issue we'll still have to contend with: What level of awareness is being asked of the human driver before the car's autopilot cuts out?

One level is that the driver is expected to pay careful attention to the road at all times. At the time of writing, Tesla's Autopilot is one such example of this approach. It's currently like a fancy cruise control: It'll steer and brake and accelerate on the motorway, but expects the driver to be alert, attentive and ready to step in at all times. To make sure you're paying attention, an alarm sounds if you remove your hands from the wheel for too long.

But that's not an approach that's going to end well. "It's impossible for even a highly motivated human to maintain effective visual attention toward a source of information, on which very little happens, for more than about half an hour," Bainbridge wrote in her essay.

Other autonomous car programs are finding the same issues. Although Uber's driverless cars require human intervention every 13 miles, getting drivers to pay attention remains a struggle. In March, an Uber self-driving vehicle fatally struck a pedestrian in Tempe, Arizona. Video footage from inside the car showed that the "human monitor" sitting behind the wheel was looking away from the road in the moments before the collision.

A PLAN FOR THE INEVITABLE

Though this is a serious problem, there is an alternative. The car companies could accept that humans will be humans, acknowledge that our minds will wander. After all, being able to read a book while driving is part of the appeal of self-driving cars.

Some manufacturers have already started to build their cars to accommodate our inattention. Audi's Traffic Jam Pilot is one example. It can completely take over when you're in slow-moving highway traffic, leaving you to sit back and enjoy the ride. Just be prepared to step in if something goes wrong. But there's a reason why Audi has limited its system to slow-moving traffic on limited-access roads. The risks of catastrophe are lower in motorway congestion.

And that's an important distinction. Because as soon as a human stops monitoring the road, you're left with the worst possible combination of circumstances when an emergency happens. A driver who's not paying attention will have very little time to assess their surroundings and decide what to do.

Imagine sitting in a self-driving car, hearing an alarm and looking up from your book to see a truck ahead shedding its load onto your path. In an instant, you'll have to process all the information around you: the motorbike in the left lane, the van braking hard ahead, the car in the blind spot on your right. You'd be most unfamiliar with the road at precisely the moment you need to know it best.

Add in the lack of practice, and you'll be as poorly equipped as you could be to deal with the situations demanding the highest level of skill.

A 2016 study simulated people as passengers, reading a book or playing on their cell phones, in a self-driving car. Researchers found that, after an alarm sounded for passengers to regain control, it took them about 40 seconds to do it.

Ironically, the better self-driving technology gets, the worse these problems become. A sloppy autopilot that sets off an alarm every 15 minutes will keep a driver continually engaged and in regular practice. It's the smooth and sophisticated automatic systems that are *almost* always reliable that you've got to watch out for.

"The worst case is a car that will need driver intervention once every 200,000 miles," Gill Pratt, head of Toyota's research institute, told technology magazine *IEEE Spectrum* in 2017.

Pratt says someone who buys a new car every 100,000 miles might never need to take over control from the car. "But every once in a while, maybe once for every two cars that I own, there would be that one time where it suddenly goes 'beep beep beep, now it's your turn!'" Pratt told the magazine. "And the person, typically having not seen this for years and years, would ... not be prepared when that happened."

ADJUSTING EXPECTATIONS

As is the case with much of the driverless technology that is so keenly discussed, we'll have to wait and see how this turns out. But one thing is for sure: As time goes on, autonomous driving will have a few lessons to teach us that apply well beyond the world of motoring — not just about the messiness of handing over control, but about being realistic in our expectations of what algorithms can do.

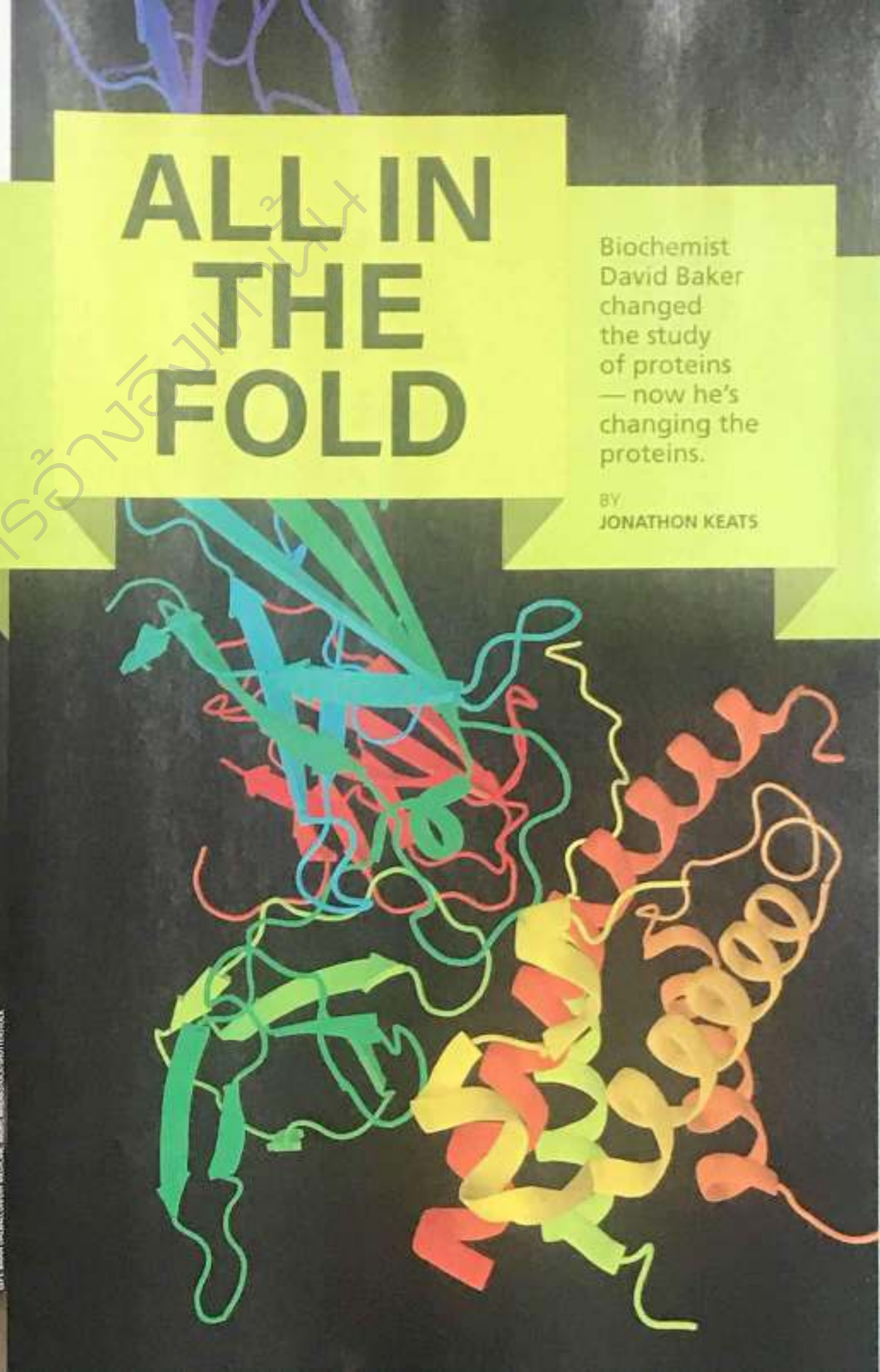
If this is going to work, we'll have to adjust our way of thinking. We're going to need to throw away the idea that cars should work perfectly every time, and accept that, while mechanical failure might be a rare event, algorithmic failure almost certainly won't be.

