HOW THE BRAIN LISTENS TO THE GUT WEIGHT-LOSS SURGERY REVEALS THE DEEP CONNECTION BETWEEN MIND AND DIGESTION PAGE 46

SCIENTIFIC AMERICAN

EVOLVED TO EXERCISE

Why humans—unlike our ape cousins—must stay active to be healthy

PLUS

THE PARTICLE CODE
New math for the world's largest accelerator PAGE 30

CAN WE REVERSE CLIMATE CHANGE?
How to pull a trillion tons of carbon from the atmosphere PAGE 52

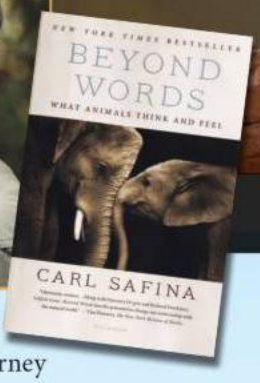
CANCER CARE
Removing barriers to lifesaving drug trials PAGE 60

JANUARY 2019
ScientificAmerican.com

Lions, Tigers and Tradewinds

A PRIVATE JET EXPEDITION

HOSTED BY *Carl Safina*



Conservationist and writer Carl Safina will host this journey throughout, offering insights on wild lands and wildlife, and humans' relationship to the living world. Author of seven books, including *Beyond Words: What Animals Think and Feel*, Dr. Safina's work has been awarded the MacArthur, Pew, and Guggenheim Fellowships, among others.

"Join me and Bushtracks Expeditions' president David Tett as we take a great-cat-sized bite out of a great swath of two continents. And, we will also experience parts of the Middle East and the Indian Ocean. Our itinerary promises lands and luxuries, coasts and comforts, lions and tigers and maybe even bears. This is an itinerary for the curious, for the seeker, for those willing to get the greatest view of all—a view at ourselves not in the mirror but from the outside, looking in. There will be an enormity of concepts to explore, and things to see and enjoy. I hope to see you at boarding!"

Carl Safina

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VOLUME 320, NUMBER 1

SCIENTIFIC AMERICAN

ON THE COVER

Humans have evolved to be far more active than our closest living relatives, the great apes. Our bodies need a good deal of exercise to function normally because unlike the plant-eating apes, humans had to adapt to a physically demanding hunting-and-gathering way of life. **Illustration by Bryan Christie.**

Photograph by Liz Tormes

SCIENTIFIC AMERICAN

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ON THE WEB

A Space-Based Building Boom?
Scientific American reports on new efforts from NASA and other federal agencies seeking to service and assemble large structures—such as life-finding telescopes—in space. *Go to www.ScientificAmerican.com/jan2019/space-based*

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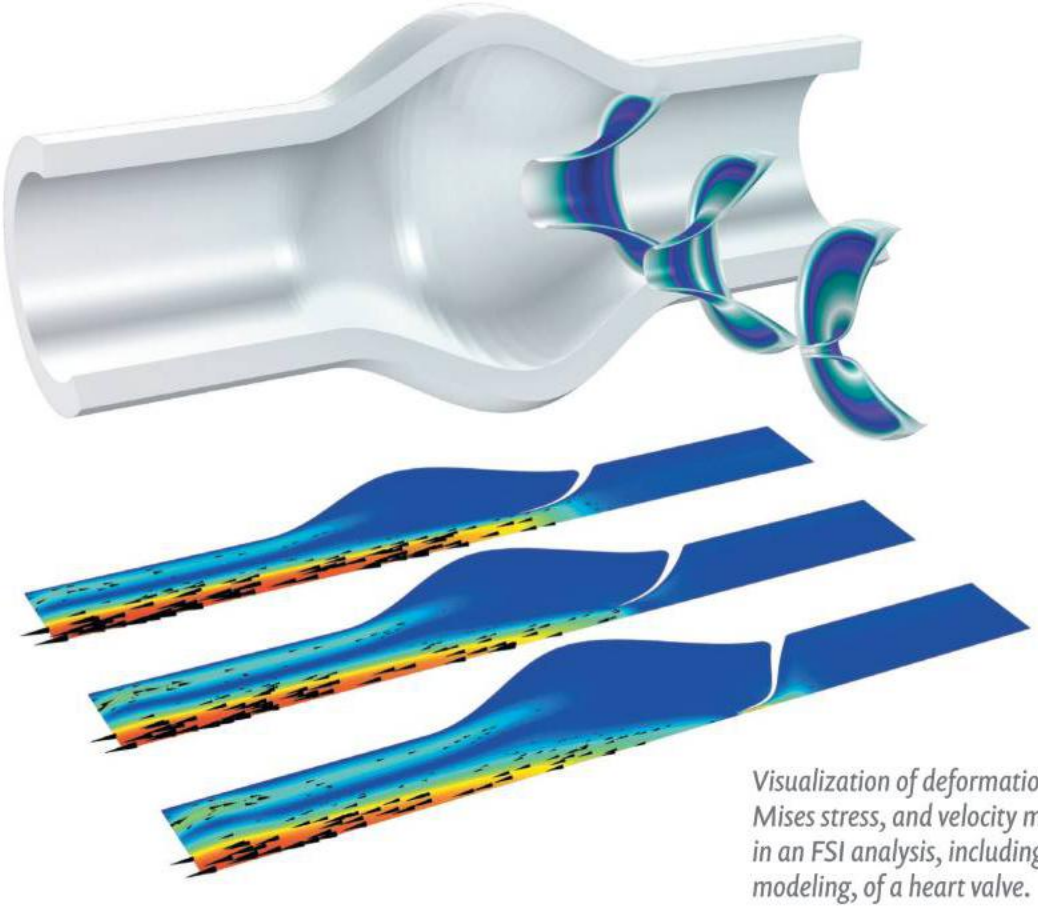
EVGENY A. PODOLSKIY (*middle*)

Visualize and predict heart valve behavior with multiphysics simulation.



Visualization of deformation, von Mises stress, and velocity magnitude in an FSI analysis, including contact modeling, of a heart valve.

Open fully, close tightly. The four valves in the human heart are expected to do this with each beat. When the valves do not function properly, cardiac health issues arise. In the quest for more effective treatments, medical researchers are studying heart valves to understand and predict their behavior. To accurately visualize a heart valve, you need to account for many coupled effects. Multiphysics simulation is up for the task.

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Mariette DiChristina is editor in chief of *Scientific American*. Follow her on Twitter @mdichristina

Running for Our Lives

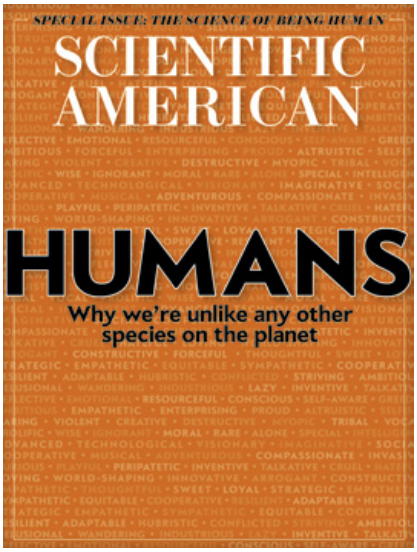
People talk a lot about the merits (or not) of the prehistoric hunting-and-gathering "Paleo diet": the idea is that eating the way we had to eat over thousands, even millions, of years would be most conducive to salubrious lives. And it makes some sense that providing the right kind of fuel for our bodies is valuable. But regardless of the exact foods in our diet, as you will learn in our cover story, it's far more important for us to be active to be healthy.

"Our taking fewer than 10,000 daily steps is associated with increased risk of cardiovascular and metabolic disease," writes Herman Pontzer of Duke University, author of the feature article "Evolved to Exercise." Unfortunately, he adds, "U.S. adults typically clock about 5,000 steps, which contributes to the alarming rates of type 2 diabetes, affecting one in 10 Americans, and heart disease, which accounts for a quarter of all deaths in the U.S." In contrast, our ape cousins are relatively sedentary yet experience none of the health ailments that we would suffer at similarly low levels of activity. And although chimpanzees have naturally high levels of cholesterol, they do not develop humanlike heart disease. Even in captivity they stay lean and rarely develop diabetes. What's going on? Why are humans the "odd ape out," as Pontzer calls us? Skip your fingers over to page 22 to learn what research is revealing about our endlessly fascinating species.

Whereas exercise has many positive effects on our well-being, Pontzer reminds us that weight loss unfortunately isn't really one of them. (He explained the reasons more fully in his feature "The Exercise Paradox" in the February 2017 issue.) Many of us struggle to avoid excess calories, even though we *know* we should be swapping in vegetables and fruit instead of reaching for those tempting bags of chips and cookies.

Are we instead being sabotaged by the microbes that live in our own gut? Recent research in rodents and in patients who have undergone bariatric surgeries suggests that may be the case. These operations reduce the size of the stomach, and they have now been found to have additional effects; namely, they can change how the brain areas involved in communicating with the gut behave. In "Mind over Meal," medical writer Bret Stetka discusses how these parts of the brain become hyperactive compared with their earlier activity. As a result, people may become satiated sooner, enabling new, beneficial eating habits. The story is ready to be consumed on page 46. Bon appétit! SA

Illustration by Nick Higgins



September 2018

LONELY LIFE

John Gribbin makes a number of excellent arguments for humans being the only intelligent life in the galaxy in "Alone in the Milky Way" ["Beyond Us," Part 3 of our single-topic issue, *A Singular Species: The Science of Being Human*]. But the same processes that eventually allowed intelligent life to emerge on our planet are still in play. As our galaxy continues to evolve, we might expect increasing opportunities for this situation to be repeated.

Greg Konesky
Hampton Bays, N.Y.

Gribbin's assumptions are preposterous. The galaxy is 100,000 light-years across. We sent our first radio transmissions around 120 years ago, so a response from beings a mere 65 light-years away would still have a distance to travel to us. And how far would our own transmissions go before they became so faint and dispersed as to become unrecognizable?

Art Cassel *Riverside, Calif.*

The accompanying graphic "Chain of Improbable Coincidences" lacks one component: at the moment of the big bang, all the laws of nature happened to exist from the get-go. Science proposes the possibility of innumerable other universes. If true, it's important that ours was just right from the start for these events to even occur.

Michael Tyler *Rochester, Mich.*

"Free will can be lost in a world managed by AI."

Brett M. Frischmann *Villanova University*

GRIBBIN REPLIES: Konesky is correct that we may be the first, rather than the only, technological civilization in the Milky Way. But will we still be here when others arise?

Cassel makes the common assumption that radio or other electromagnetic waves would provide the first signs of other civilizations in our galaxy. In fact, the best way to explore the Milky Way would be to build a few self-replicating probes called von Neumann machines, which could travel to nearby stars and make copies of themselves from the raw materials that surround them. With the exponential growth in the number of probes, they would be able to visit every star in the galaxy in a few million years. The cost would be about the same as that of an instrument such as the James Webb Space Telescope because after the first few, the rest come free. So the Fermi paradox (If there are other civilizations in our galaxy, why haven't they come here?) is as forceful as ever.

Tyler makes an excellent point, which I did not have room to go into. The question of why "our" universe is "just right" is indeed a puzzle for theorists and is a theme of my 2009 book In Search of the Multiverse.

TECH DOOM

I applaud Pedro Domingos for rejecting the sentient-AI-will-enslave-us narrative in "Our Digital Doubles" ["Beyond Us," Part 3]. But in his enthusiasm for anticipated uses of supposedly smart tech, he overlooks how overuse could be harmful.

For example, he envisions a digital double going on millions of virtual dates and living countless probable lives so that it can deliver you the optimal romantic partner and life. But life and romance are not algorithmic optimization problems comprehensible in the language of computation. What if the costs of going on some bad dates let you to learn something about yourself and others? How will you know what you want without any experiences?

Domingos assumes technology necessarily extends human capabilities. As Evan Selinger and I explore in our 2018 book *Re-Engineering Humanity,* this is a significant mistake. For millennia, humans have gained and lost capabilities as they developed and used tools. Take what might be our most fundamental capability—free will—which depends on our built sociotechnical environment. Like romance and even our humanity, free will can be lost in a world managed by AI.

Brett M. Frischmann
Charles Widger Endowed University Professor in Law, Business and Economics, Villanova University

SELF-DECEPTION

In "The Hardest Problem" ["Why Us?", Part 1], Susan Blackmore explores the debate over the nature of human consciousness and how it might differ from the experiences of other animals.

It is difficult not to anthropomorphize nonhuman behavior when observing what appears to be creative activity among some nonhuman primates and perhaps other species. It might be worth hypothesizing that creativity may be an observable marker for consciousness, if only because the animal displaying it must have some capacity for self-reflection and interpretation of its environment and its place in it.

Robert Rodgers
Emeritus professor, College of Pharmacy, University of Rhode Island

Blackmore says that animals do not share the sense of a conscious "I" that humans have. If so, how can we account for the planning shown by some animals, such as squirrels gathering nuts for the winter or dogs burying bones? Both require the sense of a persistent "I" that will be around, and hungry, in the future.

John Orlando *via e-mail*

BLACKMORE REPLIES: In answer to Rodgers: Creativity might be a marker for consciousness, which makes intuitive sense when applied to toolmaking crows or orangutan artists. But what about bowerbirds, which instinctively decorate elaborate constructions, or deep-learning algorithms that write articles? The suggestion that creativity requires a capacity for self-reflection thus fails; deep-learning

algorithms are surely not indulging in it.

Orlando claims that squirrels need "the sense of a persistent 'I'" to store nuts. While this may be true of us storing food in the freezer, squirrels' nut-hiding ability is inherited, and they need have no idea why they are doing it.

Many of us are led astray by powerful but false intuitions about the self. Our self is one of the brain's many constructions, not its controller.

COST OF CITY LIVING

Menno Schilthuizen's article "Darwin in the City" ["Beyond Us," Part 3] discusses how several species have evolved to adapt to urban environments. It made me wonder what we are doing to ourselves. Are modern medicine and the engineering of our living environments causing us to evolve into a species with low disease resistance and weaker ability to cope with different climates?

Ed Herman *Utica, Mich.*

INFORMED SPECIES

In asking the question of how human beings became "a different kind of animal" in "An Evolved Uniqueness" ["Why Us?", Part 1], Kevin Laland emphasizes copying and social learning.

Are these really the *primary* factors in shaping the difference between humans and other species? How do we use a *communal* store of experience to devise *novel* solutions to life's challenges? Someone has to think of the novel solution for the first time. The primary difference for human beings, I would suggest, is that we can imagine future possibilities, beyond what we can see or touch now.

Kevin Loughran
Belfast, Northern Ireland

Laland soft-pedals the essential role the invention of writing played in making humanity unique. Prior to that development, knowledge had to be stored in a brain and conveyed directly from one individual to another. It was thus susceptible to alteration and vulnerable to annihilation. Writing untied knowledge from the limitations of time and place and raised it to a level that made possible a pervasive, interactive, ever growing culture.

Peter Gelfan *via e-mail*

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CONTRIBUTORS
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Toxic Baby Food? Really?

It's time to get arsenic and other heavy metals out of our infants' diets

By the Editors

Many babies' first solid food is rice cereal. It is a childhood staple, commonly recommended by pediatricians. And it is often poisoned—at least a little bit. Studies have found that many brands contain measurable amounts of inorganic arsenic, the most toxic kind. It's not just rice: an August 2018 study by *Consumer Reports* tested 50 foods made for babies and toddlers, including organic and nonorganic brands such as Gerber, Earth's Best, Beech-Nut and other popular labels, and found evidence of at least one dangerous heavy metal in every product. Fifteen of the 50 contained enough contaminants to pose potential health risks to a child eating one serving or less a day.

Heavy metals can impair cognitive development in children, who are especially at risk because of their smaller size and tendency to absorb more of these substances than adults do. Inorganic arsenic in drinking water has been found to lower the IQ scores of children by five to six points. And as heavy metals accumulate in the body over time, they can raise the risk of cancer, reproductive problems, type 2 diabetes, cardiovascular disease and cognitive issues. Of course, finding out your favorite brand is contaminated is not a reason to panic. Low levels of exposure for short periods are unlikely to cause devastating effects, and parents should focus on reducing the overall levels of these toxic substances in their children's total diet to limit harm.

Heavy metals occur naturally on Earth and are present in soil and water. But pesticides, mining and pollution boost their concentrations, and farming and food manufacturing processes can contribute even more. Some crops inevitably absorb more heavy metals. Rice, for example, readily takes in arsenic both because of its particular physiology and because it is often grown in fields flooded with water, which is a primary source of the metal.

Cereal makers are clearly capable of keeping baby food poison-free: roughly a third of the products *Consumer Reports* tested did *not* contain worrisome metal levels. Companies just do not take enough safety steps. "If industry can do a better job of sourcing the raw food, that would go a long way [to reduce the danger]," says James Dickerson, chief scientific officer at *Consumer Reports*. "And then if [manufacturers] consider contamination through internal pathways—equipment, processes and the containers they use for the food—I think we can get there."

Some companies are already trying to investigate the sources of contamination in their products and reduce them. More should follow and be transparent about these efforts. But the best chance of real change from food companies most likely will come with regulation.

Currently there are no U.S. rules on acceptable levels of heavy metals in baby foods. In 2012, 2015 and 2017 Congress tried and failed to pass legislation imposing limits on arsenic and lead in fruit juice and rice products. The FDA proposed issuing new caps on the amount of arsenic allowed in rice cereal in 2016 and in apple juice in 2013, but neither of these proposals ever came to fruition. A March 2018 Government Accountability Office report found that the FDA has not moved quickly enough to finalize the rules or communicate the potential risk to the public. The agency needs to set safe and strict targets, supported by scientific studies, for these substances, ideally by establishing incremental benchmarks that lower the allowable levels over time.

And this is just a start. In 2018 a group of scientists and policy experts suggested a variety of interventions at every step of the pathway from farm to table. These steps would help fight the problem both in the U.S. and abroad, especially in developing countries where toxic substances in baby food can be devastating to children who already suffer from poor nutrition. For one, researchers should conduct more studies on which foods in our diet are the primary contributors of heavy metals and the best ways to reduce the contamination in each of those crops. Food manufacturers can do better and more frequent testing of their source crops as well as their factory methods. Scientists, doctors and governments can also better communicate these health risks and the best ways to avoid them to the public. For instance, cooking rice in copious amounts of water can help flush contaminants out, and parents should feed babies a variety of grain cereals rather than just rice.

There are many ways to deal with this problem. Congress, the FDA, the food industry, scientists and doctors should unite to tackle a serious threat to our most vulnerable population. SA

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Illustration by Francesco Zorzi

Elijah Lowenstein is a Ph.D. candidate in biology at the Max Delbrück Center for Molecular Medicine in Berlin, where he works on sensory neuron diversity.

Diversity in the Lab Makes Me a Better Scientist

It exposes my research to a wealth of different perspectives

By Elijah Lowenstein

Exposure to colleagues from many nations made both my parents better scientists, and now as I begin my own research career, I'm starting to see why. My mother and father traveled the world for their work. They grew up in Argentina during the military dictatorship, got their Ph.D.s, then moved to the U.S. Later, their jobs took them to Scotland, Wales and England before returning to the U.S.

Every time we moved, my parents' new colleagues quickly became friends, and from an early age I was exposed to many different cultural perspectives (not to mention delicious food at potlucks).

Today I am a biologist pursuing my Ph.D. in a laboratory in Berlin. My lab attracts people from all over the world, and getting to interact with them not only enriches me personally, it makes me a better scientist. I am exposed, daily, to challenges from different disciplines and perspectives—challenges that make me better explain the rationale and conclusions of my research. This back-and-forth between challenge and response drives my work forward.

Although there aren't many data on the extent of international diversity in scientific labs, about 35 percent of them on the ResearchGate information-sharing site have one or more members who come from a country outside of where the lab is based. The benefits of such a diverse environment go far beyond my personal anecdotes. The results produced by international teams receive, on average, more citations than those from groups from just one country and are generally published in journals with higher impact factors. I'm not surprised: an international environment forces you to consider different perspectives to begin with and helps you to communicate your ideas more clearly in the end.

The people I collaborate with have backgrounds in electrophysiology, molecular biology, medicine and psychology. Our different scientific backgrounds and research topics and our different ethnicities and cultural upbringings push me outside of my comfort zone. I do not have to explore my basic assumptions when I'm around only people who share my background. But this all changes in a diverse environment. I need to prepare more thoughtfully for collaborations. I need to anticipate disagreement or difficulties in explaining a concept to co-authors or colleagues, and I have to work harder to understand my own project's rationale to begin with. What is more, I consider alternatives, which makes me more flexible in my research down the line.

I also need to change the way that I present my findings to my colleagues. My lab's main language is English, but every day I hear Chinese, German, French and Spanish bouncing around the hallways. Before I begin putting together a presentation, I know that there will be people in the room who are not native English speakers and that I will need to make sure I explain everything clearly. This forces me to think hard about how I frame my research. If I can't explain concepts using clear and precise language, how can I expect colleagues to give me meaningful responses? This approach gives me a head start when I share my work more broadly, at symposia within my institution and at international conferences.

My parents showed me how important global exchanges are, and I was fortunate to be able to build on that experience at the very start of my own research career. During my undergraduate studies, the German Academic Exchange Service RISE program gave me money for a three-month internship in a neuroimaging lab at Kiel University. Other programs, such as the Erasmus Program or Fulbright Scholar Program, offer similar opportunities.

But you don't need to travel if you don't have international colleagues in your workplace. The World Wide Web was originally created to connect scientists, and it offers plenty of ways to link up. Tweet about your research and share early progress to a preprint server such as arXiv or bioRxiv with a massive international audience to get feedback. Or find me on ResearchGate and join my network of people from around the world.

I'm looking forward to meeting you, wherever you're from! SA

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Illustration by Jasu Hu

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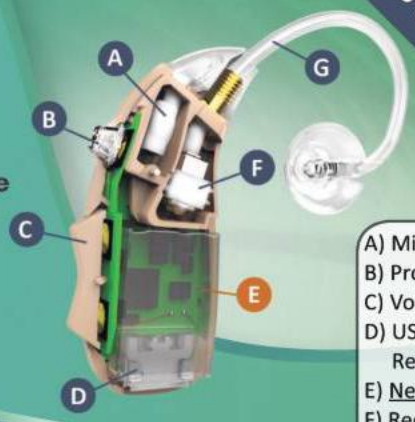

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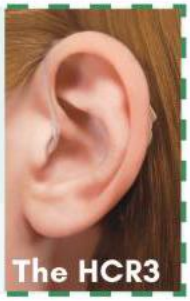

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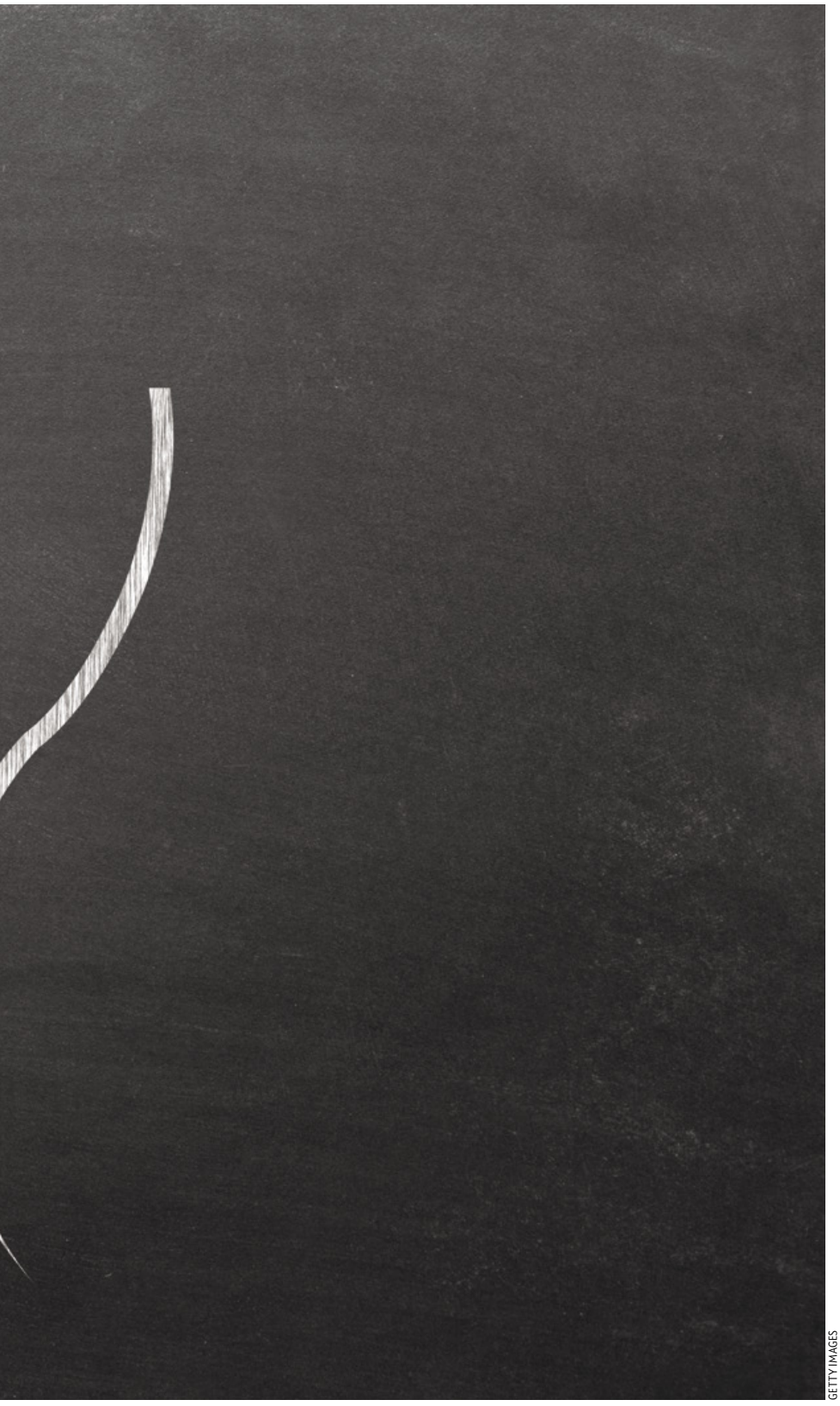
ADVANCES

Scientists are developing a method for measuring the body's inner time.

INSIDE



GETTY IMAGES

CHRONOBIOLOGY

Reading the Body's Clock

A blood test to quantify internal time could yield insight into sleep disturbances and disease

Are you an early-rising lark or a night owl? These terms have gained scientific credibility, with researchers determining such differences have a basis in genetics. The sci-fi-sounding jargon for this inclination is your "chronotype," and it can create significant discrepancies between your internal biological time and the external time shown by the clock on the wall. Now three teams of scientists are converging on a way to read a person's internal time from blood samples. A quick, accurate and cheap method for doing this could maximize the benefits of time-sensitive medical treatments and help researchers study the links between disrupted biological clocks and various chronic diseases.

The system that controls daily biological rhythms is called the circadian clock. It helps to regulate the activity of around 40 percent of our genes, orchestrating rhythms of eating, body temperature and blood pressure. Virtually every cell in the body contains its own circadian clock machinery; the master clock that synchronizes them all—a tiny brain region called the suprachiasmatic nucleus—controls levels of hormones important for the sleep-wake cycle. Chronotypes vary so widely that two people's internal time can differ by eight hours or more. "They can share the same bed without meeting," says chronobi-

ologist Achim Kramer of Charité University Medicine Berlin, who leads one of the groups developing the new technique.

The current gold-standard method of measuring internal time, called dim light melatonin onset, requires numerous blood or saliva samples, taken hourly in low-light conditions. In contrast, the three recent studies describe a simpler technique that needs only one or two blood samples (depending on the exact methods used in each study) and thus could make biological time measurements part of routine clinical practice. The general approach involves assessing fluctuating gene activity by measuring changes in RNA levels in blood. Machine-learning algorithms then "learn" which genes give the best indications of biological time. "Everybody's going in the same direction" in this area of research, says physiologist Derk-Jan Dijk of the University of Surrey in England, who leads one of the other groups. "The field is excited about this."

Computational biologist Rosemary Braun of Northwestern University led the most recent study, which was published last September in the *Proceedings of the National Academy of Sciences USA*. Braun's team claims its method is the most generalizable—it can be used with any technology for analyzing gene activity. But it requires two blood samples, whereas the studies by Kramer's team (published last September and first published online last June, in the *Journal of Clinical Investigation*) and by Dijk's team (published online in February 2017 in *eLife*) describe methods that can work with just one. Kramer and Dijk have validated their approaches against the gold standard; Braun's team has not, making direct comparisons difficult. "It may turn out their measure is better," Dijk says. "But for now we don't know."

The Kramer team's method agrees with the melatonin method to within about half an hour. One reason for this accuracy, Kramer says, is that the researchers extract just one cell type—monocytes, which display strong circadian oscillations—from blood. This requires a more complex blood analysis than the other groups' methods, but Kramer's study is the closest to clinical application, Dijk says.

The next step is to find out how well each group's method works in people whose circadian rhythms have been disrupted by jet lag, shift work or illness, Dijk says. These sleep disturbances can cause numerous ill effects, which some evidence suggests can be mitigated by realigning people's clocks using light exposure or the sleep hormone melatonin. The new technique will enable doctors to monitor the efficacy of such treatments. Circadian disruptions have also been linked to illnesses, including diabetes, heart disease, neurodegenerative diseases and depression. "We know there are links," Braun says. "But we don't know precisely how they work." Providing easy measurements of internal time will help researchers find out.

The effectiveness of some medical treatments, such as chemotherapy or blood pressure medication, varies with the time of day they are administered [see "Take Your Medicine … Now," on page 72]. Exploiting this to maximize a drug's benefits is known as chronotherapeutics. Because people's internal time most likely also makes a difference, being able to measure it more easily would help doctors personalize treatments. "This

EARTH SCIENCE

Icy Nocturnes

Nighttime cracking of Himalayan glaciers could accelerate melting

A spectacular view of Mount Everest was not what most stunned Hokkaido University geoscientist Evgeny A. Podolskiy during his first trip to the Himalayas in October 2017. What shocked him while working and living in the area were the loud, reverberating booms every night.

"The ice was cracking up," says Podolskiy, who has done research in several other glacier environments around the world, including Greenland and the Alps. "I've never come across anything like this before." Aside from one anecdotal observation made in the Arctic, there was no scientific record of such glacial fracturing at night.

The cracking is bad news for the more than a billion people in Asia who rely on these icy reservoirs for water. "This kind of wear and tear on a daily basis can make glaciers more fragile and therefore melt more easily," meaning there will be less water available over time, Podolskiy says.

Trakarding-Trambau Glacier System in Nepal

EVGENY A. PODOLSKIY

To home in on the source of the cracking, Podolskiy and his colleagues installed seismometers throughout the Trakarding-Trambau Glacier System in eastern Nepal—the first such attempt in the Himalayas. The team noticed an interesting pattern: the seismic rumbles came from ice surfaces free of debris. And larger drops in nighttime air temperatures resulted in stronger seismic signals, the team reported last September in *Geophysical Research Letters*.

In contrast, ice blanketed with a layer of loose rocks made little noise, and it was totally silent if the rubble above the ice was thicker than two feet. "The debris, in

could mean lower doses, fewer side effects, greater efficacy," Braun says. "We're really excited about the potential." How big of a difference this timing makes is not clear, however, because it has been difficult to separate patients by chronotype to investigate. This technique could help foster such studies. Grouping patients in this way could also increase success rates of new therapies in clinical trials, Kramer says.

