TESTING NEWBORNS FOR GENETIC RISKS PAGE 72

TRUE COLORS OF DINOSAURS PAGE 50

SCIENTIFIC AMERICAN

MISSION TO ALPHA CENTAURI

Tiny laser-powered probes traveling at near light speed take aim at a star

PLUS

BUG BATTLE
Gene switches fight a corn pest PAGE 64

NEW TURING TESTS
Four new ways to judge robot intelligence PAGE 58

HOW POVERTY HURTS KIDS' BRAINS
Could a simple remedy help? PAGE 44

MARCH 2017
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MARCH 2017

VOLUME 316, NUMBER 3

SCIENTIFIC AMERICAN

ON THE COVER

An ambitious project called Breakthrough Starshot would send a swarm of small, smartphonelike chips to make the first visit to another star. "Light sails" pushed by laser light beamed from Earth's surface would propel the chip satellites to near light speeds, allowing them to make a quick flyby.
Illustration by Chris Wren, Mondolithic Studios.

Photograph by Patrick Cavan Brown

SCIENTIFIC AMERICAN

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ON THE WEB

Harnessing Biological Systems
DARPA Biological Technologies Office director Justin Sanchez tells us what to expect from his research agency in 2017.
Go to www.ScientificAmerican.com/mar2017/darpa-bto

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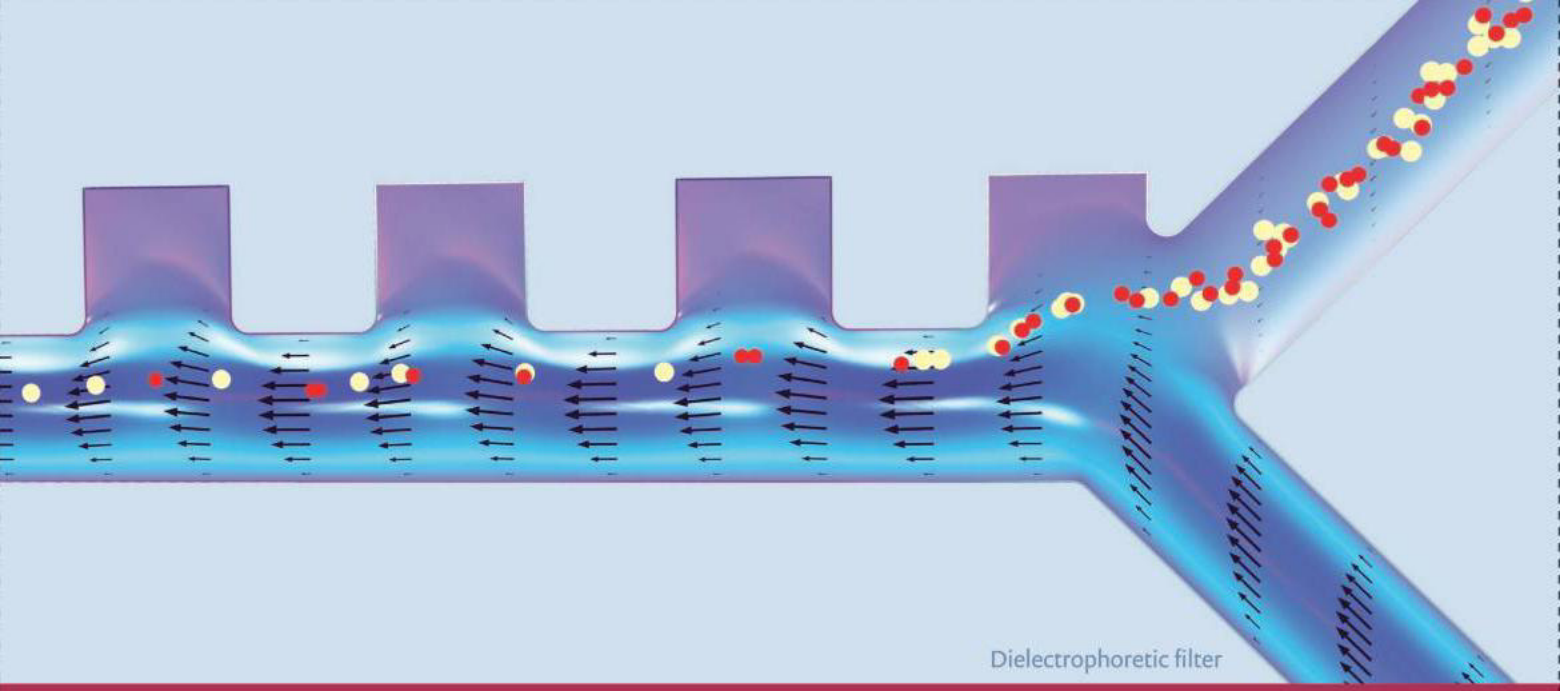

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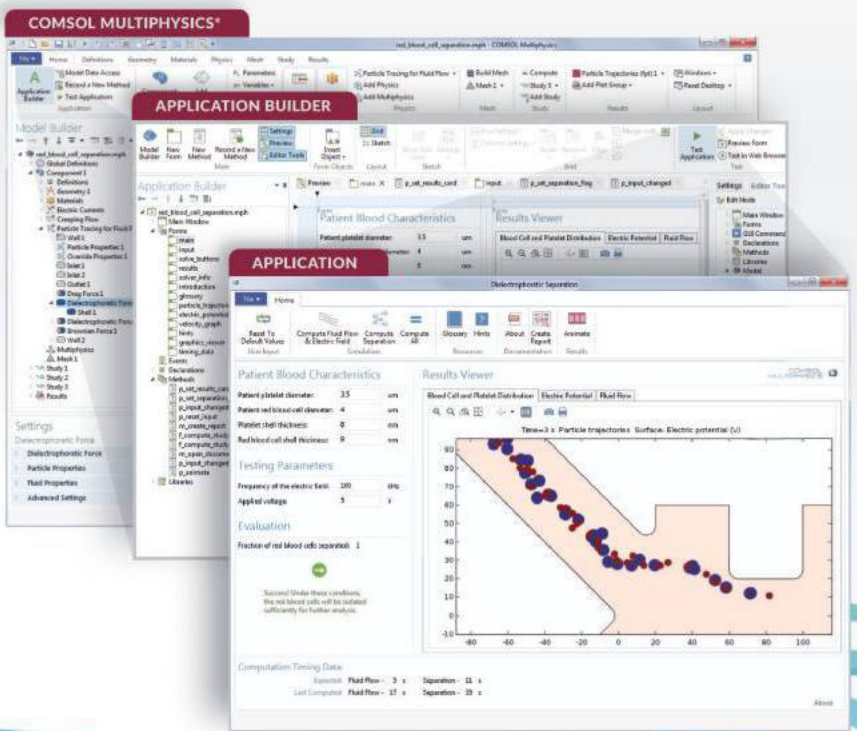

COMSOL

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

To Boldly Go

Before kindergarten, I was already dreaming about the wonders of interstellar space travel. I saw the *Apollo* astronauts walk on the moon and enjoyed the weekly exploits of the crew of the *Enterprise* on the original *Star Trek* TV episodes. It seemed we'd soon be leaping into that "final frontier." But the adult me now knows a lot more about how hard it is to explore the cold vastness of space—even if we're doing so with machines instead of us fragile humans. Robot missions to next-door neighbor Mars a mere 225 million kilometers away on average have failed with unpleasant frequency. It's almost as if the universe seems to dare us to go big or stay home.

Our cover story, then, brings you the tale of just such a big idea, which aims to reach a nearby star using something very small. A lot of millimeter-size things, actually. In "Near-Light-Speed Mission to Alpha Centauri," journalist Ann Finkbeiner relates how the Breakthrough Starshot mission plans to journey to Alpha Centauri, about four light-years away. It would use "StarChips" on light sails propelled by laser light. Based on chips similar to those in smartphones, they would take pictures and make other readings during a brief flyby. The plan is risky, expensive—and it may not work. But it's an exciting idea to tackle the hard problem, and I hope you enjoy learning about it as much as I did. Turn to page 30.

Another place that's hard to reach is the distant past. That doesn't stop us from looking for clues about it in the present—and sometimes finding them. What color were the dinosaurs, for instance? But one day biologist Jakob Vinther spied the fossilized ink of a 200-million-year-old squid relative, perfectly preserved. It looked like granules of melanin pigment. He began to wonder if melanin might survive in fossils. Voilà—an intriguing pathway to what things were like in another place and time. In "The True Colors of Dinosaurs," starting on page 50, you will learn the surprising insights scientists are gaining from this new look at old creatures.

As ever, *Scientific American* is also fully engaged with how science might solve some of humanity's greatest challenges. "Brain Trust," beginning on page 44, by neuroscientist Kimberly G. Noble, examines how growing up in poverty affects a child's cognition and brain development. Could a simple remedy—a cash stipend for families to ease financial straits—help children to reach their potential? The process of science will lead us to find out. SA

GETTY IMAGES

Illustration by Nick Higgins

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November 2016

ENTANGLED BLACK HOLES

The possible equivalency between general relativity's wormholes and quantum physics' entanglement that Juan Maldacena describes in "Black Holes, Wormholes and the Secrets of Quantum Spacetime" involves entangling a pair of black holes. To do so, he proposes creating a large number of entangled particle pairs that are separated into two sets, which are then manipulated into the two entangled black holes. But entangled quanta lose their entanglement when they interact with other quanta. Collecting entangled quanta into local sets and then manipulating them into local black holes would involve interactions that would destroy the entanglement before the black holes could be created.

Anthony Way
Dallas, Tex.

If entangled black holes share an interior, what happens to their masses?

Peter Stegner
via e-mail

MALDACENA REPLIES: In response to Way: Yes, it would be indeed extremely difficult to create entangled black holes as I describe because it is difficult to do manipulations in quantum systems while keeping coherence. And it would be most likely impossible to do it in practice for macroscopic black holes in our universe. The motivation to study these ideas is just to better understand how the quantum mechanics of spacetime works.

Regarding Stegner's question: The mass of the black holes is a property that we can measure from the outside. From there each of them has a mass (both equal). On the other hand, with these entangled black holes, there is no matter inside! Thus, we have mass purely from geometry, with no matter anywhere in the whole spacetime.

"An appalling number of my college-educated acquaintances believe that Donald Trump's unsubstantiated assertions have some basis in fact."

ELLIOT TRAMER *UNIVERSITY OF TOLEDO*

GRAMMAR WARS

In "Language in a New Key," Paul Ibbotson and Michael Tomasello criticize Noam Chomsky's linguistic theory that humans are born with a template for grammar and suggest, as an alternative, usage-based linguistics, in which children build grammatical categories and rules, based on the language they hear, with a set of general-purpose mental tools. But while this approach implies correctly that language is a form of behavior and is acquired from experiences in one's lifetime, it, like Chomsky's view, makes many untestable assumptions about unobserved mental processes.

A parsimonious and scientific theory was put forth in 1957 by experimental behavior analyst B. F. Skinner in his book *Verbal Behavior*. We might not be talking about Chomsky had he not penned a negative review of the book in 1959.

Unlike Chomsky's "theories" and those of most linguists, Skinner's was based on decades of basic experimental research. Moreover, as proof of its longevity, it has continued to generate research and is being used all over the world to help children with language deficits.

Henry D. Schlinger, Jr.
Department of psychology
California State University, Los Angeles

TRUMP'S SCIENCE FICTIONS

Before highlighting quotes from Donald Trump that show his disregard for science in "Donald Trump's Campaign for Science Illiteracy" [Science Agenda], the editors make the bland statement that they "have not fact-checked" them. Why not?! Claims that global warming is a hoax, that vaccinations cause autism or that President Barack Obama had let "Iran keep its nukes" are easily refuted.

An appalling number of my college-educated acquaintances believe, or want to believe, that Trump's unsubstantiated assertions have some basis in fact. Expanding your editorial to an additional page by the inclusion of fact-checking should have been a far higher priority than anything else contained in your November issue.

Elliot Tramer
Professor emeritus
University of Toledo

ILLICIT DRUG RESTRICTIONS

In "Get Clean or Die Trying," James Nestor says that the reason the hallucinogenic antiaddiction drug ibogaine was placed in the most restrictive category by the Drug Enforcement Administration is because it can kill users. That statement falsely makes it appear as though the DEA has been doing a fair, science-based analysis in such categorization. Ibogaine was swept into Schedule I in the same manner of cannabis and a plethora of other substances that do not directly kill people and that are orders of magnitude safer than alcohol or tobacco. That methamphetamine, cocaine and morphine are in a less restrictive category than are cannabis, peyote and psilocybin seems absurd in the light of any sort of impartial scientific analysis.

Josh Matthews
via e-mail

HALF-EMPTY EVOLUTION

In "Why Gloom Trumps Glad" [Skeptic], Michael Shermer asks why bad things seem to have more impact in politics than good ones and finds an answer in the psychology of loss aversion, in which the pain of losses outweighs the pleasure of gains. But its literature is a collection of findings rather than an explanation, and although Shermer's suggestion that the phenomenon developed as an evolutionary effect

may be true, it does not add much insight.

Negativity bias is another concept in psychology that has explored the greater impact of negative information. Here the prevailing explanation rests on the relative frequency of good and bad happenings. Positive outcomes are more common, so negative information stands out and can lead to more change. Such an explanation may lie behind loss aversion, but this area and negativity bias seem to occupy separate academic silos.

ROBERT EAST
Professor emeritus of consumer behavior
Kingston University London

SHERMER REPLIES: That loss aversion is merely a finding and not an explanation for the predominance of pessimism is debatable. I think of "aversion" as both a behavioral trait and *an emotional state. Because the world was a more dangerous place for our ancestors, it paid to be more risk-averse, cautious and pessimistic about future events. For a deeper explanation for why gloom trumps glad, see the aptly titled 2003 paper "The Second Law of Thermodynamics Is the First Law of Psychology," by John Tooby and his colleagues, which posits that any ultimate evolutionary explanation for behavior must begin with entropy: "Natural selection is the only known natural process that … offsets the inevitable increase in disorder that would otherwise take place."*

If you do nothing, entropy will take its course, and you will move toward a higher state of disorder, so the most basic purpose of life is to combat entropy by expending energy to survive, reproduce and flourish.

ERRATA

"Winds of Change," by Jeremy Hsu [Advances], should have referred to 11.5 gigawatts as the installed capacity for offshore wind power in Europe, not the total power produced every year.

"Get Clean or Die Trying," by James Nestor, incorrectly implied that a fatality rate of 19 in 3,500 would be lower than one in 300.

"The Problem with Tech Copycats," by David Pogue [TechnoFiles], should have referred to Apple, not Steve Jobs, as suing Microsoft in 1988. Jobs was not part of the company at that time.

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[insideview]

A SCIENTIST'S PERSONAL CONNECTION TO CANCER PROPELS HER RESEARCH

A conversation with JESSICA BAKER, Associate Consultant Scientist, Clinical Diagnostics Laboratory, Eli Lilly and Company

Jessica Baker's work developing cancer diagnostics took on personal significance when she was diagnosed with breast cancer almost five years ago. The Eli Lilly and Company scientist's own battle with the disease intensified her efforts to find ways to tailor cancer treatment. Baker tells *Scientific American* how her work aims to help reduce the effects of a disease that strikes 14 million people a year globally.

What led you to focus on cancer research?
My training is in medical genetics, so cancer was always a subject of interest. Before coming to Lilly, I worked in the clinical diagnostics areas at academic institutions. It was exciting research, but our job was to diagnose patients who often didn't have any treatment options. I decided to join Lilly in 2002 because I wanted to help discover cures and new medicines that make life better for people.

How did you react to your own cancer diagnosis?
I never thought it could happen to me. Even though I was in cancer research, there was no history of cancer in my family.

I knew that I needed to be strong and courageous because I had a young son. I looked for hope and dug deep for the will to fight.

I HAVE A PICTURE OF MY OWN TUMOR AT MY DESK. IT REMINDS ME WHY WE DO WHAT WE DO

How did diagnostics inform your own treatment?
I tested positive for the HER2 test using a screen that I had helped implement. The scary thing was that this was a particularly aggressive type of cancer. The hopeful part was that there is a very effective targeted treatment, which has a high success rate treating this particular kind of tumor.

In addition to the targeted treatment, I had standard chemotherapy and I continue to take anti-estrogen medication. I also elected to undergo a double mastectomy. I have been cancer-free for almost five years now.

How has this experience affected how you approach your work with Lilly?
I have a picture of my tumor at my desk, which is a good reminder of why we do what we do. When I come to work and see the picture, I think of people with cancer. They need treatment. They need it now. It gives me an extra sense of urgency.

Why is your particular work on cancer and other disease diagnosis important?
We can utilize diagnostics to help determine who will respond to a particular medicine. And as therapies continue to improve, we are better able to match them up to particular kinds of cancers — picking the right medicine for the right person.

What excites you about your work in oncology research?
I'm encouraged by the recent advances in diagnostics, targeted therapies and immuno-oncology. Just within the last year, a new breast cancer susceptibility gene was identified, a new drug combination of targeted therapies increased survival for metastatic breast cancer and a new treatment reduced recurrence for premenopausal women with hormone positive breast cancer. If these sound like buzz words, believe me when I tell you, this is amazing progress!

Developing new medicines and diagnostics is complex, difficult and only rarely successful. Why do you do it? What motivates you?
I am driven by the scientific challenge and my connection to patients. We learn from every failure; failure motivates me to try harder.

Every patient wants fewer side-effects, more time with family and friends and more time to enjoy life. Working as a researcher allows me to make an impact on this horrible disease, one tumor at a time.