So, knowing that errors are inevitable, knowing that if we proceed we have no choice but to embrace uncertainty, the conundrums within the world of driverless cars will force us to decide how good something needs to be before we're willing to let it loose on our streets. That's an important question, and it applies elsewhere. How good is good enough? Once you've built a flawed algorithm that *can* calculate something, should you let it? ◘

ALL IN THE FOLD

Biochemist David Baker changed the study of proteins — now he's changing the proteins.

BY
JONATHON KEATS

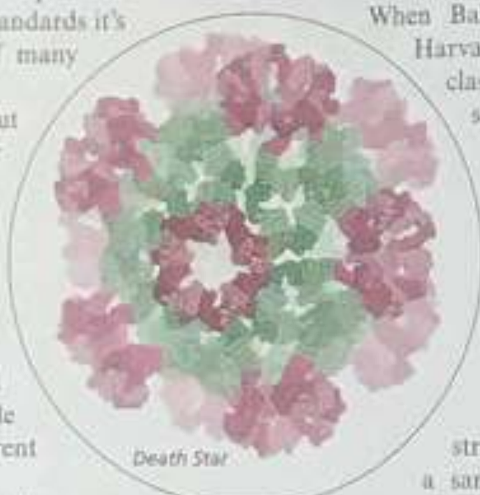


In a sleek biochemistry laboratory at the University of Washington, postdoctoral fellow Yang Hsia is watching yellowish goo — the liquefied remains of *E. coli* — ooze through what looks like a gob of white marshmallow. "This isn't super exciting," he says.

While growing proteins in bacteria and then purifying them, using blobby white resin as a filter, doesn't make for riveting viewing, the end product is extraordinary. Accumulating in Hsia's resin is a totally artificial protein, unlike anything seen in nature, that might just be the ideal chassis for the first universal flu vaccine.


Yang Hsia

David Baker, Hsia's adviser, calls this designer protein a "Death Star." Imaged on his computer, its structure shows some resemblance to the notorious *Star Wars* superweapon. Though microscopic, by protein standards it's enormous: a sphere made out of many interlocking pieces.


Death Star

"We've figured out a way to put these building blocks together at the right angles to form these very complex nanostructures," Baker explains. He plans to stud the exterior with proteins from a whole suite of flu strains so that the immune system will learn to recognize them and be prepared to fend off future invaders. A single Death Star will carry 20 different strains of the influenza virus.

Baker hopes this collection will cover the entire range of possible influenza mutation combinations. This all-in-one preview of present and future flu strains could replace annual shots: Get the Death Star vaccination, and you'll already have the requisite antibodies in your bloodstream.

As Baker bets on designer proteins to defeat influenza, others are betting on David Baker.

After revolutionizing the study of proteins — molecules that perform crucial tasks in every cell of every natural organism — Baker is now engineering them from scratch to improve on nature. In late 2017, the Open Philanthropy Project gave his University of Washington Institute for Protein Design more than $10 million to develop the Death Star and support Rosetta, the software platform he conceived in the 1990s to discover how proteins are assembled. Rosetta has allowed Baker's lab not only to advance basic science and pioneer new kinds of vaccines, but also to create drugs for genetic disorders, biosensors to detect toxins and enzymes to convert waste into biofuels.

His team currently numbers about 80 grad students and postdocs, and Baker is in constant contact with all of them. He challenges their assumptions and tweaks their experiments while maintaining an egalitarian environment in which ideas may come from anyone. He calls his operation a "communal brain." Over the past quarter-century, this brain has generated nearly [illegible] scientific papers.

"David is literally creating a new field of chemistry right in front of our eyes," says Raymond Deshaies, senior vice president for discovery research at the biotech company Amgen and former professor of biology at Caltech. "He's had one first after another."

NATURE'S ORIGAMI

When Baker was studying philosophy at Harvard University, he took a biology class that taught him about the so-called "protein folding problem." The year was 1983, and scientists were still trying to make sense of an experiment, carried out in the early '60s by biochemist Christian Anfinsen, that revealed the fundamental building blocks of all life on Earth were more complex than anyone imagined.

The experiment was relatively straightforward. Anfinsen mixed a sample of the protein ribonuclease — which breaks down RNA — with a denaturant, a chemical that deactivated it. Then he allowed the denaturant to evaporate. The protein started to function again as if nothing ever happened.

What made this simple experiment so striking was the fact that the amino acids in protein molecules are folded in three-dimensional forms that make origami look like child's play. When the denaturant unfolded Anfinsen's ribonuclease, there were myriad ways it could refold, resulting in structures as different as an origami crane and a paper airplane. Much as the folds determine whether a piece of paper can fly across a room, only one fold pattern would result in functioning ribonuclease. So the puzzle was this: How do proteins "know" how to refold properly?

"Anfinsen showed that the information for both structure and activity resided in the sequence of amino acids," says University of California, Los Angeles, biochemist David Eisenberg, who has been researching protein folding since the 1960s. "There was a hope that it would be possible to use sequence information to get three-dimensional structural information. Well, that proved much more difficult than anticipated."