Dijk's team described another breakthrough in a study published online last September in *Sleep*. Using the same approach, the researchers were able to identify—with greater than 90 percent accuracy—participants who had skipped one night's sleep. Such a test could help police identify sleep-deprived drivers involved in traffic accidents or help employers assess whether airline pilots or other staff in safety-critical jobs are fit for work. The test uses 68 genes, which show little overlap with those useful for determining internal time, but whose biological roles may offer insights into how sleep loss affects health.

The internal time and sleep-deprivation tests combined are very powerful, Dijk says: "Because how you perform at 6 A.M. depends on your circadian time but also on how long you've been awake." —*Simon Makin*

effect, protects glaciers from temperature oscillations that make the ice expand and contract cyclically," Podolskiy says. "When the temperature drops sharply, as it does at high elevations, the rapid contraction of unprotected ice breaks it up."

That protection is limited, however, because less than one fifth of the glacier surface in the Himalayas is covered with debris.

Walter Immerzeel, a glacier hydrologist at Utrecht University in the Netherlands, who has worked in the Himalayas for more than 16 years and was not involved in the study, called the finding fascinating. The study "points to a new way that the stability of glaciers can be threatened," Immerzeel says. Cracks not only cause mechanical damage; they also act as conduits for water and heat and can greatly accelerate ice loss, he adds.

As Podolskiy's team plans its future studies in the Himalayas, "a pressing issue is how cracks develop and evolve throughout the year and how this affects water flow within the ice," he says. "This is crucial for a better understanding of the future of Asia's water tower in a world of changing climate." —*Jane Qiu*

Antillean manatee

CONSERVATION TECH

Manatee Songs

New method tallies the elusive mammals based on recordings of their vocalizations

Biologists trying to count endangered Antillean manatees in Costa Rica and Panama face a major challenge: the animals live in murky waters, making them virtually impossible to see. "I rowed back and forth [along Panama's] San San River every day for two years, and all I got to see were some noses," biologist and computer scientist Mario Rivera-Chavarria says. "I could hear them, but I never saw them."

In 2013 Rivera-Chavarria, then at the University of Costa Rica (UCR), and his colleagues at the Smithsonian Tropical Research Institute launched a manatee census in Panama's San San Pond Sak wetlands, an area that borders Costa Rica and includes the San San River. Using a boat equipped with side-scan sonar, which produces images by bouncing sound waves off submerged animals and their environment, the team estimated the manatee population in an 18-kilometer stretch of the San San was as low as two individuals in some months and as high as 33 in others.

But sonar can be disruptive to these animals, so Rivera-Chavarria wanted to prove that the census could be carried out using a less invasive technique. Manatee vocalizations have specific characteristics that allow a trained ear—or computer—to distinguish one individual from another. Rivera-Chavarria recorded the animals' songs with underwater microphones suspended from his kayak as he paddled down the San San. His colleague Jorge Castro, a computer scientist now at Costa Rica's National Center for High Technology, developed an algorithm to automatically count manatees based on the recordings. Castro showed, using a sample of 54 calls that belonged to four different manatees, that his algorithm was 100 percent accurate.

The algorithm breaks the process into four main steps: chopping the recordings into short chunks, canceling out noise, labeling the manatees' calls and clustering the calls by individual. The noise cancellation step takes the longest to process; to speed things up, Castro and his colleague Esteban Meneses used a supercomputer. They translated the algorithm into a programming language that would allow them to carry out tasks in parallel, making the process 120 times faster, the team reported last July at the IEEE International Work Conference on Bioinspired Intelligence.

Next, Castro and his team plan to adjust the algorithm to identify the calls of the clay-colored thrush, Costa Rica's national bird. Roberto Vargas-Masís, an expert in bioacoustics at the National Distance Education University of Costa Rica, who was not involved in the manatee study but aims to participate in the bird research, says: "This technology will allow us to gather and analyze large quantities of data and very quickly determine if the species is present in a specific region."

—Debbie Ponchner

GIOVANNI GROTTO *Alamy*

HEALTH TECH

Googling Heroin

Internet searches offer a novel way to predict overdose deaths

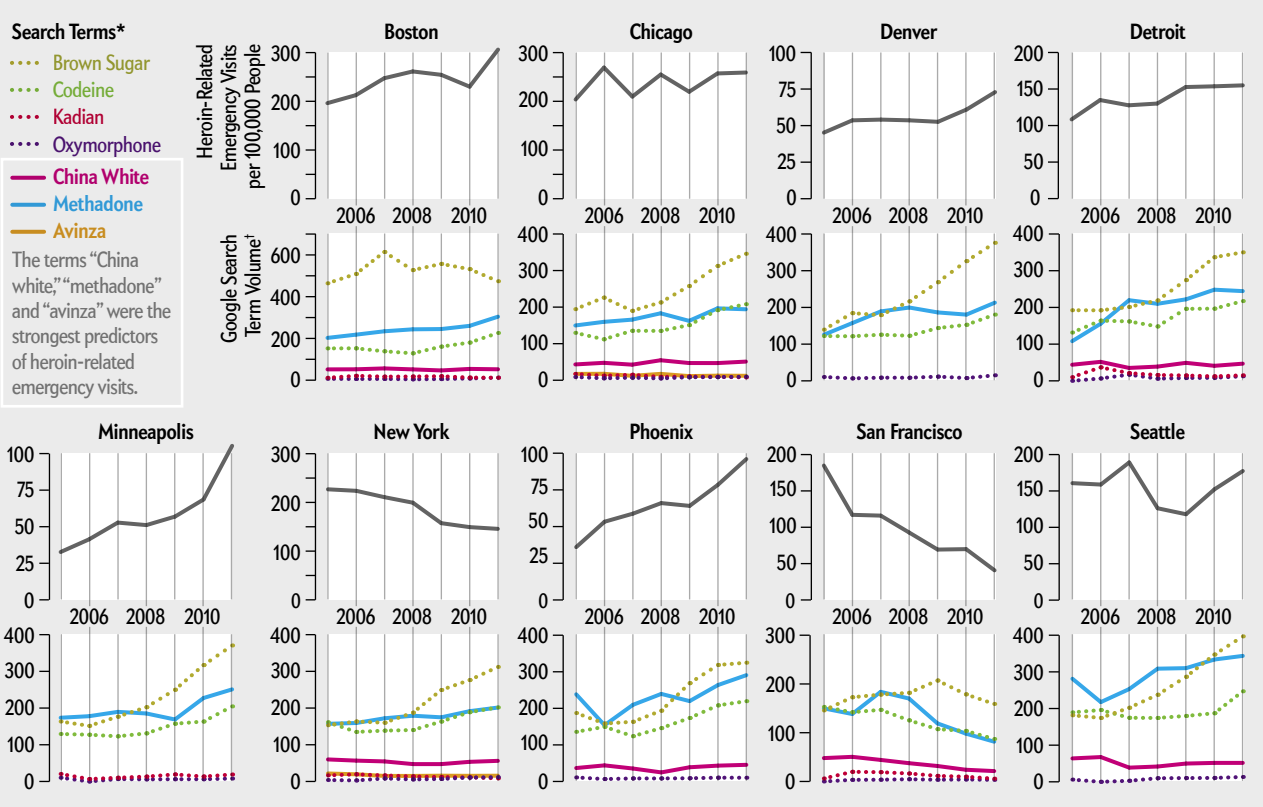
About 115 people nationwide die every day from opioid overdoses, according to the U.S. Centers for Disease Control and Prevention. A lack of timely, granular data exacerbates the crisis; one study showed opioid deaths were undercounted by as many as 70,000 between 1999 and 2015, making it difficult for governments to respond. But now Internet searches have emerged as a data source to predict overdose clusters in cities or even specific neighborhoods—information that could aid local interventions that save lives.

The working hypothesis was that some people searching for information on heroin and other opioids might overdose in the near future. To test this, a researcher at the University of California Institute for Prediction Technology (UCIPT) and his colleagues developed several statistical models to forecast overdoses based on opioid-related keywords, metropolitan income inequality and total number of emergency room visits. They discovered regional differences (*graphic*) in where and how people searched for such information and found that more overdoses were associated with a greater number of searches per keyword. The best-fitting model, the researchers say, explained about 72 percent of the relation between the most popular search terms and heroin-related E.R. visits. The authors say their study, published in the September issue of *Drug and Alcohol Dependence,* is the first report of using Google searches in this way.

To develop their models, the researchers obtained search data for 12 prescription and nonprescription opioids between 2005 and 2011 in nine U.S. metropolitan areas. They compared these with Substance Abuse and Mental Health Services Administration records of heroin-related E.R. admissions during the same period. The models can be modified to predict overdoses of other opioids or narrow searches to specific zip codes, says lead study author Sean D. Young, a behavioral psychologist and UCIPT executive director. That could provide early warnings of overdose clusters and help to decide where to distribute the overdose reversal medication Naloxone.

Still, this approach has limitations. Not everyone uses Google, and some search terms lacked important context: "brown sugar" (slang for a type of heroin) was the most popular one for opioids in the majority of cities studied, but the researchers noted that their model could not distinguish it from the baking ingredient. In addition, the overdose data in the study were relatively old.

Jeanine Buchanich, a biostatistician at the University of Pittsburgh, who was not involved in the prediction study, says that "the paper highlights the need for new, innovative approaches to analyzing data related to the opioid epidemic." —*Rod McCullom*



*Search terms may refer to slang for heroin and other opioids.

†Google search term volume is the probability of the search based on geography and time period, multiplied by 10 million for readability.

SOURCE: "INTERNET SEARCHES FOR OPIOIDS PREDICT FUTURE EMERGENCY DEPARTMENT HEROIN ADMISSIONS," BY SEAN D. YOUNG ET AL., IN *DRUG AND ALCOHOL DEPENDENCE*; VOL. 190; SEPTEMBER 1, 2018

Graphic by Amanda Montañez

JAMES BREY *Getty Images*

SUSTAINABILITY

The Grass Is Not Greener

Experts want to swap traditional lawns with something more sustainable

Cruise through many neighborhoods or parks around the world, and you will find no shortage of well-manicured expanses of grass. Lawns look attractive, but they also choke out biodiversity and can require environmentally questionable practices to maintain. In dry areas of the U.S., three quarters of annual household water use is for lawns. As climate change becomes more and more urgent, these grassy plots only make things worse.

Researchers and landscape architects are increasingly considering alternatives that are more sustainable, demand fewer resources and help people connect more intimately with nature. In an article published last October in *Science,* researchers Maria Ignatieva and Marcus Hedblom describe the drawbacks of conventional lawns and discuss possible substitutes. SCIENTIFIC AMERICAN spoke with Ignatieva, who is landscape architecture program director at the University of Western Australia. An edited excerpt of the conversation follows. —*Annie Sneed*

Why did lawns become so popular?

Lawns came to be seen as a symbol of civilization and a way of life. They were like a special frontier that separated cities and towns from the wilderness. A lawn was always a symbol of how a civilized society should be. That's why it was so powerful. And of course, they are also important for recreation.

Lawns are artificial, though; they do not exist in the natural world. They have relatives in nature, such as meadows or prairies. Those ecosystems have similar structures, but they are much more diverse and are not densely planted or developed.

What environmental problems are lawns causing?

Lawns are homogenizing the environment, not only in terms of biodiversity but also visually. You compare countries' and cities' urban landscapes around the world, and they look exactly the same.

There are a lot of ecosystem services that lawns can offer, unlike a hard surface such as cement or asphalt. Lawns sequester atmospheric carbon, produce oxygen and prevent erosion. But lawn upkeep takes resources: water; fertilizer, pesticides and herbicides that enter groundwater and runoff water; and mowers that burn fossil fuels and emit gases that heat up the atmosphere.

And not all countries have the means to support lawns, especially in dry environments. Alternatives can provide the same ecosystem services with fewer resources.

What are these alternatives?

You have to find your own local solution. We can take inspiration from the natural plant communities around us. In suburban and rural areas, that might mean having a meadow or prairie. In other places, it might be a savannalike environment or mountain plants. You can have a "grass-free lawn," with only low-growing plants that create the same effect as a lawn, and you can walk on it.

People are so used to having green grass as a symbol of wealth, but it is time now to appreciate nature as it is, by using other varieties of color and appearance and function. It is about having a heterogeneous landscape instead of a homogeneous one; it is about the benefit of bringing nature to people and making life easier, more sustainable and more economical.

How can we persuade people to adopt these alternatives?

When people see them, they appreciate them and like them. So it is all about education. We also have to try to change the minds of decision makers, including politicians. We need to show the public there are different ways of handling our urban environment and making it better.

GETTY IMAGES

GENETICS

Going the Distance

A genetic tweak may have helped give humans their running ability

Roughly two million to three million years ago, a primate moved from the forest to the savanna. It grew longer legs, larger muscles and wider feet. It developed sweat glands that allowed it to remain cool under the blazing African sun. It was also around this time, according to recent research, that a mutation in a single gene called *CMAH* spread throughout the species. Now a study in mice supports the idea that this genetic tweak enabled humans to run long distances and hunt their prey to exhaustion.

According to biologist Ajit Varki of the University of California, San Diego, the mutation rendered the *CMAH* gene completely inactive. Varki wondered if there was a link between this genetic event and a knack for long-distance running. Because all humans share the same nonfunctional gene, he could not simply compare the running abilities of people with different versions of it. But he had spent years studying mice bred to have the same *CMAH* inactivation as humans to gain insight into diabetes, cancer and muscular dystrophy. Varki's work suggested a link between *CMAH* loss and muscle biology, but he needed proof.

"For about 10 years I've been trying to convince somebody in my lab to put these mice on a treadmill," Varki says. When he finally did the experiment, "lo and behold, without any training, [the *CMAH*-deficient mice] were one and a half times better at running." The rodents' muscles—especially those in their hind limbs—used oxygen more efficiently and were more resistant to fatigue. The results were published in September in the *Proceedings of the Royal Society B.*

In 2004 Harvard University biologist Daniel Lieberman had hypothesized that running—as opposed to bipedal locomotion alone—played a major role in human evolution. Lieberman, who was not involved in the new mouse research, says it is "the first really good, careful genetic study that fits our predictions" about running's role in the rise of modern humans.

—Jason G. Goldman

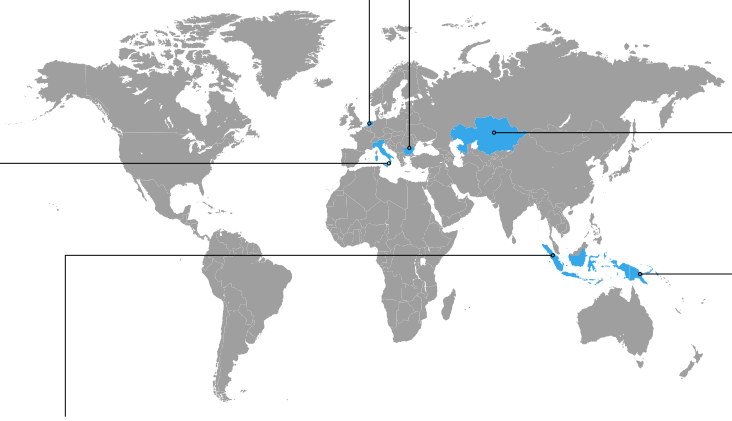
IN THE NEWS

Quick Hits

By Emiliano Rodríguez Mega

THE NETHERLANDS
A court of appeals in The Hague has ruled that the Dutch government needs to take action to help stop climate change. The ruling states that the country must reduce greenhouse gas emissions to at least 25 percent below 1990 levels by 2020.

BULGARIA
The world's oldest intact shipwreck was discovered at the bottom of the Black Sea, off the coast of Bulgaria. Radiocarbon analysis suggests the wood vessel dates back to 400 B.C.



KAZAKHSTAN
An astronaut and a cosmonaut escaped a Russian spacecraft that experienced a launch failure shortly after takeoff. Nick Hague and Alexey Ovchinin landed safely after their capsule made an emergency separation from the rocket.

ITALY
Europe's most restless volcano, Mount Etna, is slowly sliding into the sea under its own weight. If part of it collapses suddenly, researchers say it could trigger megatsunamis in the Mediterranean Sea.

PAPUA NEW GUINEA
Health authorities detected the first polio outbreak in Papua New Guinea in 18 years. The three cases were identified in Morobe Province, where sanitation is limited and vaccine coverage is low.

INDONESIA
The construction of a hydroelectric dam and power plant in North Sumatra's Batang Toru forest caused orangutans from an endangered, newly described species to flee the project site. The government has sent guards to monitor the apes, which have built their nests on local plantations.

For more details, visit www.ScientificAmerican.com/jan2019/advances

TECH

Facial Recall

App for identifying faces raises privacy concerns

Large gatherings such as weddings and conferences can be socially overwhelming. Pressure to learn people's names only adds to the stress. A new facial-recognition app could come to the rescue—but privacy experts recommend proceeding with caution.

The app, called SocialRecall, connects names with faces via smartphone cameras and facial recognition, potentially eliminating the need for formal introductions. "It breaks down these social barriers we all have in terms of initiating the protocol to meet somebody," says Barry Sandrew, whose start-up, also called SocialRecall, created the app and tested it at an event attended by about 1,000 people.

After receiving an invitation to download SocialRecall from an event organizer, a prospective user is asked to take two selfies and sign in via social media. At the event, the app is active within a previously defined geographical area. When a user points his or her phone camera at an attendee's face, the app identifies the individual, displays the person's name, and links to his or her social media profile. To protect privacy, it recognizes only those who have consented to participate. And the app's creators say it automatically wipes users' data after an event.

Ann Cavoukian, a privacy expert who runs the Privacy by Design Center of Excellence at Ryerson University in Toronto, commends the app's creators for these protective measures. She cautions, however, that when people choose to share their personal information with the app, they should know that "there may be unintended consequences down the road [with] that information being used in another context that might come back to bite you."

The start-up has also developed a version of the app for individuals who suffer from prosopagnosia, or "face blindness," a condition that prevents people from recognizing individuals they have met. (Sandrew, who has prosopagnosia himself, notes that the app has not yet been tested on others with the condition.) To use this app, a person first acquires an image of someone's face, from either the smartphone's camera or a photograph, and then tags it with a name. When the camera spots that same face in real life, the previously entered information is displayed. The collected data are stored only on a user's phone, according to the team behind the app.

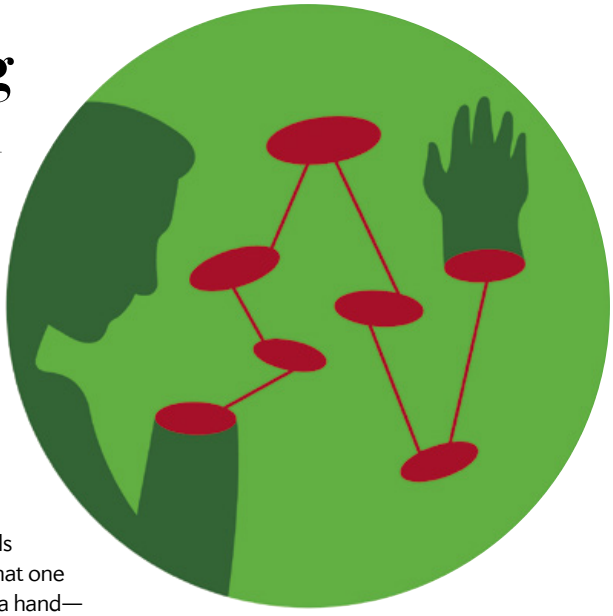
Jason Schultz, a professor of clinical law at New York University, who was not involved with the app's creation, remains wary: "The cost to everyone whom you are surveilling with this app is very, very high, and I don't think it respects the consent politics involved with capturing people's images." —*Agata Blaszczak-Boxe*

Illustrations by Thomas Fuchs

NEUROSCIENCE

Vanishing Free Will

Scientists identify the brain networks involved in the sense of agency



When Ryan Darby was a neurology resident, he was familiar with something called alien limb syndrome, but that did not make his patients' behavior any less puzzling. Individuals with this condition report that one of their extremities—often a hand—seems to act of its own volition. It might touch and grab things or even unbutton a shirt the other hand is buttoning up. Patients are unable to control the rebellious hand short of grabbing or even sitting on it. They seem to have lost agency—that unmistakable feeling of ownership of one's actions and an important component of free will. "It was one of those symptoms that really questioned the mind and how it brings about some of those bigger concepts," says Darby, now an assistant professor of neurology at Vanderbilt University.

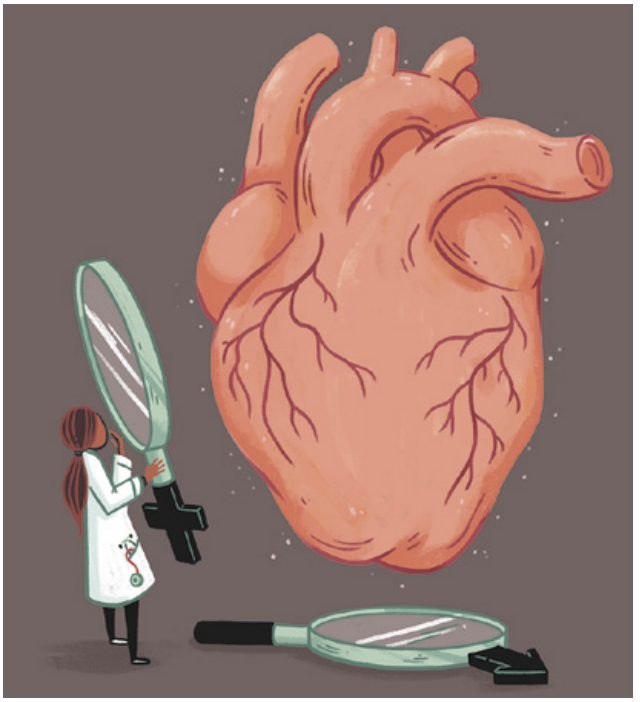
Alien limb syndrome can arise after a stroke causes a lesion in the brain. But even though patients who have it report the same eccentric symptoms, their lesions do not occur in the same place. "Could the reason be that the lesions were just in different parts of the same brain network?" Darby wondered. To find out, he and his colleagues compiled findings from brain-imaging studies of people with the syndrome. They also looked into akinetic mutism—a condition that leaves patients with no desire to move or speak, despite having no physical impediment. Using a new technique, the researchers compared lesion locations against a template of brain networks—that is, groups of regions that often activate in tandem.

Lesions associated with alien limb syndrome all mapped onto a network of areas connecting to the precuneus, a region previously linked to self-awareness and agency. In patients with akinetic mutism, the lesions were part of another network centered on the anterior cingulate cortex, which is thought to be involved in voluntary actions. These two networks also include brain regions, which, when stimulated by electrodes in previous studies, altered subjects' perceptions of free will, the team reported in October in the *Proceedings of the National Academy of Sciences USA*.

Individuals who have alien limb syndrome often report that their hand seems to act of its own volition.

The study suggests at least some components of free will—volition and agency for movements—are not localized in any one brain area but instead rely on a network of regions. The perception of will may break down with disruption to any part of that network.

"This is a creative way of using data that's been sitting around for decades and reconceptualizing it to learn something actually new and make sense of things that didn't make sense before," says Amit Etkin, an associate professor of psychiatry at Stanford University, who was not involved in the work. Studies of many other brain conditions could benefit from taking such an approach, he adds. —*Bahar Gholipour*



What Ails a Woman's Heart

The more we look, the more we find sex differences in cardiovascular disease

By Claudia Wallis

Consider almost everything you know about heart disease, particularly the garden-variety type involving high cholesterol levels, clogged coronary arteries, stents and bypass surgeries. Now I want you to rebrand all that as "male-pattern" cardiovascular disease. That's how some researchers are reframing it after taking a closer look at heart disease in women.

For years cardiologists were baffled as to why up to half of women with classic symptoms of blocked vessels—chest pain, shortness of breath and an abnormal cardiac stress test—turn out to have open arteries. Doctors called it "cardiac syndrome X." They didn't understand it, and many women were subjected to repeated angiograms in search of blockages that weren't there.

That still happens today, but more doctors now recognize that despite having open arteries, about half of women with this pattern nonetheless have ischemia—poor blood flow through the heart. The condition has gained a mouthful of a name: ischemia and no obstructive coronary artery disease, or INOCA.

Cardiologist C. Noel Bairey Merz has spent more than 20 years overseeing the Women's Ischemia Syndrome Evaluation (WISE) study, aimed at demystifying INOCA and related conditions. Although male-pattern disease is the most prevalent type in both sexes, "INOCA probably comprises 25 to 30 percent of ischemic heart disease in women and 10 percent in men," says Bairey Merz, director of the Barbra Streisand Women's Heart Center at Cedars-Sinai's Smidt Heart Institute. WISE data show that after diagnosis, women with the disorder face a 2.5 percent annual risk of dying, suffering a nonfatal heart attack or stroke, or being hospitalized for heart failure. They are also four times more likely than men to be readmitted to a hospital within 180 days of being treated for a heart attack or severe chest pain.

The initial mystery of INOCA was how the heart could be starving for blood if its main arteries are not blocked. The answer often lies in the smaller branches and twigs of the vascular system—arterioles and capillaries that deliver oxygen and nutrients to heart muscle. The walls of these vessels are too thin to accumulate plaque, but they can become dysfunctional, failing to contract or dilate as needed—when, for example, someone is walking up a flight of stairs or is hit by an emotional shock.

Half to two thirds of INOCA cases can be traced to such dysfunction, which is detected with specialized scanning or testing via catheter. Why women are so susceptible is not fully known, says cardiologist Puja K. Mehta of Emory University's Women's Heart Center. Many of the usual suspects are implicated—smoking, diabetes, high blood pressure, high cholesterol—but a history of problems during pregnancy, such as elevated blood pressure and diabetes, and of depression and autoimmune diseases, both of which are more common in women, may also contribute.

Optimal therapy remains a work in progress. Smallish studies show that many drugs used to treat male-pattern disease, including statins and ACE inhibitors, can help patients with INOCA. The first truly large-scale trial comparing an intensive drug regimen with "usual care" in 4,422 women got underway in early 2018. Its results, due out in 2022, should help set treatment standards.

Effective therapy is badly needed. Women with microvascular dysfunction often go on to develop heart failure. And not just any heart failure but a particularly female version. In men, the typical problem is that the ventricles don't squeeze effectively; this is called heart failure with reduced ejection fraction, or HFrEF (pronounced "hef-ref"). In women, the more frequent issue is that the ventricles don't relax enough to fill properly; this is heart failure with preserved ejection fraction, or HFpEF ("hef-pef").

Both types are rising in the U.S. because the population is getting older, fatter and more diabetic. As cardiologist Linda Peterson of the Washington University School of Medicine in St. Louis notes: "More people survive their heart attacks, so they are dying of heart failure down the road." HFrEF is well understood. "We have buckets of knowledge and treatment for [it]," Bairey Merz says, "but essentially no effective therapy for HFpEF. Had we studied women 50 years ago, we wouldn't be in this situation."

Just about everything we know about heart disease in women has been learned since the early 1990s, when the National Institutes of Health began requiring that women be included in the studies it funds. Before that, most medical research was conducted on guys: male patients, male rats, male mice, male monkeys, male cells. Like most gender gaps, this one is closing slowly. SA

Claudia Wallis is an award-winning science journalist whose work has appeared in the *New York Times*, *Time*, *Fortune* and the *New Republic*. She was science editor at *Time* and managing editor of *Scientific American Mind*.

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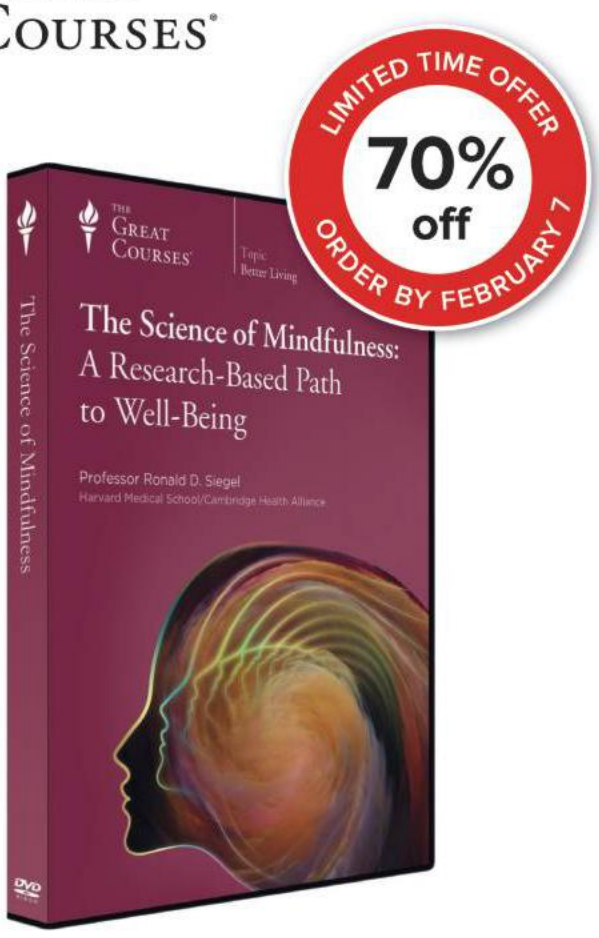

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David Pogue is the anchor columnist for Yahoo Tech and host of several *NOVA* miniseries on PBS.

Six Lessons about Technology

What's changed since my first *Scientific American* column

By David Pogue

My inaugural column in these pages, eight years ago, explored the world of crowdsourced answer Web sites. My last *Scientific American* column—well, you're reading it. My tenure here has aligned neatly with the rise of everything in the headlines today: smartphones, apps, social media, self-driving cars, AI, augmented reality, voice assistants, data breaches. So I thought I'd leave you with six lessons about technology. These are hard-won bits of wisdom, gleaned from decades of observing two fascinating populations: tech companies and the rest of us.

Just because they make it doesn't mean you need it. The big tech companies chase after new ideas like first-grade soccer players chasing the ball en masse. They're running that way not because it's strategic but because everyone *else* is running that way.

Oh, the billions of dollars blown on Amazon's DOA smartphone, Google's discontinued Glass wearables or Apple's failed social-media networks! Oh, the sadness of those early adopters who bought those pre-iPad tablets, Microsoft's smartwatches or Internet refrigerators!

Maybe we can forgive them. Not everyone can be Steve Jobs, capable of knowing what the masses want before they do themselves. Without that insight, all the companies can do is imitate their competitors so they won't be left out. If you're baffled by the appeal of some heavily hyped tech invention, there's nothing wrong with you. It's the inventor's problem, not yours.

Frictionless always wins. If you want to place bets on the success of new technologies, examine how much "friction" they eliminate: effort, steps and hassle. The remote control; microwave meals; e-mail; text messages; the iPod; Google Maps; Amazon.com; Siri and Alexa; and, yeah, self-driving cars—each, in its way, introduced a new way to let us be lazier.