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Take Nukes Off a Short Fuse

For the sake of the planet, the U.S. nuclear arsenal should not be on high alert

By the Editors

Last summer the esteemed naturalist E. O. Wilson told the Huffington Post that he fears a nuclear conflagration as a clear and present danger to the planet. A similar-sounding fear has been shared by Donald Trump. "The global warming we should be worried about is the global warming caused by NUCLEAR WEAPONS in the hands of crazy or incompetent leaders!" read a Trump tweet, fired off in 2014 and echoed during his candidacy for president.

The two men made these parallel observations for different reasons. Trump wished to downplay the risks of global warming. Wilson, while acknowledging the longer-term peril of climate change, worried that "some stupid mistake" by a nuclear-armed nation could bring on catastrophe in coming years. On an equal footing, he feared a Trump presidency as an immediate menace but at the time believed the mogul could never be elected.

Even before the election, geopolitical tensions had exacerbated the prospects of a nuclear conflict. In fact, the threat posed by nuclear weapons on high alert has persisted for decades. Both the U.S. and Russia hold about 900 nukes ready to launch, a hair-trigger status that keeps submarine- and land-based missiles prepared for immediate firing to deter a first strike—a posture intended to allow these missiles to be launched in retaliation before attacking missiles can hit their targets.

If our early-warning system detects incoming missiles, the president has 12 minutes or less to decide whether to unleash global-scale destruction and take the lives of tens of millions of civilians. So far salvos of incoming missiles have amounted to nothing more than electronic mirages.

Ominously, though, technical glitches have at times fooled both Soviet Union and U.S. warning systems into flagging attacks that were nonexistent. In 1983 a counterattack was averted only when a Soviet military officer decided to trust his gut instinct and concluded that satellite data about incoming U.S. missiles were a false alarm.

The U.S. has experienced its own mishaps. In 1979 computers at the command center in Colorado Springs signaled that a major Soviet nuclear offensive was under way. Both U.S. ballistic missile and nuclear bomber crews sprang into action, only standing down after satellite data could not corroborate the warning. It turned out that data from training software simulating a massive attack had somehow made their way into an operational computer.

The "button" can also morph into a perverse temptation for an unstable leader. In 1974, during his impeachment proceedings, President Richard M. Nixon said to reporters: "I can go into my office and pick up the telephone, and in 25 minutes, 70 million people will be dead." Worried about Nixon's state of mind at the time, Defense Secretary James Schlesinger asked to be notified before any nuclear launch order from Nixon was executed.

The existential risks of our current policy framework prompted both Barack Obama and George W. Bush to pledge during their first presidential campaigns that they would take measures to move ballistic missiles off high alert. Neither followed through, leaving an opening for the new administration.

After fluctuating wildly from one position to the next on many issues during the 2016 campaign, Trump should give the U.S. electorate some assurance that he intends to govern with a steady hand by making a commitment to take our nuclear arsenal off hair-trigger alert and buy more time to decide whether to push the button.

Trump should adopt a set of pragmatic options that the Union of Concerned Scientists (UCS) and other public-interest groups have outlined, some of which could be readily implemented. Turning a safety switch in the nuclear missile silos, a procedure called safing, used when maintenance workers are on-site, would prevent an unwarranted launch. It would take at least half a day to reverse this process because silos are not staffed, enough time to forestall an irreversible decision.

As the UCS has pointed out, by taking this step unilaterally, the U.S. could reduce the risk of a mistaken or accidental launch that could lead to nuclear retaliation on the U.S. public. It might also serve as a prelude to such measures as removing warheads and storing them elsewhere and ultimately getting rid of the land-based force entirely. The Russians might even be convinced to follow suit. Because of submarines' relative invulnerability, both the U.S. and Russia could be assured of being able to mount a counterattack.

All these moves would make the world safer and might also dissuade China, which does not have its missiles on a hair trigger, from adopting that policy. The need for better preventive steps has also become more acute because of sophisticated cybertechnologies that could, in theory, hack into a command-and-control system to fire a missile that is ready to launch.

Taking the U.S. arsenal off high alert would cost a pittance but could buy enough time to avert the cataclysmic event that once again looms as the most pressing threat to our survival. SA

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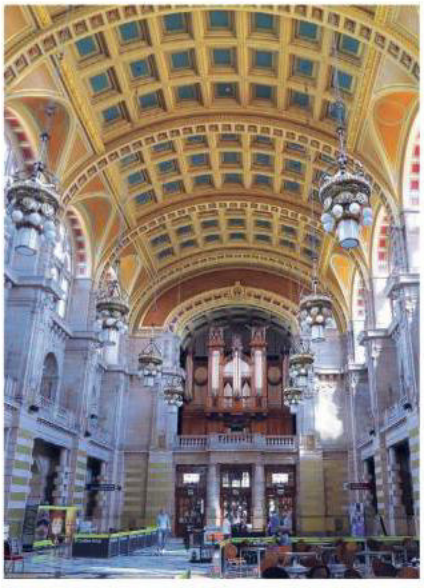

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David L. Dill is a professor of computer science and, by courtesy, electrical engineering at Stanford University. He is founder of the Verified Voting Foundation and VerifiedVoting.org.

Our Elections Are Not Secure

The Russian hacks of Democratic e-mails expose only part of the problem

By David L. Dill

The FBI, NSA and CIA all agree that the Russian government tried to influence the 2016 presidential election by hacking candidates and political parties and leaking the documents they gathered. That's disturbing. But they could have done even worse. It is entirely possible for an adversary to hack American computerized voting systems directly and select the next commander in chief.

A dedicated group of technically sophisticated individuals could steal an election by hacking voting machines in key counties in just a few states. Indeed, University of Michigan computer science professor J. Alex Halderman says that he and his students could have changed the result of the November election. Halderman et al. have hacked a lot of voting machines, and there are videos to prove it. I believe him.

Halderman isn't going to steal an election, but a foreign nation might be tempted to do so. It needn't be a superpower like Russia or China. Even a medium-size country would have the resources to accomplish this, with techniques that could include hacking directly into voting systems over the Internet; bribing employees of election offices and voting-machine vendors; or just buying the companies that make the voting machines outright. It is likely that such an attack would not be detected, given our current election security practices.

What would alert us to such an act? What should we do about it? If there is reason to suspect an election result (perhaps because it's an upset victory that defies the vast majority of preelection polls), common sense says we should double-check the results as best we can. But this is hard to do in America. Recount laws vary from state to state. Not all states even allow recounts, and many of those that do require that a candidate request the recount and pay for it himself or herself. In the 2016 election Green Party presidential candidate Jill Stein, citing potential security breaches, requested a recount in Wisconsin, Pennsylvania and Michigan, all of which unexpectedly and narrowly went to Donald Trump.

Those efforts did not change the results. Nevertheless, it has become clear that our voting system is vulnerable to attack by foreign powers, criminal groups, campaigns and even motivated amateurs. We must defend it more effectively. If elections lose their credibility, democracy can quickly disintegrate. It is not good enough to say, after every election, "We can't prove fraud." We need evidence that vote counts are accurate.

The good news is that we know how to solve this problem. We need to audit computers by manually examining randomly selected paper ballots and comparing the results with machine results. Audits require a voter-verified paper ballot, which the voter inspects to confirm that his or her selections have been correctly and indelibly recorded. Since 2003 an active community of academics, lawyers, election officials and activists has urged states to adopt paper ballots and robust audit procedures.

This campaign has had significant, albeit slow, success. Approximately three quarters of U.S. voters cast paper ballots. Twenty-six states do some type of manual audit, but none of their procedures is adequate. Auditing methods have recently been devised that are much more efficient than those used in any state. It is important that audits be performed on *every contest* in *every election* so that citizens do not have to request manual recounts to feel confident about election results. With high-quality audits, it is very unlikely that election fraud will go undetected, whether perpetrated by another country or a political party.

There is no reason we cannot implement these measures before the 2020 elections. As a nation, we need to recognize the urgency of the task, to overcome the political and organizational obstacles that have impeded progress. Otherwise, we risk losing our country to hackers armed with keyboards, without a shot being fired. SA

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Illustration by Matt Clough

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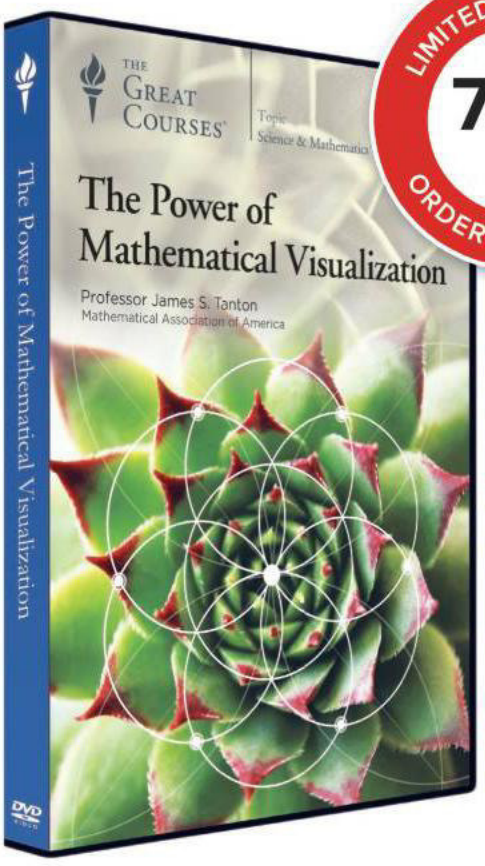

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ADVANCES

Genetic analysis suggests that humans have continuously inhabited the Tibetan Plateau as far back as the last ice age. Some nomadic people (*inset*) in the region still follow a traditional way of life.

INSIDE

EVOLUTION

Ice Age Tibetans

New studies of human migration—and resilience—suggest people populated the frozen Tibetan Plateau much earlier than thought

The first humans who ventured onto the Tibetan Plateau, often called the "roof of the world," faced one of the most brutal environments our species has ever confronted. At an average elevation of more than 4,500 meters, it is a cold and arid place with half the oxygen present at sea level. Although scientists had long thought no one set foot on the plateau until 15,000 years ago, new genetic and archaeological data indicate that this event may have taken place much earlier—possibly as far back as 62,000 years ago, in the middle of the last ice age. A better understanding of the history of migration and population growth in the region could help unravel the mysteries of Tibetans' origin and offer clues as to how humans have adapted to low-oxygen conditions at high altitudes.

As reported in a recent study in the *American Journal of Human Genetics*, researchers got a better grasp of the plateau's settlement history by sequencing the entire genomes of 38 ethnic Tibetans and comparing the results with the genomic sequences of other ethnic groups. "It has revealed a complex patchwork of prehistoric migration," says Shuhua Xu, a population geneticist at the Chinese Academy of Sciences' Shanghai Institutes for Biological Sciences. "A big surprise was the antiquity of Tibetan-specific DNA sequenc-

es," Xu says. "They can be traced back to ancestors 62,000 to 38,000 years ago, possibly representing the earliest colonization of the plateau."

As an ice age tightened its grip after that first migration, genetic mixing between Tibetans and non-Tibetans ground to a halt for tens of thousands of years—suggesting that movement into Tibet dropped to a minimum. "The migration routes were probably cut off by ice sheets," Xu says. "It was simply too harsh even for the toughest hunter-gatherers." But about 15,000 to 9,000 years ago—after the so-called last glacial maximum (LGM), when the ice age was at its harshest and Earth's ice cover had reached its peak—thousands flocked to Tibet en masse. "It's the most significant wave of migration that shaped the modern Tibetan gene pool," Xu says. This meshes well with several independent lines of evidence showing that Tibetans began to acquire genetic mutations that protected them from hypoxia 12,800 to 8,000 years ago.

Xu's team was the first to sequence the entire Tibetan genome, and "the resolution is really impressive," says archaeologist Mark Aldenderfer of the University of California, Merced, who was not involved in the research. The study, he adds, "provides fine details of how different populations from various directions may have combined their genes to ultimately create the people that we call Tibetans." It shows that 94 percent of the present-day Tibetan genetic makeup came from modern humans—possibly those who ventured into Tibet in the second wave of migration—and the rest came from extinct hominins. The modern part of the Tibetan genome reflects a mixed genetic heritage, sharing 82 percent similarity with East Asians, 11 percent with Central Asians and 6 percent with South Asians.

In addition, Xu's team identified a Tibetan-specific DNA segment that is highly homologous to the genome of the Ust'-Ishim Man (modern humans living in Siberia 45,000 years ago) and several extinct human species, including Neandertals, Denisovans and unknown groups. The segment contains eight genes, one of which is known to be crucial for high-altitude adaptation. Xu suspects that a hybrid of all these species may have been the common ancestor of the pre-LGM population on the plateau.

The study also reveals a startling genetic continuity since the plateau was first colonized. "This suggests that Tibet has always been populated—even during the toughest times as far as climate was concerned," Xu says. That idea contradicts the commonly held notion that early plateau dwellers would have been eliminated during harsh climate intervals, including the LGM, says David Zhang, a geographer at the University of Hong Kong, who was not involved in Xu's work. Aldenderfer and others contend that parts of the plateau could have provided a refuge for people to survive the ice age. "There were plenty of places for [those early populations] to live where local conditions weren't that bad, such as the big river valleys on the plateau," he says.

Also supporting the antiquity of the peopling of Tibet is a study presented at the 33rd International Geographical Congress last summer in Beijing, where a team unveiled the plateau's earliest archaeological evidence of human presence—dating to 39,000 to 31,000 years ago. The site, rich with stone tools and animal remains, lies on the bank of the Salween River in the southeastern Tibetan Plateau.

Different lines of evidence are now converging to point to much earlier and much more persistent human occupation of the plateau than previously thought, Aldenderfer says. But he notes that pieces are still missing from the puzzle: "More excavations are required to close those gaps." —*Jane Qiu*

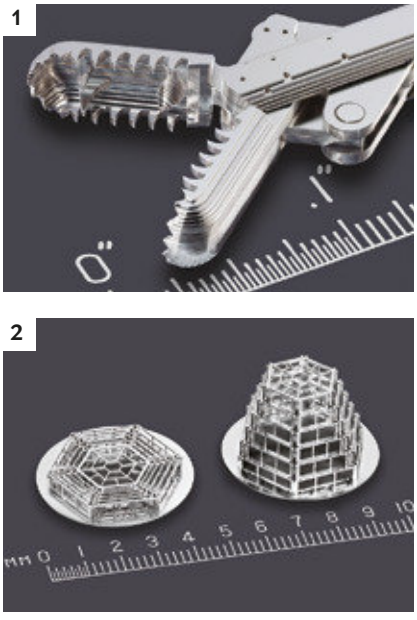
TECHNOLOGY

Metal Devices, in Miniature

A new method of 3-D printing draws inspiration from the semiconductor industry

As everything from consumer electronics to medical devices continues to shrink, manufacturers keep running up against the problem of detail: How do you make parts and pieces that are nearly microscopic while maintaining their finer points? Microfabrica, a company based in Van Nuys, Calif., has developed a process that combines 3-D printing, wherein structures are built up layer by layer, with the same manufacturing techniques used to make computer chips, whereby metal ions are essentially electroplated to a surface. The process can create objects from layers of metal with a thickness of just five microns, or 0.0002 inch, yielding extremely refined structures. (Compare that with polyjet 3-D printers, which spray plastics from nozzles at layers as small as 16 microns.)

Microfabrica's technique opens doors for new types of tools as well as old tools at new scales. For instance, the company has developed a tiny radiator for cooling computer chips under a DARPA initiative and a miniature timing mechanism for use in munitions. Microfabrica also makes minuscule surgical instruments, including biopsy forceps less than one millimeter in diameter and a tissue scaffold with linkages that allow it to expand with cell growth. Carol Livermore, a mechanical and industrial engineering professor at Northeastern University, calls Microfabrica's capabilities impressive. "I am not aware of any kind of high-end 3-D printing that exceeds that performance," she says. —*Michael Belfiore*



Biopsy forceps (*1*) and expandable tissue scaffolds (*2*) could be shipped in vials of alcohol to customers.

PRECEDING PAGES: GETTY IMAGES (*mountains*); EDWINA DEACON *Getty Images* (*Tibetan couple*); THIS PAGE: COURTESY OF MICROFABRICA (*metal devices*)

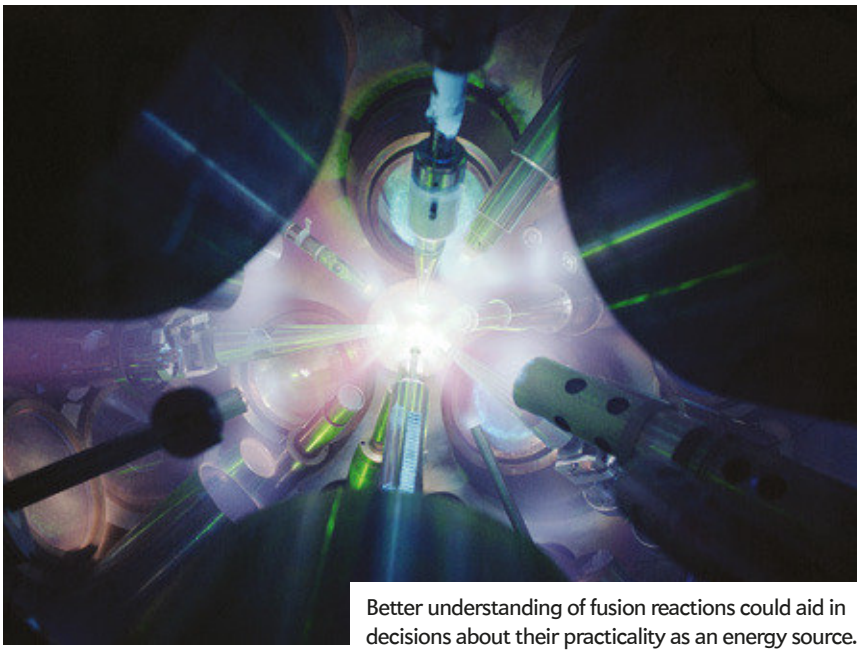
Q&A

Is Fusion in Our Future?