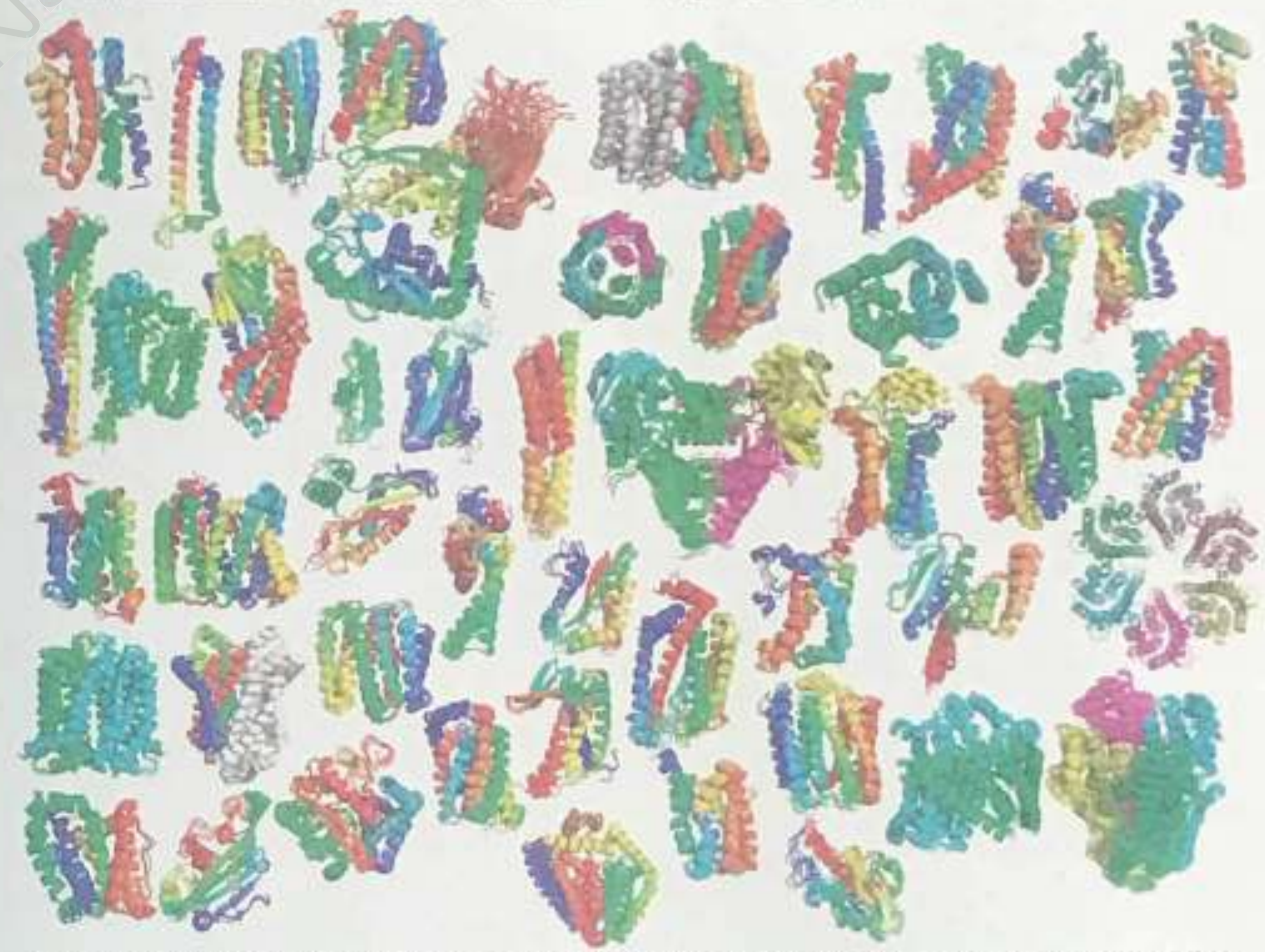
Baker was interested enough in protein folding and other unsolved mysteries of biology to switch majors and apply to grad school. "I'd never worked in a lab before," he recalls. He had only a vague notion of what biologists did on a daily basis, but he also sensed that the big questions in science, unlike philosophy, could actually be answered.

Grad school plunged Baker into the tediousness and frustrations of benchwork, while also nurturing some of the qualities that would later distinguish him. He pursued his Ph.D. under Randy Schekman, who was studying how molecules move within cells, at the University of California, Berkeley. To aid in this research, students were assigned the task of dismantling living cells to observe their internal molecular traffic. Nearly half a dozen of them, frustrated by the assignment's difficulty, had given up by the time Baker got the job.

Baker decided to follow his instincts even though it meant going against Schekman's instructions. Instead of attempting to keep the processes within a cell still functioning as he dissected it under his microscope, Baker concentrated on preserving cell structure. If the cell were a wristwatch, his approach would be equivalent to focusing on the relationship between gears, rather than trying to keep it ticking, while taking it apart.

"We've figured out a way to put these building blocks together at the right angles to form these very complex nanostructures."

"He was completely obsessed," recalls Deshaies, who was his labmate at the time (and one of the students who'd surrendered). Nobody could stop Baker, or dissuade him. He worked for months until he proved his approach was correct: Cell structure


Protein molecules play critical roles in every aspect of life. The way each protein folds determines its function, and the ways to fold are virtually limitless, as shown in this small selection of proteins visualized through the software platform Rosetta, born in Baker's lab.

drove function, so maintaining its anatomy preserved the internal transportation network. Deshaies believes Baker's methodological breakthrough was "at the core of Randy's Nobel Prize," awarded in 2013 for working out one of the fundamentals of cellular machinery.

But Baker didn't dwell on his achievement, or cell biology for that matter. By 1989, Ph.D. in hand, he'd headed across the Bay to the University of California, San Francisco, where he switched his focus to structural biology and biochemistry. There he built computer models to study the physical properties of the proteins he worked with at the bench. Anfinsen's puzzle remained unsolved, and when Baker got his first faculty appointment at the University of Washington, he took up the protein-folding problem full time.

From Baker's perspective, this progression was perfectly natural: "I was getting to more and more fundamental problems." Deshaies believes Baker's tortuous path, from cells to atoms and from test tubes to computers, has been a factor in his success. "He just has greater breadth than most people. And you couldn't do what he's done without being somewhat of a polymath."

ROSETTA MILESTONE

Every summer for more than a decade, scores of protein-folding experts convene at a resort in Washington's Cascade Mountains for four days of hiking and shop talk. The only subject on the agenda: how to advance the software platform known as Rosetta. They call it Rosettacon.

Rosetta has been the single most important tool in the quest to understand how proteins fold, and to design new proteins based on that knowledge. It is the link between Anfinsen's ribonuclease experiment and Baker's Death Star vaccine.

When Baker arrived at the University of Washington in 1993, researchers knew that a protein's function was determined by its structure, which was determined by the sequence of its amino acids. Just 20 different amino acids were known to provide all the raw ingredients. (Their particular order — specified by DNA — makes one protein fold into, say, a muscle fiber and another fold into a hormone.) Advances in X-ray crystallography, a technique for imaging molecular structure, had provided images of many proteins in all their folded splendor. Sequencing techniques had also improved, benefiting from the Human Genome Project as well as the exponential increase in raw computing power.