Innovation in a category slows down. When a new product category appears, it's a bare-bones invention. The first iPhone, for example, had no front camera, no flash, no copy/paste, no voice recognition, no video recording. The first few years of a new invention, therefore, are filled with breakthroughs as the manufacturers fill in the holes. Eventually, though, every product reaches its ultimate incarnation. Some have been there for years; when's the last time you felt the need to replace your dryer, flashlight or microwave because it doesn't have the latest features? Already it's becoming harder and harder for Apple, Google, Microsoft and Samsung to dream up new must-have features for their phones, tablets and laptops. Too bad for them—but good for you. You can keep your existing gadget that much longer.

Complexity creeps. The tech business model is: feed the upgrade cycle. Make last year's product look inadequate—usually, by adding features. Unfortunately, sooner or later, the new tweaks become increasingly inessential—and the product becomes increasingly more complex. (I'm guessing it's been a while since you used Microsoft Word's creation features for Web pages.)

Utopia never arrives. So much tech promises to make the world a better place. Social media will make us a harmonious global family! Self-driving cars will save lives! The Internet will give everyone a voice, democratizing the whole world! Alas, the law of unintended consequences means all those utopias never seem to arrive. Social media has turned into a breeding ground for hate-mongers. Self-driving cars may destroy insurance companies and ride-sharing outfits. And the Internet is becoming more cesspool than community pool.

Doomsday never arrives, either. On the other hand, we tend to overpredict the *negative* effects of new technologies, too. Every generation has its "that's gonna rot your brain" technology. My grandparents were told to quit sitting so long in front of that infernal radio. For me, it was the television. For our kids, it's the smartphone. These technologies certainly change us, but that doesn't mean they actually make us worse—and they've never actually brought the end of the world. Somehow we muddle through. Thanks for reading and for thinking. See you on Twitter, the Web, TV—or whatever the industry decides we need next. SA

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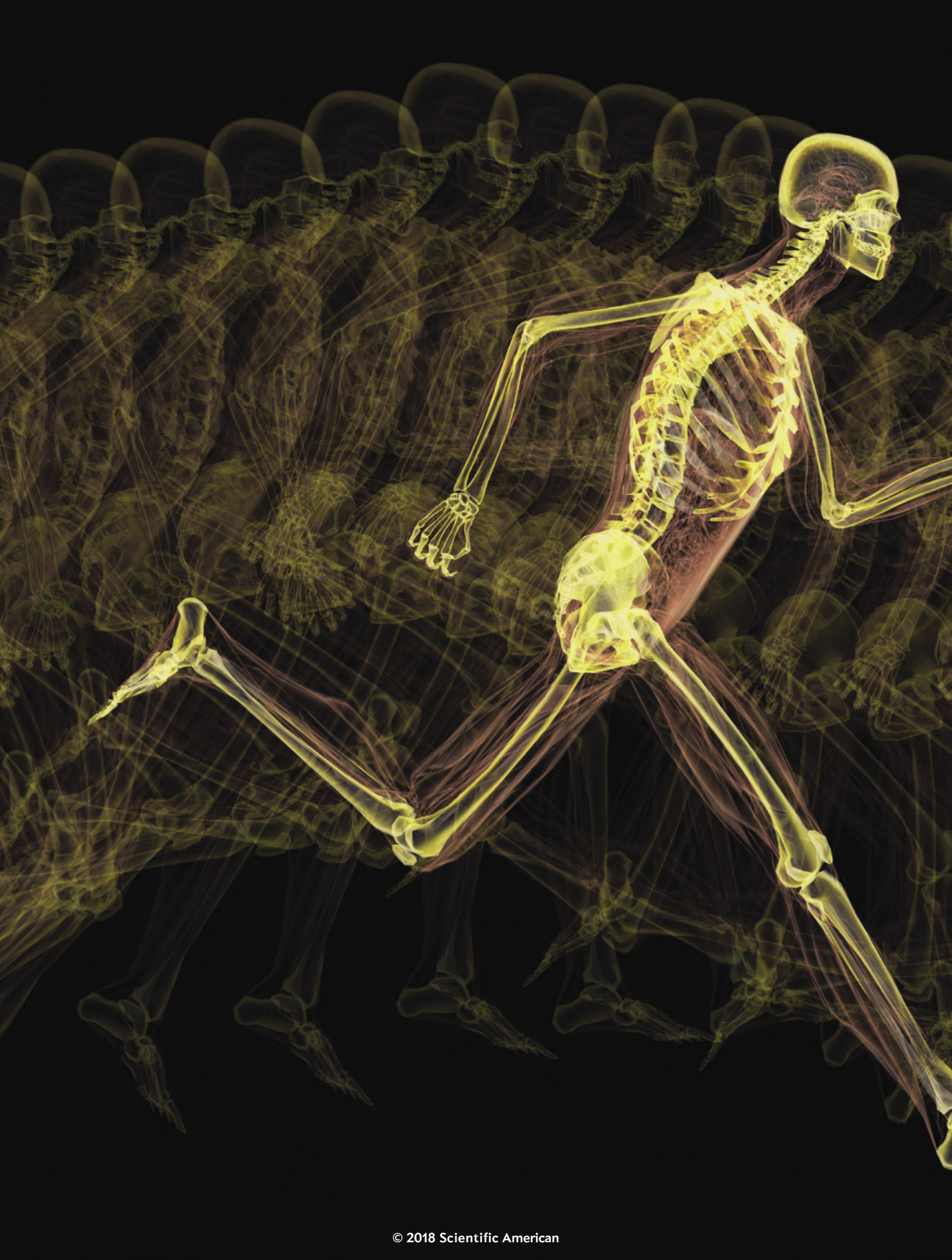
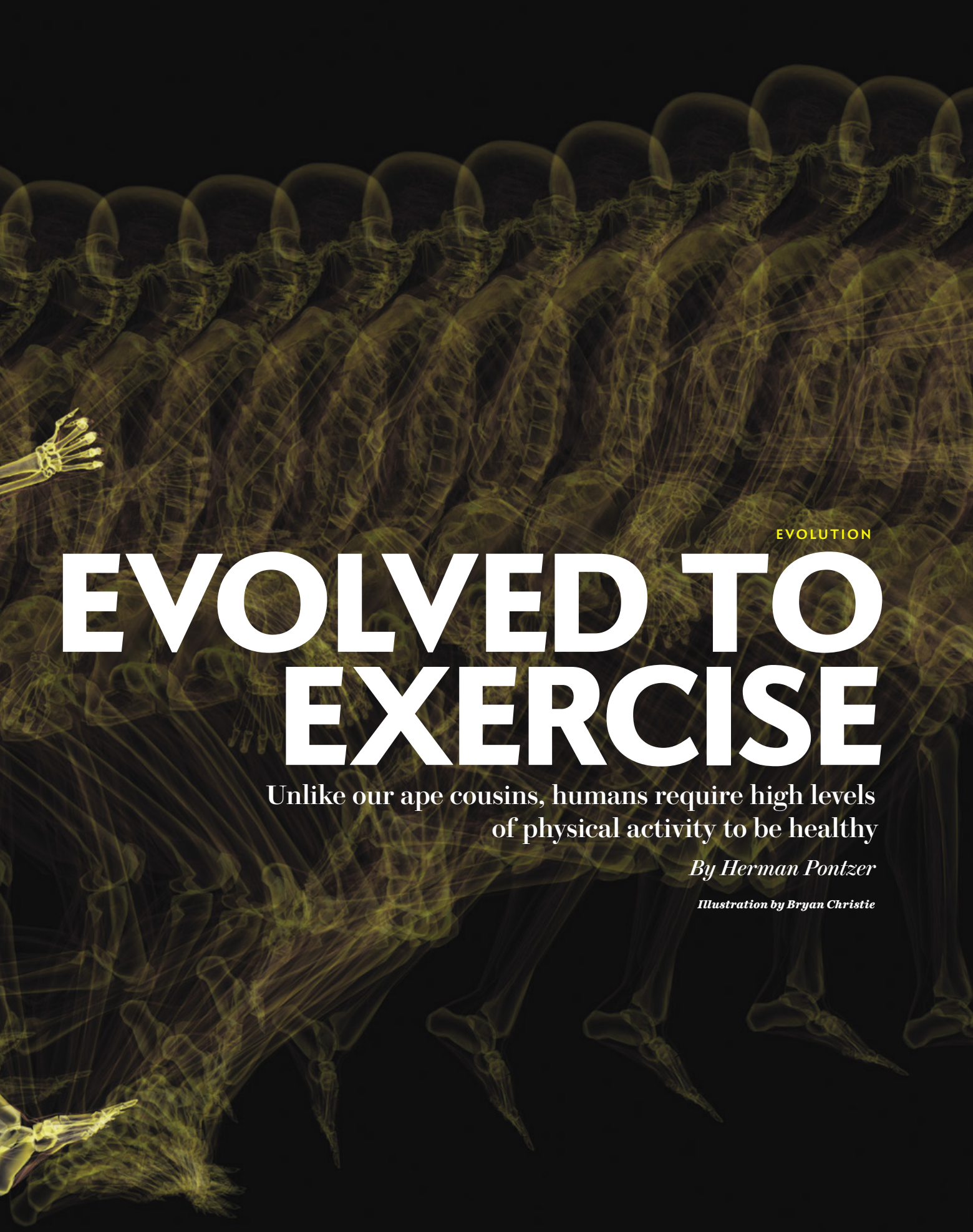




EVOLUTION

EVOLVED TO EXERCISE

Unlike our ape cousins, humans require high levels of physical activity to be healthy

By Herman Pontzer

Illustration by Bryan Christie

Herman Pontzer is an associate professor of evolutionary anthropology at Duke University. He studies how evolution has shaped human physiology and health.

IN THE PREDAWN DAMP OF A UGANDAN RAIN FOREST NEARLY 20 YEARS AGO, I STARED UP THROUGH the crowded canopy at a party of eight chimpanzees sleeping overhead. Our team of three researchers and two field assistants had woken up an hour before, wiggling into rubber boots and hastily assembling backpacks before setting out on muddy trails by headlamp. Now at our destination, the lights were off, and we stood there silently, submerged in a black ocean of forest, the surface 30 meters above, listening to the chimps chuffing and shifting in their leafy nests.

IN BRIEF

Our closest living relatives, the great apes, have habitually low levels of physical activity yet suffer no ill health effects from being lazy.
Humans have evolved to require far higher levels of exercise to be healthy.
New research reveals that as human anatomy and behavior shifted over the past two million years, so, too, did physiology.
Our physiology adapted to the intensive physical activity that hunting and gathering requires.

As a young Ph.D. student studying human and ape evolution, I was in Kibale National Park that summer to measure how much chimpanzees climb each day. It seemed to me that the energy spent climbing might be a critical factor in chimpanzee ecology and evolution, shaping their anatomy to maximize climbing efficiency, thus sparing calories for reproduction and other essential tasks. Months earlier, while mulling over summer research plans from the comfort of my desk at snowy Harvard University, I envisioned chimpanzees waging a heroic struggle for existence, working hard on a daily basis to eke out a living. But as I settled into the rhythm of fieldwork that summer, following chimpanzees from dawn to dusk, I came to a very different conclusion: chimpanzees are lazy. Only recently have I come to appreciate what ape idleness tells us about human evolution.

People are drawn to apes because we see so much of ourselves in them. It is not just that we share more than 97 percent of our DNA with orangutans, gorillas, chimpanzees and bonobos. Apes are clever, use tools, fight and make up, and sneak off to have sex. Some will kill their neighbors over turf and hunt other species for food. The kids learn from their mothers, wrestle and play with one another, and throw tantrums. And the further back in time we go in the fossil record, the more apelike our ancestors look. No species alive today is a perfect model of the past—all lineages change over time. But living apes provide the best chance to see where we came from and to understand how much of us is ancient and unchanged.

And yet it is the differences, rather than the similarities, between humans and apes that are casting new light on the way our bodies work. Discoveries from fossil excavations, zoos and laboratories around the world are revealing just how radically our bodies changed over the past two million years. For decades researchers have known that this last chapter of our evolution was marked by major anatomical and ecological changes—among them, ballooning brain size, hunting and scavenging, increasingly complex stone tools and larger body size. But they have generally assumed that these were changes in shape and behavior, not in the fundamental function of our cells. Current advances are overturning that view, showing how humans have changed physiologically as well. Unlike our ape cousins, we have evolved a dependency on physical activity. We must move to survive.

PARADISE LOST

A TYPICAL DAY'S AGENDA for a chimpanzee in the wild reads like the daily schedule for lethargic retirees on a Caribbean cruise, though with fewer organized activities. Wake up early, crack of dawn, then off to breakfast (fruit). Eat until you are stuffed, and next find a nice place for a nap, maybe some light grooming. After an hour or so (no rush!), go find a sunny tree with figs and gorge yourself. Maybe go meet some friends, a bit more grooming, another nap. Around five o'clock have an early dinner (more fruit, maybe some leaves), then it is time to find a nice sleeping tree, build a nest and call it a night. Sure, there are frenetic pant-hoot choruses when the fruit is really great and the occasional scuffle or monkey hunt, and the alpha male needs to carve some time out every day to thrash a few victims or display mightily. But in general, chimpanzee life is pretty mellow.

It is not just chimps. Orangutans, gorillas and bonobos also lead the sorts of seemingly idle lives that children's fables and high school drug programs warn you about. Great apes spend eight to 10 hours a day resting,

LOUNGING AROUND: Mountain gorilla family relaxes in Rwanda. Great apes remain healthy at low activity levels.

DAVID CAYLESS Getty Images

grooming and eating before knocking off in the evening for nine or 10 hours of sleep per night. Chimps and bonobos walk about three kilometers a day, and gorillas and orangutans travel even less. And the climbing? As I discovered that summer, chimpanzees climb about 100 meters a day, the caloric equivalent of another 1.5 kilometers of walking. Orangutans do about the same, and although their ascent has yet to be measured, gorillas surely climb less.

In humans, these activity levels would be a recipe for serious health problems. Our taking fewer than 10,000 daily steps is associated with increased risk of cardiovascular and metabolic disease. U.S. adults typically clock about 5,000 steps, which contributes to the alarming rates of type 2 diabetes, affecting one in 10 Americans, and heart disease, which accounts for a quarter of all deaths in the U.S. By these lights, apes should be in trouble. Converting their walking and climbing to steps per day for comparison across species, we see that great apes rarely accumulate even the modest step counts seen among sedentary humans and never approach the human benchmark of 10,000 steps a day.

Then there is all the sitting and resting. In humans, sitting at a desk or in front of the television for protracted periods is associated with increased risk of disease and a shorter life span, even among people who exercise. Worldwide, physical inactivity is arguably on par with smoking as a health risk, killing more than five million people annually. Among Scottish adults, those watching more than two hours of television a day had a 125 percent increase in cardiac events such as heart attack or stroke. A study in Australian adults reported that every hour accumulated watching television shortened life expectancy by 22 minutes. I will save you the math: bingeing all 63½ hours of *Game of Thrones* in its entirety will cost you one day on this planet.

Yet chimpanzees and other apes remain remarkably healthy at their habitually low levels of physical activity. Even in captivity, diabetes is rare, and blood pressures do not increase with age. Despite having naturally high cholesterol levels, chimpanzee arteries do not harden and clog. As a result, chimps do not develop humanlike heart disease or have heart attacks from occluded coronary arteries. And they stay lean. In 2016 I worked with Steve Ross at Lincoln Park Zoo in Chicago and a team of collaborators to measure metabolic rates and body composition in zoo-living apes across the U.S. The results were eye-opening: even in captivity, gorillas and orangutans average only 14 to 23 percent body fat and chimpanzees less than 10 percent, on par with Olympic athletes.

Among our primate cousins, we humans are clearly the odd ape out. Somehow humans evolved to require much higher levels of physical activity for our bodies to function normally. Sitting for hours on end, grooming and napping (or watching the tube) have gone from standard practice to a health risk. When did we trade the low-key existence of our fellow apes for a more strenuous way of life and why? Fossil discoveries are helping to piece the story together.

BRANCHING OUT

OUR LIMB OF THE PRIMATE FAMILY TREE, the hominins, split from that of chimpanzees and bonobos about six million or seven million years ago, near the end of Miocene geologic time period. Until fairly recently, there were few hominin fossils recovered from the earliest portion of the lineage. Then, in quick succession during the 2000s, paleoanthropologists working in Chad, Kenya and Ethi-

opia reported finds of three hominins from this critical period: *Sahelanthropus, Orrorin* and *Ardipithecus.*

Each of these early hominins is distinct from any of the living apes in the anatomical details of their cranium, teeth and skeleton. Nevertheless, aside from walking on two legs, it appears these species lived a very apelike existence. Their molars were similar in size and sharpness to chimpanzees, with somewhat thicker enamel, suggesting a mixed diet of fruit and other plant foods. *Ardipithecus,* found in 4.4-million-year-old deposits in Ethiopia and by far the best known early hominin, had long arms, long, curved fingers and grasping feet, indicative of a life spent partly in the trees. New biomechanical analyses, led by my City University of New York graduate student Elaine Kozma, show that *Ardipithecus* had evolved changes in its pelvic anatomy to permit fully upright, energetically efficient walking without compromising the ability to power itself into the canopy. Our early ancestors were clearly comfortable in two worlds, on the ground and in the trees.

BINGEING ALL 63½ HOURS OF *GAME OF THRONES* WILL COST YOU ONE DAY ON THIS PLANET.

From about four million to two million years ago the hominin record is dominated by the genus *Australopithecus,* with at least five species recognized today, including the famous "Lucy" and her kin. Anatomical changes in the lower limb point to improved walking ability and more time on the ground compared with earlier species. The grasping foot is gone in *Australopithecus,* the big toe in line with the others, and the legs are longer, the same ratio of leg length to body mass that we see in living humans. Analyses of the pelvis by Kozma, together with recent work on the fossilized footprints from Laetoli in Tanzania, indicate that this creature had an effectively modern gait. Long arms and fingers tell us these hominins were still regularly in the trees to forage and perhaps to sleep. Analyses of the wear patterns on their teeth suggest *Australopithecus* species primarily ate plant foods, just as the earliest hominins did before them and living apes do today. Based on their large, thick-enameled molars, *Australopithecus* diets most likely leaned more on harder and more fibrous foods, particularly when preferred foods were not available.

The evolution of an upright, striding bipedal gait in these early hominins is important, indicating a different approach for navigating their landscape. Covering more ground for fewer calories might have enabled these species to expand their range and thrive in less productive habitats than apes today. There are other notable and intriguing changes, too, such as the loss of big, sharp canines in males, which seem to reflect changes in social behavior. Yet the plant-based diet and retained climbing adaptations tell us their foraging ecology and daily activity remained quite apelike. Distances traveled per day were probably modest, with lots of time spent resting and digesting bellyfuls of fibrous plant food. It is unlikely they needed, or often got, their 10,000 steps a day.

Some two million years ago the telltale signs of curious or clever hominins experimenting with new ideas and approaches began to emerge. In 2015 Sonia Harmand of Stony Brook University and her team recovered large, unwieldy stone tools, some weighing more than 30 pounds, from 3.3-million-year-old sediments on the western shore of Lake Turkana in Kenya. In the past 15 years excavations at 2.6-million-year-old sites in both Ethiopia and Kenya have found stone tools associated with fossilized animal bones bearing the unmistakable gouges and scrapes of butchery. By 1.8 million years ago cut-marked bones and stone tools were the norm, and it was not just the sick and injured animals that fell prey to these hominins. Analyses of butchered bones at Olduvai Gorge in Tanzania show that prime-aged ungulates were targeted. Just as important, unlike every hominin before, by 1.8 million years ago hominins had expanded outside of Africa into Eurasia, from the foothills of the Caucasus Mountains to the rain forests of Indonesia. Our predecessors had jumped the ecological fence and were capable of thriving nearly anywhere.

Forget the tales of some clandestine meeting in the Garden of Eden or of Prometheus doling out fire. It was this million-year dalliance with stones and meat and the development of a hunting-and-gathering strategy that pushed our lineage away from the other apes, changing things irrevocably. This tectonic shift marked the evolutionary emergence of us, the genus *Homo.*

FOOD FOR THOUGHT

IN ECOLOGY AND EVOLUTION, diet is destiny. The foods animals eat do not just shape their teeth and guts but their entire physiology and way of living. Species evolved to eat foods that are abundant and stationary need not roam too far or be too clever to fill up; grass does not hide or run away. Eating foods that are hard to find or capture means more travel, often coupled with increased cognitive sophistication. For instance, fruit-eating spider monkeys in Central and South America have larger brains and travel five times farther every day than the leaf-obsessed howler monkeys that share their forests. Carnivores on the African savanna travel three times farther a day than the herbivores they hunt.

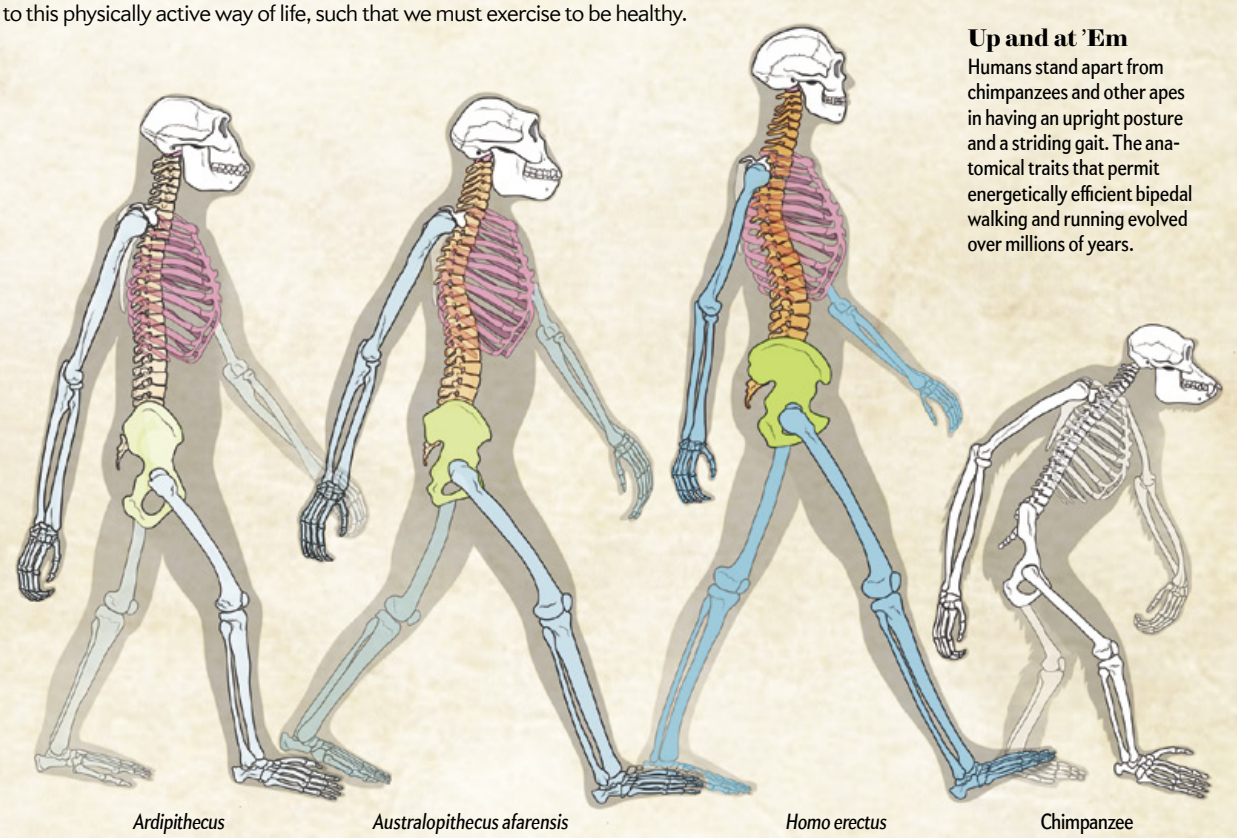
Shifting from the pure gathering lifestyle of apes and early hominins to the hunting-and-gathering strategy that marks the genus *Homo* had major ramifications. It made these social primates even more tightly knit.

Built to Move

As hominins evolved anatomical changes that facilitated upright walking (*shown*), they were able to cover more ground for fewer calories, allowing them to expand into new habitats. The subsequent advent of hunting further increased activity levels of hominins, requiring them to travel farther to find food. Our physiology has adapted to this physically active way of life, such that we must exercise to be healthy.

Up and at 'Em

Humans stand apart from chimpanzees and other apes in having an upright posture and a striding gait. The anatomical traits that permit energetically efficient bipedal walking and running evolved over millions of years.



Ardipithecus | *Australopithecus afarensis* | *Homo erectus* | Chimpanzee

Piecemeal Evolution

Early human ancestors, including *Ardipithecus* and *Australopithecus*, walked on two legs yet also retained adaptations to climbing in the trees, ate a plant-based diet like today's apes do and lived exclusively in Africa. By 1.8 million years ago *Homo* had evolved modern body proportions, adopted a dietary strategy of hunting and gathering, and spread out of Africa into Eurasia.

Vertical torso and centrally located hole in skull base to admit spinal cord		
Spine shape unknown	S-shaped spine	Enlarged lumbar vertebrae
Bowl-shaped pelvis	Smaller ischium, or "sit bone"	More robust pelvis
Short lower limbs, long upper limbs	Elongated upper and lower limbs	Long lower limbs, short upper limbs and fingers

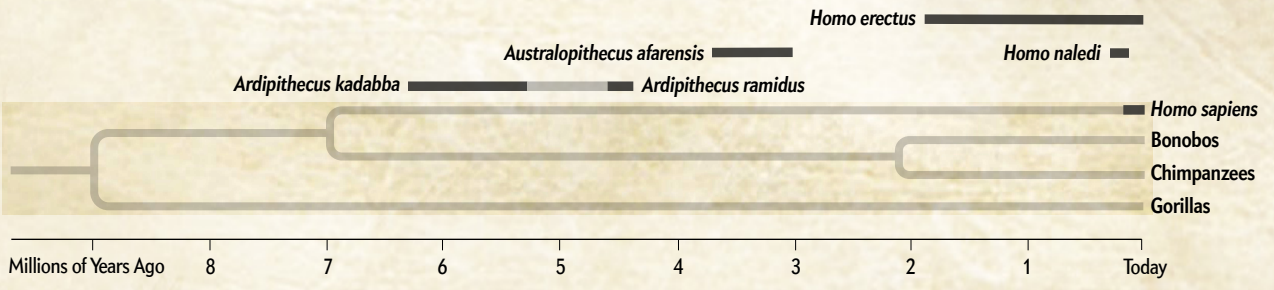


Illustration by Mesa Schumacher

Relying on meat requires cooperation and sharing—and not just because you cannot kill or eat a zebra by yourself. Meat is difficult to obtain, and sharing more predictable plant foods is what allows hunting and gathering to work. Hunter-gatherer populations today get roughly half their daily calories from plants. Recent analyses of the food trapped inside their fossilized dental calculus show that even Neandertals, masterful hunters and avatars of vegetable-boycotting Paleo diet bros everywhere, ate a balanced diet, with plenty of plants, including grains.

Hunting and gathering also put an evolutionary premium on intelligence. Technological innovation and creativity meant more calories and better odds of reproduction. Social intelligence would have proved invaluable, as coordination and communication became ingrained parts of the hominin strategy. Discoveries by Alison Brooks of George Washington University, Rick Potts of the Smithsonian National Museum of Natural History and their colleagues at the site of Olorgesailie Basin in Kenya, published in 2018, show that by 320,000 years ago, hominin cognition had blossomed into the kind of sophistication seen in modern humans, with black and red pigments for visual expression and long-distance trade networks for premium stone tool material. The age of these finds corresponds well with the oldest *Homo sapiens* fossils found to date, reported in 2017 from the 300,000-year-old site of Jebel Irhoud in Morocco.

EXERCISE IS NOT OPTIONAL; IT IS ESSENTIAL.

Moreover, hunting and gathering required hominins to work harder for their food. Simply moving up the food chain means food is harder to find; there are a lot more plant calories on the landscape than animal calories. Hunter-gatherers are remarkably active, typically covering nine to 14 kilometers a day on foot—about 12,000 to 18,000 steps. Work that David Raichlen of the University of Arizona, Brian Wood, now at the University of California, Los Angeles, and I have done with the Hadza hunter-gatherer population in northern Tanzania shows that men and women in that group log more physical activity in a day than Americans typically get in a week and travel three to five times farther every day than any of the great apes. Early members of our genus, without the benefit of technological innovations such as the bow and arrow, might have been even more active. In a landmark paper in 2004, Dennis Bramble of the University of Utah and Daniel Lieberman of Harvard argued that our genus evolved to run prey to exhaustion, pointing to a number of features in the *Homo erectus* skeleton that appear to reflect endurance running.

The steady increases in brain size and technological complexity over the past two million years seem to accumulate like a snowball rolling downhill, but any impression of momentum is an illusion. Evolution has a great memory but no plans. In 2015 Lee Berger of the University of the Witwatersrand in South Africa and his team announced their discovery of hundreds of fossils of *Homo naledi,* a new species recovered from deposits deep in the Rising Star Cave system in South Africa, dated to between 236,000 and 335,000 years old. With a brain size only 10 percent larger than *Australopithecus* and a body size similar to early *Homo,* this hominin appears to represent a lineage within our genus that stalled out in the early Pleistocene, persisting quite happily for more than a million years without the continued increase in brain size seen in other *Homo* species. *H. naledi* is an important reminder that evolution is not trying to get anywhere. We were not inevitable.

SHARKS ON THE SAVANNA

NO TRAIT EVOLVES IN ISOLATION: brains must fit snugly inside their skulls, teeth inside their jaws; muscles, nerves and bones must function harmoniously. Behavioral traits are no different. When a behavioral strategy—such as hunting and gathering—becomes the norm, physiology adapts to accommodate and even depend on it.

Take vitamin C, for instance. Early mammals evolved a multistep process to make this crucial nutrient on their own, a cascade involving several genes that remains functional in rodents, carnivores and many other mammals. Tens of millions of years ago our primate ancestors became so fixated on eating fruits rich in vitamin C that making their own became an unnecessary cost. Their physiology adapted to their behavior, with mutations accumulating in the gene needed in the final step of synthesis. Consequently, today's anthropoid primates—monkeys, apes and humans—cannot make vitamin C. Without it in our diets, we get scurvy and die.

Further afield, yet closer to home, is the evolution of a specialized form of breathing called ram ventilation in several species of sharks and scombrid fish (the group that includes tuna and mackerel). These lineages evolved highly active foraging behavior, swimming nonstop day and night. Their anatomy and physiology adapted, using the constant forward motion to ram water into their mouths and past their gills. This change eliminated the need to pump water past the gills, leading to the evolutionary loss of the associated gill musculature. This loss saved energy but left these species vulnerable to suffocation. If they stop moving, they die.

Although we have long known that exercise is good for us humans, we are only beginning to appreciate the myriad ways our physiology has adapted to the physically active way of life that hunting and gathering demands. Nearly every organ system is implicated, down to the cellular level. Some of the most exciting work in this area has focused on the brain. For one thing, our brain has evolved to get less sleep, even in societies without artificial lighting or other modern nighttime distractions.

Humans around the globe—whether it is the Hadza on the African savanna, the Tsimane horticulturalists in the Amazonian rain forest or urbanites in New York—clock about seven hours of sleep a night, far less than apes. Raichlen and his colleagues have shown that our brain has evolved to reward prolonged physical activity, producing endocannabinoids—the so-called runner's high—in response to aerobic exercise such as jogging. Raichlen and others have even argued that exercise helped to enable the massive expansion of the human brain and that we have evolved to require physical activity for normal brain development. Exercise causes the release of neurotrophic molecules that promote neurogenesis and brain growth, and it is known to improve memory and stave off age-related cognitive decline.