The U.S. is grossly underinvested in energy research, says Obama's science adviser. And that includes fusion power

John Holdren has heard the old joke a million times: fusion energy is 30 years away—and always will be. Despite the broken promises, Holdren, who early in his career worked as a physicist on fusion power, believes passionately that fusion research has been worth the billions spent over the past few decades—and that the work should continue. In December, SCIENTIFIC AMERICAN talked with Holdren, outgoing director of the federal Office of Science and Technology Policy, to discuss the Obama administration's science legacy. An edited excerpt of his thoughts on the U.S.'s energy investments follows.

—*Fred Guterl*



Better understanding of fusion reactions could aid in decisions about their practicality as an energy source.

SCIENTIFIC AMERICAN: Have we been investing enough in research on energy technologies?

John Holdren: I think that we should be spending in the range of three to four times as much on energy research and development overall as we've been spending. Every major study of energy R&D in relation to the magnitude of the challenges, the size of the opportunities and the important possibilities that we're not pursuing for lack of money concludes that we should be spending much more.

But we have national labs that are devoted—

I'm counting what the national labs are doing in the federal government's effort. We just need to be doing more—and that's true right across the board. We need to be doing more on advanced biofuels. We need to be doing more on carbon capture and sequestration. We need to be doing more on advanced nuclear technologies. We need to be doing more on fusion, for heaven's sake.

Fusion? Really?

Fusion is not going to generate a kilowatt-hour before 2050, in my judgment, but—

Hasn't fusion been 30 years away for the past 30 years?

It's actually worse than that. I started working on fusion in 1966. I did my master's thesis at M.I.T. in plasma physics, and at that time people thought we'd have fusion by 1980. It was only 14 years away. By 1980 it was 20 years away. By 2000 it was 35 years away. But if you look at the pace of progress in fusion over most of that period, it's been faster than Moore's law in terms of the performance of the devices—and it would be nice to have a cleaner, safer, less proliferation-prone version of nuclear energy than fission.

My position is not that we know fusion will emerge as an attractive energy source by 2050 or 2075 but that it's worth putting some money on the bet because we don't have all that many essentially inexhaustible energy options. There are the renewables. There are efficient breeder reactors, which have many rather unattractive characteristics in terms of requiring what amounts to a plutonium economy—at least with current technology—and trafficking in large quantities of weapon-usable materials.

The other thing that's kind of an interesting side note is if we ever are going to go to the stars, the only propulsion that's going to get us there is fusion.

Are we talking warp drive?

No, I'm talking about going to the stars at some substantial fraction of the speed of light.

When will we know if fusion is going to work?

The reason we should stick with ITER [a fusion project based in France] is that it is the only current hope for producing a burning plasma, and until we can understand and master the physics of a burning plasma—a plasma that is generating enough fusion energy to sustain its temperature and density—we will not know whether fusion can ever be managed as a practical energy source, either for terrestrial power generation or for space propulsion. I'm fine with taking a hard look at fusion every five years and deciding whether it's still worth a candle, but for the time being I think it is.

To read more of the conversation with John Holdren—which includes his assessment of the future of U.S. science policy, the prospects for continued progress on brain science, and more—visit ***www.ScientificAmerican.com/john-holdren***

ROGER RESSMEYER *Getty Images (fusion);* HARAZ N. GHANBARI *AP Photo (Holdren)*

Colonies of the bacterium that causes gonorrhea.

R. PARULAN JR. *Getty Images*

PUBLIC HEALTH

STD Results in Minutes

A clinic sets up a new—and fast—model for STD testing

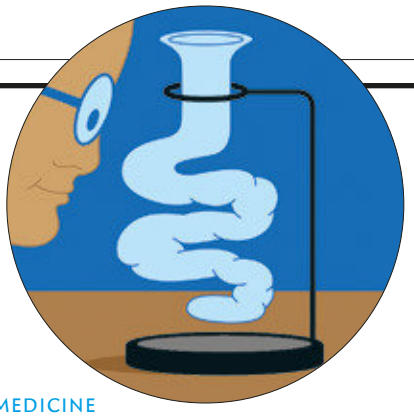
Getting tested for an STD is a pain. There's a doctor's appointment, a week of waiting for results and a wealth of opportunity for embarrassing human interaction. These hassles may be part of the reason STD infection rates are on the rise—so now a clinic in London has begun to reimagine the process for the digital age. Its walk-in facility, called Dean Street Express, seeks to provide a self-service, stigma-free experience that requires almost no eye contact with strangers. And the system is working thanks to a miniaturized version of molecular-testing technology.

After scheduling a time online, a person concerned about STDs arrives at the Dean Street clinic and checks in on a computer screen. A technician then hands the subject a tube with the appropriate swabs for tests that were selected from a menu (which includes all the standards such as syphilis, gonorrhea and chlamydia). Next the individual enters a private room where a video shows how to provide samples. Results are texted to a mobile phone within six hours.

The technology that makes this possible was developed by Cepheid, a U.S.-based diagnostics company whose portable tuberculosis test hit the market in 2011, then skyrocketed in popularity for its ability to get from sample to result in just 15 minutes. Just like laboratory tests, Cepheid's method relies on genetic markers to pinpoint disease—but it all takes place inside a machine that is small enough to be carried around. Within five years the company has sold nearly 12,000 testing systems in countries that, in some cases, had never seen molecular testing before. Hoffmann–La Roche, Abbott and other companies have since developed similar systems.

In London, the Dean Street model has been so popular that the company's founders recently introduced HIV testing and opened a second location. Five more are planned for the city, and Cepheid says it is also providing systems for walk-in clinics in Barcelona, Paris, Brisbane, Australia and San Francisco (with one about to launch in Florida). Says Dave Persing, the testing company's chief medical officer: "Everybody sees the potential here to shorten the time to result and get patients on therapy much more quickly, reduce transmission, reduce anxiety and provide an overall better experience. Nobody likes getting surprised 11 days later that they're positive for chlamydia or gonorrhea. That's just unacceptable."

—Erin Biba



MEDICINE

It Takes Guts

Functional intestine becomes the latest lab-grown organ

When it comes to growing intestines, the first inch is the hardest—especially in a petri dish. Scientists at Cincinnati Children's Hospital Medical Center have met that benchmark: they recently reported in *Nature Medicine* that they had grown a piece of gut—nerves, muscles and all—from a single line of human stem cells. In the future such tissue could be used for studying disease and more.

In 2011 researchers at the same center announced that they had grown intestinal tissue—but it was missing nerve cells and so was unable to contract in the undulating motion that pushes food along a colon. This time around, the scientists grew neurons separately and then combined them with another batch of stem cells that had been induced to become muscle and intestinal lining. Voilà: an inch-long piece of gut formed. "Just like in developing human bodies, the nerve cells knew where to go," says Michael Helmrath, surgical director of the Intestinal Rehabilitation Program at Cincinnati Children's.

The scientists then transplanted the tissue onto a living mouse's intestine so it could mature. After harvesting it for testing, they stimulated the bespoke chunk with a shock of electricity. It contracted and continued to do so on its own. "The function was quite remarkable," Helmrath says. Intestines now join kidneys, brain matter and a few other kinds of tissue that can be grown in the lab.

Next, Helmrath and his colleague Jim Wells would like to coax longer pieces of intestine by working with pigs. Eventually the researchers hope to help treat people with gastrointestinal problems by making copies of a patient's gut to observe how a disease manifests—or even to transplant the tissue. "Intestines are a complex structure to grow," Wells says. "That we've even gotten this far in such a short time gives me hope that we can grow something therapeutically useful in the long run." —*Ryan F. Mandelbaum*

Illustrations by Thomas Fuchs

ENVIRONMENT

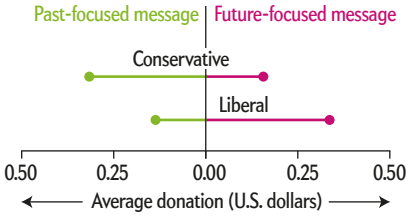
Make Earth Great Again

Would more people care about the environment if conservation focused on the past?

Political conservatives become more open to environmentalism after seeing climate change messages rooted in nostalgia, found a new study in the *Proceedings of the National Academy of Sciences USA*.

Researchers at the University of Cologne in Germany ran several experiments with self-identified liberals and conservatives to evaluate their feelings about environmental conservation, depending on how the issue was presented. For example, participants were given a $0.50 donation to split between two fictional climate change charities: one that emphasized preventing future environmental degradation and one that highlighted reinstating a healthier Earth from yesteryear. In all experiments, conservatives were more willing to embrace environmentalism after confronting climate change messaging that emphasized the past (including donating more to the past-focused charity).

Natural Selections



Asked to allocate $0.50 between a fictional charity focused on creating a new Earth for the future and one aiming to restore the planet to its past state, conservatives favored the latter.

Matthew Baldwin, a co-author on the paper, attributes the findings to the inherent value that conservatives place on the past. For him, the experiments demonstrate the power of framing to change how people respond to information.

Others are skeptical that this insight will lead to change. Riley Dunlap, an environmental sociologist at Oklahoma State University, says the study is well executed, but he doubts that reframing climate change messages can influence conservatives—especially in today's highly polarized political arena. "If you're a good conservative, you need to be a climate change skeptic," he says. "Global warming has joined God, guns, gays, abortion and taxes. It's part of that ideology."

Still, Baldwin thinks that approaching climate change as a marketing problem rather than a political issue may be the key to rising above the political quagmire. "If you want to sell a product, you sit down and figure out who your audience is, and you market the product to the audience," he says. "[My colleagues and I] don't think science is really all that much different."

—*Catherine Caruso*

Graphic by Amanda Montañez

SOURCE: "PAST-FOCUSED ENVIRONMENTAL COMPARISONS PROMOTE PROENVIRONMENTAL OUTCOMES FOR CONSERVATIVES." BY MATTHEW BALDWIN AND JORIS LAMMERS, IN *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA*, VOL. 113, NO. 52; DECEMBER 27, 2016

PALEONTOLOGY

Fossil Octopus Is a Jurassic Jewel

Paleontologists provide a new look at a beautifully preserved cephalopod

Octopus body shapes diversified widely earlier in evolutionary history than previously thought.

A good cephalopod fossil is hard to find. Although ammonite shells, belemnite guards and other indicators of hard body parts are abundant in the fossil record, paleontologists seldom get to see the characteristic soft-tissue anatomy of these many-armed swimmers. Finds are so rare that one from 1982 still stands out: a 165-million-year-old fossilized octopus uncovered in France.

J. C. Fischer and B. Riou named the eight-armed invertebrate *Proteroctopus ribeti* and described its suckers to the delight of other paleontologists. But despite its unprecedented level of detail, the fossil looked deflated—an animal preserved as a squished version of its former self. That made it difficult to figure out the particulars of the specimen's anatomy and how it related to other octopuses. More than three decades later paleontologist Isabelle Kruta of Pierre and Marie Curie University in Paris and her colleagues have provided more detail about what this emblematic cephalopod looked like when alive. They reconstructed the animal in 3-D using synchrotron microtomography, a high-definition imaging technique.

Reinflated and restored, *Proteroctopus* most likely falls within a major octopus group called Vampyropoda—which contains the common octopus as well as the vampire "squid." With the new images, the researchers found that *Proteroctopus* looked something like today's deep-sea forms of Vampyropoda—with a few differences. For instance, the ancient specimen has eight arms and a fin sticking out on either side of its body. *Proteroctopus* also lacks an ink sac, like the modern *Vampyroteuthis.* But the suckers of this Jurassic invertebrate are obliquely offset from one another rather than occurring side by side as in many extant octopuses. The study was published last fall in *Palaeontology.*

What *Proteroctopus* can tell us about the ancestral octopus will rely on finding more fossils, but the specimen adds to an emerging consensus that octopus body shapes were already widely diversified by about 164 million years ago. "[Characteristics] we thought were quite recent in the evolution of the group, such as the shape of some suckers, were already present in the Jurassic," Kruta says. As for what else the fossil record holds, paleontologists would surely give an arm and a leg to know. —*Brian Switek*

FROM "*PROTEROCTOPUS RIBETI* IN COLEOID EVOLUTION," BY ISABELLE KRUTA ET AL., IN *PALAEONTOLOGY*, VOL. 59; NOVEMBER 2016

IN THE NEWS

Quick Hits

FRANCE

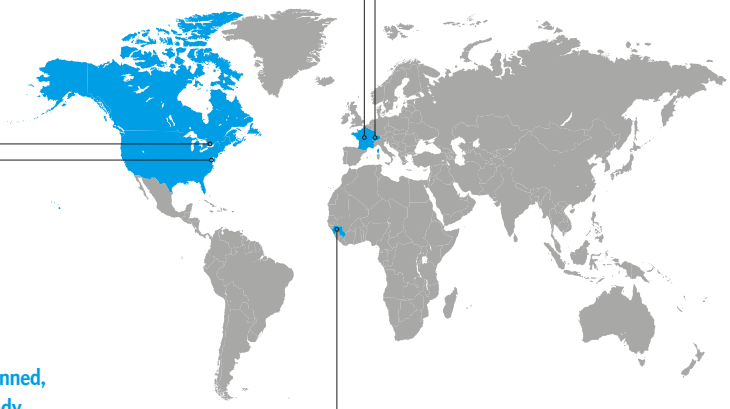
In 1963 Lascaux, a cave with magnificent ice age artwork painted on its walls, was closed to the public. A replica of the entire cave—its chambers, animal paintings, humidity and all—recently opened near the original in southwestern France. The project has been six years in the making.

SWITZERLAND

In a world's first, physicists at CERN near Geneva measured how much light antimatter absorbs. The atoms are notoriously difficult to work with given that, by definition, they annihilate matter.

CANADA

Researchers at the University of Toronto announced that they have recovered the world's oldest water. Found in a mine at a depth of nearly three kilometers, the liquid dates to at least two billion years ago.



U.S.

The U.S. Office of Naval Research demonstrated the latest version of its "drone" boats in the Chesapeake Bay off Virginia. The navy hopes to use the unmanned, autonomous craft—which are not yet ready for deployment—to escort ships, conduct surveillance and carry out other missions.

GUINEA

A clinical trial of a new Ebola vaccine wrapped up with 100 percent effectiveness. It has not yet received regulatory approval—and it may not be effective for all strains of the virus—but Merck has already begun stockpiling the vaccine in case of another outbreak.

For more details, visit www.ScientificAmerican.com/mar2017/advances

ANIMAL BEHAVIOR

How to Get Elephants to Buzz Off

Researchers exploit a fear to reduce elephant-human confrontation

Mice don't actually scare elephants, but there *is* one tiny animal that the pachyderms definitely steer clear of: bees. It's a fear conservationists have begun to harness to keep elephants out of crops in Africa—a point of conflict that leaves hundreds of humans and elephants dead every year. —*John R. Platt*

The Elephants and Bees Project, run by the nonprofit Save the Elephants, seeks to keep elephants from trampling and eating crops by building bee fences: wire fences strung with hives. The experimental project first began in Kenya in 2008 and has since expanded to six African countries. According to an upcoming paper in *Conservation Biology,* the buzzing fences have kept out 80 percent of the elephants that have approached them. These special barriers also provide locals with revenue from honey, says project leader Lucy King.

Air Shepherd, a program of the Charles A. and Anne Morrow Lindbergh Foundation, is simulating the threat of bee stings to minimize conflict. Last summer researchers brought drones to Malawi to search for poachers—and found that the noise of the quadcopters could spook elephants. "They sound like bees," explains Otto Werdmuller Von Elgg, the program's head of drone operations. In addition to its antipoaching efforts, Air Shepherd now also spends nearly every night flying the buzzing quadcopters along crop fences and around Liwonde National Park as an elephant deterrent. Drones are not yet legal in every African country, but Von Elgg thinks the idea will eventually fly in more locations. "One drone is enough to move a herd of 100 elephants," he says.

Schooner Bay, Point Reyes National Seashore, California

ENERGY

It's Electric—With the Right Mix

Freshwater-saltwater ecosystems could provide bountiful renewable energy

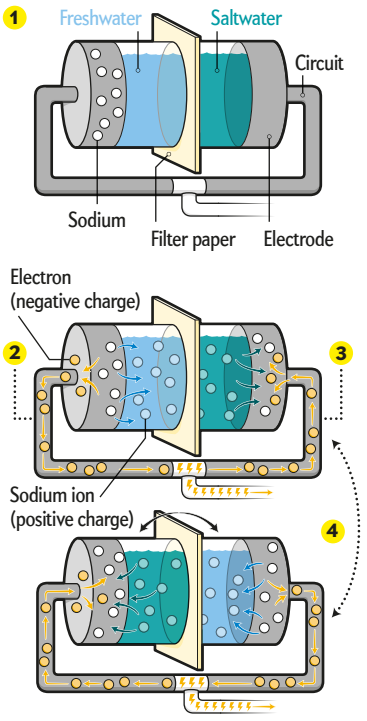
There is great opportunity where rivers and oceans meet: the salinity gradient that forms at these freshwater-saltwater boundaries holds a substantial amount of potential energy. Estuaries, for instance, could cover an estimated 40 percent of global electricity generation.