"There's a right time for things," Baker says in retrospect. "To some extent, it's just luck and historical circumstance. This was definitely the right time for this field."

Which is not to say that modeling proteins on a computer was a simple matter of plugging in the data. Proteins fold to their lowest free energy state. All of

Proteins 101

Each 6-foot-long strand of DNA packed into our cells has the information to create 20 different amino acids. These amino acids form chains and fold in a seemingly endless number of ways to create about 100,000 different proteins. Each protein has a specific purpose, most of them crucial to keeping our bodies functioning.

1 DNA
Stored in the nucleus of the cell and made up of four chemical building blocks — A, C, T and G, for short. DNA contains an organism's blueprints, or instructions, for life.

2 mRNA
Because a cell's protein-making factory cannot directly interpret the instructions encrypted in DNA, an enzyme converts the directives into a message know as mRNA.

3 RIBOSOME
The cellular factory known as the ribosome builds proteins according to mRNA instructions. The ribosome links the corresponding amino acids together into a protein chain.

4 PROTEIN
Tireless workers in the cell, proteins function as tiny molecular machines. Each protein performs a specific job, which, like any widget, depends entirely on its precise shape.

Protein Structures

Made of long chains of amino acids, each protein folds into elaborate, precise structures that determine how they function. While the folding patterns are unique and complicated, they can be thought of in four different levels of complexity:

PRIMARY PROTEIN STRUCTURE
Sequence of a chain of amino acids.

SECONDARY PROTEIN STRUCTURE
The amino acids fold into repeating patterns in the shape of pleated sheets or an alpha helix.

TERTIARY PROTEIN STRUCTURE
Three-dimensional folding patterns of protein.

QUATERNARY PROTEIN STRUCTURE
Protein consisting of more than one amino acid chain.

Folded Protein

The complex ways proteins fold are determined by their individual amino acids, which naturally arrange themselves in a state of equilibrium with each other.

Two Tracks of Research

PREDICTING HOW PROTEINS WILL FOLD
Using a software platform called Rosetta, researchers try to predict all the ways a sequence of amino acids can fold. The goal is to find a protein's most stable structure. Baker's lab has identified this state of equilibrium for about 600 of the 15,000 known naturally occurring protein families.

CREATING NOVEL PROTEINS
Researchers also use Rosetta to design new proteins from scratch. Because the folding pattern, or structure, determines function, once researchers find the right shape, they can reverse engineer the correct amino acid sequence that will create that specific folding pattern.

Rosetta's impressive computational power allows researchers to predict how proteins — long, complex chains of amino acids — will fold; the platform also helps them reverse engineer synthetic proteins to perform specific tasks in medicine and other fields.

their amino acids must align in equilibrium. The trouble is that the equilibrium state is just one of hundreds of thousands of options — or millions, if the amino acid sequence is long. That's far too many possibilities to test one at a time. Nature must have another way of operating, given that folding is almost instantaneous.

Baker's initial approach was to study what nature was doing. He broke apart proteins to see how individual pieces behaved, and he found that each fragment was fluctuating among many possible structures. "And then folding would occur when they all happened to be in the right geometry at the same time," he says. Baker designed Rosetta to simulate this dance for any amino acid sequence.

Baker wasn't alone in trying to predict how proteins fold. In 1994, the protein research community organized a biennial competition called CASP (Critical Assessment of Protein Structure Prediction). Competitors were given the amino acid sequences of proteins and challenged to anticipate how they would fold.

The first two contests were a flop. Structures that competitors number-crunched looked nothing like folded proteins, let alone the specific proteins they were meant to predict. Then everything changed in 1998.

FUNCTION FOLLOWS FORM

That summer, Baker's team received 20 sequences from CASP, a considerable number of proteins to model. But Baker was optimistic: Rosetta would transform protein-folding prediction from a parlor game into legitimate science.

In addition to incorporating fresh insights from the bench, team members — using a janky collection of computers made of spare parts — found a way to run rough simulations tens of thousands of times to determine which fold combinations were most likely.

They successfully predicted structures for 12 out of the 20 proteins. The predictions were the best yet, but still approximations of actual proteins. In essence, the picture was correct, but blurry.

Improvements followed rapidly, with increased computing power contributing to higher-resolution models, as well as improved ability to predict the folding of longer amino acid chains. One major leap was the 2005 launch of Rosetta@Home, a screensaver that runs Rosetta on hundreds of thousands of networked personal computers whenever they're not being used by their owners.

Yet the most significant source of progress has been RosettaCommons, the community that has formed around Rosetta. Originating in Baker's laboratory and growing with the ever-increasing number of University of Washington graduates — as well as their students and colleagues — it is Baker's communal brain writ large.

Dozens of labs continue to refine the software, adding insights from genetics and methods from machine learning. New ideas and applications are constantly emerging.

The communal brain has answered Anfinsen's big question — a protein's specific amino acid alignment creates its unique folding structure — and is now posing even bigger ones.

"I think the protein-folding problem is effectively solved," Baker says. "We can't necessarily predict every protein structure accurately, but we understand the principles.

"There are so many things that proteins do in nature: light harvesting, energy storage, motion, computation," he adds. "Proteins that just evolved by pure, blind chance can do all these amazing things. What happens if you actually design proteins intelligently?"

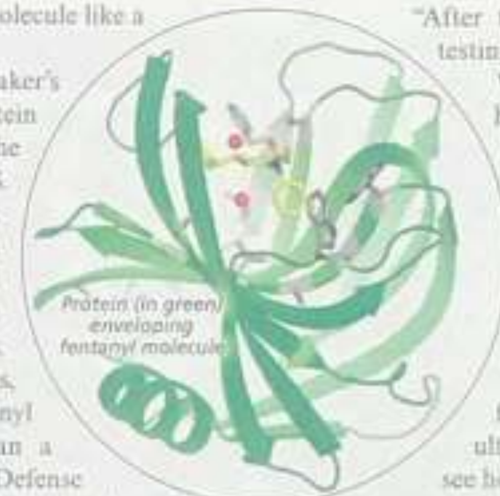
"Proteins that just evolved by pure, blind chance can do all these amazing things. What happens if you actually design proteins intelligently?"

DE NOVO DESIGN

Matthew Bick is trying to coax a protein into giving up its sugar habit for a full-blown fentanyl addiction. His computer screen shows a colorful image of ribbons and swirls representing the protein's molecular structure. A sort of Technicolor Tinkertoy floats near the center, representing the opioid. "You see how it has really good packing?" he asks me, tracing the ribbons with his finger. "The protein kind of envelops the whole fentanyl molecule like a hot dog bun."