Our metabolic engines have evolved to accommodate increased activity as well. Humans' maximum sustained power output, our VO_{2max}, is at least four times greater than that of chimpanzees. This increase stems largely from changes in our leg muscles, which are 50 percent bigger and have a much greater proportion of "slow-twitch" fatigue-resistant fibers than the leg muscles of other apes. We also have more red blood cells to carry oxygen to working muscles. But the adaptations to exercise appear to go even deeper, accelerating the rate with which our cells function and burn calories. My work with Ross, Raichlen and others has shown that humans have evolved a faster metabolism, providing fuel for increased physical activity and the other energetically costly traits that set humans apart, including bigger brains.

All of this evidence points toward a new way of thinking about physical activity. Since the sweaty spandex excitement of the 1980s, exercise has been sold as a way to lose weight or as a health-conscious buffet item to add to our lifestyle, like oat bran muffins. But exercise is not optional; it is essential, and weight loss is probably the one health benefit it largely fails to deliver. Our bodies are evolved to require daily physical activity, and consequently exercise does not make our bodies work *more* so much as it makes them work *better*. Research from my lab and others has shown that physical activity has little effect on daily energy expenditure (Hadza hunter-gatherers burn the same number of calories every day as sedentary Westerners), which is one reason exercise is a poor tool for weight loss. Instead exercise regulates the way the body spends energy and coordinates vital tasks.

Recent advances in metabolomics have shown that exercising muscles release hundreds of signaling molecules into the body, and we are only beginning to learn the full extent of their physiological reach. Endurance exercise reduces chronic inflammation, a serious risk factor for cardiovascular disease. It lowers resting levels of the steroid hormones testosterone, estrogen and progesterone, which helps account for the reduced rate of reproductive cancers among adults who exercise regularly. Exercise may blunt the morning rise in cortisol, the stress hormone. It is known to reduce insulin insensitivity, the immediate mechanism behind type 2 diabetes, and helps to shuttle glucose into muscle glycogen stores instead of fat. Regular exercise improves the effectiveness of our immune system to stave off infection, especially as we age. Even light activity, such as standing instead of sitting, causes muscles to produce enzymes that help to clear fat from circulating blood.

No wonder populations such as the Hadza do not develop heart disease, diabetes or the other maladies that afflict industrial countries. But we do not need to cosplay as hunter-gatherers or run marathons to reap the benefits of a more evolutionarily informed life. The lesson from groups such as the Hadza, Tsimane and others is that volume matters more than intensity. They are on their feet and moving from sunrise until dusk, racking up more than two hours of physical activity a day, most of it as walking. We can emulate these same habits by walking or biking instead of driving, taking the stairs, and finding ways to work and play that keep us off our butts. A recent study of Glaswegian postal workers shows us what this can look like. These men and women were not committed athletes but were active throughout the day, handling the mail. Those who got 15,000 steps or spent seven hours a day on their feet (numbers similar to what we see with the Hadza) had the best cardiovascular health and no metabolic disease.

While we are at it, we might take other lessons for living well from groups like the Hadza. Beyond the copious amounts of exercise and whole food diets, daily life for these cultures is full of fresh air, friendships and family. Egalitarianism is the rule, and economic inequality is low. We do not know exactly how these factors affect the health of hunter-gatherers, but we know their absence contributes to chronic stress in the developed world, which in turn promotes obesity and disease.

Embracing more physically active life habits would be easier if we did not have to wrestle with the 400-pound gorilla in our head. Like vitamin C for our anthropoid ancestors, exercise was unavoidable and plentiful during the last two million years of hominin evolution. There was no need to seek it out, no evolutionary pressure to lose the ancient, simian weakness for gluttony and sloth. Today, as masters of our environments, we are giving our inner apes too much say in how the modern world is engineered: filling up on easy food, bingeing *The Walking Dead* instead of actually walking, sitting for hours at our desks grooming one another on social media. We are fascinated when we see ourselves in great apes, but we should worry when we see them in us. Underneath the surface, we are more different than we seem. SA

MORE TO EXPLORE

The Crown Joules: Energetics, Ecology, and Evolution in Humans and Other Primates. Herman Pontzer in *Evolutionary Anthropology,* Vol. 26, No. 1, pages 12–24; January/February 2017.

Economy and Endurance in Human Evolution. Herman Pontzer in *Current Biology,* Vol. 27, No. 12, pages R613–R621; June 19, 2017.

FROM OUR ARCHIVES

The Exercise Paradox. Herman Pontzer; February 2017.

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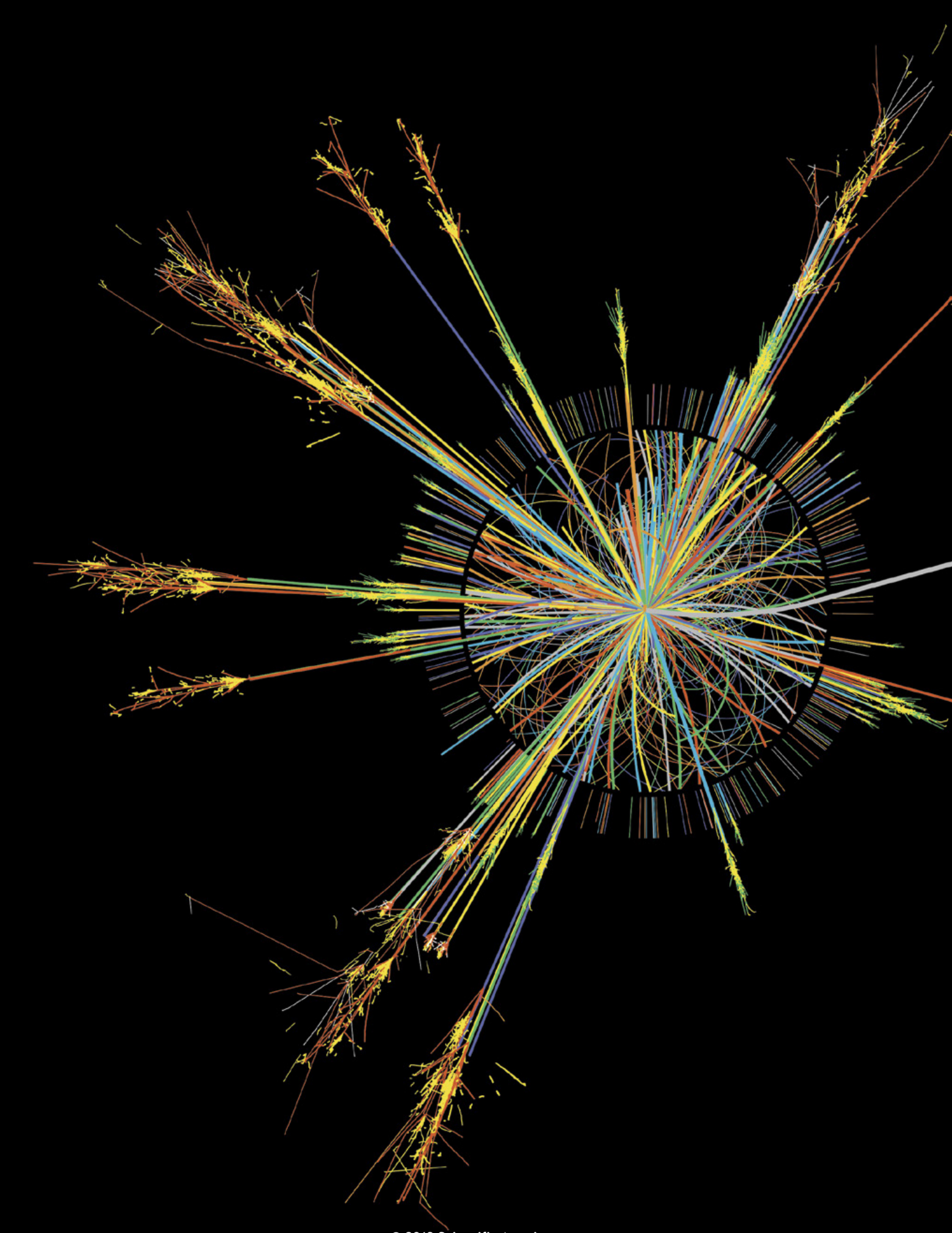


THE PARTICLE CODE

Scientists are creating mathematical tools to identify novel particles and phenomena at the world's largest particle accelerator

By Matthew von Hippel

ATLAS EXPERIMENT, © 2016 CERN

IN BRIEF

To search for new phenomena at the Large Hadron Collider, physicists must be able to precisely calculate the odds of different particle collisions and reactions. **Scientists in a field** called amplitudeology are designing cutting-edge mathematical techniques to deal with these difficult computations. In particular, they are building an "alphabet" of logarithms they can combine in different ways to complete previously impossible calculations.

A recent advance in the alphabet could enable the precision necessary for physicists to identify never before seen particles that open the door to a deeper theory of physics.

THE LARGE HADRON COLLIDER, OR LHC, IS THE BIGGEST machine humans have ever built. Pooling the resources of more than 100 countries, it accelerates protons to within a millionth of a percent of the speed of light. When they collide, the protons break into their component parts (quarks and the gluon particles that glue them together) and create particles that were not there before. This is how, in 2012, the LHC achieved the first detection of a Higgs boson, the final missing particle predicted by the Standard Model of particle physics. Now physicists hope the LHC will find something genuinely new: particles not already in their current theory—particles that explain the mystery of dark matter, for instance, or offer solutions to other lingering questions. For such a discovery, scientists must pore through the 30 petabytes a year of data the machine produces to identify tiny deviations where the results do not quite match the Standard Model.

Of course, all of that effort will be useless if we do not know what the Standard Model predicts.

That is where I come in. The questions we want to ask about the LHC come in the form of probabilities. "What is the chance that two protons bounce off each other?" "How often will we produce a Higgs boson?" Scientists compute these probabilities with "scattering amplitudes," formulas that tell us how likely it is that particles "scatter" (essentially, bounce) off each other in a particular way. I am part of a group of physicists and mathematicians who work to speed up these calculations and find better tricks than the old, cumbersome methods handed down by our scientific forebears. We call ourselves "amplitudeologists."

Amplitudeologists trace our field back to the research of two physicists, Stephen Parke and Tomasz Taylor. In 1986 they found a single formula that described collisions between any number of gluons, simplifying what would ordinarily be pages of careful case-by-case calculations. The field actually kicked off in the 1990s and early 2000s, when a slew of new methods promised to streamline a wide variety of particle physics computations. Nowadays amplitudeology is booming: the Amplitudes 2018 conference had 160 participants, and 100 attended the summer school the week before, aimed at training young researchers in the tricks of the field. We have gotten some public attention, too: physicists Nima Arkani-Hamed and Jaroslav Trnka's Amplituhedron (a way to describe certain amplitudes in the language of geometry) made the news in 2013, and on television *The Big Bang Theory*'s Sheldon Cooper has been known to dabble in amplitudeology.

Lately we have taken a big step forward, moving beyond the basic tools we have already developed into more complex techniques. We are entering a realm of calculations sensitive enough to match the increasing precision of the LHC. With these new tools we stand ready to detect even tiny differences between Standard Model predictions and the reality inside the LHC, potentially allowing us to finally reveal the undiscovered particles physicists dream of.

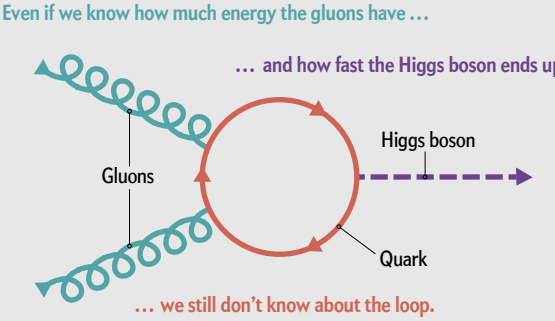
LOOPS AND LINES

TO ORGANIZE OUR CALCULATIONS, scientists have long used pictures called Feynman diagrams. Invented by physicist Richard Feynman in 1948, these figures depict paths along which particles travel. Suppose we want to know the chance that two gluons merge and form a Higgs boson. We start by drawing lines representing the particles we know about: two gluons going in and one Higgs boson coming out. We then have to connect those lines by drawing more particle lines in the middle of the diagram, according to the rules of the Standard Model. These additional particles may be "virtual": that is, they are not literally particles in the way the gluons and Higgs are in our picture. Instead they are shorthand, a way to keep track of how different quantum fields can interact.

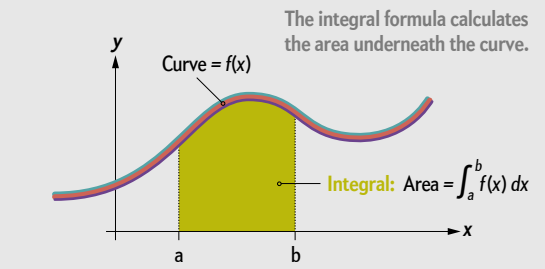
Feynman diagrams are not just pretty pictures—they are instructions, telling us to use information about the particles we draw to calculate a probability. If we know the speed and energy of the gluons and Higgs boson in our diagram, we can try to work out the properties of the virtual particles in between. Sometimes, though, the answer is uncertain. Trace your finger along the particle paths, and you might find a closed loop: a path that ends up back where you started. A particle traveling in a loop like that is not "input" or "output": its properties never get measured. We do not know how fast it is going or how much energy it has. Though counterintuitive, it is a consequence of the fundamental uncertainty of quantum mechanics, which prevents us from measuring two traits of a particle, such as speed and position, at the same time. Quantum mechanics tells us how to deal with this uncertainty—we have to add up every possibility, summing the probabilities for any speed and energy the virtual particles could have, using a technique you might remember from high school calculus: an integral.

Matthew von Hippel is a postdoctoral scholar at the Niels Bohr International Academy in Copenhagen. He has been working on amplitudes since he stumbled into his adviser's office in graduate school, looking for a summer project. He has also been doing science outreach since he got into a discussion with *Ars Technica*'s science editor about the definition of "theory." He blogs at https://4gravitons.wordpress.com

Feynman Diagram: Two gluons in, one Higgs boson out



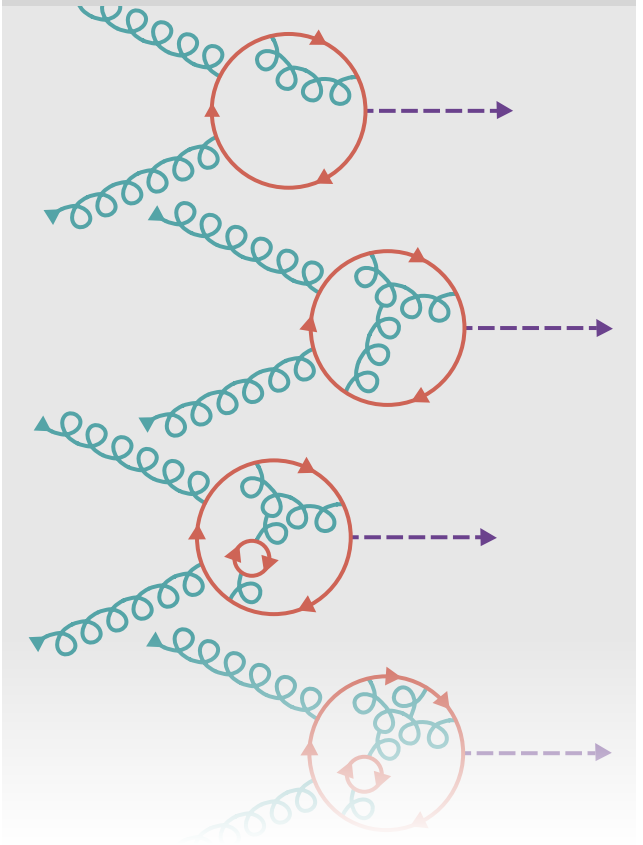
Integral: The area under the function's curve



In principle, to calculate a scattering amplitude we have to draw every diagram that could possibly connect our particles, every way the starting ingredients could have turned into the finished products (here the pair of gluons and the Higgs boson). That is a lot of diagrams, an infinite number, in fact: we could keep drawing loops inside loops as far as we like, requiring us to calculate more and more complicated integrals each time.

Graphics by Jen Christiansen

Loops inside Loops

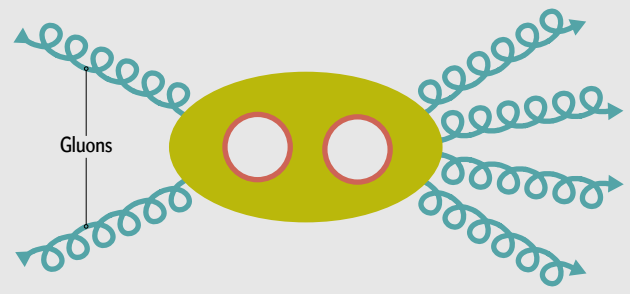


In practice, we are saved by the low strength of most quantum forces. When a group of lines in a diagram connect, it depicts an "interaction" among different types of particles. Each time this happens we have to multiply by a constant, related to the strength of the force that makes the particles interact. If we want to draw a diagram with more closed loops, we have to connect up more lines and multiply by more of these constants. For electricity and magnetism, the relevant constants are small: for each loop you add, you divide by roughly 137. This means that the diagrams with more and more loops make up a smaller and smaller piece of your final answer, and eventually that piece is so small that the experiments cannot detect it. The most careful experiments on electricity and magnetism are accurate up to an astounding 10 decimal places, some of the most precise measurements in all of science. Getting that far requires "only" four loops, four factors of $^1/_{137}$ before the number you are calculating is too small to measure. In many cases, these numbers have actually been calculated, and all 10 decimal places agree with experiments.

The strong nuclear force is a tougher beast. It is the force that glues together protons and neutrons and the quarks inside them. It is quite a bit stronger than electricity and magnetism: for calculations at the LHC, each loop means dividing not by 137 but by 10. Getting up to 10 digits of precision would mean drawing 10 loops.

The LHC is not as precise as those electricity and magnetism experiments. At the moment, measurements from the machine are just starting to match the precision of two-loop calculations. Still, those results are already quite messy. For example, a two-loop calculation in 2010 by physicists Vittorio Del Duca, Claude Duhr and Vladimir Smirnov computed the chance that two gluons collide and four gluons come out. They made their calculation using a simplified theory, with some special shortcuts, and the resulting formula still clocked in at 17 pages of complicated integrals. That length was not too surprising; everyone knew that two-loop calculations were hard.

Two-Loop Example: Two gluons in, four gluons out



Until a few months later, when another group managed to write the same result on two lines. That group was a collaboration among three physicists—Marcus Spradlin, Cristian Vergu and Anastasia Volovich—and a mathematician, Alexander B. Goncharov. The trick they used was extraordinarily powerful, and it exposed amplitudeologists to an area of mathematics that most of us had not seen before, one that has driven my career to this day.

PERIODS AND LOGS

SHOW A MATHEMATICIAN like Goncharov one of the integrals we get out of Feynman diagrams, and the first thing you will hear is, "That's a period."

Periods are a type of number. You might be familiar with the natural numbers (1, 2, 3, 4 …) and the rational numbers (fractions). The square root of 2 is not rational—you cannot get it by dividing two natural numbers. What it is, though, is algebraic: you can write an algebraic equation, say $x^2 = 2$, where the square root of 2 is the solution. Periods are the next step up: although you cannot always get them from an algebraic equation, you *can* always get them from an integral.

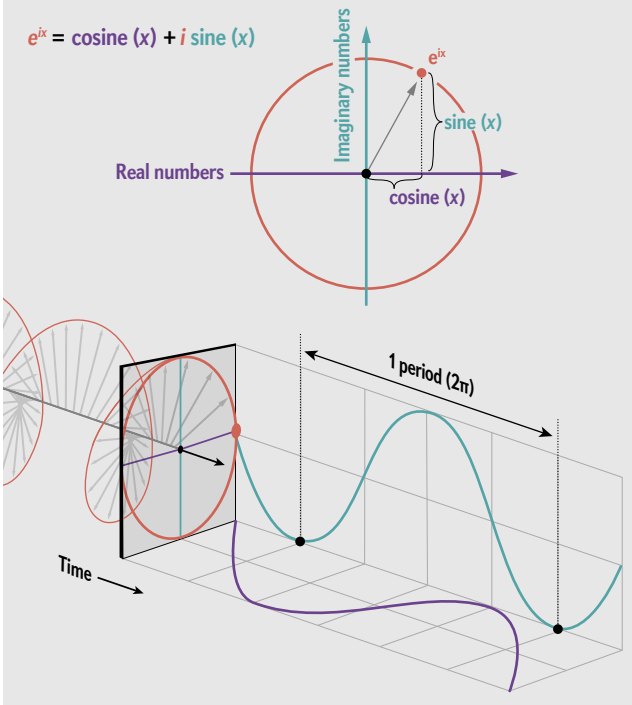
Why call them periods? In the simplest cases, that is literally what they are: the distance before something repeats. Thinking back to high school, you might remember grappling with sines and cosines. You might even remember that you can put them together with imaginary numbers (the square roots of negative numbers—in other words, numbers that would not normally exist) using Euler's formula: $e^{ix} = \cos(x) + i \sin(x)$ (here e is a constant, and i is the square root of -1). All three of these—$\sin(x)$, $\cos(x)$, and e^{ix}—*have* period 2π: if you let x go from 0 to 2π, the function repeats, and you get the same numbers again.

Euler's Formula

$$e^{ix} = \text{cosine}\,(x) + i\,\text{sine}\,(x)$$

2π is a period because it is the distance before e^{ix} repeats, but you can also think of it as an integral. Draw a graph of e^{ix} in the complex plane: imaginary numbers on one axis; real numbers on the other. It forms a circle. If you want to measure the length of that circle, you can do it with an integral, adding up each little segment all the way around. In doing so, you will find exactly 2π.

Euler's formula visualized as a circle, then projected through time

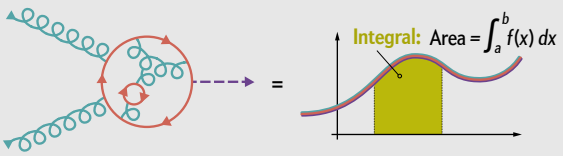


What happens if you go partway around the circle, to some point z? In that case, you must solve the equation $z = e^{ix}$. Thinking back again to high school, you might remember what you need to solve that equation: the natural logarithm, ln (z). Logarithms might not look like "periods" in the way 2π does, but because you can get them from integrals, mathematicians call them periods as well. Besides 2π, logarithms are the simplest periods.

The periods mathematicians and physicists care about can be much more complicated than this scenario, of course. In the mid-1990s physicists started classifying periods in the integrals that come out of Feynman diagrams and have since found a dizzying array of exotic numbers. Remarkably, though, the high school picture remains useful. Many of these exotic numbers, when viewed as periods, can be broken down into logarithms. Understand the logarithms, and you can understand almost everything else.

That was the secret that Goncharov taught Spradlin, Vergu and Volovich. He showed them how to take Del Duca, Duhr and Smirnov's 17-page mess and chop it up into a kind of "alphabet" of logarithms. That alphabet obeys its own "grammar" based on the relations between logarithms, and by using this grammar, the physicists were able to rewrite the result in terms of just a few special "letters," making a messy particle physics calculation look a whole lot simpler.

With Goncharov's trick, a complex Feynman diagram is represented by an integral …



… which we can then break down into letters that act like logarithms.

A C B A D E …

The letters have a "grammar," based on relations between logarithms.

Natural log — $\ln(AB) = \ln(A) + \ln(B)$

For instance, the log of A times B equals the log of A plus the log of B.

C F AB E D = C F A E D + C F B E D

And the log of C to the nth power equals n times the log of C.

$$\ln(C^n) = n \times \ln(C)$$

We can apply these same rules to manipulate our alphabet for Feynman diagram calculations.

D A C^n B A = n × D A C B A

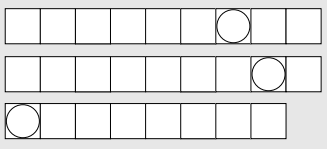
To recap, physicists calculate scattering amplitudes using Feynman diagrams, which require doing integrals. Those integrals are always periods, sometimes complicated ones, but we can often break those complicated periods apart into simpler periods (logarithms) using Goncharov's trick, which was what ignited my area of the amplitudes field. We can divide many of the integrals we use into an alphabet of letters that behave like logarithms. And the same rules that apply to logarithms, such as basic laws like $\ln(xy) = \ln(x) + \ln(y)$ and $\ln(x^n) = n \times \ln(x)$, work for the alphabet.

WORD JUMBLE

GONCHAROV'S ALPHABET TRICK would not be nearly as impressive if all it did was save space in a journal. Once we know the right alphabet, we can also do new calculations, ones that would not have been possible otherwise. In effect, knowing the alphabet lets us skip the Feynman diagrams and just guess the answer.

Think about that newspaper mainstay, the word jumble. The puzzle tells you which letters you need and how long the word is supposed to be. If you were lazy, you could have a computer write down the letters in every possible order, then skim through the list. Eventually you would find a word that made sense, and you would have your solution.

Word Jumble: Unscramble the letters



The list of possibilities can be quite long, though. Luckily in physics, we start with hints. We begin with an alphabet of logarithms that describe the properties our particles can have, such as their energy and speed. Then we start writing words in this alphabet, representing integrals that might show up in the final answer. Certain words do not make physical sense: they describe particles that do not actually exist or diagrams that would be impossible to draw. Others are needed to explain things we already know: what happens when a particle gets very slow or very fast. In the end, we can pare things down from what might have been millions of words to thousands, then tens, and finally just one unique answer. Starting with a guess, we end up with the only possible word that can make sense as our scattering amplitude.

Lance J. Dixon, James M. Drummond and Johannes Henn used this technique to find the right "word" for a three-loop calculation in 2011. I joined the team in 2013, when I snuck away from graduate school on Long Island to spend the winter working for Dixon at SLAC National Accelerator Laboratory at Stanford University. Along with then grad student Jeffrey Pennington, we got the result into a form we could compare with the old two-loop calculation from Del Duca, Duhr and Smirnov. Now instead of 17 pages, we had a formula that was 800 pages long—and all without drawing a single Feynman diagram.

Since then, we have pushed to even more loops, and our collaboration has grown, with Duhr, Andrew McLeod, Simon Caron-Huot, Georgios Papathanasiou and Falko Dulat joining the team. We are at seven loops, and I do not know how many pages the new formulas will take to write out. Goncharov's trick is not enough to simplify the result when the calculation is this complicated. Here we are just happy it makes the calculation *possible!* We store our results in computer files now, big enough that you would think they were video files, not text.

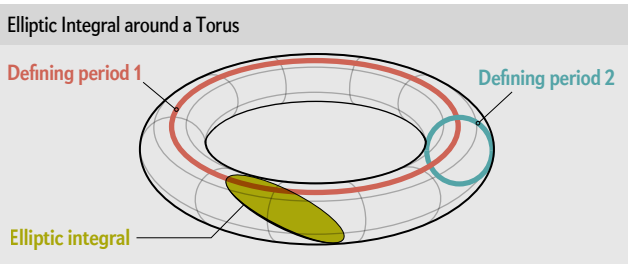
THE ELLIPTIC FRONTIER

RECALL THAT THE MORE LOOPS you include in your scattering amplitude calculation, the more precise your prediction will be. Seven loops would be more precise than the two or so loops the LHC can measure, more precise than the four-loop state of the art in quantum electromagnetism. I say "would be" here, though, because there is a catch: our seven-loop calculations use a "toy model"—a simpler theory of particle interactions than any that can describe the real world. Upgrading our calculations so they describe reality will be difficult, and there are numerous challenges. For one, we will need to understand something called elliptic integrals.

The toy model we use is very well-behaved. One of its nicer traits is that for the kind of calculations we do, Goncharov's method always works: we can always break the integral up into an alphabet of logarithms, of integrals over circles. In the real world, this tactic runs into problems at two loops: two integrals can get tangled together so they cannot be separated.

Think about two hooked rings that cannot be pulled apart. If you move one ring around the other, you will draw a doughnut shape, or a torus. A torus has two "periods," two different ways you can draw a line around it, corresponding to the two different rings. Integrate around a circle by itself, and you get a logarithm. Try to draw a ring around a torus, and you will not always get a circle: instead you might get an ellipse. We call such integrals around a torus elliptic integrals—integrals over an elliptic curve.

Understanding elliptic curves involves some famously complex mathematical problems. Some of these problems are so difficult to solve that organizations like the National Security Agency use them to encode classified information, on the assumption that no one can solve them fast enough to crack the code. The problems we are interested in are not quite so intractable, but they are still tricky. With the LHC's precision increasing, though, elliptic integrals are becoming more and more essential, spurring on groups around the world to tackle the new mathematics. The machine shut down in late 2018 for upgrades, but scientists still have hordes of data to sort through; it will start up again in 2021 and will go on to produce 10 times more collisions than before.



At times the speed at which the field is moving leaves me breathless. Last winter I holed up at Princeton University with a group of collaborators: McLeod, Spradlin, Jacob Bourjaily and Matthias Wilhelm. Within two weeks we went from a sketched-out outline to a full paper, calculating a scattering amplitude involving elliptic integrals. It was the fastest I have ever written a paper, and the entire time we worried that we were going to be scooped, that another group would do the calculation first.

We did not end up getting scooped. But not long after, we received a bit of an early Christmas present: two papers by Duhr, Dulat, Johannes Broedel and Lorenzo Tancredi that explained a better way to handle these integrals, building on work by mathematicians Francis Brown and Andrey Levin. Those papers, along with a later one with Brenda Penante, gave us the missing piece we needed: a new alphabet of "elliptic letters."

With an alphabet like that, we can apply Goncharov's trick to more complicated integrals and start to understand two-loop amplitudes, not just in a toy model but in the real world as well.