Scientists have been working for decades to turn this potential into a usable power source and have developed a number of techniques. One of the latest comes from Pennsylvania State University, where Chris Gorski, an assistant professor of civil engineering, and his colleagues say they have come up with a way to generate electricity from freshwater-saltwater ecosystems that is potentially more efficient and cheaper than previous attempts. The system, a variation on a process called capacitive mixing, works a little like a battery. It employs battery electrodes and relies on an electrochemical gradient—but unlike a battery, it is an open system (*graphic at above right*).

So far Gorski and his team have tested only a cell-phone-sized prototype in the laboratory. As reported in *Environmental Science & Technology,* it produced 0.4 watt per square meter—twice the power density achieved in previous capacitive mixing studies. The researchers still need to boost output and determine if the system is cost-effective and scalable (the power plant would be the size of a small warehouse in a real-world setting). They also need to investigate the potential for ecosystem disruption because the "river battery" requires the passage of large amounts of estuary water.

Yale University chemical and environmental engineering researcher Anthony Straub and other scientists are skeptical about the possibility of building an efficient system on a river-ocean junction—and say technologies like Gorski's may ultimately only work in places with relatively extreme salt gradients, such as hypersaline lakes, geothermal wells or wastewater facilities. But if it proves viable and safe, such a system may one day join solar and wind power as a form of renewable energy. —*Annie Sneed*

How It Works



1. Saltwater and freshwater are pumped into opposite sides of a cell, immersing battery electrodes composed of copper hexacyanoferrate. Filter paper keeps mixing between the two sides to a minimum.
2. On the freshwater side, the electrode is primed with sodium. In the presence of freshwater, the iron in the electrode reacts with sodium to release sodium ions into the water. The iron simultaneously releases electrons, which travel through a circuit.
3. On the saltwater side, the iron in the electrode absorbs sodium ions from the water and pulls in electrons coming from the freshwater side. These two reactions are coupled, and electricity is generated as electrons flow through the circuit from one side of the cell to the other.
4. Every 60 seconds, the liquids are switched (the saltwater side of the cell now receives freshwater, and vice versa) so that the current is maintained.

ROLF SCHULTEN *Getty images (estuary);* SOURCE: "HARVESTING ENERGY FROM SALINITY DIFFERENCES USING BATTERY ELECTRODES IN A CONCENTRATION FLOW CELL," BY TAEYOUNG KIM ET AL., IN *ENVIRONMENTAL SCIENCE & TECHNOLOGY,* VOL. 50, NO. 17; SEPTEMBER 6, 2016

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Gasping for Air

Shortness of breath can arise from a bewildering number of conditions, complicating diagnosis and treatment

By Robin Lloyd

The healthy adult at rest involuntarily inhales and exhales some 20,000 times a day, as naturally as seawater slides back and forth in a tidal zone. This cycle is so routine and rhythmic that we hardly notice it—except when something goes wrong, such as when we can't seem to get enough air into our lungs.

A number of easily identified disorders can cause such shortness of breath (dyspnea, in technical terms), including asthma, lung infections and chronic obstructive pulmonary disease (or COPD, an umbrella term for various conditions that permanently impair airflow through the lungs). Congestive heart failure, in which the heart no longer pumps normally and so cannot deliver enough oxygen and nutrients to the body, is also well known to disrupt breathing. But absent any of those conditions, patients who are out of breath are also often out of luck in terms of getting an accurate diagnosis—or an effective treatment.

Indeed, it turns out that the seemingly basic act of breathing is more complex than scientists have traditionally understood it to be. New research efforts are under way to figure out how it works and why it goes awry. The science of why breathing falters is still young, but already fresh insights are spurring investigators to develop new tools for pinpointing the causes of mysterious cases and devising ways that clinicians can help patients breathe easier.

A DIFFICULT DIAGNOSIS

TO GET A SENSE of how complicated it can be to identify why someone is short of breath, consider a hypothetical scenario described by pediatric pulmonologist J. Tod Olin of National Jewish Health in Denver. A shy 16-year-old who is under a lot of stress says she "just can't get a good breath." By the time the young woman reaches a pulmonary or respiratory specialist, she may already have visited four or five other doctors and come up empty.

The specialist puts her through standard tests for the most obvious causes, starting with asthma, which is marked by inflammation that can lead the lungs' airways to swell, constrict and fill with mucus temporarily. As a result, patients may become short of breath or wheeze, making a whistling sound in their chest. Exercise can trigger asthma symptoms, but this patient is sedentary and has not responded to asthma medications. Spirometry, a test that measures airflow during breathing, does not demonstrate a pattern consistent with asthma or COPD. Moreover, when the specialist listens to lung and heart sounds for signs of decreased function and observes the motions of the chest, throat and other relevant body parts, the inhalations and exhalations resemble frequent deep sighing breaths rather than the wheezes common in asthmatics.

The doctor orders a chest x-ray, electrocardiogram and CT scans to check for infection, a foreign object in the windpipe or food pipe, or signs of possible cancer or heart disease. But these tests all look normal, as does a check of the patient's vocal cords to see if they might be constricted and blocking her airway.

So the doctor examines the patient's breathing more closely. The patient dons a plastic mask that connects to a device that collects samples of exhaled air. The samples get channeled to sensors that instantaneously measure airflow, oxygen levels, carbon dioxide levels, and more. The data reveal an erratic pattern in the amount of air the patient inhales: she alternates between drawing in 20 liters one minute and eight liters the next. A blood test shows standard levels of dissolved oxygen and slightly low carbon dioxide levels, signaling that the patient is taking in sufficient quantities of oxygen but exhaling excessively.

By process of elimination, the doctor finally diagnoses the young woman with "dysfunctional breathing," a mysterious disorder that researchers have only recently begun to recognize. Dysfunctional breathing, also known as dysfunctional breathlessness, may accompany and worsen symptoms of asthma, COPD and other conditions, but it can also stand alone. As Olin's scenario suggests, there is no medical consensus on gold-standard diagnostic criteria for dysfunctional breathing. Further

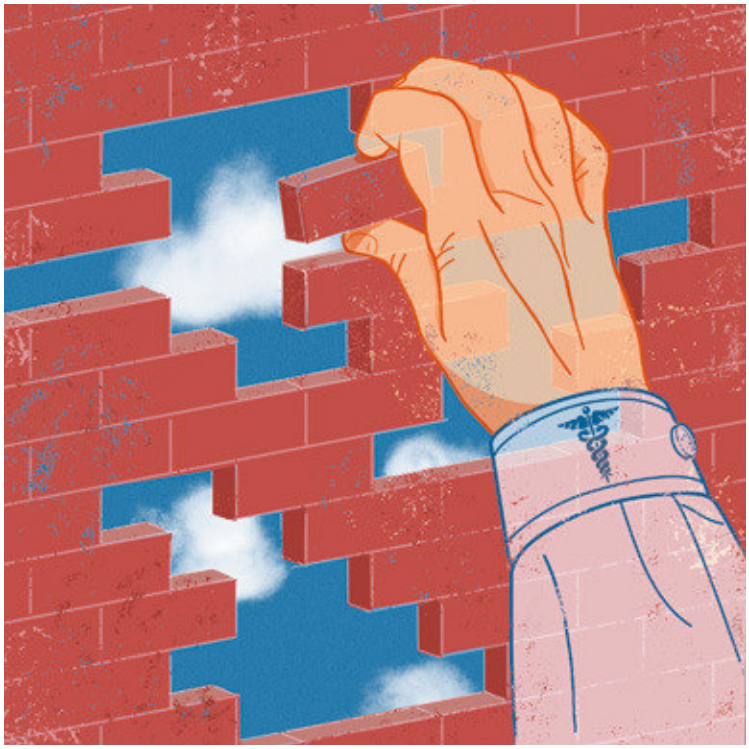

Illustration by Brucie Rosch

Robin Lloyd is a science writer based in New York City and a contributing editor at *Scientific American*.

complicating matters, patients may not seek medical attention, because they have adapted their behavior to avoid symptoms—giving up singing or a competitive sport, for instance—notes Mark L. Everard of the University of Western Australia. People with the disorder, which by some estimates may affect 10 percent of adults at some point in their life, are often thus undiagnosed or misdiagnosed or receive inappropriate care.

Exactly what causes dysfunctional breathlessness is uncertain, but many experts suspect that it originates from biomechanical or psychological disturbances, or some combination of the two. One possible culprit is breathing that stems from the upper chest rather than the entire chest and abdomen.

Treatment for dysfunctional breathing is not standardized yet. By the time patients are diagnosed with it, they have most likely already tried drugs known as beta-agonists that relax the airways to ease breathing, with disappointing results. Switching to other combinations of beta-agonists may help, however. Some people with the condition may receive coaching on how to breathe normally at rest and in motion, as well as psychological counseling if a doctor thinks that stress or emotions are involved. Over time patients usually take more control over their breathing, and the condition fades. Still, treatment may have resolved the symptoms but done nothing to address the root cause.

CLEARING THE AIR

EXPERTS AGREE that better care for breathless patients will require sharper understanding of the processes surrounding inhalation and exhalation and the mechanisms behind breathing disorders. Improved technology for measuring breathing patterns and clearer diagnostic criteria for dysfunctional breathing will also be key.

Of course, the body's controls on breathing are far from unknown. Scientists understand that signals sent from the brain stem instruct the throat, chest and abdominal muscles, especially the diaphragm, to expand and contract involuntarily, drawing in and expelling air. And it is clear that we also have some behavioral control over breathing—we can intentionally slow it down, speed it up, and take deeper breaths or shallower ones. Likewise, we can coordinate it with swallowing, speaking, singing and eating. But dig much deeper into the science of dysfunctional breathing, and the picture becomes murkier.

To be fair, pulmonary and respiratory researchers face particular challenges. Lungs perform at least three functions: they bring in oxygen and clear out carbon dioxide, they regulate the body's balance of acidic and basic compounds required for proper organ functioning, and they filter out the soup of foreign particles we constantly inhale. A lung is thus a more complicated organ in some ways than the kidney or the heart, says Richard Castriotta of the University of Texas Health Science Center at Houston.

Further, the process of breathing involves many systems in the body, from the central and peripheral nervous systems to the respiratory and digestive systems. "If you go to the doctor and say, 'I have trouble breathing,' there are so many different diseases, disorders, maladaptive positions and techniques that could be the cause of the problem," says Gina Vess of Duke University. "You might go to a cardiologist, a pulmonologist, an [ear, nose and throat] surgeon, a laryngologist, a speech pathologist, a physical therapist, a respiratory therapist or a psychiatrist."

Even so, the developing field of breathing research (which is distinct from the larger field of pulmonology) is delivering new insights into various breathing disorders. For example, Olin has figured out how to obtain real-time images of the voice boxes, or larynxes, of athletes suffering from exercise-induced breathlessness, which is distinct from dysfunctional breathing. He outfits patients with a helmet-mounted digital endoscope that shows the larynx while they cycle on stationary bikes. He and his team have found that the larynx becomes more severely constricted in these athletes when they exercise at maximum intensity than when they exercise less arduously or are at rest. The observations hint that the athletes may differ from the general population in the structure of the upper part of their airway or in their behavioral response to intense exercise. Surveys of the existing medical literature on dysfunctional breathing have also proved enlightening. Stephen J. Fowler of the University of Manchester in England and his colleagues recently reviewed dozens of reports on the condition to take stock of the ways in which it manifests and is assessed and treated. Their analysis revealed five common types of dysfunctional breathing and the breathing patterns associated with each of them—findings that could eventually help doctors tailor treatments more closely to patients' needs.

Clinical applications of those discoveries may be a way off, however. In the near term, the best hope for those suffering from breathing problems lies in better agreement on standards for diagnosis and treatment. To that end, Fowler and others who treat and study dysfunctional breathing have met in England every week for the past six months to discuss difficult cases.

Pulmonary specialists agree on where we should aim to end up: breathing naturally. Vess notes that people can often help themselves reach that goal by avoiding clothing that restricts movement of the chest and abdomen and relaxing the gut to likewise liberate the breathing muscles. Excess fat in the abdominal area can impede inhalation and exhalation in extreme cases, Castriotta says, so maintaining a healthy weight is important, too.

As for when to worry about shortness of breath, Castriotta offers the following recommendation: people who struggle to keep up with others their own age during activities such as walking or climbing stairs should seek medical attention.

Some people who have no shortness of breath may wonder whether they should take measures anyway to tone their breathing apparatus. The answer, says Michael Koehle of the University of British Columbia, is no. Deep-breathing exercises such as yoga breathing may help reduce stress and anxiety. But even during exercise our innate respiratory-control system usually does quite well at providing adequate oxygen supply and removing carbon dioxide produced by metabolism. "In the strictest definition of health—absence of disease—it is not necessary to do specific breathing practices," Koehle notes. In other words, you may now exhale. SA

Your Echo Is Listening

A murder case raises concerns about the "Internet of Things"

By David Pogue

In November 2015 James Bates invited some friends over to watch a Razorbacks football game at his house in Bentonville, Ark. The next morning one of them, Victor Collins, was found dead in Bates's hot tub—apparently strangled. Bates was charged with murder; he pled not guilty. But in their investigation, the police discovered something intriguing. He had an Amazon Echo, the popular black cylinder that's always listening for voice commands and questions, something like Siri for the home.

The police served Amazon with a search warrant. Their hope: to retrieve recordings the Echo might have made on that fateful night, with clues to what happened. That's a mighty slim hope. The Echo is indeed listening all the time but only for the word "Alexa," which you must utter at the beginning of any request. No audio is recorded or transmitted until you do so. At that point, the Echo's bright blue LED lights up while your request is sent to Amazon's computers for an answer. But very occasionally the Echo *thinks* it hears "Alexa" and responds nonsensically to whatever sentence comes next. If that freak occurrence happened on the night of the murder, then maybe the police could retrieve a few seconds of audio.

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

But never mind. Amazon gave them the customer's subscriber and purchase information but refused to supply any recordings or data that pertained to what Bates said to his Echo. "Amazon objects to overbroad or otherwise inappropriate demands as a matter of course," the company said in a statement. Between the lines, you can sort of hear: "If the public thinks that we record conversations in their homes and make them available to law enforcement, that's the end of our Echo product line!"

That's not the first time a big electronics company has refused to cooperate with the law on privacy grounds. You may recall that last year the FBI asked Apple to give it backdoor access to the San Bernardino shooter's iPhone, and Apple refused. (The FBI was able to gain access to the phone's data through other means.)

In the Arkansas case, the police ended up striking possible gold, not with the Echo but with Bates's smart water meter. Its records revealed that someone used 140 gallons of water between 1 and 3 A.M. the night of the murder. Investigators doubt that Bates took a *really* long shower; instead they believe that he used the water to rinse away evidence on his patio.

Legally, of course, Amazon could land in some hot water of its own. "Amazon risks being held in contempt of court for its refusal to comply fully," says Peter Guffin, who heads up the privacy and data security practice at law firm Pierce Atwood. "If the parties are unable to reach an agreement for obtaining the data, a contempt proceeding could be commenced against Amazon."

That, in fact, is exactly where things stand. As I write this, Nathan Smith, the attorney for the Bates prosecution, has told me that the case will likely go to trial later this year and that his office still hopes to work something out with Amazon. But if the company refuses to budge, he may have to take it to court.

These conflicts will only become more frequent. At this year's enormous International Consumer Electronics Show in Las Vegas, the hottest trend was Echo compatibility. An astonishing number of newly unveiled appliances can respond to commands you speak to your Echo: refrigerators, light switches, power strips, lamps, speakers, robotic vacuums, satellite boxes, TVs, security cameras, door locks, air purifiers, washers and dryers, cars, and on and on.

As we fill our homes with machines that are always listening or watching, clashes between electronic privacy and law enforcement will occur ever more frequently. "There are no laws that govern this," Guffin says. "We haven't enacted laws that deal with this burgeoning array: the movements in our house, what we're putting in our refrigerators, how much energy we're using, the conversations we might be having in our homes." Dear lawmakers: The Internet of Listening Things is now upon us. Might be worth looking into. SA

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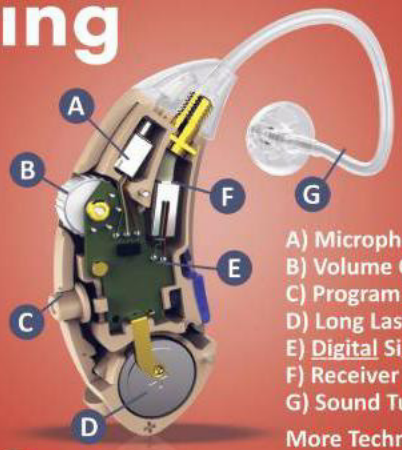

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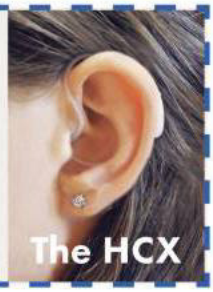

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SPACEFLIGHT

NEAR-LIGHT-SPEED MISSION TO ALPHA CENTAURI

A billionaire-funded plan aims to send a probe to another star. But can it be done?