Matthew Bick

A postdoctoral fellow in Baker's lab, Bick engineers protein biosensors using Rosetta. The project originated with the U.S. Department of Defense. "Back in 2002, Chechen rebels took a bunch of people hostage, and there was a standoff with the Russian government," he says. The Russians released a gas, widely believed to contain a fentanyl derivative, that killed more than a hundred people. Since then, the Defense Department has been interested in simple ways to detect fentanyl in the environment in case it's used for chemical warfare in the future.



Protein (in green) enveloping fentanyl molecule

Proteins are ideal molecular sensors. In the natural world, they've evolved to bind to specific molecules like a lock and key. The body uses this system to identify substances in its environment. Scent is one example; specific volatiles from nutrients and toxins fit into dedicated proteins lining the nose, the first step in alerting the brain to their presence. With protein design, the lock can be engineered to order.

For the fentanyl project, Bick instructed Rosetta to modify a protein with a natural affinity for the sugar xylotetraose. The software generated hundreds of thousands of designs, each representing a modification of the amino acid sequence predicted to envelop fentanyl instead of sugar molecules. An algorithm then selected the best several hundred options, which Bick evaluated by eye, eventually choosing 62 promising candidates. The protein on Bick's screen was one of his favorites.

"After this, we do the arduous work of testing designs in the lab," Bick says.

With another image, he reveals his results. All 62 contenders have been grown in yeast cells infused with synthetic genes that spur the yeasts' own amino acids to produce the foreign proteins. The transgenic yeast cells have been exposed to fentanyl molecules tagged with a fluorescing chemical. By measuring the fluorescence — essentially shining ultraviolet light on the yeast cells to see how many glow with fentanyl — Bick can determine which candidates bind to the opioid with the greatest strength and consistency.

Baker's lab has already leveraged this research to make a practical environmental sensor. Modified to glow when fentanyl binds to the receptor site, Bick's customized protein can now be grown in a common plant called thale cress. This transgenic weed can cover terrain where chemical weapons might get deployed, and then glow if the dangerous substances are present, providing an early warning system for soldiers and health workers.

The concept can also be applied to other biohazards. For instance, Bick is now developing a sensor for aflatoxin, a residue of fungus that grows on grain,

Cassie Bryan, a senior fellow at Baker's Institute for Protein Design at the University of Washington, checks on a tube of synthetic proteins. The proteins, not seen in nature, are in the process of thawing and being prepped to test how they perform.

causing liver cancer when consumed by humans. He wants the sensor to be expressed in the grain itself, letting people know when their food is unsafe.

But he's going about things differently this time around. Instead of modifying an existing protein, he's starting from scratch. "That way, we can control a lot of things better than in natural proteins," he explains. His *de novo* protein can be much simpler, and have more predictable behavior, because it doesn't carry many million years of evolutionary baggage.

For Baker, *de novo* design represents the summit of his quarter-century quest. The latest advances in Rosetta allow him to work backward from a desired function to an appropriate structure to a suitable amino acid sequence. And he can use any amino acids at all — thousands of options, some already synthesized and others waiting to be designed — not only the 20 that are standard in nature for building proteins.

"The current world is quite a bit different than the world in which we evolved. We live much longer, so we have a whole new class of diseases."

Without the freedom of *de novo* protein design, Baker's Death Star would never have gotten off the ground. His group is now also designing artificial viruses. Like natural viruses, these protein shells can inject genetic material into cells. But instead of infecting you with a pathogen, their imported DNA would patch dangerous inherited mutations. Other projects aim to take on diseases ranging from malaria to Alzheimer's.

In Baker's presence, protein design no longer seems so extraordinary. Coming out of a brainstorming session — his third or fourth of the day — he pulls me aside and makes the case that his calling is essentially the destiny of our species.

"All the proteins in the world today are the product of natural selection," he tells me. "But the current world is quite a bit different than the world in which we evolved. We live much longer, so we have a whole new class of diseases. We put all these nasty chemicals into the environment. We have new needs for capturing energy.

"Novel proteins could solve a lot of the problems that we face today," he says, already moving to his next meeting. "The goal of protein design is to bring those into existence." ◻

Contributing editor ***Jonathon Keats'*** *most recent book is You Belong to the Universe: Buckminster Fuller and the Future.*

Know Your Enemy

A surge of research into ancient killers may help us outsmart them in the future.

BY GEMMA TARLACH

Two key developments allowed the current flood of research into ancient pathogens: powerful new data-crunching software and many more ancient genomes available for study, such as from these 4,500-year-old skeletons in Mongolia (left) and a partial jaw from Germany (right), both of which contained the hepatitis B virus (above).

The deadliest and most devastating opponents our species has faced have never been across a battlefield. They've been on our skin and in our blood and bones.

Viruses and bacteria have killed or debilitated millions during the course of human history — and well before. Researchers have unraveled the story of a few, most notably the bacterium *Yersinia pestis*, which causes plague. But findings about the origins and evolution of other scourges, including leprosy, hepatitis B and syphilis, have been elusive or contradictory.

Now, two key advances — a surge in ancient DNA samples and powerful computer programs to process the data — are allowing scientists to study disease-causing bacteria and viruses like never before.

"There were very few ancient human virus samples even six months ago," says Terry Jones, a computational biologist at the University of Cambridge. "In terms of being 'ancient,' 300 years was considered old, and that was only two or three samples. Now we're finding viruses up to 7,000 years old. ... We've gone from zero to this almost out of the blue."

Jones and fellow Cambridge computational biologist Barbara Mühlemann were key members of a team that published the oldest known genome of the hepatitis B virus (HBV) in *Nature* in May. The roughly 4,500-year-old sample was one of a dozen ancient HBV genomes found as the researchers sifted through one of the largest databases of ancient human DNA ever assembled.

Mühlemann, a co-lead author of the paper, says advances are being made not just in how far back researchers can find ancient pathogens, but in how many they're finding: "Where before we saw maybe one genome sequenced, now we see three, or 10, or 12."

A partial skull from a 7,000-year-old site in Kärsdorf, Germany, provided DNA from the hepatitis B virus, the oldest sample ever obtained.

The reign of Jones and Mühlemann's HBV genome as world's oldest was short-lived: That same week, in the online journal *eLife*, a separate team reported additional HBV genomes up to 7,000 years old, including now-extinct strains previously unknown to science.

NEEDLES IN A HAYSTACK

Hunting ancient pathogens is a recent offshoot of paleogenetics, which focuses on the extraction and sequencing of ancient DNA (aDNA) from animals, including humans, and plants. The primary challenges of working with aDNA from these macroorganisms are degradation — genetic material breaks down over time — and contamination.