If we can do two-loop calculations in the real world, if we can figure out what the Standard Model predicts to a new level of precision, we will get to see if the LHC's data match those predictions. If it does not, we will have a hint that something genuinely new is going on, something our theories cannot explain. It could be the one piece of data we need to move particle physics to the next frontier, to unlock those lasting mysteries we cannot seem to crack. SA

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THE SOCIAL LIVES OF AMBOSELI

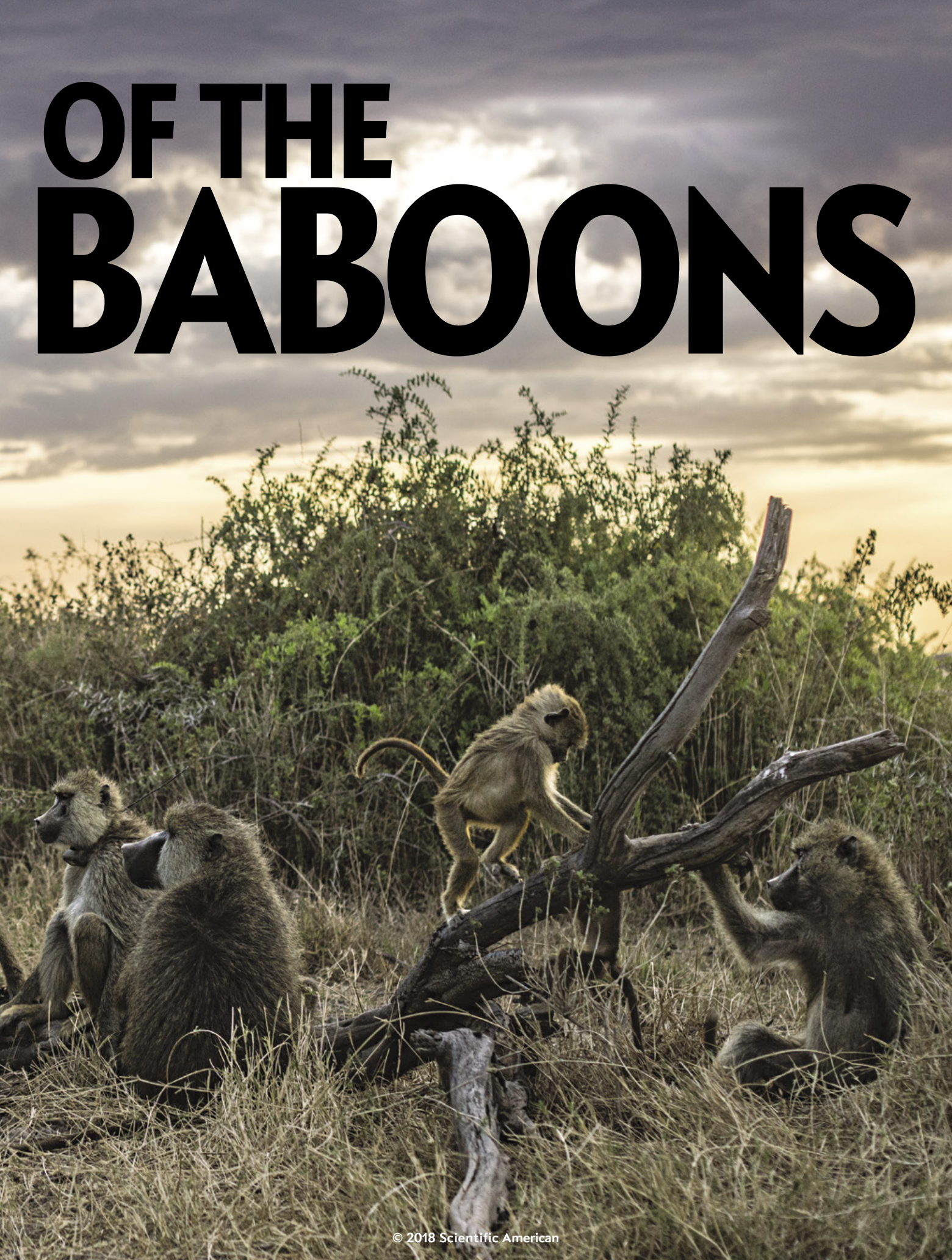
Strong relationships seem to help baboons overcome early life adversity, and that could have big implications for human health

By Lydia Denworth

Photographs by Nichole Sobecki

TROOP OF YELLOW BABOONS gathers at dusk at Amboseli National Park in Kenya. Researchers here are observing them to understand how social habits affect health.

OF THE BABOONS



Lydia Denworth is a Brooklyn-based science writer and author of *I Can Hear You Whisper: An Intimate Journey through the Science of Sound and Language* (Dutton, 2014). She is working on a book about the science of friendship.

It's just after daybreak on a plain at the edge of Amboseli National Park in southern Kenya. In a fever tree grove, a troop of nearly 70 yellow baboons is getting an easy start to the morning. A few late risers sleep on in the upper branches, but the others have been dropping down to the scrubby grass, one by one.

Hiawatha, a six-year-old female, is picking through the coat of her older sister, Hoja, removing dirt and bugs. "It's like somebody waking up, taking a shower, brushing your teeth and combing your hair," Kinyua Warutere, a senior field assistant for the Amboseli Baboon Research Project, says quietly. "Before they set out, they'll socialize in such a way. Mothers will groom kids. Friends will groom friends."

Some of the kids are already playing. The smallest, Huawey, is younger than two months and a little wobbly. He still has the distinctive black coat and bright pink facial features of an infant, although soon his fur will turn golden and then grayish brown. He rolls around with a playmate, and they bat at each other's heads like kittens. Every couple of minutes, though, Huawey retreats to his mother, Hiawatha, and tucks himself under her arm for a moment before venturing out again.

The fate of Huawey and his playmates is of particular interest to Susan Alberts, who stands by a mud-spattered 4×4 peering through binoculars. An evolutionary biologist at Duke University and co-director of the project, Alberts has been studying this group of baboons for 34 years. Since the Amboseli project was founded in 1971 by primatologists Jeanne and Stuart Altmann, its goal has been to dig for the deep evolutionary roots of social behavior in the lives of these animals. The focus of the team's latest work is the long-term consequences of what happens early in life.

The odds are already long for Huawey and his peers. They must navigate what Alberts calls "the Darwinian gauntlet." Thirty to 50 percent of wild baboons do not survive their first year, mostly because of nutritional stress, disease and predators. But some individuals have it harder than others—if they are born in a drought, say, or orphaned. In the first prospective, longitudinal study of its kind, published in 2016, the Amboseli researchers found that early adversity reduces life expectancy dramatically, by as much as half.

Recently, however, the Amboseli researchers have found a potential source of protection from early adversity: strong, stable relationships with other baboons. Now they are trying to figure out how much agency an individual baboon has to use relation-

IN BRIEF

For nearly 50 years researchers at the Amboseli Baboon Research Project have been recording the behaviors of wild baboons, using precise observational tools. The data reveal that baboons that have early adversity tend to die younger than those that do not.

There is new evidence, however, that a baboon might be able to overcome a tough early life by building strong relationships with others in its community. Amboseli researchers suggest that stable social connections might play a role in biological health.

These new ideas in evolutionary science could change our understanding of (and approach to) public health. Humans with childhood adversity tend to get sicker: Could strong relationships help rescue people from their rough starts?

FIELD RESEARCHER Longida Siodi uses an antenna to find baboons, some of which wear tracking collars (*1*). Members of Yoda's Group are located on the plain (*2*). Project manager Raphael Mututua searches for the baboons he will be studying that day (*3*).

ships to bend the trajectory of its fate. This is a critical question not just for baboons but for people with rough starts in life, too.

There are obviously significant differences between baboons and humans. But the parallels in the fundamental elements that shape a life are striking—from the earliest environment to the social relationships of adulthood and patterns of mortality. Indeed, research into developmental origins of human health has found that low birth weight and poor maternal nutrition lead to a higher risk of a range of health problems later in life. And retrospective studies find that early psychological traumas such as abuse and loss of a parent are also associated with a greater likelihood of psychological and medical problems in adulthood.

With fewer confounding variables and shorter (but not too short) life spans, the baboons offer an intriguing opportunity to bridge research in evolution and human health—and to better understand the origins of illness and how to protect against it. As Elizabeth Archie, an associate director at Amboseli and a behavioral ecologist at the University of Notre Dame, says: "The fact that we see a relationship between social support and longevity in animals where they don't have hospitals or someone to drive them to hospitals means that there must be something else fundamentally biological going on." Being well, in other words, is not just about access to health care. Understanding that fact could have sweeping implications for public health.

GROWING ROOTS IN AMBOSELI

WHEN THE ALTMANNS FIRST CAME to Africa in 1963, few primatologists were working in the wild. They spent months searching Kenya and Tanzania before choosing Amboseli as a field site. Stretching across 150 square miles, the acacia woodland and open grassland offered good visibility and thousands of baboons to observe, along with elephants, zebras and giraffes. After they set up a permanent field site in 1971, Jeanne Altmann, who originally studied mathematics and ultimately assumed responsibility for the project, thought hard about how to rigorously record observational data. She developed a methodical technique in which researchers follow individual animals in a certain order for a set period, carefully logging what each does and with whom. Her eventual paper on sampling methods, published in 1974, made possible the valid measurement of behavior in the wild. It has become a bible in primatology.

Altmann also pushed to do two things that were highly unusual. The first was to pay attention to female animals when male aggression—and the assumption that violent competition deter-

NOTES ON social interactions among members of Acacia's Group (*1*). Feces from a yellow baboon from Yoda's Group—to test for hormone levels and track lineage within the troop (*2*).

mined an animal's fate—tended to steal the limelight. "There was this attitude, sometimes explicit, sometimes implicit, that males were where all the action of evolution was," she said when we met in the summer of 2017 in her office at Princeton University, where Altmann is a professor emerita of ecology and evolutionary biology. Yet baboon society is organized along matrilineal lines. Females usually stay in one group all their lives, whereas males move at sexual maturity. "I felt that particularly in mammals and even more so in primates, including humans, females had not only control over their own lives—to the extent that anybody does—but also over the next generation. Why should that be irrelevant to evolution?" Altmann also knew that she needed to be in for the long haul, collecting data on the same groups of animals for generations. "It was so obvious that the outcomes came down the road," she says. "The real action was in lifetimes."

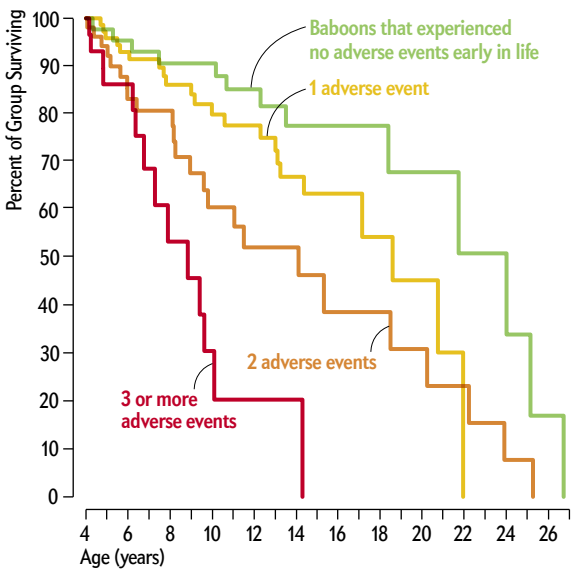
The team of scientists at Amboseli today represents its own matriline—an academic one. Altmann remains a director. Alberts came to Amboseli a year out of college in 1984 and was one of Altmann's first graduate students before becoming a director. The two associate directors, Archie and Jenny Tung, an evolutionary biologist at Duke, were Alberts's graduate students. Between them, they study everything from the demographics of the six groups they follow to the microbiome and genetics of the animals. Of the three Kenyan senior field assistants, Warutere is the most junior, with only 23 years of experience. Project manager Raphael Mututua and second-in-command Serah Sayialel both started work for the project in the 1980s. Even the camp staff—drivers and a cook—are old-timers.

The benefits of such deep institutional knowledge are evident in the field. Warutere, like Mututua and Sayialel, knows every animal on sight—even on the move or glimpsed in the trees. As we watch the troop start its day, he uses a small, yellow binder to record field notes on births, deaths, visible wounds and reproductive states, which females advertise by the variable swelling and color of their posteriors. When the census is done, Warutere begins to collect data in exactly the manner Altmann devised years ago. He observes individual baboons for 10 minutes at a time, noting what they are doing—eating, resting, grooming, and so on—and with whom. He and his colleagues ensure that every animal is observed for the same total amount of time.

Multiply this morning's data by two sessions a day, six days a week, 52 weeks a year and 48 years, and the result is a database that is nearly unmatched in any other wild population. It includes some 1,800 animals across six and a half generations. Yet the records are also intimate. The coded spreadsheets retell the stories of thousands of individual interactions such as those we have just witnessed among Hoja, Hiawatha and Huawey.

How Early Adversity Affects Survival

An analysis of the lives and deaths of 196 wild female baboons from Amboseli showed that sources of early adversity add up—with far-reaching implications for longevity. Females that experienced three or more harsh conditions early in life, such as drought, having siblings close in age or the death of a mother, died an average of 10 years earlier than those that got off to an easier start.



SOURCE: "CUMULATIVE EARLY LIFE ADVERSITY PREDICTS LONGEVITY IN WILD BABOONS," BY JENNY TUNG ET AL., IN *NATURE COMMUNICATIONS*, VOL. 7, ARTICLE NO. 11181; APRIL 19, 2016

Graphic by Amanda Montañez

OUT IN THE FIELD: Mututua and Siodi observe Acacia's Group of yellow baboons at dusk in early November (*1*). One of the baboons from Acacia's Group eats in a tree (*2*).

THE POWER OF BEGINNINGS

AFTER MORE THAN FOUR DECADES of accumulating details about the lives of the baboons, the scientists in Amboseli began to think their research might have relevance to a growing field within human epidemiology: the developmental origins of health. Theories about the impact of early environments on adult disease had been gaining influence since the 1980s. But they remained untested. And in humans, it is difficult to disentangle the effects of early adversity from differences in health habits and access to health care.

The idea that developmental origins might matter appeared in 1986, when the late British epidemiologist David Barker published the first of a series of papers highlighting a link between malnutrition in utero and adult disease such as diabetes, hypertension and heart attacks. Among other things, Barker found that higher rates of type 2 diabetes in British adults in their 60s were associated with low birth weights. Barker and his colleagues came up with the idea that fetal undernutrition might be setting up long-term risk for chronic diseases that we traditionally associate with overweight adults, explains anthropologist Chris Kuzawa of Northwestern University. A handful of other unfortunate natural experiments suggested something similar. At the end of World War II, for instance, residents of a region of the Netherlands under German occupation faced a famine during the winter of 1944–1945, when a railway strike cut off access to food. The long-running Dutch Hunger Winter study of the survivors has shown effects on cardiovascular disease, metabolism and cognitive function in Dutch adults born during that season of starvation.

In light of such findings, in 1992 Barker and C. Nicholas Hales, a biochemist at the University of Cambridge, developed the thrifty phenotype hypothesis, which suggested that an organism faced with harsh early conditions must compromise aspects of development in the interests of short-term survival (fetal under-

nutrition, for instance, might alter glucose metabolism). About a decade later they noticed that in some species, notably insects, early conditions could actually be used to predict adult environments. They refined their hypothesis and renamed it "predictive adaptive response," which suggests that adapting to difficult early conditions better prepares an organism for similar conditions later in life. The theory emphasizes that a mismatch—early malnutrition followed by plenty of food—would be a recipe for disease. The idea rapidly caught on among experts in public health. "It's hard to overstate how widely accepted these models are," Alberts said in a recent presentation.

Variation in adaptive responses depends on the notion of developmental plasticity, which is the ability of an organism to find more than one way to cope with and adapt to its environment. The best demonstrations of the principle are in short-lived animals, such as a species of Siberian vole. Based on cues from maternal melatonin received while in utero, voles born early in the summer mature and reproduce quickly, whereas those born as days shorten experience slower development and do not reproduce until the sun returns.

Other researchers inadvertently stumbled on the long shadow cast by early psychological and social stresses. In the 1980s Vincent J. Felitti was a physician running an obesity clinic in California. He had a patient whose weight appeared to be related to sexual abuse she had suffered as a child. That spurred Felitti to seek connections between childhood family dysfunction and adulthood disease and risky behavior.

Felitti joined forces with Robert Anda, then at the Centers for Disease Control and Prevention, and others, and they launched the Adverse Childhood Experiences (ACE) Study in 1995. It established seven categories of formative experiences, such as abuse, living amid domestic violence, and having family members who were imprisoned or suicidal. Among the more than 9,500 adults who answered the questionnaire, there was a strong relation between the number of categories to which someone had been exposed and that person's likelihood of engaging in substance abuse, suicide attempts and other risky behavior. Exposure to four or more categories resulted in a four-fold to 12-fold increase in risk. The study also found an increased risk of heart disease, cancer and other biomedical diseases.

In the baboons of Amboseli, Alberts, Tung and their colleagues saw an opportunity to test these ideas. In 2015 the team evaluated the predictive adaptive response hypothesis using data they had collected in 2009—a year of such terrible drought that 98 percent of Amboseli's wildebeests died. The researchers focused on adult female baboons born in previous years of either low rainfall or high rainfall. Because reproductive success is the most critical measure in evolutionary biology, they compared the fertility of these individuals in 2009 with one another. As expected, all animals were less likely to reproduce during a bad drought. But in a direct contradiction of the predictive adaptive response model—which would suggest that being born in a dry year prepares a female for drought, making her fertility less susceptible to its effects—those born in low rainfall years did not fare better than the high rainfall group. In fact, they did worse. Alberts and her colleagues propose that something nearly opposite to the predictive adaptive response is at work: a developmental constraints model. It predicts that "being born in a poor early environment gives you a deficit in *all* environments," Alberts says.

1

2

The team also designed a baboon version of the ACE Study. Because baboons are nonseasonal breeders, no two have the same experience. "Everybody's born at a different time, and so many aspects of the early environment are highly particular to your mother," Alberts says. Published in 2016 in *Nature Communications,* the study analyzed the life histories of 196 females and considered six categories of early adversity from the first four years of life: drought; group size (which affects competition and fertility); maternal dominance rank and social integration; a sibling born within 18 months; and death of the mother.

The results were unequivocal. Baboons with three or more sources of adversity died an average of 10 years earlier than those with one or none (the median life span of the group was 18.5 years). Those that suffered the most adversity were also the most socially isolated adults. "That's an astonishing effect," Alberts says. "It explains 12 percent of the variation in life span, which is a lot for a fitness component."

Northwestern's Kuzawa, who oversees a long-term study of the developmental origins of human health in the Philippines, was pleased to see Amboseli's empirical tests of the predictive adaptive response model, which he had always found limited. Early life conditions may predict adult conditions for a short-lived animal such as the vole, for whom environmental factors at birth are more like-

AMBOSELI Baboon Research Project is studying animals from Acacia's Group (*1*, *3*), Yoda's Group (*2*) and others. The baboons give an opportunity to bridge research in evolution and human health.

3

ly to stay the same into reproduction, Kuzawa says. But the model is not necessarily valid in humans, who live into their 70s and beyond. "You see the same ideas get repeated, and there's actually no evidence for it," he says. Baboons, which can live for up to 30 years, are more comparable. That is why Kuzawa calls the Amboseli project "a unique resource for looking at these long-term effects."

RESILIENCE FROM RELATIONSHIPS

FOR PEOPLE WHO FACE early adversity while they are young, the big question is: How much can later circumstances compensate for the effects of a rough start? The recent Amboseli studies may offer some clues. Not every unfortunate baboon came to an unfortunate end. Indeed, there was enough variation in longevity to suggest that some animals do alter their fate. The Amboseli researchers have found signs that strong relationships help animals push back against the damaging effects of early adversity. Being born in a drought, for example, is mitigated by having a high-ranking mother. Females' grooming relationships with males, as opposed to females, were less affected by early adversity, suggesting a possible buffer. Maternal early experience echoes down the baboon generations. "If your mother dies and she had no early adversity, your survival is compromised, but it's not terrible compared with kids whose mothers are still alive," Alberts says. "But if your mother dies and she had early adversity, you're toast."

These findings fit with earlier pioneering work from Amboseli on the functional significance of social bonds. By the mid-1990s the project had complete data (birth, reproduction, death) on about 100 female baboons and was reaping the rewards of Jeanne Altmann's long-range approach. Altmann and Alberts teamed up with evolutionary anthropologist Joan Silk, now at Arizona State University, to investigate just how much social relationships might figure in an animal's prospects for reproductive success.

Silk had spent a year at Amboseli as a postdoctoral researcher. In the late 1990s and early 2000s, when a few primatologists started saying that animals have friends, she wondered if they really did and if it mattered. Conventional wisdom held that the critical variable in hierarchical monkey societies was dominance rank. But Silk was intrigued by emerging evidence that human social relationships were linked with health. A pivotal 1988 paper in *Science* by sociologist James House and his colleagues at the University of Michigan had concluded that a lack of connection could be as deadly as obesity and smoking.

So Silk, Alberts and Altmann turned to Amboseli's database. Alberts had already created something they called the sociality index, a measure that reflected the strength of social bonds based on proximity, grooming and other social behaviors—basi-

cally how often females interacted nicely. They measured that against the number of surviving infants. To their surprise, social integration predicted reproductive success more than dominance rank or any other variable they measured. That result, which Silk calls "stunning," was published in 2003 in *Science*.

To be sure the finding was not unique to Amboseli, Silk did a similar analysis with Robert Seyfarth and the late Dorothy Cheney, evolutionary biologists at the University of Pennsylvania, using data from their baboon research at Moremi Game Reserve in Botswana. "The results from both studies were striking in their convergence," Seyfarth says. By 2014 further studies at both Amboseli and Moremi had found that social connectedness was linked not just to reproduction but to longevity.

Overall, the negatives of getting a bad start still tend to outweigh the positive effects of social connection among the baboons. But because social relationships do have some protective power in extending life spans, the team at Amboseli is now asking, as Archie puts it, "Can friendship rescue you?" If it can, the reasons why are likely to be found in biology. "What's happening at the molecular and physiological level?" asks Tung, who focuses on the interplay between genes and behavior. "How does [social behavior] get under the skin and influence how the genome functions?"

Applying evolutionary science to public health could provide important clues to figuring out the causes of disease.

Tung's most intriguing finding so far, published in 2016 in *Science,* came not from the baboons but from a group of captive rhesus macaques. Her Duke laboratory manipulated the animals' social status by creating and then rearranging groups of females. When the scientists tested cells from different animals to see how they handled infection, they found clear differences in immune gene regulation according to social status. "We think that social integration and social isolation probably do have direct effects on how our immune system functions," Tung says.

Although Tung cannot manipulate the wild baboon groups, she is now using fecal samples, collected in Dixie cups, to look for similar patterns. Led by Archie, the team is sequencing the microbiomes of those 20,000 samples. So far the researchers have found that the baboon microbiome is socially structured—animals in the same group have more similar gut microbes. Furthermore, within a group animals that groom one another more often are more similar than those that do not. Once the sequencing is done, they will look for aspects of the microbiome that predict an animal's health, survival or reproductive success.

The new ideas about developmental plasticity arising from the work of the Amboseli Baboon Research Project are stirring debate as well as excitement. When the scientists published a review in 2017 in *Evolution, Medicine, & Public Health,* it generated five commentaries in response, including one from Kuzawa, who questioned the researchers' definition of "early life," which they extend from conception to reproductive maturity. Others argued that they did not give enough attention to the role of parents as mediators of early conditions. And a few researchers remain unconvinced that animal models are useful for thinking about disease in people.

Nearly everyone agrees, however, that applying evolutionary science to public health could provide important clues to figuring out the causes of disease and developing better interventions. A 2017 review in the *Lancet* noted: "It is no exaggeration to suggest that ... [it] could revolutionise the discipline." It will deepen our understanding, the authors explain, of why poverty and deprivation have such a powerful impact on health and life span and emphasizes that factors such as bad health habits do not explain everything. After all, Alberts says, "baboons don't have health habits."

At the end of our morning in the field, Alberts and I perch on a rocky hillside above the baboons with zebras and wildebeest grazing in the distance. She sums up the project's work by drawing a chart in my notebook. It consists of three boxes in a row. She marks the first "EA" for early adversity, the middle "ASC" for adult social connectedness, and the third "H + S" for health and survival. Then she adds arrows between the boxes—each pointing to the right—to show the influence of adversity on connectedness and of connectedness on survival. Based on the new research, she inserts a third arrow, which arcs high above the boxes from early adversity directly to health and survival, skipping over connectedness. This represents how too much adversity swamps the help provided by strong relationships.

The arrows are all-important. Clearly, early adversity must precede survival. But how does connectedness fit in? How much healthier does it make you? It is still possible that healthier individuals are more likely to connect in the first place.

Alberts hands back my notebook and says, "I think that all those arrows are real." She means that each element exerts its influence in the way she has laid out. If she is right, connectedness has the power to alter the course of an individual's life in the face of early adversity. Even if that does not prove true, Alberts is convinced the baboons have more to tell us about ourselves. "When a phenomenon that we are very concerned about in humans has evolutionary roots," she says, "it has huge consequences for how we think we're going to fix the problems that arise from it." SA

MORE TO EXPLORE

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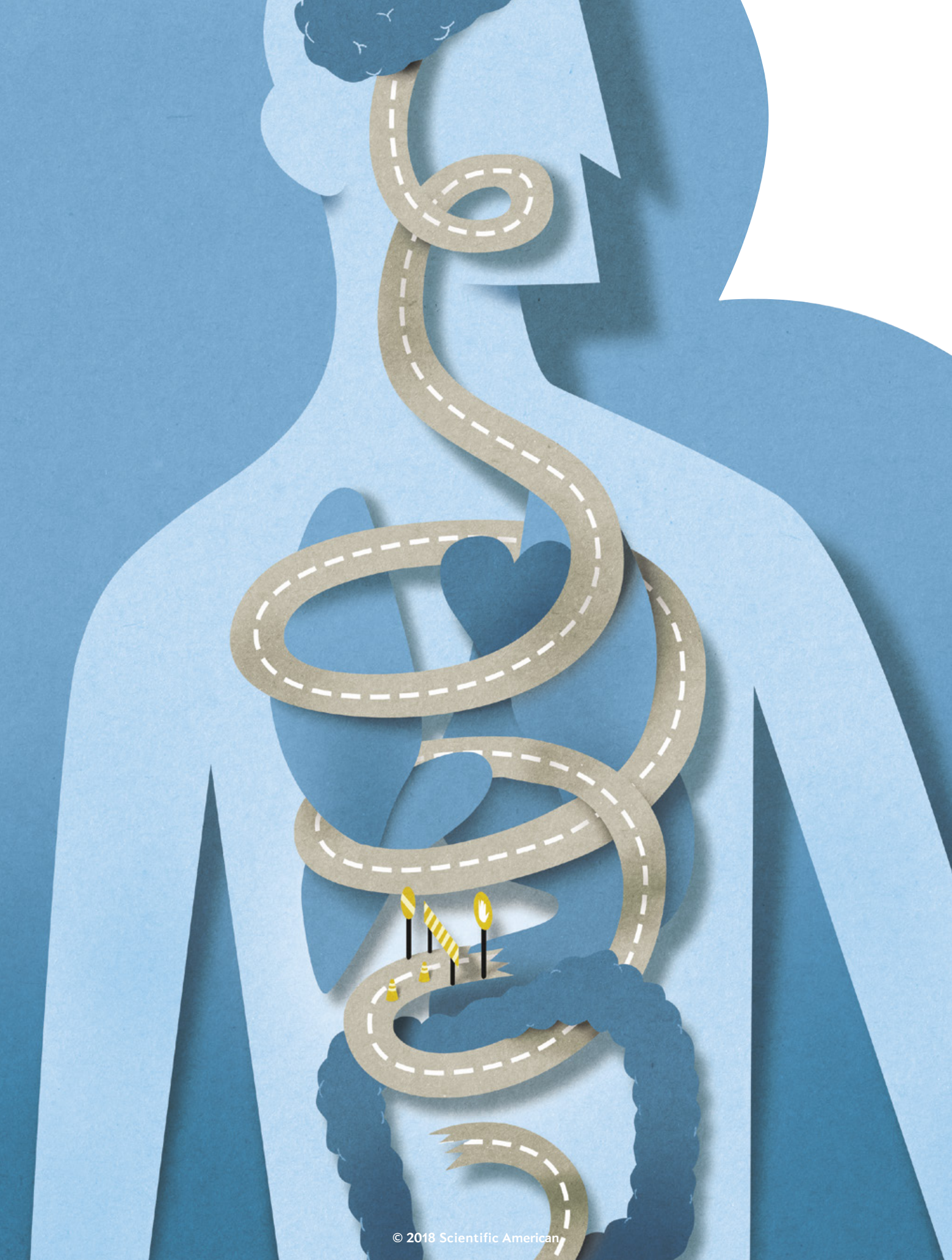


MIND OVER MEAL

Does weight-loss surgery rewire gut-brain connections?

By Bret Stetka

Illustration by Bomboland

For Teresa, the first plate of scrambled eggs was a transcendent experience.

THE STANFORD UNIVERSITY MEDICAL CENTER nurse coordinator, 41 years old at the time, had completely lost her appetite in the days after her surgery. She consumed only liquids and only at her surgeon's request. Yet when her interest in eating returned, it was as though something about her relationship with food had fundamentally changed.

Bret Stetka is a writer based in New York City and an editorial director at Medscape (a subsidiary of WebMD). His work has appeared in *Wired,* NPR and the *Atlantic.* He graduated from the University of Virginia School of Medicine in 2005.

The eggs, Teresa's first solid meal in four weeks, were a revelation: simple, soft and buttery. To her surprise, they constituted a completely satisfying meal. Gone was the desire for sweets and excessively salted savories. Her once beloved french fries and rich desserts no longer enticed her. Her desire to eat was back, but for the first time in her life eating "right" came easy.

Teresa had undergone a sleeve gastrectomy, one of a variety of procedures—known as bariatric surgeries—that manipulate the stomach and intestines to promote weight loss. Yet more than shedding pounds, which she did, it was the complete change in cravings that Teresa considers the most surprising result of her 2012 operation.

She had struggled with her weight since childhood. Years of hormone therapy while trying to get pregnant did not help, nor did pregnancy itself. "Before I knew it, I was 270 pounds," Teresa recalls. "And I just couldn't get the extra weight off despite trying everything: every diet, lots of exercise." The surplus pounds also made it hard to manage a toddler. "I couldn't keep up with my son," she says.

A sleeve gastrectomy can shrink the stomach from the size of a football to that of a banana, roughly 15 percent of its original size. One year later—after months of eating healthier and eating less—Teresa was down to 150 pounds. "That was actually even low for me," she says, "but the surgery really changed how I ate."

Since the 1960s, when these techniques were introduced, doctors have considered bariatric surgery primarily a mechanical fix. A smaller stomach, the reasoning went, simply cannot hold and process as much food. Patients get full faster, eat less and therefore lose weight.

This idea is in part true. But now scientists know that it is not nearly that simple. Teresa's weight loss was in all likelihood caused by the drastic change in how her gut speaks to her brain, and vice versa. The procedure had indirectly spurred new neural connections, changing how she thought about and craved food.

Recent science has revealed that appetite, metabolism and weight are regulated through a complex dialogue between bowel and brain—one in which

IN BRIEF

Doctors have long suspected that bariatric surgeries help patients lose weight by reducing the size of the stomach—but new work suggests other mechanisms are involved.

In patients who undergo the procedure, the brain areas involved in communicating with the gut become hyperactive compared with their earlier activity.

These interventions also change the microbial populations living within digestive systems in ways that could further adjust signaling along the gut-brain axis and contribute to new, healthier eating habits.

mechanical influences, hormones, bile acids and even the microbes living in our gut all interact with labyrinthine neurocircuitry. Bariatric surgery, scientists are discovering, engages and may change all these systems. In the process, it is helping researchers map how this complicated interplay manipulates our eating behaviors, cravings and frenzied search for calories during starvation. This work could also reveal new targets—including microbes and possibly the brain itself—that render the risky surgical procedure obsolete altogether.

BRAIN MEETS BOWEL

WE HAVE ALL FELT the physical effects of the gut-brain communion: the gastric butterflies that come with love, the rumbles that arise before delivering a speech. These manifestations result from the brain signaling to the gastrointestinal tract, both through hormones and neuronal signals.