By Ann Finkbeiner

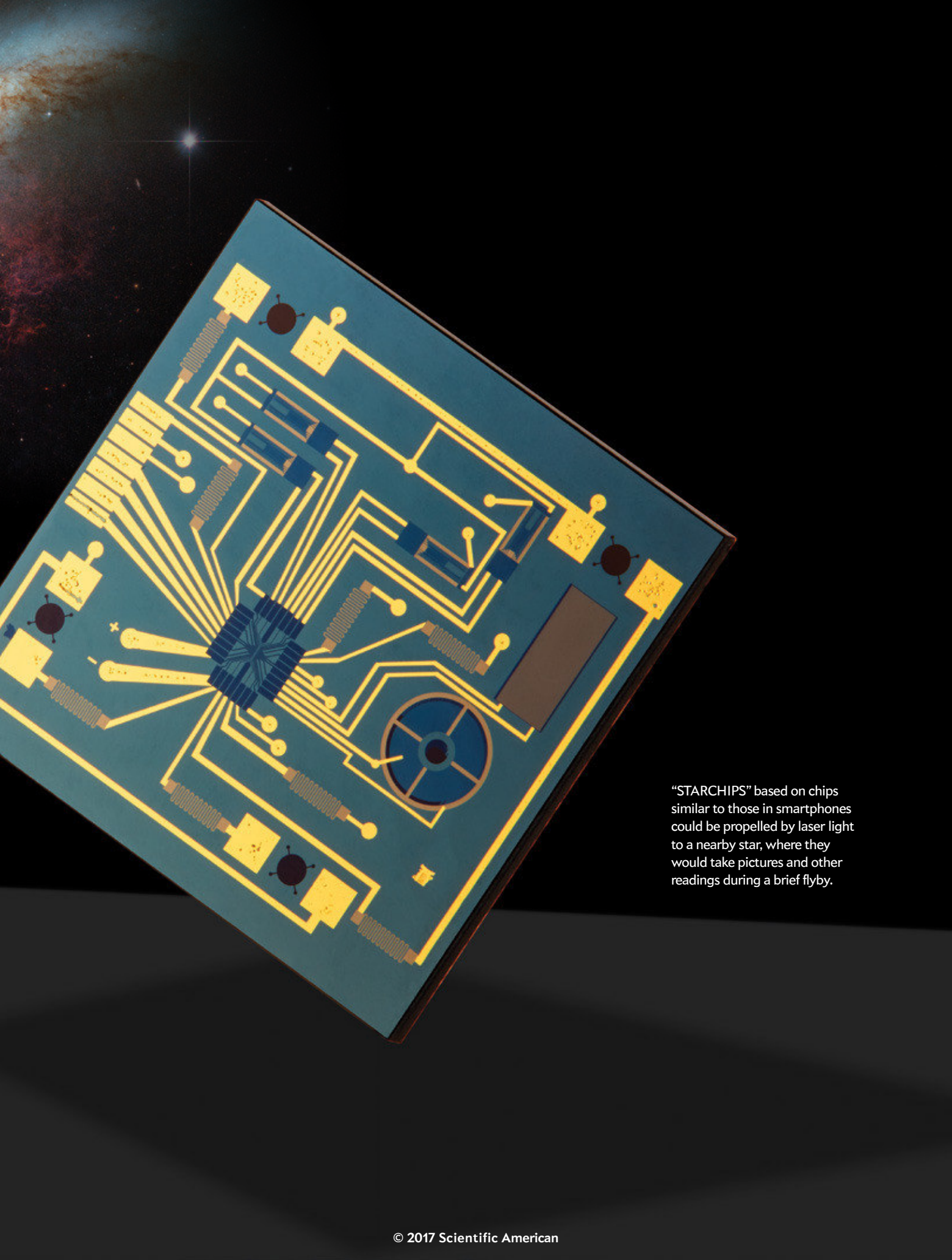
IN BRIEF

A Silicon Valley billionaire is funding an audacious plan to send a spacecraft to one of the sun's closest stellar neighbors.

The mission, called Breakthrough Starshot, would use lasers to propel "light sails" attached to small, smartphonelike chips that could take pictures, make measurements and beam their findings back to Earth.

Experts say the plan is risky and expensive and may not work—but is nonetheless exciting, offering a chance to send the first man-made object to another star.

Photographs by Stan Musilek



"STARCHIPS" based on chips similar to those in smartphones could be propelled by laser light to a nearby star, where they would take pictures and other readings during a brief flyby.

Ann Finkbeiner is a science writer based in Baltimore. She specializes in writing about astronomy, cosmology, and the intersection of science and national security and loves unlikely technologies. Her most recent book is *A Grand and Bold Thing* (Free Press, 2010) about the Sloan Digital Sky Survey project to map the entire night sky.

In the spring of 2016 I was at a reception with Freeman Dyson, the brilliant physicist and mathematician, then 92 and emeritus at the Institute for Advanced Study in Princeton, N.J. He never says what you expect him to, so I asked him, "What's new?" He smiled his ambiguous smile and answered, "Apparently we're going to Alpha Centauri." This star is one of our sun's nearest neighbors, and a Silicon Valley billionaire had recently announced that he was funding a project called Breakthrough Starshot to send some kind of spaceship there. "Is that a good idea?" I asked. Dyson's smile got wider:

"No, it's silly." Then he added, "But the spacecraft is interesting."

The spacecraft is indeed interesting. Instead of the usual rocket, powered by chemical reactions and big enough to carry humans or heavy instruments, Starshot is a cloud of tiny, multifunction chips called StarChips, each attached to a so-called light sail. The sail would be so insubstantial that when hit by a laser beam, called a light beamer, it would accelerate to 20 percent of the speed of light. At 4.37 light-years away, Alpha Centauri would take the fastest rocket 30,000 years to reach; a StarChip could get there in 20. On arrival, the chips would not stop but rather tear past the star and any of its planets in a few minutes, transmitting pictures that will need 4.37 years to return home.

The "silly" part is that the point of the Starshot mission is not obviously science. The kinds of things astronomers want to know about stars are not the kinds of things that can be learned from a quick flyby—and no one knows whether Alpha Centauri even has a planet, so Starshot could not even promise close-ups of other worlds. "We haven't given nearly as much thought to the science," says astrophysicist Ed Turner of Princeton University, who is on the Starshot Advisory Committee. "We've almost taken for granted that the science will be interesting." But in August 2016 the Starshot team got lucky: a completely unrelated consortium of European astronomers discovered a planet around the next star over, Proxima Centauri, a tenth of a light-year closer to us than Alpha Centauri. Suddenly, Starshot became the only semifeasible way in the foreseeable future to visit a planet orbiting another star. Even so, Starshot sounds a little like the dreams of those fans of science fiction and interstellar travel who talk seriously and endlessly about sending humans beyond the solar system with technologies that would surely work, given enough technological miracles and money.

Starshot, however, does not need miracles. Its technology, though currently nonexistent, is based on established engineering and violates no laws of physics. And the project has money behind it. Yuri Milner, the entrepreneur who also funds other research projects called Breakthrough Initiatives as well as yearly science awards called Breakthrough Prizes, is kick-starting Starshot's initial development with $100 million. Furthermore, Milner has enlisted an advisory committee impressive enough to convince a skeptic that Starshot might work, including world experts in lasers, sails, chips, exoplanets, aeronautics and managing large projects, plus two Nobel Prize winners, the U.K.'s Astronomer Royal, eminent academic astrophysicists, a cadre of smart, experienced engineers—and Dyson, who, despite thinking Starshot's mission is silly, also says the laser-driven sail concept makes sense and is worth pursuing. On the whole, few would make a long-range bet against an operation with this much money and good advice and so many smart engineers.

Whatever its prospects, the project is wholly unlike any space mission that has come before. "Everything about Starshot is unusual," says Joan Johnson-Freese, a space policy expert at the U.S. Naval War College. Its goals, funding mode and management structure diverge from all the other players in space travel. Commercial space companies focus on making a profit and on manned missions that stay inside the solar system. NASA, which also has no plans for interstellar travel, is too risk-averse for something this uncertain; its bureaucratic procedures are often cumbersome and redundant; and its missions are at the mercy of inconsistent congressional approval and funding. "NASA has to take time; billionaires can just do it," says Leroy Chiao, a former astronaut and commander of the International Space Station. "You put this team together, and off you go."

THE GAME PLAN

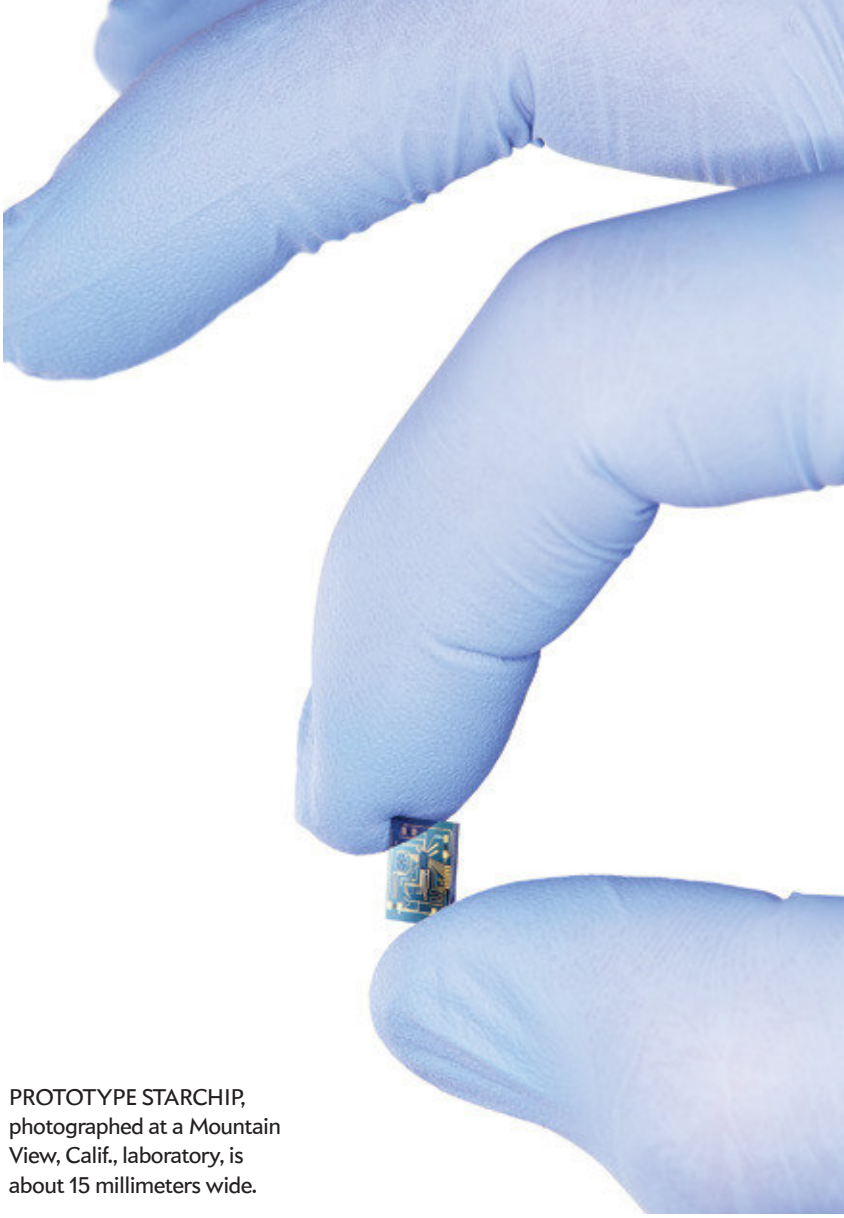
THE MAN DRIVING the Starshot project has always been inspired by the far reaches. Yuri Milner was born in Moscow in 1961, the same year Yuri Gagarin became the first human to go into space. "My parents sent me a message when they called me Yuri," he says—that is, he was supposed to go somewhere that no one had ever been. So he went into physics—"it was my first love," he says. Milner spent 10 years getting educated, then worked on quantum chromodynamics. "Unfortunately, I did not do very well," he says. Next he went into business, became

PAGE 30: COURTESY OF NASA, ESA, A. GOOBAR *Stockholm University* AND HUBBLE HERITAGE TEAM (STScI/AURA) (*galaxy*)

an early investor in Facebook and Twitter, and amassed a fortune reported to be nearly $3 billion. “So maybe four years ago,” Milner says, “I started to think again about my first love.”

In 2013 he set up the Breakthrough Prizes, one each for the life sciences, mathematics and physics. And in 2015 he started what he calls his hobby, the Breakthrough Initiatives, a kind of outreach to the universe: a $1-million prize for the best message to an extraterrestrial civilization; $100 million for a wider, more sensitive search for extraterrestrial intelligence; and now $100 million to Starshot.

In early 2015 Milner recruited a central management team for Starshot from people he had met at various Breakthrough gatherings. Starshot’s Advisory Committee chair and executive director, respectively, are Avi Loeb, chair of Harvard University’s astronomy department, and Pete Worden, who directed the NASA Ames Research Center and was involved in a DARPA/NASA plan for a starship to be launched in 100 years. Worden recruited Pete Klupar, an engineer who had been in and out of the aerospace industry and had worked for him at Ames, as Starshot’s director of engineering. They in turn pulled together the impressive committee, which includes specialists in the relevant technologies who are apparently willing to participate for some or no money, as well as big names such as Facebook’s Mark Zuckerberg and cosmologist Stephen Hawking. Starshot’s management policy seems to be a balance between NASA’s hierarchical decision-tree rigor and the Silicon Valley culture of putting a bunch of smart people in a room, giving them a long-term goal and standing back. One committee member, James Benford, president of Microwave Sciences, says the charge is to “give us next week and five years from now, and we’ll figure out how to connect the two.”



PROTOTYPE STARCHIP, photographed at a Mountain View, Calif., laboratory, is about 15 millimeters wide.

The assembled team members began by agreeing that they could rule out sending humans to Alpha Centauri as too far-fetched and planned to focus on an unmanned mission, which they estimated they could launch in roughly 20 years. They then agreed that the big problem was spacecraft propulsion. So in mid-2015 Loeb’s postdocs and graduate students began sorting the options into the impossible, the improbable and the feasible. In December of that year they received a paper by Philip Lubin, a physicist at the University of California, Santa Barbara, called “A Roadmap to Interstellar Flight.” Lubin’s option for propulsion was a laser phased array—that is, a large number of small lasers ganged together so that their light would combine coherently into a single beam. The laser beam would push a sail-carried chip that would need to move at a good fraction of light speed to reach another star within a couple of decades. (A similar idea had been published 30 years earlier by a physicist and science-fiction writer named Robert Forward; he called it a Starwisp.) Although the technology was still more science fiction than fact, “I basically handed Starshot the road map,” Lubin says, and he joined the project.

In January 2016 Milner, Worden, Klupar, Loeb and Lubin met at Milner’s house in Silicon Valley and put together a strategy. “Yuri comes in, holding a paper with sticky notes on it,” Lubin says, “and starts asking the right science and economic questions.” The beauty of the project’s unusual approach was that, rather than going through a drawn-out process of soliciting and reviewing proposals as NASA would or being concerned about the potential for profit like a commercial company, the Starshot team was free to hash out a basic plan based purely on what sounded best to it.

Starshot’s only really expensive element was the laser; the sails and chips would be low cost and expendable. The latter would be bundled into a launcher, sent above the atmosphere and released like flying fish, one after another—hundreds or thousands of them—so many that like the reptilian reproduction strategy, losing a few would not matter. Each one would get hit by the laser and accelerated to 20 percent the speed of light in a few minutes. Next the laser would cut off, and the chip and sail would just fly. When they got to the star, the chips would call back home. “Ten years ago we couldn’t have had a serious conversation about this,” Milner says. But now, what with lasers and chips improving exponentially and scientists designing and building new materials, “it’s not centuries away, it’s dozens of years away.”

Starshot management sent the idea out for review, asking sci-

How to Visit a Star

Breakthrough Starshot is an ambitious plan to send tiny spacecraft to one of our neighboring stars to snap pictures and make measurements during a quick flyby. The mission would be the first interstellar voyage humanity has launched. Funded by the Breakthrough Initiatives, the plan calls for the pressure of laser light, beamed from the surface of Earth, to propel ultrafine sheets called light sails attached to tiny spacecraft called StarChips (together called nanocraft), which would then beam their messages back home to us.