Paleogeneticists interested in sequencing human aDNA, for example, will extract a sample from human remains, filter out both modern and non-human genetic material — generally the result of microbial contamination — and look at what's left. The ancient pathogen hunters, on the other hand, will take that same sample and try to identify every single fragment of genetic code.

That's where things get chaotic. Researchers estimate that there may be up to a trillion species of bacteria and closely related archaea, compared with about 8 million species *combined* of plants, animals, fungi and algae. To complicate matters, bacteria in particular are notorious for horizontal gene transfer: picking up bits of DNA from other organisms and integrating it into their own. Then there are viruses, some of which carry their genetic code in DNA, and others in RNA, complicating identification.

"We don't choose what to study. We look at the data and see what comes out," says Jones. "It may be genetic material from the host, or a parasite, or bacteria, or another virus, or DNA from the food they ate the day before they died, or even from something they came into contact with."

Powerful new software tools can sort through all the ancient genetic fragments in a sample and match them to millions of sequences from organisms across a broad spectrum of biodiversity.

Researchers estimate that there may be up to a trillion species of bacteria and closely related archaea, compared with about 8 million species *combined* of plants, animals, fungi and algae.

Limits remain, however. Viruses in particular are wily targets. Blood-borne HBV, for example, lingers in an individual, including their bones, for years. But many other viruses cause acute infections, fatal or otherwise, without leaving a trace of their presence behind.

"The number of viruses you can expect to find in ancient human DNA samples is not very large," Jones says.

WRITTEN IN BONE

Bacteria, however, can be easier to find. Some bacterial diseases, such as leprosy and syphilis, can leave distinctive marks on victims' bones. *Mycobacterium leprae*, which causes leprosy, damages peripheral nerves, reducing sensation. Over time, this leads to increased risk of injuries and infections that cause localized cell death. Bones, especially of the extremities, appear to dissolve. Syphilis, one of a handful of diseases caused by the bacterium *Treponema pallidum*, leads to inflammation of the connective tissues surrounding bones and can cause bone lesions.

In June, University of Zurich paleogeneticist Verena Schuenemann and colleagues published three *T. pallidum* genomes after sampling human remains with bone lesions. The genetic material may not seem ancient — the individuals were buried in a 17th-century Mexico City cemetery — but they are the oldest *T. pallidum* genomes known, and the first to be sequenced from archaeological material, a feat researchers in an earlier study considered "not possible."

Paleogeneticist Verena Schuenemann (above) and colleagues typically examine bones for signs of disease to determine which are most likely to retain traces of certain pathogens. Her team recently found genetic material from the bacterium that causes leprosy in a medieval Danish skull (right) with pitting indicative of the disease.

Schuenemann credits a new program called MALT that can process hundreds of millions of genetic sequences in a few hours.

Schuenemann also used MALT to find 10 new samples of ancient *M. leprae* DNA in individuals with telltale skeletal deformities from several medieval European cemeteries. The genomes, reported in May in *PLOS Pathogens*, included the oldest published *M. leprae* genome: an English sample that's about 1,500 years old.

In 2005, an early attempt to understand the evolution of *M. leprae* concluded that the pathogen most likely arose in the Middle East or Eastern Africa, with only a few strains making it to Europe. But the newly published ancient genomes reveal almost all of the major strains of the bacterium were present in Europe.

"The evolutionary history of *M. leprae* is much more complex than previously thought to be," says Schuenemann. "Already in [medieval] Europe we find a much higher diversity than assumed."

> "The evolutionary history of *M. leprae* is much more complex than previously thought to be," says a paleogeneticist.

In fact, the newest findings hint that *M. leprae* may have originated in Western Eurasia, perhaps Europe itself.

THE BIG PICTURE

Ideas about the origins of syphilis are also up for revision. It's often been called a New World disease, thought to have spread globally only after widespread European contact with Native Americans. But there's some inconclusive skeletal evidence that syphilis and related diseases have been present worldwide for millennia. The three new *T. pallidum* genomes are too few to answer the question definitively, but they are valuable puzzle pieces researchers will be able to use, one day, to see the big picture.

Likewise, a *Current Biology* study published in July described the earliest evidence of *Salmonella enterica*, which causes deadly enteric fever, in northern Europe. The bacterium was found in the bones and teeth of a young woman who died about 800 years ago in Norway. What's surprising is that the particular variety found is rare today in Europe and North America; it's much more common in Asia and Africa. A bacterium of the same type was also identified in 16th-century victims in Mexico, according to a January study in *Nature Ecology & Evolution*.

Combined, the data allowed researchers to dig deep into

Different subspecies of *Treponema pallidum* (left) cause syphilis and other treponemal diseases. Researchers long thought it impossible to find the bacterium in archaeological remains due to DNA degradation. In June, however, a team identified and sequenced *T. pallidum* genomes from bones (above) interred at a centuries-old Mexican cemetery.

S. enterica's past, something that was previously impossible to do because only modern genomes of the pathogen were available for study. Their conclusions: The bacterium was once much more widespread globally and thousands of years older than thought — and may have jumped to humans through contact with early domesticated pigs.

Similar recent studies on lesser-known pathogens are redefining our shared histories. Jones and Mühlemann collaborated with colleagues on a study published in July in *PNAS* that used aDNA to change our understanding of human parvovirus B19 (B19V). The virus causes a common, mild childhood disease but can have more serious consequences in adults. Previous research based on modern strains suggested B19V arose in the early 1900s, but the *PNAS* study found it in human remains that were up to 6,900 years old.

Just how far back will ancient pathogen hunters find their quarry?

"The general assumption for the survival of aDNA is 1 million years," says Schuenemann, who adds that some microbes are more likely than others to be preserved. "I actually have hope to find very old *M. leprae* DNA; it has a very thick additional cell wall layer that seems to also protect its DNA."

> **While the chronological cutoff point for finding genetic material from ancient pathogens is still unknown, each new genome found offers hints about an even deeper past.**

While the chronological cutoff point for finding genetic material from ancient pathogens is still unknown, each new genome found offers hints about an even deeper past.

The three ancient HBV genomes presented in the *eLife* study earlier this year, for example, are more closely related to strains that still infect non-human primates in Africa than they are to modern strains. That could bolster a theory that the virus may have found its first human hosts on that continent. Jones believes it's even possible that HBV was present in species ancestral to our own.

"What's the chance of it not infecting an earlier species?" he asks. "The virus has been around for hundreds of millions of years. We've just started to open the window to see what the truth is, but we're nowhere near the bottom of it."

The new research is not just about hindsight. Nearly a million people die each year from complications of hepatitis B infection, and leprosy still infects more than 200,000 people annually. Syphilis is considered a re-emerging global public health threat, with about 6 million new cases each year.