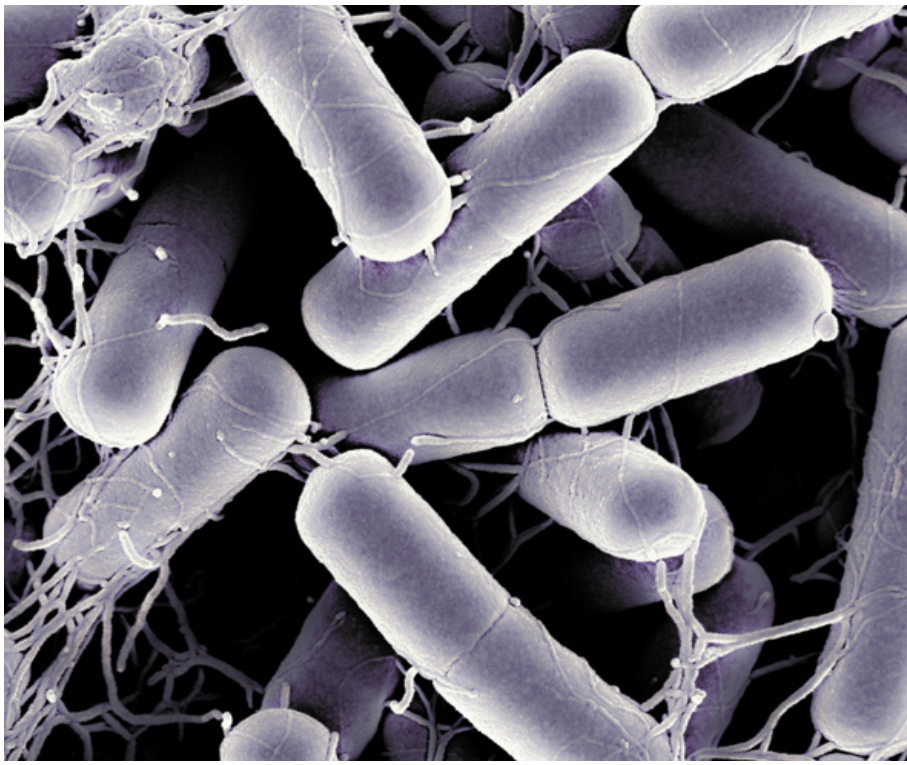
Conversely, the gut can send signals back to the brain, too. In fact, coursing through our abdomen is the enteric nervous system, colloquially known as the second brain. This neural network helps to control food digestion and propulsion through the 30 feet of our gastrointestinal tract. It also communicates directly with the brain through the vagus nerve, which connects the brain with many of our major organs.

Two primary gut-brain pathways regulate appetite. Both systems involve a small, central brain region called the hypothalamus, a hotbed of hormone production that helps to monitor numerous bodily processes. The first system comes into play during fasting. The stomach secretes the hormone ghrelin, which stimulates the arcuate nucleus, a region within the hypothalamus. This structure then releases neuropeptide Y, a neurotransmitter that, in turn, revs up appetite centers in the cerebral cortex, the outer folds of the brain, driving us to seek out food. In anticipation of mealtime, our brain sends a signal to the stomach via the vagus nerve, readying it for digestion. "This can occur simply at the sight, smell or thought of food," says Mayo Clinic gastroenterologist and obesity expert Andres Acosta Cardenas. "Our brain is preparing our body for a meal."

The second gut-brain pathway suppresses our appetite. As we eat, several other hormones, including leptin and insulin, are secreted from fat tissue, the pancreas and the gastrointestinal tract. Separately, these hormones play many roles in digestion and metabolism. Acting together, they signal to another area of the hypothalamus that we are getting full. Our brain tells us to stop eating.

The appetite and satiety loop constantly hums along. Yet hunger pathways also interact with brain regions such as the amygdala, involved in emotion, and the hippocampus, the brain's memory center. Hence, our "gut feelings" and "comfort foods" are driven more by moods and nostalgic recollections of Grandma's rhubarb pie than mealtimes. As a result of higher thinking processes, food now has context. Food is culture. As playwright George Bernard Shaw expressed it, "there is no sincerer love than the love of food."

Then there is the hedonistic thrill of sitting down to a meal. Eating also lights up our reward circuitry, pushing us to eat for pleasure independent of energy needs. It is this arm of the gut-brain axis that many scientists feel contributes to obesity.



GUT MICROBES may play a role in obesity. Gastric bypass surgery can lead to lasting changes in the microbial populations that reside in the digestive system.

Neuroimaging work confirms that, much like sex, drugs and gambling, food can cause a surge of dopamine release in the brain's reward circuitry. This neurotransmitter's activity serves as a powerful motivator, one that can reinforce dining for its own sake rather than subsistence. Researchers have found that for rats, sweetness surpasses even cocaine in its desirability. In humans, psychiatrist Nora Volkow, director of the National Institute on Drug Abuse, has confirmed what chocolate lovers everywhere already know: food's effects on the reward system can override fullness and motivate us to keep eating. Such findings hint at a neurobiological overlap between addiction and overeating, although whether eating can be an outright addiction remains a controversial question.

THE SURGICAL SOLUTION

THANKS TO THE MOVEMENT of messenger hormones and neurotransmitters, our mind and stomach are in constant communication. Disrupting this conversa-

SCIENCE SOURCE

tion, as bariatric procedures must do, will therefore have consequences.

Research has shown that in the days and weeks after bariatric surgery, sugary, fatty and salty foods become less palatable (as Teresa discovered). One study, published in 2010 by Louisiana State University neurobiologist Hans-Rudolf Berthoud, found that rats lost their preference for a high-fat diet following gastric bypass surgery. In the 1990s multiple research teams had reported that after such surgery, patients often lose the desire to consume sweet and salty foods. More recently, a 2012 study by a team at Brown University found that adult patients had significantly reduced cravings for sweets and fast food following bariatric surgery. Similar findings in adolescent surgery patients also appeared in a 2015 study.

The alteration in cravings and taste may be caused by changes in the release and reception of neurotransmitters throughout the gut-brain system. In 2016 Berthoud and his colleagues found that in the short term—around 10 days postprocedure—bariatric surgery in mice caused additional meal-induced neural activity in brain regions known to communicate with the gut compared with brain activity before the surgery. Specifically, the boost in activity was seen in a connection leading from stomach-sensing neurons in the brain stem to the lateral parabrachial nucleus, part of the brain's reward system, as well as the amygdala.

"Obesity is a disease of the gut-brain axis. We need to identify which part of the axis is abnormal in each patient to personalize treatment."
—Andres Acosta Cardenas *Mayo Clinic*

An expert in this area is biochemist Richard Palmiter of the University of Washington. In a 2013 study published in *Nature,* Palmiter's group used complex genetic and cell-stimulation techniques—including optogenetics, a means of controlling living tissue using light—to activate or silence specific neurons in the brain stem parabrachial nucleus pathway in mice. He found that engaging this circuit strongly reduced food intake. Yet deactivating it left the brain insensitive to the cocktail of hormones that typically signaled satiety—such that mice would keep eating.

Palmiter's work suggests that engagement of the brain stem parabrachial pathway helps us curb our appetite. Because it is this same pathway that becomes unusually active postsurgery, it is probable that the hyperactivation Berthoud discovered is part of the gut-brain's effort to assess satisfaction postsurgery. As he puts it, "the brain must relearn how to be satisfied with smaller portions."

In other words, bariatric surgery is certainly a mechanical change: with less space, the body needs to adjust. Still, there is clearly more to the story. After the procedure, more undigested food may reach the intestine, and, Berthoud speculates, it would then trigger a hormonal response that alerts the brain to reduce food intake. In the process, it would alter the brain's activity in response to eating. If he is correct, the surgery's success—at least in the short term—may have as much to do with its effects on the gut-brain axis as it does on the size of a person's stomach.

THE MICROBIAL MIND

THERE IS ANOTHER PLAYER in the complex communications of mind and gut that might explain bariatric surgery's effects. Experts have implicated the microbiota—the trillions of single-celled organisms bustling about our digestive system—in countless disorders, including many that affect the brain. Our co-denizens and their genome, the "microbiome," are thought to contribute to autism, multiple sclerosis, depression and schizophrenia by communicating with the brain either indirectly via hormones and the immune system or directly through the vagus nerve.

Research carried out by gastroenterologist Lee Kaplan, director of the Massachusetts General Hospital Weight Center, suggests that the microbiota may play a role in obesity. In a study published in 2013 in *Science Translational Medicine,* Kaplan and his colleagues transferred the gut microbiota from mice that had undergone gastric bypass surgery to those that had not. Whereas the surgery group lost nearly 30 percent of their body weight, the transplanted mice lost a still significant 5 percent of their body weight. (Meanwhile a control group that did not have surgery experienced no significant weight change.) The fact that rodents could lose weight without surgery, simply by receiving microbes from their postoperative fellows, suggests that these microbial populations may be at least partly responsible for the effectiveness of bariatric procedures.

A similar study, published in 2015 by biologist Fredrik Bäckhed of the University of Gothenburg in Sweden, found that two types of bariatric surgery—the Roux-en-Y gastric bypass and vertical banded gastroplasty—resulted in enduring changes in the human gut microbiota. These changes could be explained by multiple factors, including altered dietary patterns after surgery; acidity levels in the gastrointestinal tract; and the fact that the bypass procedure

causes undigested food and bile (the swamp-green digestive fluid secreted by the liver) to enter the gut farther down the intestines.

As part of the same research, Bäckhed and his colleagues fed mice microbiota samples from obese human patients who either had or had not undergone surgery. All the rodents gained varying degrees of body fat, but mice colonized with postsurgical microbiota samples gained 43 percent less.

How might changes in our gut's flora alter their interactions with the gut-brain axis and affect weight? Although the answer is still unclear, there are a few promising leads. Specific gut microbial populations can trigger hormonal and neuronal signaling to the brain such that they influence the development of neural circuits involved in motor control and anxiety. Bäckhed suspects gut flora after bariatric surgery could have a comparable effect on brain regions associated with cravings and appetite.

The neurotransmitter serotonin could play a special role as well. About 90 percent of our body's serotonin is produced in the gut, and in 2015 researchers at the California Institute of Technology reported that at least some of that production relies on microbes. Change the microbes; change the serotonin production. And that could make quite a difference because, as numerous studies have confirmed, stimulating the brain's serotonin receptors can significantly reduce weight gain in rodents and in humans.

TREATING THE GUT-BRAIN AXIS

IT IS A WELCOME TURN of fate that bariatric surgery is illuminating new directions in treating obesity—which affects more than 600 million people worldwide. Some of these avenues could render surgery obsolete or at least reserved for the most extreme cases. Thus, at the forefront of battling excess weight may be hijacking the gut-brain axis.

In 2015, for example, the U.S. Food and Drug Administration approved a device that stimulates the vagus nerve to quell food cravings. A surgeon implants the device, made up of an electric pulse generator and electrodes, in the abdomen so that it can deliver electric current to the vagus nerve. Although precisely how it works is unknown, the study leading to its approval found that patients treated for one year with this tool lost 8.5 percent more of their excess weight than those without the device.

That approach offers some patients a less invasive alternative to bariatric surgery, but for the moment, vagus nerve stimulators are not as effective as many other obesity therapies. Meanwhile a number of intrepid neurosurgeons are investigating the use of a technique called deep-brain stimulation. Approved for use in Parkinson's disease and obsessive-compulsive disorder, the procedure involves stimulating specific brain regions using implanted electrodes. Although this research is in its infancy, numerous brain regions involved in appetite control are being explored as possible targets.

The Mayo Clinic's Acosta Cardenas believes that in the future the best approach to treating obesity will be highly personalized. "Obesity is a disease of the gut-brain axis," he says, "but I think we need to identify which part of the axis is abnormal in each patient to personalize treatment. I'm trying to identify which patients have a problem with the microbiome, or hormones, or emotional eating so we can maximize response to treatment."

In 2015 Acosta Cardenas and his colleagues looked at numerous factors potentially related to obesity in more than 500 normal-weight, overweight and obese patients. Among the factors were how quickly the study subjects got full, how quickly their stomachs emptied, and how hormone levels fluctuated in response to eating and psychological traits. Acosta Cardenas's findings support the idea that there are clear subclasses of obesity and that the cause and ideal treatment of obesity are most likely unique to each patient. For example, 14 percent of the obese individuals in his study have a behavioral or emotional component that would steer his treatment recommendation away from surgery and medication and toward behavioral therapy. He can also foresee a future in which he might prescribe a probiotic or antibiotic for obesity patients with an abnormal microbiota.

At the moment there is no telling with certainty which perturbations of the gut-brain axis caused Teresa's weight gain. But it is clear that she benefited from surgery, maintaining her desired weight of 160 pounds for at least the next four years.

Her feet do not hurt anymore. She has more energy. She can keep up with her son. And although she admits certain cravings have crept back during the years, they are not as intense as they once were and are far more manageable.

"Before my surgery I had no self-control. I couldn't hold back," Teresa recalls. "Now if french fries show up at the dinner table, I may have a few, but I don't have to deprive myself. I just don't have the drive to eat that way anymore. I will inevitably take half of my meal home." SA

MORE TO EXPLORE

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SUSTAINABILITY

THE LAST

Can we remove enough CO_2 from the atmosphere to slow or even reverse climate change?

By Richard Conniff

Photographs by Liz Tormes

INJECTION WELLS at Iceland's Hellisheiði geothermal power plant send brine down into deep bedrock, along with carbon dioxide pulled from the air.

RESORT

Richard Conniff is an award-winning science writer. His books include *The Species Seekers: Heroes, Fools, and the Mad Pursuit of Life on Earth* (W. W. Norton, 2011).

NOT LONG AGO IT SEEMED AS IF REDUCING GREENHOUSE GAS emissions would be enough to save the world from climate change. Replace fossil-fuel power plants with clean energy sources, make cars and buildings more efficient, switch to LED lights, eat less meat, and so on. Slashing emissions and boosting renewables looked like the answer even to the Intergovernmental Panel on Climate Change as recently as 2005. But the strategy has not worked out as planned. Global emissions have gone up instead of down. It now appears that even cutting annual net emissions worldwide to zero by 2050 will not be enough.

To prevent economic and environmental devastation, climate experts maintain that we will now also have to achieve *negative* emissions. Doing so means removing billions of tons of carbon dioxide from the atmosphere every year. That is like saying we can no longer put out the garbage—and we need to steadily take back the garbage we put out in the past.

Negative emissions on a massive scale have become "a biophysical requirement" to meeting climate change goals, according to a 2018 study led by Jan C. Minx of Germany's Mercator Research Institute on Global Commons and Climate Change. Figuring out how to get there is a matter of "immediate urgency," he and his co-authors warn in *Environmental Research Letters,* if the world hopes to limit warming to 1.5 degrees Celsius. Almost every nation on the planet subscribed to that target—with a fallback of "well under" two degrees C—as part of the 2016 Paris Agreement on climate change. Warming is currently about one degree above preindustrial levels. But it is increasing at 0.2 degree C per decade. In a special report in October 2018, the Intergovernmental Panel on Climate Change warned that we have just 12 years to act if we hope to avoid slipping past 1.5 degrees C, the level regarded by most scientists as the furthest we can go if we hope to preserve life more or less as we know it.

Staying under that threshold mandates a specific "carbon budget," an overall amount of carbon dioxide we can add to the atmosphere without pushing warming beyond that temperature. At today's emissions—about 40 billion to 50 billion tons a year—"there may be only five years' worth of CO_2 emissions left" in the 1.5-degree scenario, Minx and his co-authors say. (For the remainder of this article, we use "tons" to mean "metric tons.") After that, every additional ton would require an equal withdrawal. His group estimates the world will need to remove 150 billion to more than one trillion tons of CO_2 from the atmosphere by 2100—roughly two billion to 16 billion tons a year, starting in 2050, with the number increasing significantly later in the century.

To do that, Minx and his team note, we will have to start building "several hundred" carbon capture and storage installations a year beginning in 2030, just 11 years from now. That could mean deploying big machines to pull carbon dioxide from the air or developing bioenergy power plants that burn trees—grown in continuous rotation—in a facility that captures emissions and sends them deep underground for permanent burial. Low-tech options would include replanting cut forests or expanding existing ones, improving farm and pasture soils so they hold more carbon, and crushing and spreading certain kinds of rock that soak up CO_2.

Most of the higher-tech carbon capture methods are still in the early stages of development, however. They require enormous investment at considerable risk of failure and entail major side effects, including competition for land that is already being used to feed people or provide habitat for wildlife.

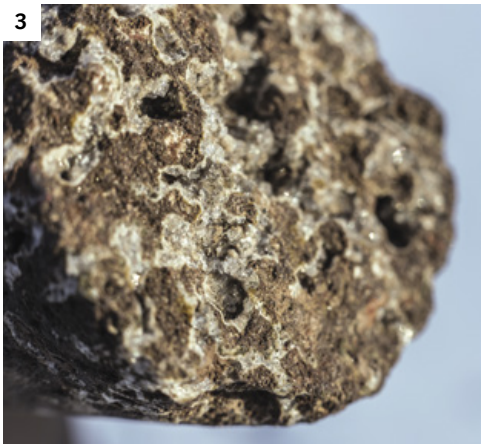
And yet pursuing carbon capture on a massive scale appears to be our only option. When University of Washington statistician Adrian E. Raftery and his co-authors of a 2017 study in *Nature Climate Change* looked at current trends—not including negative emissions technologies—they found that we are on track to reach 3.2 degrees C of warming by the end of the century, with a range from two to 4.9 degrees C. In a subsequent study in the *Proceedings of the National Academy of Sciences USA,* Tex-

IN BRIEF

To limit global warming to 1.5 degrees Celsius, nations will have to remove one trillion tons of carbon dioxide emissions from the planet's atmosphere this century.

Finding the optimal mix of carbon capture methods will be critical. Machines that pull CO_2 from the air could remove 250 billion tons by 2100. Replanting clear-cut forests could achieve 180 billion tons.

Net costs range from $0 to $300 per ton. Unless big markets are developed to use the captured CO_2, a carbon tax may provide the best support for the techniques.



CLIMEWORKS MACHINE extracts carbon dioxide from the atmosphere (*1*). An injector inside a nearby dome (*2*) sends the gas more than 700 meters underground, where it reacts with basalt bedrock to form carbonate, visible as white streaks in a core sample from the basalt (*3*).

as A&M climate scientist Yangyang Xu and a colleague categorized warming greater than three degrees C as "catastrophic" and greater than five degrees C as posing "existential threats to a majority of the [human] population."

So let us assume that one trillion tons of negative emissions in this century—an average of 20 billion tons a year from 2050 to 2100—is necessary. What share of that pie could each method account for and at what cost? Given competition among methods for certain resources, such as land, what is the best mix to pursue? And can we muster the political will to pursue negative emissions—while drastically cutting our current carbon dioxide output?

CLEAN THE WIND

ON A HARDENED LAVA FIELD OF BOULDERS and moss in the foothills just outside Reykjavík, Iceland, a machine the size of a one-car garage pulls air through a chemical filter that extracts carbon dioxide. It is powered by waste heat from the geothermal power plant next door, and it pumps the captured carbon dioxide more than 700 meters underground, where the gas reacts with basalt rock and becomes solid mineral. Climeworks, a Swiss start-up, calls the operation the first direct air capture and storage plant in the world. It sequesters a modest 50 tons of carbon dioxide a year.

Direct air capture and storage may be the most straightforward path to negative emissions: banks of fans would harvest CO_2 from the sky and bury it. Scientific scenarios project that this technology could remove 10 billion to 15 billion tons of carbon dioxide a year by the end of the century; a few experts think 35 billion or 40 billion tons may be possible. This is such a tantalizing prospect that many climate scientists worry it could pose a moral hazard: people might think they can delay fossil-fuel reductions now in the hope of technological salvation later.

The most thorough review of removal methods—another 2018 study in *Environmental Research Letters*—takes a more sober view. Sabine Fuss of Mercator and her colleagues examined costs, side effects, environmental sustainability and other factors to project the carbon sequestration potential for seven major removal methods. Fuss and her co-authors put that potential for direct air capture in 2050 at only 500 million to five billion tons a year—adding up to 25 billion to 250 billion tons this century—at a cost of $100 to $300 per ton. For perspective, our cars each typically emit 4.6 tons of carbon dioxide a year.

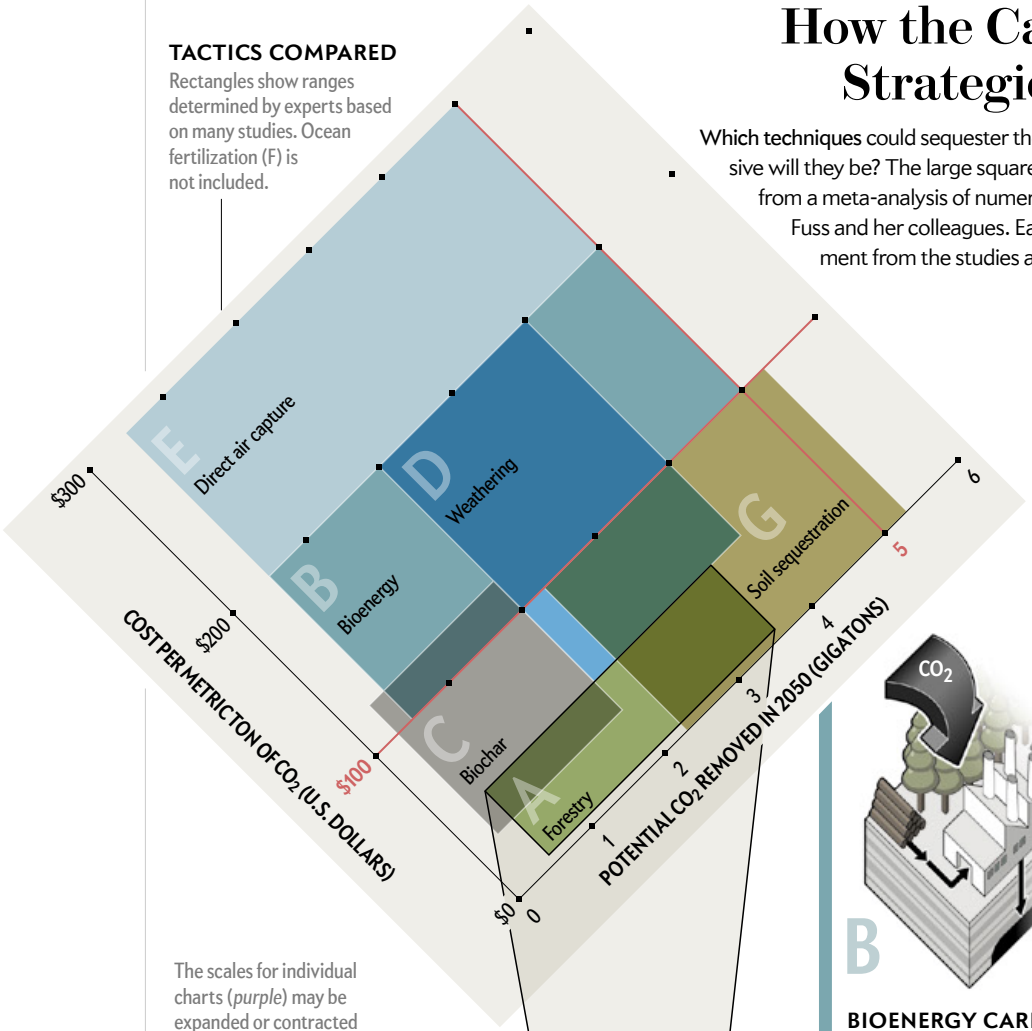
Indeed, air capture "is not a silver bullet," says James S. Mulligan of the World Resources Institute's Food, Forests, and Water Program. "It's not a shiny object. It's kind of a cruddy object. But we need it." Some researchers claim they could get the cost below $100 per ton. Yet if the time line for doing that at scale is anything like the 60-plus years it took solar power to move from satellites in the 1950s to broad marketplace penetration today, Minx says "it may be too late."

Direct air capture also consumes enormous amounts of energy. Removing a million tons of carbon dioxide a year would require a 300- to 500-megawatt power plant, according to Jennifer Wilcox, a chemical engineering professor at Worcester Polytechnic Institute. If that were a coal-fired plant, it would create more emissions than it would remove. If power came from solar or wind farms, it would cover a lot of land that might already be in

How the Carbon Capture Strategies Stack Up

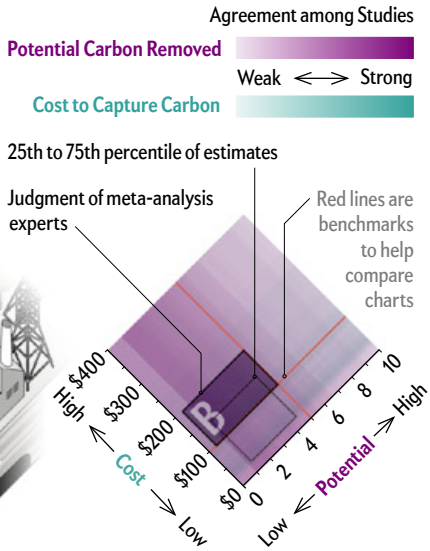
Which techniques could sequester the most carbon dioxide in 2050? How expensive will they be? The large square compares approaches. The numbers come from a meta-analysis of numerous studies, performed by economist Sabine Fuss and her colleagues. Each breakout chart shows a detailed assessment from the studies and the expert judgment of Fuss's team.

TACTICS COMPARED
Rectangles show ranges determined by experts based on many studies. Ocean fertilization (F) is not included.



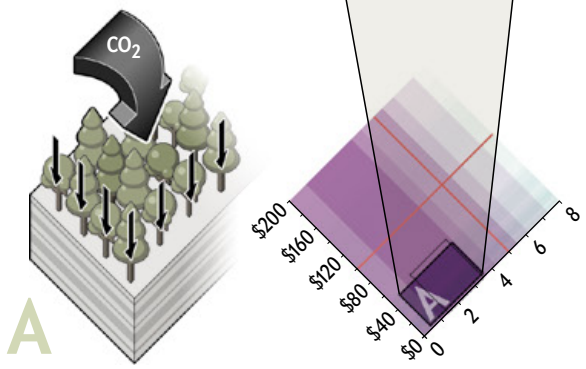
The scales for individual charts (*purple*) may be expanded or contracted for easier reading.

HOW TO READ THE PURPLE CHARTS
Colors depict the range of values from numerous studies. Darker shades indicate heavier overlap.



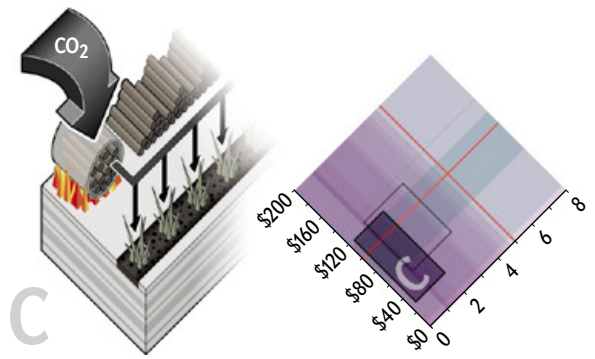
BIOENERGY CARBON CAPTURE AND STORAGE

Plants, which breathe in CO_2, are burned to produce energy or fermented into fuel. The CO_2 is removed and pumped deep underground for permanent storage. The products create revenue, but wide adoption could eat up land needed for food crops.



REFORESTATION AND AFFORESTATION

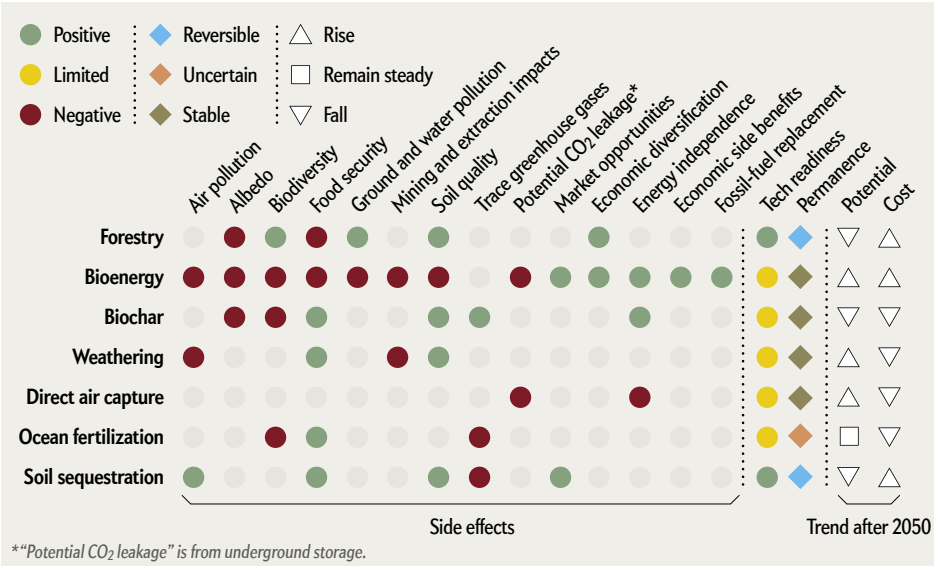
Trees are planted to replace clear-cut forests or expand existing ones. They absorb CO_2 from the air and convert it into new wood growth, including roots. Timber markets and management practices would have to be reformed.



BIOCHAR

Crops, manure or organic waste is heated, without oxygen, creating biofuel and biochar—a charcoal-like residue rich in carbon. It is spread onto agricultural fields to improve soil, which can also bind additional carbon. Large-scale production with minimal energy inputs could be a challenge.

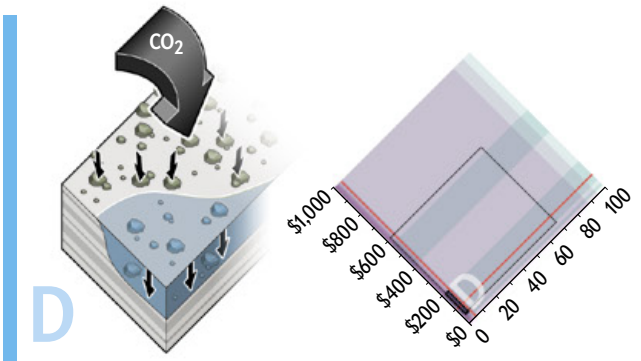
Graphics by Pitch Interactive, Illustrations by Ben Gilliland



*"Potential CO_2 leakage" is from underground storage.

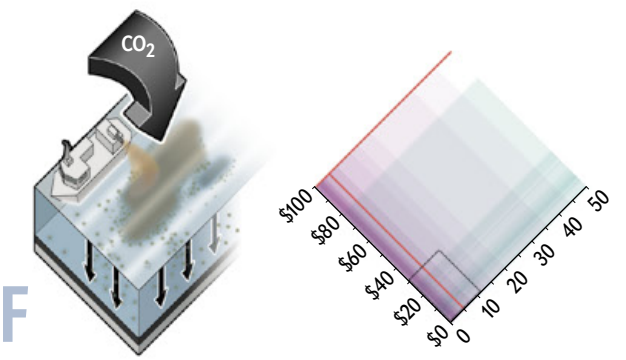
PROS AND CONS

Techniques that capture carbon in 2050 (*rows*) may come with positive or negative side effects (*dots*). The "tech readiness" column indicates how set for deployment an approach may be at that time. "Permanence" is whether stored CO_2 might escape back into the atmosphere: "reversible" indicates high risk; "stable" indicates low risk (*diamonds*). Whether the potential for sequestration or costs will rise or fall beyond 2050 is shown at the far right (*triangles*), based on factors such as land limitations. Effects are judged on how they are predominately assessed in published papers (if few papers exist, entries may be blank).