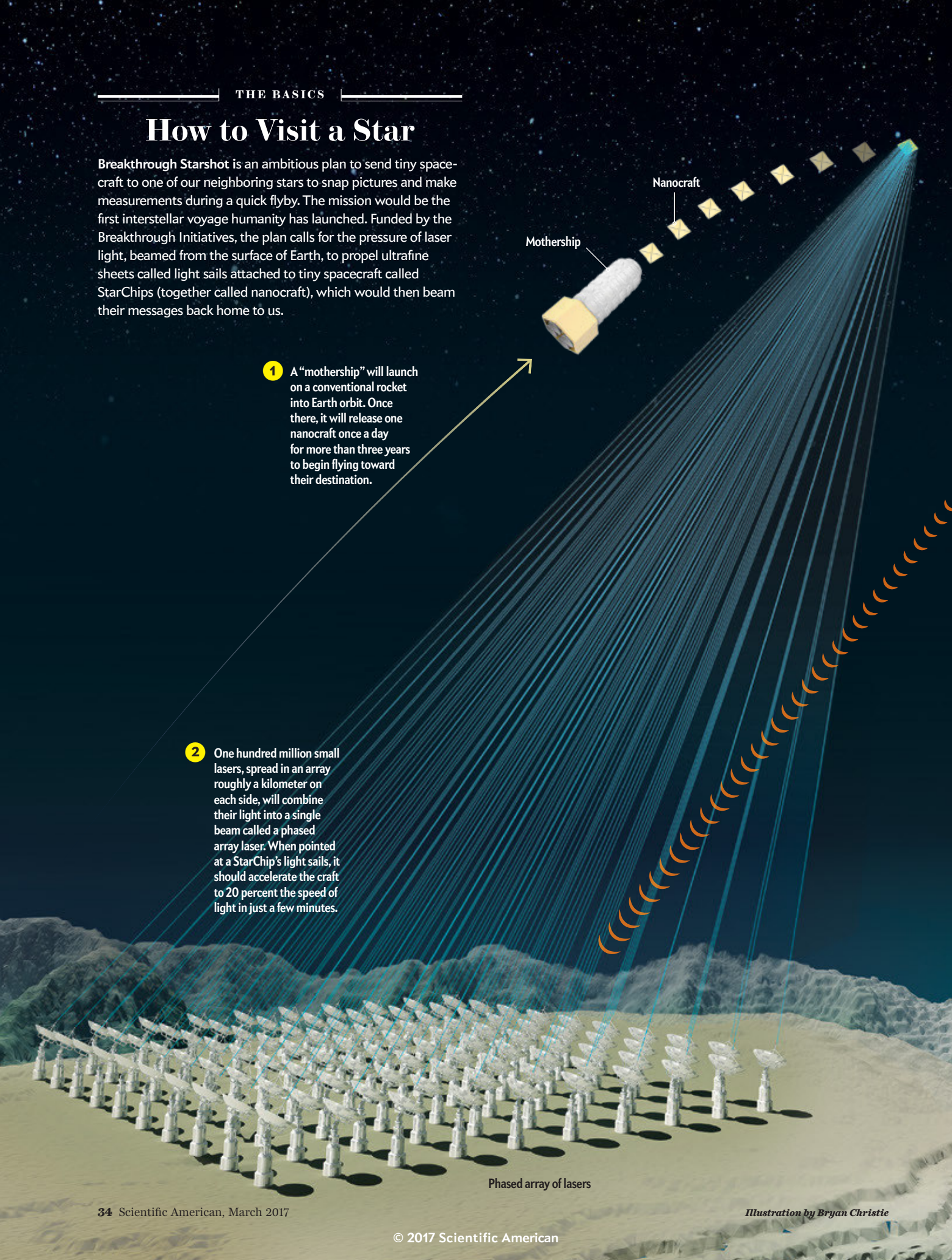
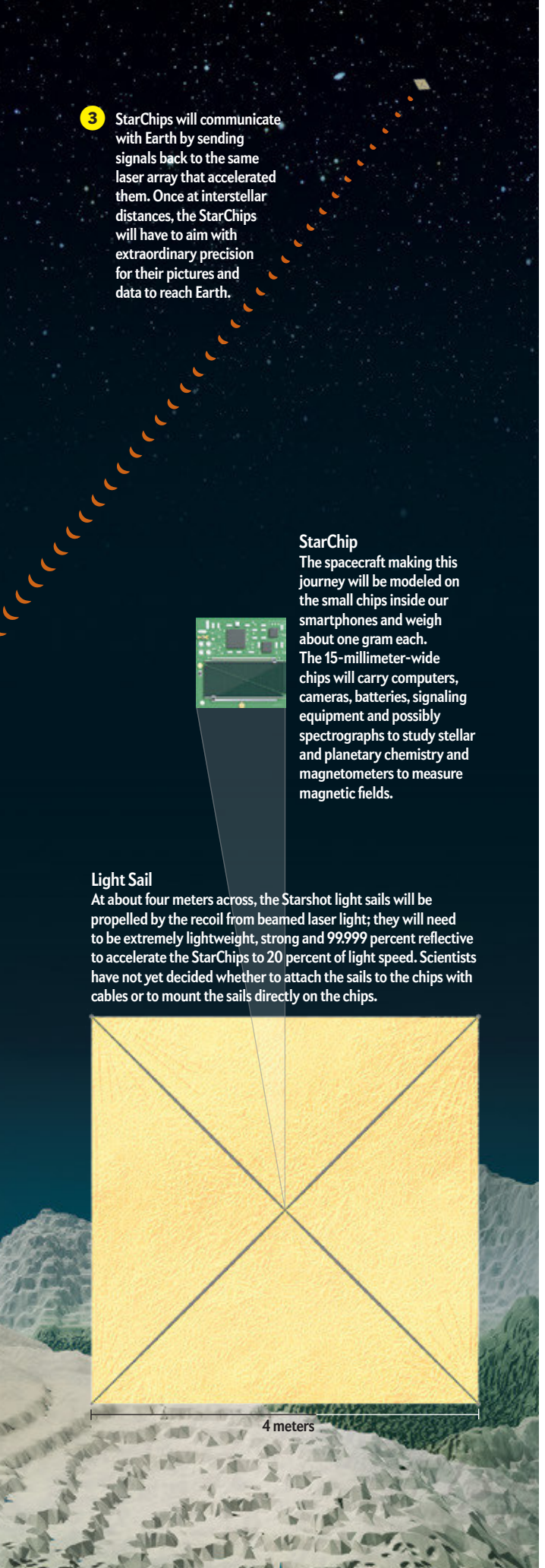


Illustration by Bryan Christie



entists to look for deal breakers. None found any. "I can tell you why it's hard and why it's expensive," Lubin says, "but I can't tell you why it can't be done." By April 2016 the team had agreed on the system, and on April 12 Milner arranged a press conference atop the new Freedom Tower in New York City, featuring videos, animations and several members of the advisory committee. He announced an "interstellar sailboat" driven by a wind of light. The researchers spent the following summer outlining what had to happen next.

STARCHIPS AND LIGHT SAILS

THE TEAM SOON FOUND that, though technically feasible, the plan would be an uphill climb. Even the easiest of the technologies, the StarChip, poses a lot of problems. It needs to be tiny—roughly gram-scale—yet able to collect and send back data, carry its own power supply and survive the long journey. Several years ago engineer Mason Peck's group at Cornell University built what they call Sprites, smartphonelike chips that carry a light sensor, solar panels and a radio and weigh four grams each. The Starshot chips would be modeled on the Sprites but would weigh even less, around a gram, and carry four cameras apiece. Instead of heavy lenses for focusing, one option is to place a tiny diffraction grating called a planar Fourier capture array over the light sensor to break the incoming light into wavelengths that can be reconstructed later by a computer to any focal depth. Other equipment suggested for the chip include a spectrograph to identify the chemistry of a planet's atmosphere and a magnetometer to measure a star's magnetic field.

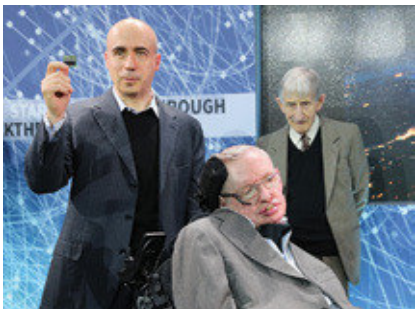
The chips would also need to send their pictures back over interstellar distances. Satellites currently use single-watt diode lasers to send information but over shorter distances: So far, Peck says, the longest distance has been from the moon, more than 100 million times closer than Alpha Centauri. To target Earth from the star, the laser's aim would need to be extraordinarily precise. Yet during the four-year trip the signal will spread out and dilute until, when it reaches us, it will come in as just a few hundred photons. A possible solution would be to send the pictures back by relay, from one StarChip to a series of them flying at regular distances behind. Getting the information back to Earth, says Starshot Advisory Committee member Zac Manchester of Harvard, "is still a really hard problem."

The chips also need batteries to run the cameras and onboard computers to transmit data back during the 20-year voyage. Given the distance to Alpha or Proxima Centauri and the few watts achievable on a small chip, the signal would arrive on Earth weak but "with just enough photons for Starshot's receiver to pick it up," Peck says. To date, no power source simultaneously works in the dark and the cold, weighs less than a gram and has enough power. "Power is the hardest problem on the chip," Peck says. One possible solution, he offers, is to adapt the tiny nuclear batteries used in medical implants. Another is to tap the energy the sail gains as it travels through the gas- and dust-filled interstellar medium and heats up via friction.

The same interstellar medium could also pose hazards for the Starshot chips. The medium is like highly rarefied cigarette smoke, says Bruce Draine, an astronomer at Princeton University who is also a committee member. No one knows exactly how dense the medium is or what size the dust grains are, so its potential for devastation is hard to estimate. Collisions near the

speed of light between the StarChips and grains of any size could create damage that would range from minor craters to complete destruction. If the StarChips are a square centimeter, Draine says, "you'll collide with many, many of these things" along the way. One protectant against smaller particles might be a coating of a couple of millimeters of beryllium copper, although dust grains could still cause catastrophic damage. "The chip will either survive, or it won't," Peck says, but with luck, out of the hundreds or thousands sent off in the chip swarm, some will make it.

The next-hardest technology is the sail. The StarChips would be propelled by the recoil from light reflected off their sails, the way the recoil from a tennis ball pushes a racket. The more light gets reflected, the harder the push and the faster the sail; to get to 20 percent of light speed, the Starshot light sail has to be 99.999 percent reflective. "Any light that isn't reflected ends up heating the sail," says Geoffrey Landis, a scientist at the NASA Glenn Research Center and a member of the advisory committee—and given the extraordinary temperatures of the light beamer, "even a small fraction of the laser power heating the sail would be disastrous." Compared with today's solar sails, which have used light from the sun to propel a few experimental spacecraft around the solar system, it also has to be much lighter, of a thickness measured in atoms or about "the thickness of a soap bubble," Landis says. In 2000, in the closest approximation yet, Benford used a microwave beam to accelerate a sail made of a carbon sheet. His test achieved about 13 *g*s (13 times the acceleration felt on Earth caused by gravity), whereas Starshot's sail would need to withstand an acceleration up to 60,000 *g*s. The sail, like the StarChip, would also have to stand up to dust in the interstellar medium punching holes in it. So far no material exists that is light, strong, reflective and heat-resistant and that does not cost many millions of dollars. "One of the several miracles we'll have to invent is the sail material," Klupar says.



BILLIONAIRE ENTREPRENEUR Yuri Milner, who is funding Breakthrough Starshot, holds up a prototype of the StarChip during an April 12, 2016, press conference in New York City announcing the mission. Scientists Stephen Hawking and Freeman Dyson, who are advising the project, also spoke.

JEMAL COUNTESS *Getty Images*

Other sail-related decisions remain. The sail could attach to the chip with cables, or the chip could be mounted on the sail. The sail might spin, allowing it to stay centered on the light beamer. After the initial acceleration, the sail could fold up like an umbrella, making it less vulnerable during the journey. And once it got to Alpha Centauri, it could unfold and adjust its curvature to act like a telescope mirror or an antenna to send the chip's messages back to Earth. "It sounds like a lot of work," Landis says, "but we've solved hard problems before."

Yet all these challenges are still easier than those of the light beamer that will push the sail. The only way Starshot could reach a good fraction of light speed is with an unusually powerful 100-gigawatt laser. The Department of Defense has produced lasers more powerful, says Robert Peterkin, chief scientist at the Directed Energy Directorate at the U.S. Air Force Research Laboratory, but they shine for only billionths or trillionths of a second. The Starshot light beamer would have to stay on each sail for minutes. To reach this kind of power for that long, small fiber lasers can be grouped into an array and phased together so that all their light combines into one coherent beam. The Defense Department has also built phased array lasers, but theirs include 21 lasers in an array no more than 30 centimeters across, Peterkin says, which achieves a few tens of kilowatts. The Starshot light beamer would have to include 100 million such kilowatt-scale lasers, and the array would spread a kilometer on each side. "How beyond the state of the art is that?" Peterkin says.

"And it all gets worse and worse," he adds. The 100 million little lasers would be deflected by the normal turbulence of the atmosphere, each one in its own way. In the end, the light beamer would need to bring them all to a single focus 60,000 kilometers up on a four-square-meter sail. "At the moment," says Robert Fugate, a retired scientist at the Directed Energy Directorate who is on the committee, drily, "phasing 100 million lasers through atmospheric turbulence on a meter-class target 60 megameters away has my attention." The light could miss the sail completely or more likely hit it unevenly so parts of the sail would be pushed harder, causing it to tumble, spin or slip off the beam.

Again, the Starshot team has a potential solution but one that comes with its own set of problems. A technology called adaptive optics, already used by large telescopes, cancels out the distortion created by the atmosphere's turbulence with a flexible mirror that creates an equal and opposite distortion. But this technology would need major adaptations to work for Starshot. In the case of the beamer, instead of an adjustable mirror scientists would have to minutely adjust each laser fiber to make the atmospheric correction. Current adaptive optics on telescopes can resolve at best a point 30 milliarcseconds across (a measure of an object's angular size on the sky). Starshot would need to focus the beamer within 0.3 milliarcsecond across—something that has never been done before.

And even if all these disparate and challenging technologies could be built, they must still work together as a single system, which for the Starshot managers is like creating a puzzle with pieces whose shapes evolve or do not yet exist. Worden calls the process "the art of a long-term hard-research program." The system has "no single design yet," says Kevin Parkin of Parkin Research, a systems engineer who is on the committee. The plan, for the first five years, Klupar says, is to "harvest the technologies"—that is, with the guidance of the relevant experts on the committee, the team members will carry out small-scale experiments and make mathematical models. They began in the winter of 2015–2016 by scoping out existing technologies and requesting proposals for not yet developed technologies; in spring 2017 they intend to award small contracts of several hundred thousand to $1.5 million each. Prototypes would come next, and, assuming their success, construction of the laser and sail could begin in the early 2030s, with launch in the mid-2040s. By that

time Starshot will likely have cost billions of dollars and, with any luck, have collected collaborators in governments, labs and space agencies in the U.S., Europe and Asia. "I will make the case, and I hope more people will join," Milner says. "It has to be global," he adds, citing the reasonable national security concerns of an enormous laser installation. "If you start something like this in secrecy, there will be many more question marks. It's important to announce intentions openly."

STARWARD, HO!

GIVEN ALL THESE HURDLES, what are the odds of success? Technologically savvy people not connected to Starshot estimate they are small; several people told me flatly, "They're not going to Alpha Centauri." David Charbonneau of the Harvard-Smithsonian Center for Astrophysics says the project will ultimately be so expensive that "it may amount to convincing the U.S. population to put 5 percent of the national budget—the same fraction as the Apollo program—into it."

Those connected with Starshot think the odds are better but are pragmatic. "We can certainly use lasers to send craft to Alpha Centauri," says Greg Matloff of the New York City College of Technology, a member of the committee. "Whether we can get them there over the next 20 years, I don't know." Harvard's Manchester says, "Within 50 years the odds are pretty good; in a century, 100 percent." Worden thinks their approach is purposefully measured, "and maybe in five years we'll find we can't do it." Milner sees his job on Starshot, besides funding it, as keeping it practical and grounded. "If it takes more than a generation," he says, "we shouldn't work on that project."

Until late last August I thought Dyson was right; the Starshot technology was intriguing, but Alpha Centauri was silly. The star is a binary system (Alpha Centauri A and B), and both stars are sunlike, neither one unusual. Astronomers' understanding of such stars, Charbonneau says, "is pretty good," and although comparing their flares and magnetic fields with our sun's might be useful, "what we'd learn about stellar physics by going there isn't worth the investment."

Now that astronomers know Alpha Centauri's neighbor has a planet, the science case is more promising. The star, Proxima Centauri, is a tad nearer to Earth and is a red dwarf, the most common kind of star. The planet, Proxima Centauri b, is at a distance from its star that could make it habitable. When the discovery was announced, the Starshot team celebrated over dinner. Would members consider changing the project's target? "Sure," Milner says. "We have plenty of time to decide." The laser array should have enough flexibility in pointing that it could "accommodate the difference, about two degrees," Fugate says.

Ultimately the Breakthrough Initiatives' general goal is to find all the planets in the solar neighborhood, Klupar says, and Proxima Centauri b might be just the first. "I feel like an entomologist who picks up one rock, finds a bug, then thinks every rock after that will have a bug under it, too," he says. "It's not true, but it's encouraging somehow."

Of course, even the presence of Proxima Centauri b still does not make Starshot slam-dunk science. The chip could take images, maybe look at the planet's magnetic field, perhaps sample the atmosphere—but it would do this all on the fly in minutes. Given the time to launch and the eventual price, says Princeton astrophysicist David Spergel, "we could build a 12- to 15-meter optical telescope in space, look at the planet for months and get much more information than a rapid flyby could."

But billionaires are free to invest in whatever they wish, and kindred souls are free to join them in that wish. Furthermore, even those who question Starshot's scientific value often support it anyway because in developing the technology, its engineers will almost certainly come up with something interesting. "They won't solve all the problems, but they'll solve one or two," Spergel says. And an inventive solution to just one difficult problem "would be a great success." Plus, even if Starshot does not succeed, missions capitalizing on the technologies it develops could reach some important destinations both within and beyond our solar system.

Milner's own fondness for the project stems from his hope that it can unite the world's humans in a sense of being one planet and one species. "In the past six years I've spent 50 percent of my time on the road, a lot of time in Asia and Europe," he says. "I realized that global consensus is difficult but not impossible." That theme fits with the other Breakthrough Initiatives, which chiefly want to find aliens to talk to, and with Milner's considerable investments in the Internet and social media, which have changed the nature of conversation and community. But in the end, even he acknowledges that wanting to go to a star is inexplicable. "If you keep asking me why, eventually I'll say I don't know. I just think it's important."

Almost everyone I asked said the same: they cannot explain it to someone who does not already understand—they just want to go. James Gunn, emeritus professor in Princeton's department of astrophysical sciences, who thinks Starshot's chances of success are slim and who dismissed the scientific motivations, still says, "I'm rational about most things, but I'm not particularly rational about the far reach of humanity. I dreamed of going to the stars since I was a kid." Many of the advisory committee said the same thing. "It is just *so* cool," Landis says, echoing the exact words of other members.