"Working on ancient pathogens has implications for modern-day pathogens: Understanding the evolution of a bacterium, its past spread and diversity leads to a better knowledge of how this bacterium changed over time and adapted to environmental changes," Schuenemann says.

And thanks to gene transfer and other quirks of evolution, bacteria and viruses are especially wily at adapting.

"Fossilized animals that are extinct are not coming back, but in the case of viruses, they can come back," says Jones. "Parts of them can come back. You'll never see, for example, an elephant with a mammoth head, but that can happen with viruses. When we study the past, we know what may happen in the future. It gives us a way to anticipate future changes." ◼

Gemma Tarlach is senior editor at Discover.

The shoebox-sized KickSat releases numerous tiny Sprite satellites in this illustration. The cheap, abundant and self-contained Sprites could represent the next step in space tech.

A Sprite-ly Spacecraft

Scientists hope the world's smallest satellites will boldly go where no probe has gone before. BY STEVE NADIS

During an interview at a Boston-area cafe, Zac Manchester apologized for not bringing along a copy of his latest satellite — one of many duplicates due to enter orbit this fall during a mission to the International Space Station (ISS). "Don't worry," says Manchester, a Stanford University professor of aeronautics and astronautics. "I'll put one in an envelope and mail it to you."

Even a small envelope would suffice, given that Manchester has created the tiniest satellite yet. The Sprite, as it's called, weighs just 4 grams and measures less than 2 square inches — roughly the size and weight of a standard sugar packet.

Such diminutive spacecraft, assembled from off-the-shelf components at a cost of about $25 apiece, could play a big role in future space exploration, Manchester says. They may even represent our best chance of getting a human-made device to a star other than the sun. An upcoming ISS mission should show him just how close we already are.

SLOW STARTS

Manchester started working on the project in 2009, shortly after he began graduate studies at Cornell University, following up on earlier work by his adviser Mason Peck and fellow graduate student Justin Atchison. By early 2011, he had already produced some preliminary versions of the Sprite. When a last-minute spot opened up on a space shuttle flight that year, he and Peck managed to get their experiment to the ISS. Astronauts mounted three of the devices to the outside of the space station during a space walk. Three years later, all were still working, proving the electronics could withstand the harsh space environment.

The next big challenge is to get Sprites flying freely in space, where they can talk with each other and with Earth-based command posts.

Zac Manchester holds the original 2014 KickSat, full of Sprites. A new version, KickSat-2, should launch in November.

Manchester's Sprites went on to fly on the hulls of the Latvian-German Venta 1 satellite and the Italian-German Max Valier satellite, which launched into low-Earth orbit in June 2017. The Sprites are still attached to their host satellites today, having demonstrated they can harness solar energy and successfully communicate with ground stations.

The next big challenge is to get Sprites flying freely in space, where they can talk with each other and with Earth-based command posts. The first attempt came in April 2014, with the launch of around 120 Sprites aboard a shoebox-sized satellite called KickSat-1 — so named because Manchester financed the mission through a crowdfunded KickStarter campaign.

But the Sprites' release had to wait more than two weeks because of a NASA request to keep the area clear for a Russian Soyuz launch. After that delay, KickSat-1 failed to discharge its Sprites because of an electrical problem likely caused by exposure to radiation. As a result, the whole spacecraft burned up during atmospheric re-entry without having released the Sprites.

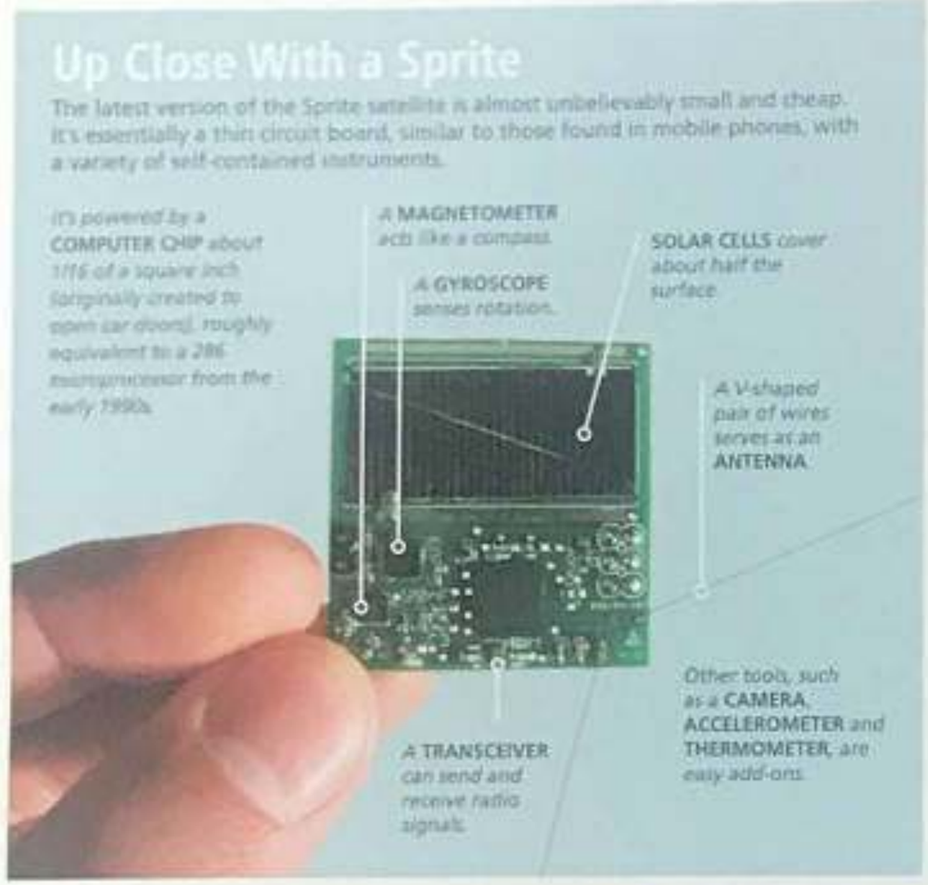
A LOOMING LAUNCH

Hopes now rest on KickSat-2, another shoebox-sized craft set to launch in November from NASA's Wallops Flight Facility in Virginia. It took Manchester more than four years to try again because of difficulties securing a Federal Communications Commission (FCC) license, required to communicate with ground facilities in the United States. The FCC was also concerned about orbital debris and the ability to detect the minute spacecraft, which can be difficult to track.

"That has posed a problem for the entire small-satellite research community," says Manchester. He managed to skirt this issue by handing over responsibility for the mission to NASA Ames Research Center, for whom he had previously worked.