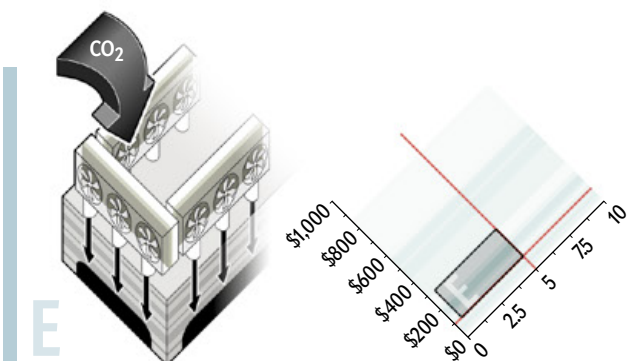
ENHANCED WEATHERING

Rock is pulverized into dust. When spread on fields, it draws CO_2 from the air and fertilizes soil. When sprinkled on the ocean, it reacts with seawater, converting CO_2 into carbonates that fall to the seafloor. Grinding and transporting rock economically are key.



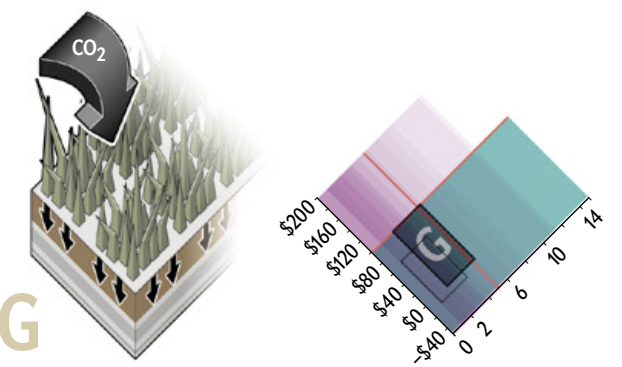
OCEAN FERTILIZATION

Iron filings are sprinkled at sea, helping plankton grow. They breathe in CO_2 and convert it into sugar or cellular material. When they die, they sink to the seafloor. Gains would be short-lived, and altering the ecosystem would be risky, so experts dropped it from the composite chart (*opposite page*).



DIRECT AIR CAPTURE

Machines pull in ambient air and chemically separate out CO_2, pumping it underground for permanent storage. Projected costs are high but could decline with technology development. (Data for "potential" were not available.)



SOIL CARBON SEQUESTRATION

Grasses or crops breathe in CO_2 and convert it into root material, fixing carbon in the soil. Soil-management techniques could enhance sequestration and plant yield. Long-term potential may be limited because soils can hold only so much carbon.

SOURCE: "NEGATIVE EMISSIONS—PART 2: COSTS, POTENTIALS AND SIDE EFFECTS," BY SABINE FUSS ET AL., IN *ENVIRONMENTAL RESEARCH LETTERS*, VOL. 13, NO. 6, ARTICLE NO. 063002; JUNE 2018

demand for farming or nature. And of course, a million tons would barely make a dent in the target of 20 billion tons a year.

Constructing such plants now might be essential to developing the know-how for building them on a much larger, more efficient scale later in the century. "But if you went out and built 20 million tons of direct air capture today, that would be the wrong thing to do with your money," says Roger Aines, chief scientist of Lawrence Livermore National Laboratory's energy program. "It would take a lot of solar and wind power, and if you had that much solar and wind power, the best thing to do would be to put it on the grid and turn off a coal plant." Preventing new emissions is still the overwhelming priority.

PORTFOLIO OF FIXES

THE FUSS STUDY DOES NOT simply add up the potential of the seven carbon capture methods, because some of them compete for the same resources. For example, too much reforestation would take away land needed to grow the fuel for bioenergy power plants, and too much bioenergy might compete with direct air capture for underground carbon sequestration. Climate scientists say we need to optimize a portfolio of methods.

One immediate way to start building this portfolio, says Pete Smith, a professor of soils and global change at the University of Aberdeen in Scotland, is by scaling up "stuff we already know how to do. We know how to plant trees. We know how to restore peatlands, basically by raising the water table," so the peat captures carbon dioxide instead of emitting it. "We know how to improve soil carbon content…. Incentivizing those sorts of things is [relatively] easy and could be done immediately. It would get us some of the way there."

Consider reforestation. Tragically, the world's tropical forests have become a source, rather than a sink, for carbon dioxide emissions, as trees are cut down and burned or as ravaged forests degrade. Getting forests back into negative emissions territory would first require major reforms in an international timber market that is heavily influenced by illegal trade. Beyond that, the obvious place for reforestation is land that had been clear-cut for farming or grazing but was abandoned as unproductive. Restoring five million square kilometers of such land could sequester 3.7 billion tons of carbon dioxide a year if adequate funding were available, according to a 2015 study in *Nature Climate Change* led by Richard Houghton of the Woods Hole Research Center.

Turning all livestock grazing lands that used to be forested back into forests again could create as much as 10 billion tons of negative emissions a year, according to Bronson Griscom, director of forest carbon science at the Nature Conservancy and lead author of a study on "natural climate solutions" in *PNAS*. That is a sizable portion of the annual carbon dioxide recovery needed annually. But the move would require a global shift away from meat eating, the opposite of the current trend.

Fuss and her co-authors foresee more modest potential. Trees live and die, meaning they will store carbon now but give it up again later this century or the next. The amount of carbon dioxide sequestered will also likely decline as forests mature, growing more slowly. Wildfires, deforestation and climate change raise the risks. Even so, forest expansion could provide a critical stopgap while direct air capture or other technologies are scaling up. Fuss puts the potential somewhere between 500 million and 3.6 billion tons of carbon dioxide removal a year by midcentury.

BIOCHAR fertilizer was made by heating chicken waste and wood chips that would otherwise emit carbon dioxide as they decay.

JEFF HUTCHINS Getty Images

That could take 25 billion to 180 billion tons off our target of one trillion tons this century, at a cost of $5 to $50 per ton.

Better management could raise the gains. Griscom notes, for example, that tree plantation managers in the southeastern U.S. knowingly harvest loblolly pine trees several years before their optimal yield. Allowing them to sell carbon credits to cover the extra years of growth could delay harvesting to the optimal age, adding on more timber and more carbon storage.

Likewise, growing nitrogen-fixing plants in pastures and moving to a smarter system of pasture rotation could make grazing more productive while improving carbon storage in soils. Fuss conservatively estimates that improvements in soil sequestration can yield up to 5.3 billion tons a year—265 billion tons this century—at $0 to $100 per ton.

That would be in addition to biochar. In this form of carbon removal, a specialized furnace applies heat in the absence of oxygen to biomass, turning it into a form of charcoal and generating useful by-products such as bio-oil or synthetic gas. When the charcoal is applied to farm fields, it binds carbon in the soil and can improve crop yields. But no one has yet attempted to deploy biochar on a large scale. Fuss and her co-authors consider it a plausible source of 300 million to two billion tons of annual carbon dioxide removal, at $90 to $120 per ton. That is 15 billion to 100 billion tons in this century.

Another land-based approach is called bioenergy with carbon capture and storage, or BECCS. Early plans from many countries for meeting their Paris commitments depend on it, yet it is deeply controversial. A power plant burns wood, agricultural wastes or other biomass such as switchgrass. These sources take carbon dioxide out of the atmosphere as they grow or accumulate. Combustion releases it again, and the power plant recaptures it from the smokestack, sending it down into deep geologic formations for permanent storage. But reforestation for biofuel production at the scale suggested by some proponents could eat up much of the world's arable land, threatening food production and nature conservation, as well as carbon dioxide removal by other methods such as reforestation or soil sequestration. Pulling emissions from the smokestack also sharply reduces power plant efficiency, at least with current technologies. Hence, Fuss puts the sustain-

able yield from BECCS at just two billion tons a year, well below the forecast by other researchers, at a cost of $100 to $200 per ton. Fuss's estimate would account for 100 billion tons of negative emissions by 2100.

That leaves two other carbon capture methods now under consideration. Enhanced weathering exploits a natural process: carbon dioxide in the air converts into carbonate when exposed to certain kinds of crushed rock. The question is whether researchers can find a way to grind the right rocks into powdered form economically, to speed up the natural process. Fuss puts the potential at two billion to four billion tons a year, at $50 to $200 per ton. Her team concludes that ocean fertilization—sprinkling iron or other nutrients into the ocean to stimulate growth of algae and other plankton, which take up carbon dioxide—would be too inefficient and short-lived to justify potential ill effects on ecosystems. It is "not a viable negative emissions strategy," they write.

PROFIT RATHER THAN COST

WHERE DOES THE ACCOUNTING LEAVE US? The ranges in the Fuss study add up to as little as 150 billion tons or a bit more than one trillion tons by 2100. The latter number might sound as if it solves our problem. But we cannot just add up the numbers because of conflicts between methods. What we can do, Fuss says, is manage the portfolio to take advantage of beneficial overlaps. Enhanced weathering, for instance, could be deployed on the same land being used to grow biomass for BECCS.

What all the approaches need, scientists argue, is massive investment in research and development. "This is going to be a long, hard battle," says Lawrence Livermore's Aines. But governments have been reluctant to foot the bill for negative emissions technologies because of ideological resistance to "picking winners" and because some past investments have been notorious failures. The U.S. Department of Energy, for instance, has spent huge sums of money on carbon capture projects intended to make "clean coal" power generation a reality. Southern Company abandoned the latest attempt in 2017, switching the Kemper County clean coal plant in Mississippi to natural gas after spending $7.5 billion.

A carbon tax would bypass picking winners by imposing a cost on emissions—a cost for putting garbage into the atmosphere. That would create a marketplace motivation both to reduce emissions now and to claw back past emissions later. The U.K. imposed such a tax, currently at about $25 per ton, primarily on fossil-fuel power plants, which cut coal emissions in half just from 2015 to 2016. Most governments shy away, however, seeing a tax as too drastic for economies built on fossil fuels.

With few exceptions, corporations have also been reluctant to invest in CO_2-removal technologies because, until recently, they saw no marketplace. To them, fixing the climate is a public benefit, not something from which they can earn a profit. But that may be changing because of a surprisingly bipartisan package of tax incentives approved by the U.S. Congress in early 2018. The so-called 45Q legislation significantly increases the tax credits companies can claim over the next 12 years, not just for capturing carbon dioxide and sequestering it underground—at as much as $50 per ton in tax credits—but for using CO_2 in a variety of ways.

The most controversial use is "enhanced oil recovery." An oil company purchases carbon dioxide, transports it by pipeline and injects it into depleted oil wells, pushing out extra oil it could not extract by conventional means. A climate change solution that entails producing *more* fossil fuels may sound Orwellian, and some environmental critics have attacked 45Q as just another fossil-fuel subsidy program in disguise. But enhanced oil recovery appears to reduce current emissions because the captured carbon dioxide, typically from natural gas or ethanol refineries, gets sequestered underground. Some environmentalists, such as Kurt Waltzer of the Clean Air Task Force, argue that turning carbon capture into an energy technology, rather than an emissions technology, is the first step toward broad commercial adoption of carbon dioxide removal. It turns recaptured CO_2 into a product to be bought or sold rather than simply a cost to be endured. That could be the key to eventual negative emissions.

TIME TO START

COULD A PORTFOLIO OF CARBON capture methods, taxes and markets get us to the goal of one trillion tons by 2100? The overheated summer of 2018 may have been a turning point. The American West was on fire. People on four continents experienced severe heat waves. In Japan, thousands of heatstroke victims went to the hospital in a single week. Climate scientists shook off cautious language and warned, in *PNAS,* that further warming risks tipping the planet into a "Hothouse Earth … likely to be uncontrollable and dangerous to many." In case that message was not strong enough, senior author Hans Joachim Schellnhuber, director emeritus of the Potsdam Institute for Climate Impact Research in Germany, told reporters that the cascading effects could lead to a world capable of supporting just one billion human beings, down from 7.5 billion today.

For some political leaders even now, climate change still seems shrouded in uncertainty, despite the overwhelming evidence that it is our grim present and grimmer future. The disconcerting thing about negative emissions technologies is that so much can seem uncertain even for the scientists themselves. "Everyone is talking about how it depends on what the substrate is, what part of the world you're in, what the rainfall is like there and what the temperature is," says University of Virginia ecologist Stephanie Roe, speaking about soil carbon enhancement.

Researchers also get caught up in arguing about whether any of the carbon-removal methods, much less all of them, can scale up to billions of tons annually. "There's maybe a bit too much focus in this debate about what's the eventual scale," says Brendan Jordan of the Great Plains Institute in Minneapolis. "I fear that it paralyzes us, and we really can't afford paralysis." That is, we need to start to achieve negative emissions despite uncertainties because they are trivial compared to a world in which the climate change game of musical chairs stops, and there's no room for 6.5 billion people to sit down. SA

MORE TO EXPLORE

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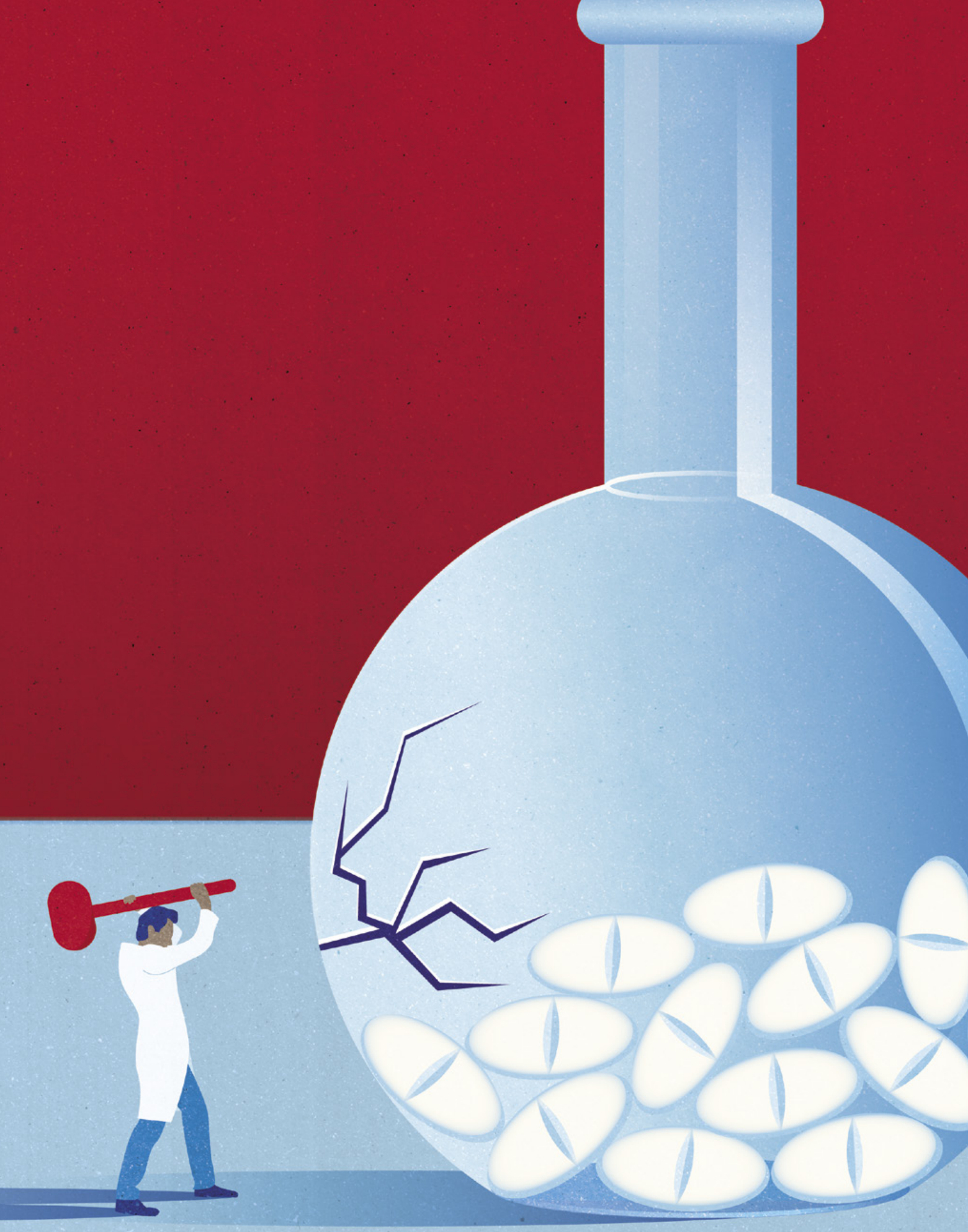


Out of Reach

MEDICINE

Most cancer patients never get into lifesaving drug trials because of barriers at community hospitals

By David H. Freedman

IN BRIEF

The newest and best medicine is first offered to patients in clinical trials, and cancer patients in trials often do better than those on standard treatments.

Yet trials, particularly in cancer but also in other diseases, have many empty patient slots. The vast majority of people are not offered the chance to enroll.

Obstacles to trials need to be overcome in community hospitals by reducing the burden on local doctors and improving patient-trial matching technology.

Illustration by Kotryna Zukauskaite

JEAN REIMERS, A 75-YEAR-OLD RETIRED supermarket cashier, enjoys her life in Grand Island, Neb., a small city near the Platte River that boasts attractions such as the Stuhr Museum of the Prairie Pioneer and a sandhill crane nature reserve. Nearly two years ago Reimers found out from her local doctor that she had cancer. The worse news was that it was late-stage metastatic lung cancer, hard to treat and with a dismally low survival rate. The standard approach in such cases is palliative care to keep dying patients comfortable. "It looked like I probably wouldn't be around another year," she says.

David H. Freedman is a science writer based in Boston.

Today not only is Reimers still around, but she says she feels great. She has lots of energy and no pain. This past fall CT scans showed all her tumors have shrunk or disappeared entirely. And she was anticipating the birth of her 11th grandchild. "I've got a lot of things I still want to do," she says.

Her high-quality time, Reimers says, comes thanks to experimental drugs she received as part of a clinical trial. The treatment, a combination of two immunotherapies called ipilimumab and nivolumab, is not yet approved for lung cancer by the U.S. Food and Drug Administration. The trial Reimers took part in was one of the tests to see if the regimen works.

This would not be an unusual story if Reimers was a patient at a big-name, big-city academic medical center. The very top cancer hospitals, such as the University of Texas MD Anderson Cancer Center in Houston and New York City's Memorial Sloan Kettering Cancer Center, enroll about 25 percent of their patients in trials. But Reimers, like Grand Island's other 51,000 residents, lives closest to CHI Health St. Francis, a typical small community hospital that is part of a regional network but has no formal ties to any major medical institution. "I didn't think people in small towns had the same chances for trials that people in big cities do," Reimers says. Her only option, she thought, was to drive nearly three hours every two weeks to a bigger hospital in Omaha. She would likely have had to stay overnight instead of going straight home to rest, and she probably would not have done it. But the head oncologist at St. Francis's cancer treatment center found out that Reimers met the criteria for the double-drug trial, filled out the forms, followed up and got her in.

The drugs available in clinical trials often represent the latest in research, and many turn out to be significantly more effective than standard treatments. Half of all drugs that make it into the last of three phases of drug trials, when most patients enter those trials, end up being approved by the FDA because of these improved results. The drug Herceptin, for instance, was only available in trials before it became a mainline treatment for breast cancer in 1998 and since then has been prescribed to 420,000 women. More recently, some 90,000 breast cancer patients have been treated with Ibrance, but before 2015 the drug was given only in trials. Another medication, Keytruda, was approved after clinical trials in 2014; now some 70,000 patients with a number of different types of cancer have used it.

But whereas about one third of cancer patients in the U.S. meet the criteria for a trial with a new drug, only about 4 percent end up in such tests, according to National Cancer Institute estimates, and some experts say the real number is even lower. The main reason for the massive shortfall: in the nonacademic community hospitals where most cancer patients are treated, doctors do not feel they have the time, the incentives or the support to learn about available trials, to qualify and enroll patients, or to provide the extra follow-up care such trials often call for. A National Academies of Sciences, Engineering, and Medicine study concluded that "community practitioners lack the needed infrastructure and support to actively participate in clinical trials." A study in the clinical cancer journal *CA* called trial enrollment "embarrassingly low" and blamed it, in part, on "a lack of knowledge about available studies by community oncologists, a lack of time or interest, or a lack of resources to support the cost of performing clinical trials." Because nationally about 85 percent of cancer patients end up at community hospitals, most of the low participation in cancer trials is attributable to the failure of those hospitals to enroll their patients.

Low trial enrollment, which effectively cuts patients off from lifesaving medicine, is a giant national health problem. For example, fewer than 1 percent of patients who have Alzheimer's disease enter a trial. But for cancer, the missed opportunities are especially painful, experts say, because drug development in this area has been particularly strong. "Many of our drug trials involve the most promising agents we've seen," says Tufia Haddad, an oncology researcher at the Mayo Clinic. Thanks to new ways of identifying and targeting mutations in tumors and to immunotherapies that help muster the body's natural defenses against cancers, there are more than 600 experimental cancer drugs that have shown good results in animals and in early small studies in humans. And contrary to common belief, patients in the vast majority of cancer drug trials do not risk getting a placebo—these trials test the best standard treatment against a new medication.

The enrollment problem also handicaps research. Lack of patients forces many trials to stop before getting results, ending the progress of many promising treatments. Most trials are at least delayed by patient enrollment shortages. About one out of six of all trials never manage to recruit a single patient. "The biggest problem in developing new drugs is a lack of patients to treat with them," says John T. Cole, an oncologist at the Ochsner Health System based in New Orleans, who oversees a network of oncology practices. "We can't meet that challenge unless we solve the problem of low enrollment in community hospitals."

Politicians and regulators have done little to help community hospitals and doctors surmount the obstacles, according to R. Alta

Charo, a law professor at the University of Wisconsin–Madison, who studies medical research policy. Instead they have passed "right to try" legislation, which prohibits the FDA from denying terminal patients access to experimental drugs that are not available to them in clinical trials. In fact, the FDA almost never denies such access, so the law is unlikely to help more than a handful of patients and does nothing to improve access to clinical trials. "Helping overwhelmed and underresourced doctors at community hospitals would be a much better approach," Charo says.

Finding effective ways to help, however, is not easy. There are partial solutions, such as artificial-intelligence programs that crunch through reams of data to match patients to trials. Other attempted remedies are low tech and involve a range of outreach, education and marketing tools that can change the antitrial culture of community hospitals. To succeed, however, these approaches need to help doctors cope with the time constraints, lack of expertise and financial obstacles that keep them from getting patients into trials. St. Francis, which shares those small hospital disadvantages, manages to place some 35 percent of its cancer patients in trials. That achievement is due almost entirely to the determination and dedication of Mehmet Copur, the head oncologist at the time of Reimers's treatment. But counting on every other community hospital to display the same fervor is a risky gamble.

ONE DOCTOR'S MISSION

WHEN REIMERS BECAME ILL, Copur was willing to put in the extra work required to find out about appropriate trials and get her into one—work built into the infrastructure of academic centers but not community hospitals—just as he has been doing for his other patients. To refuse to go that extra mile is to fail to provide seriously ill patients with their best possible prospects, insists Copur, who recently moved to the Morrison Cancer Center in the nearby community of Hastings, where he is building a similar clinical trial program. "The standard of care today is what was in trials 10 years ago," he says. "To put patients in a trial is to give them a chance to get a drug that will be the standard of care 10 years from now."

In 1995 Copur was a young medical scientist from Turkey doing basic research at the National Institutes of Health outside of Washington, D.C., when a change in government policy—an alteration in temporary work permit numbers—suddenly left him in imminent danger of losing his visa. His only hope for staying in the U.S. was a program that grants permanent visas to doctors who spend three years treating patients in an underserved community. He saw a listing for a job at Grand Island's St. Francis. Copur grabbed the position.

"But when I got here I said to myself, 'My God, my career is over,'" he recalls. Copur had intended to continue some clinical research in the job, but he found that St. Francis had no medical library and no Internet access at the time. Clinical trials were almost nonexistent, and when Copur proposed that he at least try to participate in some, neither his fellow oncologists nor the hospital administration seemed open to the idea. "It was a fight from the beginning," he says. "Even in big-city hospitals people don't always see how important clinical trials are, let alone a small-town hospital."

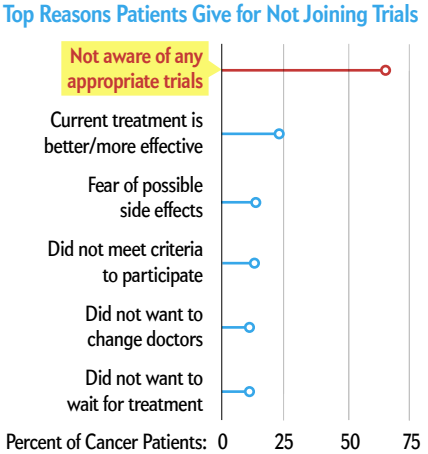
The problem was that to earn his salary Copur had to see a stream of patients, five days a week. But clinical trials require extra work, with each patient taking up on average about three times as much time as a nontrial patient, thanks to extra record keeping and close patient-monitoring requirements. In academic centers, doctors are given that extra time and can draw on a trial-focused support staff. Copur had to do it all on his own, including establishing rigorous data collection, performing extra diagnostic tests,

Losing Patients

When ill people get into clinical trials, they often do better than patients on standard treatments. Yet only a fraction of trial-eligible patients are offered a chance to participate. Many are not told about trials by their doctors. Trials do have plenty of room for more patients; indeed, many halt without robust results because they do not get enough people.

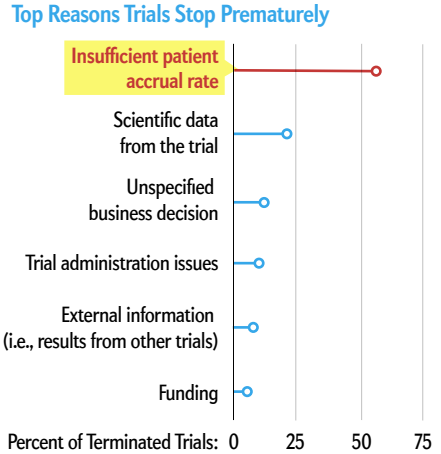
Cancer Patients in the Dark

Eighty-one percent of cancer patients reported they did not discuss any clinical trial participation with their physicians. That is one finding from a study of 406 cancer patients and 200 oncologists, published in 2009. Patients cited lack of awareness of appropriate trials as the major reason they did not enroll in one.



Desperately Seeking Participants

An analysis of all U.S. clinical trials that shut down prematurely, published in 2015, found the main cause was that they did not enroll enough patients. Of the 905 trials, 57 percent closed for this reason. In contrast, only 21 percent stopped for scientific causes, such as when the drugs being tested did not perform well.



SOURCE: "CLINICAL TRIAL AWARENESS, ATTITUDES, AND PARTICIPATION AMONG PATIENTS WITH CANCER AND ONCOLOGISTS," BY LAURIE FENTON ET AL., IN *COMMUNITY ONCOLOGY*, VOL. 6, NO. 5; MAY 2009 *(patient responses)*; "TERMINATED TRIALS IN THE CLINICALTRIALS.GOV RESULTS DATABASE: EVALUATION OF AVAILABILITY OF PRIMARY OUTCOME DATA AND REASONS FOR TERMINATION," BY REBECCA J. WILLIAMS ET AL., IN *PLOS ONE*, VOL. 10, NO. 5, ARTICLE NO. E0127242; MAY 26, 2015 *(trial termination)*

Graphic by Jen Christiansen

conducting extra patient visits, producing reports, training staff, and more. He also brought in funding from the NCI and joined a research consortium of hospitals that made more trials available.

Many of his patients hesitated to join a trial, saying they did not want to be guinea pigs who might end up with a highly toxic drug or a placebo—widely held misconceptions that are particularly common among rural patients, says James Atkins, an oncologist at the Southeastern Medical Oncology Center in North Carolina. Copur patiently explained to them that cancer trials today are designed with patient benefit in mind and that the worst case was usually getting the drug they would have received anyway. Most of his patients consented. Then other oncologists at St. Francis started to notice that Copur's trial patients sometimes did surprisingly well. Of course, they were doing well, Copur explained: some of them were receiving much better drugs. Soon his colleagues began looking for trials for their own patients.

MEHMET COPUR, a cancer physician who finds clinical trials for his patients, hugs one of them.

"Copur has done a great job in a completely rural environment," says Praveen Vikas, an oncologist at the University of Iowa Health Care. "He's that rare kind of community physician who can provide the kind of care that often beats physicians in academic settings in terms of value and patient satisfaction, while staying on top of research."

As of 2018, Copur's team at St. Francis had enrolled patients in 74 different trials. But to do so, Copur worked nonstop from dawn, taking off one hour at 7 P.M. to have dinner at home with his ailing father before returning to spend another three hours at the clinic. "These trials are my whole life," he says. "Sometimes I dream about making that big fundamental research contribution, but then my patients remind me that what I am doing here is a bigger contribution."

One of those patients is a young man (he asked not to be identified) who learned two years ago that his kidney cancer was spreading. Approved chemotherapies did not offer much hope, so he started searching out clinical trials, assuming he would have to go far from his home near Grand Island to get in one. He traveled to Washington, D.C., to meet with a specialist—who told him to get right back to Nebraska and see Copur. "To be honest, I was a little skeptical when I met Dr. Copur, and he told me he'd get me in the right trial," he recalls. "But my phone started pinging with e-mails about trials by the time I was pulling out of the parking lot." Today the patient is thriving and credits the immunotherapy drugs he received through the trial that Copur enrolled him in.

BREAKING BARRIERS

COPUR'S EXPERIENCE at St. Francis proves that community hospitals can succeed as clinical trial centers. And if he can deliver on his quest to duplicate that success at the even smaller Morrison Cancer Center, which is part of the Mary Lanning Healthcare community hospital in Hastings, the evidence will be all the more impressive. Community hospitals do not need to hit 35 percent enrollment, as St. Francis has, to make a big dent in the trial gap. If only one fourth of community hospitals boosted their trial enrollment to an average of 10 percent, it would result in an increase of 50 percent in the number of cancer patients enrolled in trials. In a survey of a wide range of cancer patients, 81 percent reported their doctors did not discuss the possibility of trials with them. In a separate survey of women with cancer, more than half reported that their oncologists either did not mention trials or even actively discouraged patients from participating in one.

The St. Francis work also highlights the obstacles that community hospitals face. But a 10 percent gain in enrollment does not require daunting personal sacrifice, say clinicians who have helped other community hospitals make the jump. Atkins, who directs a large clinical trial consortium across the southeastern U.S., is working with 25 hospitals in five states to help them boost clinical trial enrollment. Many physicians have gotten onboard, Atkins says. It means going beyond the typical physician's 50-or-so-hour week but only by five hours or less. "It's extra work for doctors, but if a doctor doesn't want to do it for patients, that seems a little lazy to me," he says.

Clinical trials can also be redesigned to reduce the burden on community hospital physicians, shifting more of the workload to the research centers that originate the trials. A study led by the University of Pittsburgh Medical Center, along with six other academic medical centers and the National Institutes of Health, looked at 38 steps that clinical trial leaders can take to get more doctors at other hospitals involved in their trials, steps mostly aimed at raising doctors' interest while reducing the workload involved in opening the trial and in enrolling patients. The steps included sending researchers out to hospitals to speak to staff about the trial's relevance, the benefits to patients and the patients' qualifications; providing follow-up teleconference meetings; writing articles for the hospital newsletter and for local and physician publications; establishing 24/7 access for researchers to get questions answered; putting up a Web site dedicated to the trial; and making available patient-recruitment aids such as multilingual brochures and consent forms. The study, published in 2014 in *Clinical Pediatrics,* found there was a 38 percent jump in recruitment after the steps were taken.