The contradictions inherent in such dreams are perhaps best expressed by Freeman Dyson. Starshot's laser-driven sail with its chip makes sense, he says, and those behind the project are smart and "quite sensible." But he thinks they should stop trying to go to Alpha or Proxima Centauri and focus on exploring the solar system, where StarChips could be driven by more feasible, less powerful lasers and travel at lower speeds. "Exploring is something humans are designed for," he says. "It's something we're very good at." He thinks "automatic machines" should explore the universe—that there is no scientific justification for sending people. And then, being Dyson and unpredictable, he adds, "On the other hand, I still would love to go." SA

MORE TO EXPLORE

A Roadmap to Interstellar Flight. Philip Lubin in *Journal of the British Interplanetary Society*, Vol. 69, pages 40–72; 2016.

Alpha Centauri or Bust. Mark Alpert in Guest Blog, ScientificAmerican.com. Published online April 13, 2016. https://blogs.scientificamerican.com/guest-blog/alpha-centauri-or-bust

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FROM OUR ARCHIVES

Starship Humanity. Cameron M. Smith; January 2013.

scientificamerican.com/magazine/sa

IMMUNOLOGY

CANCER KILLERS

Some advanced cancers can now be successfully treated by synthetic immune cells that are more powerful and longer-lasting than any found in the body

By Avery D. Posey, Jr., Carl H. June and Bruce L. Levine

Illustration by James Yang

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Carl H. June is a professor of pathology and laboratory medicine at the University of Pennsylvania Perelman School of Medicine.

Bruce L. Levine is a professor of cancer gene therapy at the University of Pennsylvania Perelman School of Medicine.

TUMOR IMMUNOLOGISTS HAVE known for decades that the immune system can be an important ally in the fight against cancer. Most early attempts to recruit its potential proved disappointing, however. It turns out that investigators had not done enough to stimulate a key component of the immune system, a kind of master sergeant called the T cell. Without enhancing the ability of T cells both to identify and to attack cancer cells, researchers were, in effect, asking the immune system to go into battle with the biological equivalent of paper airplanes and pellet guns.

The first clues that T cells needed to be greatly fortified to fight cancer emerged in the 1980s. Researchers tried to strengthen the immune responses by drawing T cells from patients, multiplying them in the laboratory and then infusing the expanded number of cells back into the body. That approach helped some people but typically did not work for long: the cells tended to exhaust themselves and shut down soon after delivery.

Various groups of investigators then began addressing the problem in different ways. One strategy that we and our colleagues have developed is now showing exciting promise in clinical trials. Back in the mid 1990s, while trying to discover new treatments for HIV, two of us (June and Levine) created an improved technique to turbocharge T cells drawn from patients, making the cells more abundant, powerful and longer-acting than previous methods could achieve. Then, about a decade ago, a new way of genetically altering T cells became available that would allow them to efficiently home in on and attack certain kinds of cancer—such as leukemia and lymphoma—that originate in various types of white blood cells.

In the past few years these synthetic immune cells, known as chimeric antigen receptor T—or CAR T—cells, have been tested in dozens of studies collectively involving close to 1,000 patients with advanced cases of leukemia or lymphoma. Depending on the disease, half or more of those patients are now living longer than expected, and hundreds appear to be cancer free.

A consensus is building among cancer researchers that treatment with CAR T cells—either alone or in combination with other therapies—will eventually provide durable cures for certain blood cancers. The next hurdles will include confirming if this type of therapy can be effective against other kinds of tumors and better controlling the side effects, some of which can be fatal. But the success so far, which involved tackling a series of difficult challenges over the course of about 20 years, is heartening.

TURBOCHARGE T CELLS

WHEN WE STARTED on the road that ultimately led us to CAR Ts, our first task—simply figuring out how to enhance the cell-killing powers of T cells from patients—was anything but simple. To become activated, T cells must receive signals from a different group of immune system players called dendritic cells. Only after receiving such instructions can T cells achieve their full potential: dividing and producing extra copies of themselves (all primed against the same target) and releasing chemicals called cytokines that boost the body's immune response even further. After a few days, the T cells quiet down, allowing the body—and the immune system—to return to normal.

In the mid-1990s, while working on HIV, June and Levine decided to improve on this natural process by stimulating T cells in the lab. Our goal was to take some T cells out of a patient, activate them, encourage them to multiply many more times than was possible within the body and inject them back into the same person—where we hoped they would boost the ability of the patient's immune system to fight HIV and the other infections that plague people with AIDS (the end stage of HIV infection).

But first we needed to find a good way to activate the T cells. In theory, we could expose them to dendritic cells that were also isolated from each patient, but dendritic cells vary substantially in number and quality, especially in people with HIV or with cancer. To get around the problem, we decided to develop artificial substitutes for the dendritic cells. Eventually we settled on tiny, magnetic beads that we coated with two proteins able to mimic and improve on the dendritic cells' stimulatory behavior.

Then we collected T cells from the blood of patients and energized them with our all-purpose beads. By the end of the five- to 10-day process, each of our patients' T cells had given rise to 100 more cells. Our microbead-based method is now one of the primary tools that investigators use to grow activated T cells for use in many different research experiments and clinical trials.

REDESIGN THE T CELL

THE BODY FACES two major challenges in mounting an immune response to cancer. One is that malignant cells spring up from our

IN BRIEF

Synthetic immune cells, known as chimeric antigen receptor T, or CAR T, cells have proved remarkably effective at treating leukemia and lymphoma. **CAR T cells boost and enhance** the body's ability to fight malignant cells. But they can trigger unwanted side effects and, in some cases, death. **Researchers are now designing** new CAR T cells they hope will treat other forms of cancer and cause fewer deleterious side effects.

Synthetic Immune Cells

Researchers have developed a variety of experimental treatments in recent years to boost the immune system's ability to identify and destroy malignant tumor cells. Among these therapies, delivery of synthetic immune cells, known as CAR T cells, has proved particularly effective for the treatment of advanced cases of leukemia and lymphoma. Built into each custom-designed CAR T cell are two powerful shortcuts, depicted here, to soup up the immune response.

Normal Immune Response Is Complicated

Although a healthy immune system can recognize and destroy cancer cells, the process is complex and prone to breakdown. So-called dendritic cells absorb and process some of the proteins found either on the surface or inside of a malignant cell. Then, the next time the immune defender meets other immune cells called T cells, it "presents" them with bits of those proteins, known as antigens. This action prompts the T cells to do two things: (1) search out and identify any cells that contain both the antigen that had been presented by the dendritic cell and another protein called an MHC and (2) attack the antigen-bearing cell if it also possesses yet a third protein, called a co-stimulatory ligand.

CAR T Cell Therapy Is Streamlined

CAR (for chimeric antigen receptor) T cells are much more potent than anything the body could produce on its own. Whereas typical T cells normally call off their attack after a few weeks, investigators have genetically engineered CAR T cells so that they will remain active for months if not years against targets of the researchers' own choosing, such as a protein called CD19.

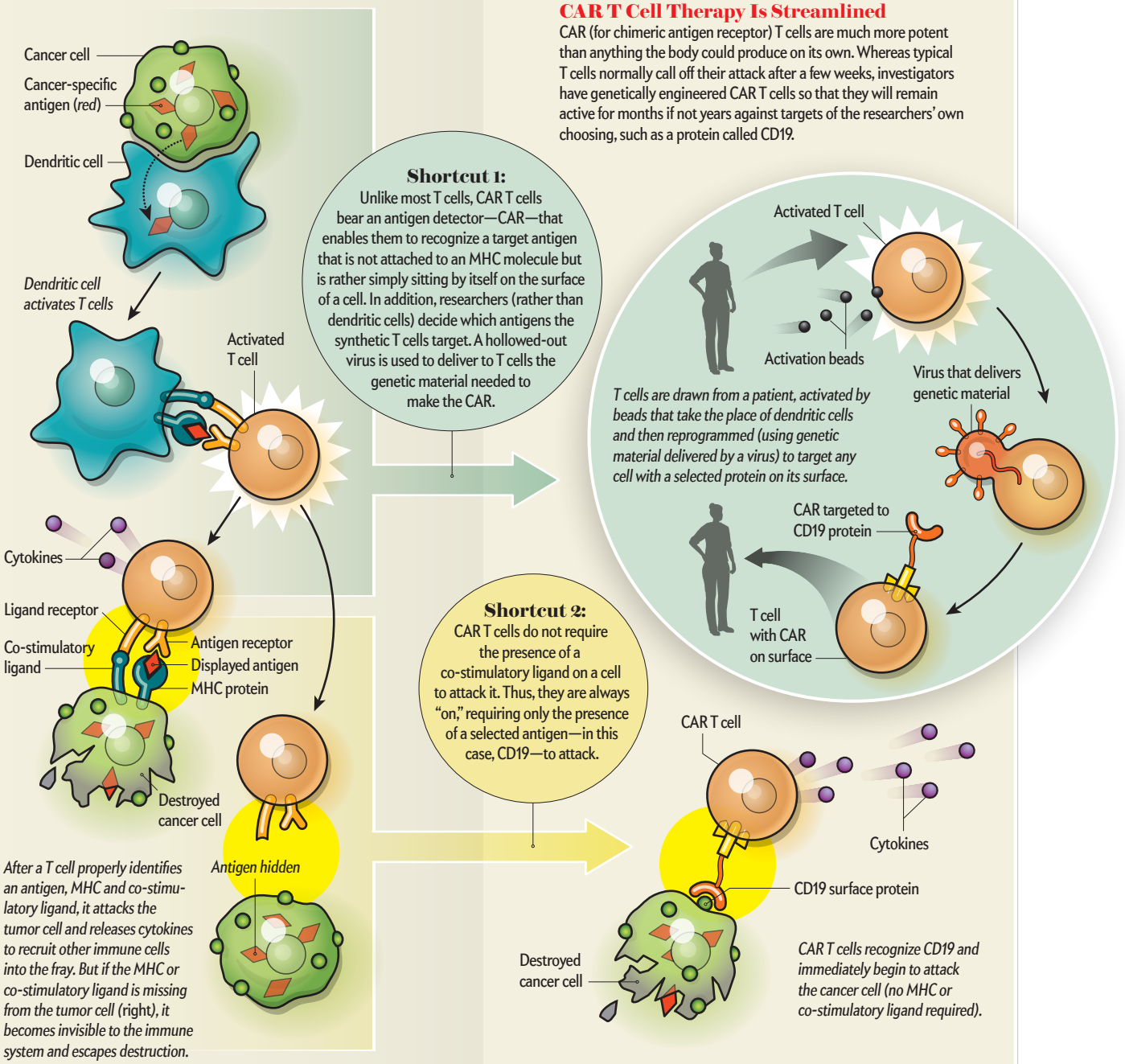

Illustration by Jen Christiansen

own cells. Because our immune system has evolved so as not to attack our tissue, it often has trouble distinguishing cancer cells from normal cells. The second challenge is that many cancer cells exploit various tricks to thwart an immune response. They have learned how to hide from the immune cells, as well as how to interfere with an effective immune response.

As part of the mechanism for protecting healthy tissue from "friendly fire," a T cell inspects a cancer cell for the presence on its surface of two requisite molecules before it will attack. One consists of a large protein complex, known as an MHC molecule, that cradles a protein fragment, or antigen—the target "presented" to the T cells by dendritic cells. The second required molecule—a so-called co-stimulatory ligand—provides the on signal that tells the T cell to attack. If either the antigen-MHC unit or the co-stimulatory ligand is absent, the T cell simply moves on. Thus, a malignant cell has at least two ways to fool immune cells into leaving it alone: it can stop producing MHC on its surface, or it can display a form of co-stimulatory ligand that acts as an off switch to T cells.

Unlike regular T cells, CAR T cells attack a cancer cell immediately after detecting their target.

But what if T cells could be genetically modified so that researchers, instead of dendritic cells, could choose the target antigen—say, one that is naturally abundant on cancer cells but is not necessarily presented by an MHC molecule? And what if these T cells did not need to follow the usual two-step process to begin to attack tumor cells? It was not until CAR T cell technology came along that investigators could easily try to make this happen.

The solution, in principle, was to outfit T cells with genes that would give rise to a synthetic molecule (CAR) that could do two things at once: detect the selected antigen and activate the T cell—even in the absence of the usual on signals. We could accomplish this goal by combining elements of specialized proteins known as antibodies (which normally target bacteria and viruses) with other proteins known to stimulate T cells. More specifically, we designed the antibodylike part of CAR, which juts out a bit from the surface of the cell, to bind to the cancer antigen of choice. And we constructed the rest of CAR, which plunges through the T cell membrane, to generate the proper signals and activate the T cell as soon as the cancer antigen is detected.

The concept of targeting cancer-specific antigens to fight malignancy is not new, of course. In the 1990s physicians began treating patients with so-called monoclonal antibodies, which seek out specific proteins found primarily on the surface of different types of tumors. But antibodies do not last more than a few weeks in the body. Engineered into T cells, however, they would live for as long as the T cells lasted, for years at a time.

The challenge became getting the T cells to produce the selected antibody-activator molecule. We decided to take advantage of HIV's well-known proclivity for infecting T cells by removing the genes that make HIV a killer and replacing them with genes that contained the necessary information for building our antibody-activator chimera. We then allowed these now harmless HIV particles to infect the T cells that we had removed from our patients. The altered viruses acted like a Trojan Horse to deliver the genes into the T cells; the cells took it from there, producing CAR and fitting it onto the cells' surface. Using this and other techniques, several different groups of investigators, including our own, have refashioned T cells so that they can attack tumor cells after recognizing only a single protein on the cells' surface. (No MHC or co-stimulatory ligand required.) Furthermore, this new custom-tailored T cell can be designed to go after exactly whatever antigen—or perhaps even combination of antigens—investigators choose.

In the mid-1990s and early 2000s, collaborating with others, we learned how to turn T cells drawn from HIV patients into CAR T cells and tested these in human clinical trials. We continue to improve our technique and expect to have more advanced therapies for HIV in another few years.

CAR T cells were also beginning to be tested in patients with cancer by several groups. We sought to combine technologies—taking what we had learned about activating T cells with microbeads, with the CAR technology to redesign and redirect T cells, and the harmless HIV as the Trojan Horse to deliver the CAR payload to T cells.

We soon discovered how powerful these CAR T cells could be.

TEST THE NEW DESIGN

NOW WE HAD THE RIGHT AMOUNT of firepower, and we were also pretty sure we had a fairly good target. The perfect homing beacon for our CAR T cells, of course, would be an antigen found only on tumor cells, but these antigens are very rare. Because all cancer cells arise from what were once normal cells, tumor cells and healthy cells mostly display the same antigens. Developing a CAR T cell against these shared antigens would inevitably destroy a lot of healthy tissue along with the tumor.

There are, however, noted exceptions to this quandary. Certain types of leukemia and lymphoma, for example, arise from a group of white blood cells called B cells. People can survive without B cells, which are the body's normal source of antibodies, provided they receive the occasional infusion of manufactured antibodies. B cells—as well as any malignant cells that they might become—bear a surface protein known as CD19. We and others in the field thought CD19 could be an attractive target for CAR T cell therapy because it is not found on any other healthy tissue.

We tested the idea in mice. Then, in early 2010, we began a clinical trial of CAR T cells that targeted CD19. The initial three patients were adults with advances cases of chronic lymphocytic leukemia (CLL) that was not responding to other treatments.

The first was William Ludwig, a retired corrections officer who had learned he was sick a decade earlier and was now carrying over five pounds of leukemic cells dispersed throughout his body. He received one billion of his own genetically modified CAR T cells in August 2010. Ten days later he developed a fever, low blood pressure and breathing difficulties—serious side effects that landed him in intensive care. We later learned that Ludwig's symptoms occurred because his immune system had gone into triple overdrive in response to the high number of cytokines now coursing through his body—a reaction, known as cytokine release syndrome, that can kill if it gets out of hand.

Fortunately, Ludwig came through, and one month later his

SCIENTIFIC AMERICAN ONLINE Watch a video about CAR T cell therapy at ScientificAmerican.com/mar2017/cart

doctors could find no evidence of leukemic B cells in his body. This outcome was so extraordinary and unexpected that clinicians performed a second biopsy, which confirmed the results. We then treated the two other patients, who also had extraordinary responses. More than six years later Ludwig and one of the other patients are still alive and free of leukemia. Further testing showed that the CAR T cells multiplied in the bloodstream and bone marrow, where blood cells are made; each CAR T cell that had been infused (or its daughter cells) in these three patients was ultimately responsible for killing between 1,000 and 93,000 tumor cells. When the CAR T cells were isolated from blood samples months later, they still retained the ability to kill leukemic cells bearing the CD19 molecule in the lab. In effect, these long-term sentinels had become a "living drug" that continued to patrol the body, hunting for any potential recurrence.

EXPAND THE REPERTOIRE

AS SIGNIFICANT AS OUR INITIAL RESULTS WERE, we were out of money and unable to try our experimental treatment on any more patients. Review panels at federal research agencies deemed the therapy too risky and thus not worth further funding. Nevertheless, we submitted two papers describing the first three patients that were quickly accepted and published simultaneously in August 2011 in the *New England Journal of Medicine* and *Science Translational Medicine*. Extensive media coverage followed, as did inquiries from biotechnology start-ups and companies that were interested in licensing the technology from the University of Pennsylvania, where we work.

Eventually one of our grant applications came through, which allowed another trial to begin in 2012, this time in children. Then we decided to form an alliance between the University of Pennsylvania and Novartis to finance development and the future submission of our results to the FDA for commercial approval. News of the partnership triggered a licensing and investment frenzy, with many medical centers around the world forming new biotechnology companies dedicated to producing new variations of CAR T cells. Our latest results in children show an overall survival rate after 12 months of 62 percent, compared with less than 10 percent after a year using standard treatments.