Once KickSat-2 enters its prescribed orbit, Manchester and his team can issue commands from the ground to release its roughly 100 Sprites from a spinning container, so that they'll naturally spread out in space. "They'll fly for a few days to a couple of weeks, at most, before they burn up, which makes for a short-lived experiment," he says.

The mission's primary goal is to establish communications among the minute satellites through an approach called mesh networking, which involves passing messages to nearby satellites so that information eventually propagates to all the Sprites. Although it's a




Along with large light sails, Sprites could be part of an ambitious plan to send a spacecraft to the nearest exoplanet within 20 years.

standard technique on Earth, it has never been done in space.

Secondary goals will be to test the Sprites' positioning and navigational abilities, such as determining the distance between individual satellites by sending radio signals and measuring the transit times. "All of these steps are building blocks toward enabling large-scale spacecraft swarms to act collectively," Manchester says.

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THE FUTURE IS NOW

Although KickSat-2 is meant to be a technology demonstration project, Manchester is eager to start doing actual science, too. The swarms of low-cost, disposable flying objects could perform tasks that no single spacecraft can do on its own.

He's already teamed up with Harvard University astronomer Blakesley Burkhart, devising a plan to deploy a separate swarm of small satellites to survey the sky in the low-frequency radio range. These observations cannot be done from the ground, Burkhart explains, because Earth's ionosphere interferes with those frequencies. Such radio waves also have huge wavelengths, in the tens and hundreds of meters, so observations could require a telescope a few kilometers across, Manchester estimates. If researchers can overcome a few minor bugs, an array made up of Sprites could perform the job of a giant telescope at a much lower cost. "This truly is the last frontier for radio astronomy," Burkhart says.

Sprites are also key to another ambitious endeavor, Breakthrough Starshot. Its goal is to launch a squadron of the tiny probes in about 20 years to the Alpha Centauri star system, 4.3 light-years away. These Sprites would likely be equipped with super-lightweight, lens-free cameras 100,000 times smaller than conventional cameras because, Manchester notes, "it's all on a chip."

He's already looking forward to one photo in particular, taken as his satellites race by at 20 percent the speed of light: a snapshot of the planet Proxima Centauri B. The picture he has in mind is something like the famous Pale Blue Dot photographs of Earth taken by the Voyager 1 space probe in 1990 as it started leaving the solar system.

"I'm hopeful that in a few decades, we'll get a picture like this," Manchester says, "not looking back at Earth, but looking toward a new Earth." ◼

Steve Nadis, a contributing editor to Discover and Astronomy, plays handball and volleyball in Cambridge, Massachusetts, where he also lives.

20 Things You Didn't Know About ...

Lasers

BY ERIKA K. CARLSON

Counterclockwise from top right: Laser tattoo removal; workers at the world's largest laser facility, in California; a beam reflected off a mirror; a map of hidden buildings found through lidar; mirrors placed on the moon decades ago to measure distance using Earth-based lasers.

1 Chances are, you can thank a laser for helping you get through the day. The technology lets us do everything from scan groceries at the checkout to remove regretted tattoos. **2** The word *laser*, coined in 1957, is an acronym for "light amplification by stimulated emission of radiation." Since that -*er* ending makes a laser seem like a doer of something, it soon spawned the verb "to lase." **3** Unlike the sun or a flashlight, which shines in a broad range of colors combined to produce white light, lasers lase by producing a concentrated beam of a single wavelength, or color. **4** In 2016, scientists created a new type of microlaser, smaller than a red blood cell, which could lead to innovations in medical imaging. **5** That same year, the world's most powerful laser, China's Superintense Ultrafast Laser Facility (SULF), fired a single pulse equivalent to 5.3 petawatts — 5.3 *quadrillion* watts! **6** SULF isn't the world's largest laser, however. That would be California's National Ignition Facility (NIF), about the size of three football fields. The megalaser can deliver the same amount of energy released by a couple pounds of TNT to a target the size of a pea. **7** Ultimately, researchers want to use NIF's energy to trigger a nuclear fusion reaction, squishing the nuclei of hydrogen atoms together to make helium and producing energy the same way stars do. **8** Speaking of stars, give a big gold one to the true inventor of lasers, whomever that may be. Three scientists shared the 1964 Nobel Prize for work leading to the first lasers, but grad student Gordon Gould designed one before the laureates — one of whom was also his adviser. **9** Gould sued and finally received patent rights in 1977. A fifth scientist actually built the first working laser, in 1960. **10** Since then, lasers have landed a lot of Nobels, including in 2017. That award went to team leaders at the Laser Interferometer Gravitational-wave Observatory (LIGO), who were first to measure long-predicted ripples in space-time. **11** Lasers play a starring role in another measuring method: light detection and ranging. A lidar system shoots out a laser pulse, calculates how long it takes the pulse to bounce back, and determines how far away an object is, like bats using echolocation to find dinner. **12** It's not batty to think lidar will be part of driverless car technology. Engineers are experimenting with it to monitor the vehicle's surroundings and judge when to brake. **13** Archaeologists use aircraft-based lidar to map a different kind of surrounding: sites hidden beneath dense forest canopies. **14** In 2016, researchers using lidar described vast ancient cities in Cambodia's rainforests. The extensive urban network reached its zenith in the 12th century and may have been the largest empire on Earth at the time. **15** Astronomers, meanwhile, use lasers to measure real-time turbulence in Earth's atmosphere. With this information, they can adjust telescope mirrors to account for atmospheric blurring and make sharper images, a technique called adaptive optics. **16** If an aircraft flew into one of these laser beams, the crew could be disoriented. Facilities that use adaptive optics employ spotters whose sole job is to watch the night skies for planes straying too close, ready to flip an emergency shut-off switch. **17** The precision afforded by adaptive optics has resulted in images of exoplanets in other star systems and even two supermassive black holes colliding hundreds of millions of light-years away. **18** The laser-based Strategic Defense Initiative, proposed in 1983 and nicknamed "Star Wars," soon fell into a metaphorical black hole, but laser weapons aren't all fiction. The Department of Defense is developing systems that can take down drones and even small planes and boats. **19** *Star Wars* the movie featured a giant planet-destroying laser, but when scientists shoot lasers at our moon, it's for peaceful purposes. The beams fire at mirror arrays placed on the lunar landscape by astronauts from several Apollo missions. **20** Aiming lasers at these moon mirrors measures the precise distance to our satellite sidekick, and has revealed that the moon is slowly moving away from us. Hey, Moon, was it something we said? ■

Erika K. Carlson grew up in Livermore, the home of NIF. She writes this in fond memory of physics professor Alfred Kwok, who had an infectious enthusiasm for lasers.