Sonika Bhatnagar, lead author and an associate professor of pediatrics at the University of Pittsburgh School of Medicine, notes that some factors stood out during the study. "The biggest physician barrier was time constraints," she says. "Minimizing their workload was critical, and we found making everything as simple as possible made a big difference." Among the aids Bhatnagar and her colleagues provided physicians were prepack-

MARY LANNING HEALTHCARE AND ALAN JACKSON STUDIOS

aged talking points to use with patients, so the doctors did not have to study a trial's methodology in detail to explain it accurately. The researchers also offered to reach out directly to a patient's family to address their concerns. And physicians worry that putting a patient in a trial will compromise his or her autonomy in making care decisions, Bhatnagar adds, because trials often tightly circumscribe some treatment options. She has found that the best way to counter that concern is for researchers to go to hospitals to meet as many physicians as possible in person to build trust in the trial's protocol and to create enthusiasm about what the trial might do both for individual patients and for the countless patients everywhere who might ultimately be helped by the trial's findings. "Most physicians would take a lot of pride in contributing to research that could ultimately change treatment guidelines for the field," Bhatnagar says.

Another study gave doctors materials designed to streamline the process of patient screening—that is, determining which patients qualify—and to make it easier to follow trial protocols during treatment. The study also involved adding one-on-one meetings between local physicians and trial researchers and onsite discussions about the disease being treated. In that study, enrollment at the targeted facilities more than doubled.

Some trial outreach efforts are being facilitated by the fact that academic medical centers are looking to expand in their states, and sometimes beyond, via acquiring or partnering with community hospitals. Existing big health networks are also pushing outreach. Kaiser Permanente—a nonprofit health care company—has nudged and supported all its 27 northern California hospitals, many of them community hospitals, into enrolling cancer patients into trials. "Instead of having to drive 50 miles or more to an academic medical center, our patients can be treated in a clinical trial in the same place they delivered their babies and got their flu shots," says Lou Fehrenbacher, a Kaiser Permanente oncologist who oversees the region's cancer trials program. Likewise Yale University's main hospital, based in New Haven, has been bringing in affiliated community oncology clinics around Connecticut into clinical studies. Unfortunately, most of the nation's 4,000 community hospitals are not closely allied with an academic center, so this approach may be limited.

THE HIGH-TECH FIX

IT MAY BE, THOUGH, that technology can help close that particular gap. The Mayo Clinic has been testing a pilot of an ambitious approach, based on IBM's Watson cognitive-computing platform. That system has been looking at all the details in the records of every breast cancer patient at the medical center and matching them against the 16 different clinical trials for breast cancer available there. The Mayo claims that after 11 months the system was able to increase combined enrollment in those trials by 80 percent—though so far only at the clinic itself and not yet at community hospitals. According to the Mayo's Haddad, who is helping to run the pilot, the big jump is owed in part to the fact that the project included increased staffing and focus around patient-trial matching. But she adds that Watson's ability to zip through not only tightly specified data fields in the health records but also clinical notes and other unstructured data has made a big difference in the system's hit rate. "Most electronic health record systems aren't sophisticated enough to be able to answer questions such as which treatments the patient has already had," she says. "More than 90 percent of the data in records is in unstructured form, and cognitive systems can go after it."

A study run by the NCI and Case Western Reserve University, using another experimental cognitive-computing-based system called Trial Prospector, scoured the records of 60 new gastrointestinal cancer patients across several clinics and matched 57 percent of them to at least one of 15 different trials. A group of oncologists brought into the study gave the system a big thumbs-up, deeming all the matches to be accurate. Another system tested at Cincinnati Children's Hospital Medical Center was found to reduce the time needed to match patients to trials by 85 percent.

Exciting results, but they come with serious qualifications. For one thing, such systems generally require that a hospital have a sophisticated electronic health record system in place to feed them data. Most community hospitals currently have systems that are too rudimentary to allow programming in trial-matching capabilities. But given medicine's growing reliance on mining electronic health records for advancing patient care, those systems will inevitably be upgraded to the point where automating trial matching will become feasible—especially as more community hospitals become affiliated with larger hospitals and even academic medical centers.

Copur, for his part, maintains that what will ultimately bring clinical trial options to that great majority of cancer patients will be a slowly growing wave of peer pressure as more clinicians in community settings start to see the light. Copur himself keeps publishing—63 papers and articles to date, such as a study in the *Journal of Clinical Oncology* evaluating treatments for metastatic pancreatic cancer—and giving talks about what a community hospital can accomplish. "I tell doctors that if they're not looking for ways to put their patients in clinical trials, they should be referring them to a doctor who will," he says.

What seems poised to effect change, if slowly, is a combination of all those approaches: Trial researchers who get out into communities and market their work to local doctors, trial designs that reduce physician workload, and tools that automate patient-trial matching and related tasks. It will also take strong advocates like Copur and the NCI willing to sound a constant, loud drumbeat that links trials to the duty that all physicians—not just those in academia—have to the profession and to their patients. It will only be then, if those efforts on multiple fronts put more people in trials, that patients win the real right to try. SA

MORE TO EXPLORE

Clinical Trial Awareness, Attitudes, and Participation among Patients with Cancer and Oncologists. Laurie Fenton et al. in *Community Oncology,* Vol. 6, No. 5, pages 207–213; May 2009.

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Reliability of Adverse Symptom Event Reporting by Clinicians. Thomas M. Atkinson et al. in *Quality of Life Research,* Vol. 21, No. 7, pages 1159–1164; September 2012.

Alzheimer's Disease Drug Development Pipeline: 2017. Jeffrey Cummings et al. in *Alzheimer's & Dementia: Translational Research & Clinical Interventions,* Vol. 3, No. 3, pages 367–384; September 2017.

FROM OUR ARCHIVES

Understanding Clinical Trials. Justin A. Zivin; April 2000.

scientificamerican.com/magazine/sa

RECOMMENDED

By Andrea Gawrylewski

Picturing Science and Engineering

by Felice C. Frankel.
MIT Press, 2018
($39.95)

IMAGE OF AGATE slice shows how a flatbed scanner can reveal details at 30 to 50 microns.

While on a fellowship at Harvard University, photographer Frankel audited a course by chemist George Whitesides. She was captivated by pictures from his laboratory—but knew she could do better. She continued to hone her skills and has spent her career making striking images that have been featured on many notable journal covers. This beautiful and engaging book is her latest practical guide to help other scientists use their creativity and basic lab tools (even the seemingly prosaic flatbed scanner) to create standout visualizations of their work and research subjects. "I am convinced," she writes, "that smart, accessible, and compelling representations of science can be doors through which others can enter."

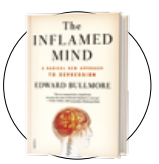
The Second Kind of Impossible: The Extraordinary Quest for a New Form of Matter

by Paul J. Steinhardt.
Simon & Schuster, 2019 ($27)

"Quasicrystals" are a kind of matter that should not exist—they break centuries-old rules about how atoms can arrange into solids. Unlike regular crystals, whose atoms assemble in repeating patterns, quasicrystal particles are ordered but not periodic—their arrangements never repeat. In 1984 physicist Steinhardt predicted quasicrystals with a graduate student; independently that same year, chemists announced they had discovered them in a lab. Steinhardt tells the story behind his theory—a crazy math caper that includes a reclusive amateur genius, the "golden ratio" and even an old *Scientific American* column that plays a crucial role in his breakthrough. The tale culminates in a trek to a remote Russian peninsula in search of quasicrystals in the wild. *—Clara Moskowitz*

The Inflamed Mind: A Radical New Approach to Depression

by Edward Bullmore. Picador, 2018 ($28)



The development of new antidepressant drugs has stalled. Many efforts to discover novel treatments for depression have only led to dead ends. In 2010 professor of psychiatry Bullmore witnessed this failure when the pharmaceutical giant he worked for suddenly stopped all ongoing projects on mental health. "I was a 50-year-old psychiatrist working for a company that didn't want to do psychiatry any more," he writes. But in recent years scientists have spotted signs of hope for what seemed to be a barren research field. The immune system, not the brain, they say, is where the root causes of depression can be found. Bullmore draws from the latest research and his own experiences to defend the heretic idea that the link between brain inflammation and depression could revolutionize the way we understand, and maybe treat, disorders of the mind. *—Emiliano Rodríguez Mega*

The Misinformation Age: How False Beliefs Spread

by Cailin O'Connor and James Owen Weatherall.
Yale University Press, 2019 ($26)

Sharing information and influencing one another's beliefs are partly what makes humans special. Of course, not all information that gets shared is factual. In fact, some false information has particularly strong spreading power—an unavoidable element of the human condition, write O'Connor and Weatherall, an associate professor and a professor, respectively, of logic and philosophy of science. The two deftly apply sociological models to examine how misinformation spreads among people and how scientific results get misrepresented in the public sphere. They offer scientific case studies—the discovery that CFCs were responsible for the ozone hole in the 1980s, for example—to explore the question of what constitutes truth and to consider the role that information plays in a healthy democracy.

FELICE C. FRANKEL

Michael Shermer is publisher of *Skeptic* magazine (www.skeptic.com) and a Presidential Fellow at Chapman University. His new book is *Heavens on Earth: The Scientific Search for the Afterlife, Immortality, and Utopia.* Follow him on Twitter @michaelshermer

Stein's Law and Science's Mission

The case for scientific humanism

By Michael Shermer

In the April 2001 issue of *Scientific American,* I began this column with an entry entitled "Colorful Pebbles and Darwin's Dictum," inspired by the British naturalist's remark that "all observation must be for or against some view, if it is to be of any service." Charles Darwin penned this comment in a letter addressing those critics who accused him of being too theoretical in his 1859 book *On the Origin of Species*. They insisted that he should just let the facts speak for themselves. Darwin knew that science is an exquisite blend of data and theory. To these I add a third leg to the science stool—communication. If we cannot clearly convey our ideas to others, data and theory lie dormant.

For 214 consecutive months now, I have tried to communicate my own and others' thoughts about the data and theory of science as clearly as I am able. But in accordance with (Herb) Stein's Law—that things that can't go on forever won't—this column is ending as the magazine redesigns, a necessary strategy in the evolution of this national treasure, going on 174 years of continuous publication. I am honored to have shared a fleeting moment

of that long history, grateful to the editors, artists and production talent for every month I was allowed to share my views with you. I will continue doing so elsewhere until my own tenure on this provisional proscenium ends (another instantiation of Stein's Law)—many years in the future, nature and chance willing—so permit me to reflect on what I think science brings to the human project of which we are all a part.

Modern science arose in the 16th and 17th centuries following the Scientific Revolution and the adoption of scientific naturalism—the belief that the world is governed by natural laws and forces that are knowable, that all phenomena are part of nature and can be explained by natural causes, and that human cognitive, social and moral phenomena are no less a part of that comprehensible world. In the 18th century the application of scientific naturalism to the understanding and solving of human and social problems led to the widespread embrace of Enlightenment humanism, a cosmopolitan worldview that esteems science and reason, eschews magic and the supernatural, rejects dogma and authority, and seeks to understand how the world works. Much follows. Most of it good.

Human progress, which has been breathtaking over the past two centuries in nearly every realm of life, has principally been the result of the application of scientific naturalism to solving problems, from engineering bridges and eradicating diseases to extending life spans and establishing rights. This blending of scientific naturalism and Enlightenment humanism should have a name. Call it "scientific humanism."

It wasn't obvious that the earth goes around the sun, that blood circulates throughout the body, that vaccines inoculate against disease. But because these things are true and because Nicolaus Copernicus, William Harvey and Edward Jenner made careful measurements and observations, they could hardly have found something else. So it was inevitable that social scientists would discover that people universally seek freedom. It was also inevitable that political scientists would discover that democracies produce better lives for citizens than autocracies, economists that market economies generate greater wealth than command economies, sociologists that capital punishment does not reduce rates of homicide. And it was inevitable that all of us would discover that life is better than death, health better than illness, satiation better than hunger, happiness better than depression, wealth better than poverty, freedom better than slavery and sovereignty better than suppression.

Where do these values exist to be discovered by science? In nature—human nature. That is, we can build a moral system of scientific humanism through the study of what it is that most conscious creatures want. How far can this worldview take us? Does Stein's Law apply to science and progress? Will the upward bending arcs of knowledge and well-being reach a fixed upper ceiling?

Remember Davies's Corollary to Stein's Law—that things that can't go on forever can go on much longer than you think. Science and progress are asymptotic curves reaching ever upward but never touching omniscience or omnibenevolence. The goal of scientific humanism is not utopia but protopia—incremental improvements in understanding and beneficence as we move ever further into the open-ended frontiers of knowledge and wisdom. *Per aspera ad astra.* SA

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Illustration by Izhar Cohen

Not your average cruise.

Cruise prices start at $2,809 per person (pp) based on double occupancy. For those attending our SEMINARS, there is a $1,575 fee. Add'l pp fees: gov't taxes and fees ($210), a non-refundable Booking Service Fee ($150), and the Tour Leader gratuities ($10 pp per day). Program, cruise pricing and options are subject to change. Scientific American is a registered trademark of Springer Nature America, Inc.

Steve Mirsky has been writing the Anti Gravity column since a typical tectonic plate was about 36 inches from its current location. To hear our interview with the Ravenmaster, go to www.scientificamerican.com/podcast/01/2019

Birdman

His job is for the avians

By Steve Mirsky

The Ravenmaster awoke at the crack of dawn. He emerged from his quarters and onto the grounds. He then prepared water and food for the seven ravens he lives with before releasing six of them for the day. Merlina was already out—she prefers to sleep outside. None of the ravens has three eyes or carries messages. This wasn't Winterfell; it's the Tower of London. And it wasn't a portentous day in 1215 or 1455 or 1605 or 1837. It's today.

Unless the Ravenmaster, Christopher Skaife, is on holiday. Such was the case in October, when Skaife came to New York City, where I interviewed him about his new book, *The Ravenmaster: My Life with the Ravens at the Tower of London* (Farrar, Straus and Giroux, 2018). Our conversation took place before an avian aficionado audience at Caveat, the lower Manhattan spot that bills itself as the "speakeasy bar for intelligent nightlife." The ravens do not bill themselves—they hatch that way.

Skaife spent more than two decades in the military before becoming, in all its officialdom, Yeoman Warder of Her Majesty's Royal Palace and Fortress the Tower of London and a member of the Sovereign's Body Guard of the Yeoman Guard Extraordinary. But what's truly extraordinary are the birds. "I used to think that my military career came to an end when I left the army," Skaife writes, "but now I see that it was merely my apprenticeship."

Indeed, life among the ravens takes discipline and courage—he must maintain his composure up close with large birds (three times the weight of crows) blessed with big beaks and formidable talons. But why are there resident ravens at the Tower in the first place?

In the book, Skaife says that the usual explanation begins with sky watcher John Flamsteed complaining to King Charles II about the wild ravens interfering with the celestial observations he performed at the Tower. Charles agreed to shoo them away, "until someone pointed out that the birds had always been at the Tower and were an important symbol." Ultimately, Skaife explained at Caveat: "Charles II stated … that [at least] six ravens should live at the Tower of London forevermore" or the kingdom would fall. But, he continued, "it's myth and legend."

"The truth," Skaife writes, "is that there was no Royal Decree … though there was … a Royal Warrant issued in June 1675, which provided John Flamsteed, who became the first Royal Astronomer, with the funding to set up a proper observatory in Greenwich"—site of the prime meridian, longitude 0 degrees. "So it's possible that the confounded ravens played a small part in the history of astronomy and navigation … simply by being so bloody annoying that Flamsteed had to move out to Greenwich to get away from them."

The real reason for ravens at the Tower is probably to impress tourists, most of whom see the birds only once. But the ravens continue to impress Skaife, who sees them daily. "Experts in avian cognition have designed all sorts of tests and experiments to measure birds' cognitive abilities and behavior," Skaife writes, "and I'm proud to say that our ravens at the Tower have assisted in many a scientific study. The consensus among the experts seems to be that ravens can carry out all sorts of tasks that it was previously thought only primates could handle." Like mess with tourists.

"I've seen Merlina lying on her back, playing dead," Skaife told me, "much to the dismay and horror of the visitors who come to the Tower of London. We had two … ladies the other week, actually, who were in tears watching Merlina lying there. She puts her wings out, legs in the air. Honestly, she stays as still as she possibly can. For up to 10 minutes…. And everybody walks past and says, 'A raven's dead! Raven's dead!' and I say, "No. Watch her. She's just doing it either because she's bored or she's getting a bit of a suntan…. It's something that they do, and they do it in the wild as well."

As another Briton once famously said of another bird, a Norwegian Blue parrot: "He's not dead, he's, he's restin'!" Because keeping a kingdom from falling, even apocryphally, must be exhausting. SA

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Illustration by Matt Collins

JANUARY

1969 Abortion Debate

"Abortion is still the most widespread, and the most clandestine, method of fertility control in the modern world. In recent years several nations have legalized the practice, and as a consequence, induced abortion is emerging from the shadows and has become a topic of worldwide discussion and controversy. The debate ranges over a wide spectrum of considerations: moral, ethical, medical, social, economic, legal, political and humanitarian. The experience of countries that have made abortion legally permissible is now beginning to provide a body of reliable data with which to evaluate the pros and cons of the practice. Abortion did not become a statutory crime in the U.S. until about 1830. Today it is still prohibited in most states of the U.S. except in cases of serious hazard to the mother's life."

Dance of the Solids

"All things are Atoms:
Earth and Water, Air
And Fire, all, *Democritus* foretold.
Swiss *Paracelsus,* in's alchemic lair,
Saw Sulfur, Salt, and
Mercury unfold
Amid Millennial hopes
of faking Gold.
Lavoisier dethroned
Phlogiston; then
Molecular Analysis made bold
Forays into the gases: Hydrogen
Stood naked in the dazzled sight
of Learned Men.

—John Updike"

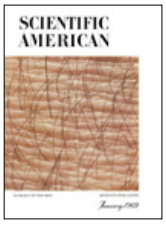
The original 11-stanza poem by Updike was inspired by the September 1967 issue on "Materials."

1919 Airships and Fire

"What has come pretty near superannuating the airship as an instrument of warfare is not the airplane; it is the unduly high fire risk involved in the use of hydrogen, the gas wherefrom airships have hitherto derived flotation. Helium, an inert, non-inflammable gas, the second lightest known (the lightest being hydrogen), is relatively abundant in all minerals which contain radium, thorium, or uranium, such as thorianite, cleveite, etc., but the operation of separating helium from these minerals has involved such a great expense—from $1,500 to $6,000 per cubic foot—that its use as a hydrogen substitute was never seriously considered. By next spring helium will be produced in this country on an industrial basis and at a cost of approximately $100 per 1,000 cubic feet, and the magnitude of the achievement will be fully realized."

The Helium Control Act of 1927 halted export of the gas. Foreign entities, such as the German Zeppelin Transport Company, which operated the airship Hindenburg, *had to make do with flammable hydrogen.*

1919: A disarmed Renault FT light tank is pressed into postwar service as a canal-side barge tractor. It would have been fairly inefficient, but so many horses had been killed in the Great War that it may have been necessary.



1969

1919

1869

1869 Herring Fishery

"Dr. Louis Feuchtwanger has lately returned from a trip 'Down East' [Maine] and sends us some facts in regard to the eastern herring fishery. He says this season has been one of the most prolific known for many years. On the 12th of October 80 hogsheads of herrings were taken at one haul, and 30 hogsheads two tides before. Every two hogsheads will yield one barrel of fish oil worth in the market $22.50 per barrel, the oil being used in currying leather and for mixing with other fish and lubricating oils. Besides this product the remains of five hogsheads of fish will produce one tun of pumice or fish guano, the best fertilizer known, and worth by itself $20 per tun."

Plague of Rabbits

"The rabbit originally brought from England into Australia is now threatening to become a plague of almost Egyptian magnitude in the distant and thinly populated plains. Only a year or two ago not a rabbit was to be seen save as a curiosity in a hutch. Now that the plague is in full force we can, of course, all very easily account for what no one foresaw. In England the wild rabbit meets with many destroyers; here there are very few."

Whisky Fraud

"The *New York World* has been doing the country a service by investigations into the quality of liquors sold at the different bars in this city. A large number of samples of brandy sold at from thirty to fifty cents a glass, and of whisky sold at from twenty to thirty cents per glass, were examined and found to be genuine in only two instances. If such be the case with liquors sold in the best places, what must be the character of the fluids retailed at the low grog shops where whisky can be obtained for from five to ten cents a glass."

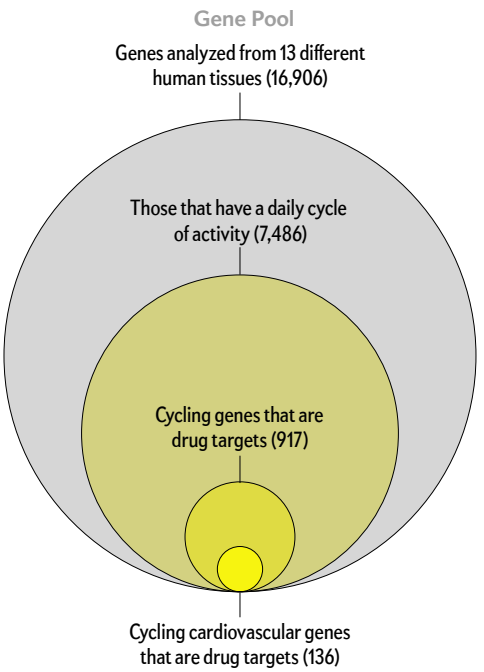
SCIENTIFIC AMERICAN, VOL. CXX, NO. 2; JANUARY 11, 1919

Text by Mark Fischetti | Graphic by Martin Krzywinski

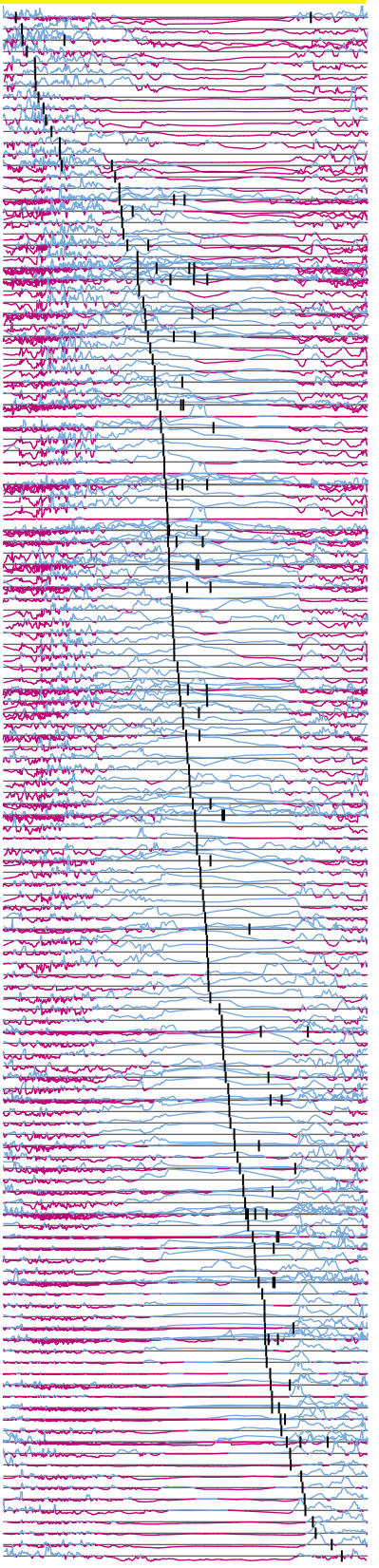
Take Your Medicine ... Now

Drugs could be more effective if taken when the genetic proteins they target are most active

Doctors may tell patients to pop their pills in the morning or evening or perhaps with meals. But a new study finds many genes that direct production of proteins targeted by drugs have a daily cycle of activity driven by the body's circadian rhythms. Medication to manage a hyperactive thyroid, for example, could therefore be most effective if consumed when certain thyroid genes are most active. Conversely, taking the drug when the genes are idle could be ineffective. Also, says Marc D. Ruben, a research fellow at Cincinnati Children's Hospital, who led the study, smart timing "could reduce the amount of drug needed to achieve a desired effect or lessen side effects at the same dose."



Expression of Cardiovascular Genes That Cycle across 24 Hours

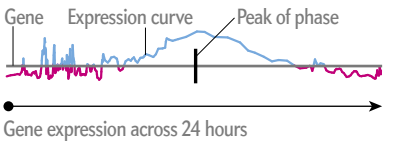


Cardiac Case Study

The 136 genes that affect a heart chamber, aorta, coronary artery or leg artery have a daily cycle (*tall graphic*). There is a pattern to when they are very active (*blue*) and underactive (*pink*), and most of these phases last for a stretch of time. By comparison, for cardiac genes that do not have a daily cycle (*subset shown in short graphic*), enhanced and depressed activity is random and not sustained. Some common drugs, such as beta blockers for high blood pressure, act for only a short time, so they could be most effective if taken when cycling genes are active.

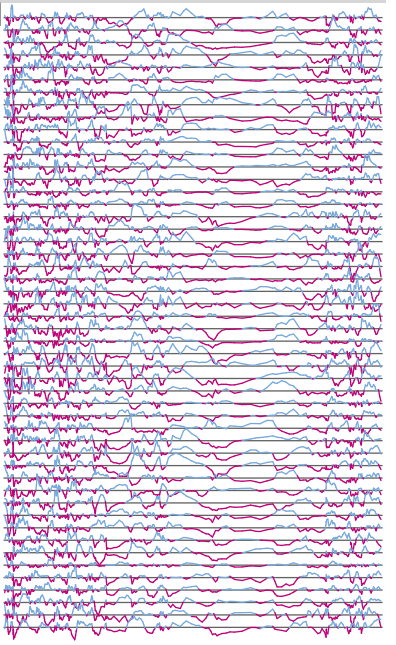
How to Read the Stacks

Each horizontal line represents a gene. The jagged curve shows gene activity, or expression, across 24 hours: pink indicates underactivity; blue indicates heightened activity. The short, vertical bar is the peak of the daily phase; it occurs early for genes at the top of the chart and late for genes at the bottom.



Some genes affect up to four different cardiac tissues and may be expressed differently in each one (noted on a given line by superimposed curves and multiple vertical bars).

Expression of Cardiovascular Genes That Do Not Cycle



SOURCE: "A DATABASE OF TISSUE-SPECIFIC RHYTHMICALLY EXPRESSED HUMAN GENES HAS POTENTIAL APPLICATIONS IN CIRCADIAN MEDICINE," BY MARC D. RUBEN ET AL., IN *SCIENCE TRANSLATIONAL MEDICINE*, VOL. 10, SEPTEMBER 12, 2018

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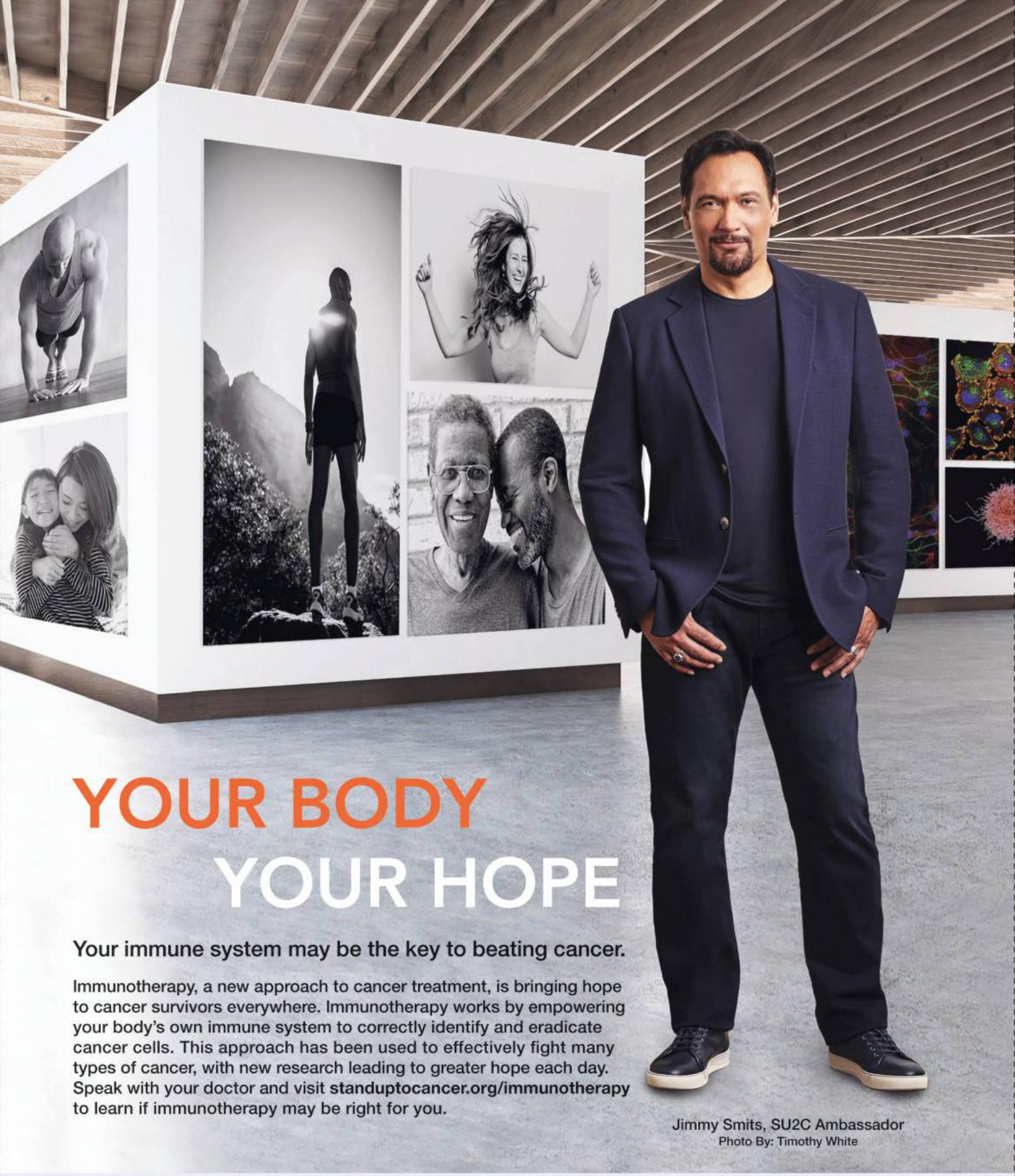

YOUR BODY
YOUR HOPE

Your immune system may be the key to beating cancer.

Immunotherapy, a new approach to cancer treatment, is bringing hope to cancer survivors everywhere. Immunotherapy works by empowering your body's own immune system to correctly identify and eradicate cancer cells. This approach has been used to effectively fight many types of cancer, with new research leading to greater hope each day. Speak with your doctor and visit **standuptocancer.org/immunotherapy** to learn if immunotherapy may be right for you.

Jimmy Smits, SU2C Ambassador
Photo By: Timothy White

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