Over the past few years many groups—including Memorial Sloan Kettering Cancer Center, Seattle Children's Hospital, the Fred Hutchinson Cancer Research Center allied with Juno Therapeutics, the National Cancer Institute allied with Kite Pharma, and others—have reported astonishing responses in advanced cases of leukemia and lymphoma. At our center, we have treated 300 patients with CAR T cells targeting B cell malignancies. The response rates vary by disease: about half of our patients with advanced chronic lymphocytic leukemia show marked clinical improvement (based on the decrease in leukemic cells in their body, among other factors), whereas about 90 percent of children with acute lymphoblastic leukemia have shown a complete response—no evidence of cancer cells—one month after treatment.

No one really knows why CAR T cell therapy does not work for everyone with CD19 malignancies. Some relapses seem to occur because the infused CAR T cells did not multiply in the patient or because new leukemic cells evolved that did not produce the CD19 molecule and thus were unaffected by treatment. Even so, the magnitude of the response for these malignancies is unprecedented. Two companies are expected this year to ask the FDA to approve CAR T cells for the treatment of cancer: Novartis, for pediatric acute lymphoid leukemia and later for lymphoma, and Kite for a type of lymphoma.

Many challenges remain. As a research community, we are still developing ways to manage and possibly to prevent the most severe side effects. Although fatalities among patients are generally rare, a number of people with acute lymphoblastic leukemia have died from treatment-related problems, which may stem in part from the fragile health of these patients, as well as from differences in the design of CAR T cells at different institutions.

We are now in the "Model T" stage of CAR T cell development. Making it more widely available to patients with B cell cancers and other tumors is a priority, and a number of recent scientific and technological advances will be tested in clinical trials over the next several years. To treat cancers other than B cell malignancies, investigators will probably need to identify and target certain combinations of antigens that are more commonly found on cancer cells than healthy tissue. One of us (Posey), for example, is trying to develop an immune-based treatment for breast and pancreatic cancer. These and other so-called solid tumors are even better at hiding from and suppressing the native immune system than leukemia and lymphoma, which are more accessible because they circulate in the blood. To smoke out such cells, Posey is designing a CAR T cell that will search for two targets instead of just one: the first is a certain sugar molecule that is found solely on the surface of cancer cells and that allows those cells to reproduce faster than normal cells do; the second is a protein found on both cancerous and healthy cells. In theory, this specific combination of sugar and protein targets should occur in abundance only on cancer cells, which should limit this particular CAR T cell's ability to harm normal tissues.

Progress is rarely linear, of course. Disappointments, failed hypotheses and setbacks are inevitable. But there is no doubt in our mind that the success we have already seen in advanced leukemias and lymphomas justifies future research into the development of yet more CAR T cells. SA

DISCLOSURE: Like many cancer researchers, the authors have some commercial ties to for-profit companies. Avery D. Posey, Jr., has intellectual property licensed to Novartis and to Tmunity Therapeutics, which develops anticancer therapies. Carl H. June and Bruce L. Levine receive royalties and laboratory funding from Novartis based on an intellectual-property licensing agreement and alliance with the University of Pennsylvania. Novartis and the University of Pennsylvania have applied for drug patents based on some of the work summarized in this article. June and Levine are co-founders of and have equity in Tmunity Therapeutics and also receive consulting fees from and advise several other companies involved in cell therapy and cancer research. These relationships are managed in accordance with University of Pennsylvania policy and oversight.

MORE TO EXPLORE

Fire with Fire. Video on CAR T therapies. Directed by Ross Kauffman. Red Light Films, 2013. www.youtube.com/watch?v=h6SzI2ZfPd4

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FROM OUR ARCHIVES

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scientificamerican.com/magazine/sa

BEHAVIORAL NEUROSCIENCE

Brain Trust

POVERTY MAY AFFECT THE SIZE, SHAPE AND FUNCTIONING OF A YOUNG CHILD'S BRAIN. WOULD A CASH STIPEND TO PARENTS HELP PREVENT HARM?

By Kimberly G. Noble

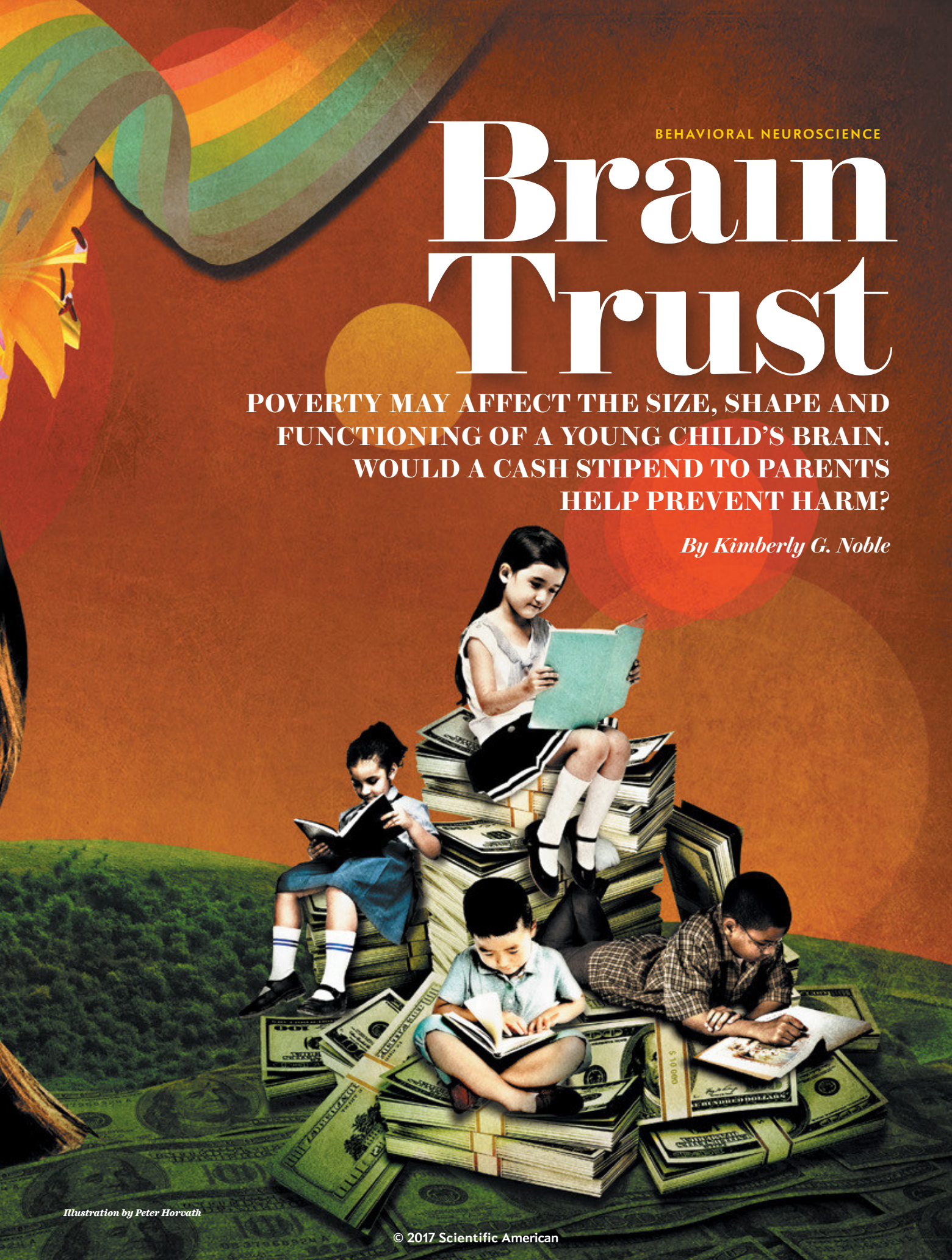


Illustration by Peter Horvath

Kimberly G. Noble is an associate professor of neuroscience and education at Columbia University's Teachers College. Her research focuses on socioeconomic disparities in children's cognitive faculties and brain development.

GROWING UP POOR DOES MORE THAN DEPRIVE A BILLION children and adolescents worldwide of basic material necessities. Poverty places the young child's brain at much greater risk of not going through the paces of normal development to eventually become the three-pound wonder able to perform intellectual feats, whether composing symphonies or solving differential equations.

Children who live in poverty tend to perform worse than their more advantaged peers on IQ, reading and other tests. They are less likely to graduate high school, less apt to go on to college and receive a degree, and more prone to be poor and underemployed as adults. These correlations are not new, and brain development is only one contributing factor among many. Until the past decade, however, we had only the vaguest idea of what impact poverty actually has on the developing brain.

My laboratory, along with a few others, has begun to explore the relation between a family's socioeconomic status (SES)—a measure that gauges income, educational attainment and occupational prestige—and children's brain health. We have found that socioeconomic disadvantage is associated with tremendous differences in the size, shape and actual functioning of children's brains.

The recognition of poverty's potential to hijack normal brain development has led us to propose a simple remedy to alleviate the hardships of being poor. We are planning a study to gauge the effect on a young child's health of giving a cash stipend to families to help ease their financial straits. The study is the first to probe whether a modest elevation in income could help build a better brain. If it succeeds, it could provide a clear path that proceeds directly from basic brain science to the formulation of new public policy.

LOOKING FOR ANSWERS

WHEN I BEGAN THIS RESEARCH 15 years ago, I was a graduate student at the University of Pennsylvania. At the time, my adviser, Martha Farah, wanted to know more about how poverty affected early brain development. Luckily for me, she asked me to be her first student to tackle this challenge.

The project required careful deliberation about what research methods we would use. The splashiest techniques involved brain imaging, in which powerful machines take pictures that are analyzed to reveal structure (how the brain looks) as well as function (how the brain operates). As enticing as brain imaging is, it is also expensive: a single scan typically costs hundreds of dollars, which does not include compensation to study participants or research assistants who analyze the data.

Because we were taking on a research question that had not been addressed before, we decided to look for techniques that were simple and inexpensive and would allow us to recruit as many study participants as possible. The search led us to a straightforward solution: the use of standard methods to measure cognition. Unlike previous studies that looked at the effects of poverty, we decided not to rely on broad indices of achievement, such as high school graduation rate. This is because no one part of the brain is responsible for graduating from high school. Rather different brain circuits are involved in processing distinct cognitive skills, many of which are important for academic and life achievement. For instance, we know that when people have strokes or develop lesions in a region of the left side of the brain known as Wernicke's area, they have difficulty understanding language. We have also found, from neuroimaging studies, that healthy individuals use this same area when they listen to speech. From this work, scientists have deduced that healthy individuals recruit this region whenever they participate in a task that involves listening to and understanding speech. We do not need to take a picture each time to know that is so.

In this way, we decided to use well-established psychological testing methods to assess children's language capabilities with-

IN BRIEF

Children who live in poverty tend to perform worse than peers in school on a bevy of different tests. They are less likely to graduate from high school and then continue on to college and are more apt to be underemployed once they enter the workforce.

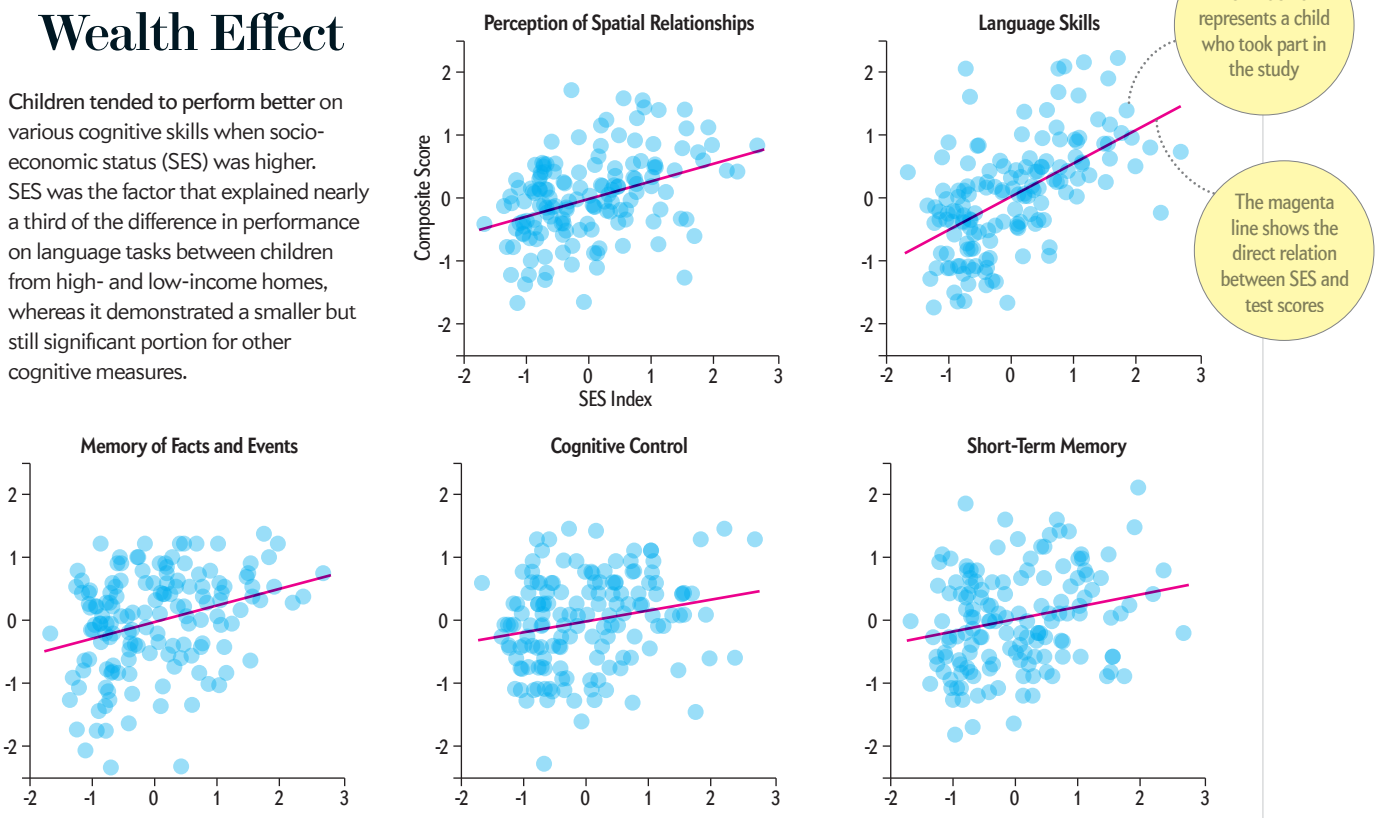
Research that crosses neuroscience with sociology has begun to show that educational and occupational disadvantages that result from growing up poor can lead to significant differences in the size, shape and functioning of children's brains.

Poverty's potential to hijack normal brain development has led to plans for studying whether a simple intervention might reverse these injurious effects. A study now in the planning stages will explore if a modest subsidy can enhance brain health.

PRECEDING PAGES: GETTY IMAGES (*illustration reference for children*); FOR ILLUSTRATION PURPOSES ONLY

Wealth Effect

Children tended to perform better on various cognitive skills when socioeconomic status (SES) was higher. SES was the factor that explained nearly a third of the difference in performance on language tasks between children from high- and low-income homes, whereas it demonstrated a smaller but still significant portion for other cognitive measures.



out having to scan their brain. The question we posed was: How do socioeconomic disparities relate to brain function?

In conducting our study, we recruited several groups of families from varied socioeconomic backgrounds whose children ranged in age from kindergarten through adolescence. We then administered to the children cognitive tests that served as a measure of the integrity of different brain circuits. Our results were remarkably consistent across multiple studies. In general, children from more disadvantaged homes tended to perform more poorly on tasks that tested their language and memory skills and the ability to exert self-control and avoid distraction.

In some cases, we and other groups carrying out similar research did need access to more advanced imaging tools to determine if family SES relates to differences in the size and shape of key brain areas involved in higher cognitive processes. Four independent research groups have now reported that children whose parents earn higher incomes tend to have a larger hippocampus, a structure located deep in the brain that is critical for memory formation. Other work has focused on the size and shape of the cerebral cortex, the wrinkled outer layer of brain cells that does most of the cognitive "heavy lifting." Several early studies have examined whether SES correlates with the volume of the cortex.

To understand what is meant by volume, picture the cortex as if it were shaped roughly like a can of soup. We can calculate the amount, or volume, of soup that the can holds by multiplying the height of the can—known in brain parlance as the cortical thickness—by the area of the circle on top of the can, which is analogous to the cortical surface area.

Measurements of cortical volume must be done with care. It is easy to be misled because the same cortical volume can exist with a large surface area and a small cortical thickness or with a substantial thickness and a tiny surface. Cortical thickness tends to decrease with age—our hypothetical soup can might shrink down to the size of a tuna fish can—but our cortical surface area tends to increase with age. It is as if we started out with a small can of tomato paste, which grows wider over time to the width of a full-fledged can of soup.

With our set of software-measuring tools in hand, we recently looked at whether socioeconomic disparities affect both cortical surface area and thickness. In the largest study of its kind to date, published in 2015 in *Nature Neuroscience,* we analyzed the brain structure of 1,099 children and adolescents, recruited from socioeconomically diverse homes from 10 sites across the U.S. We found that both parental educational attainment and family income were associated with differences in the surface area of the cerebral cortex. Children from families that earned less than $25,000 a year had 6 percent less cortical surface area than those from families that earned more than $150,000. These associations were found across much of the brain but were particularly pronounced in areas that process language and govern impulse control and other forms of self-regulation—abilities that have repeatedly shown substantial differences across socioeconomic lines.

For this study, we took into account several key variables. First, as a proxy for race, we controlled for the proportion of genetic background each individual had from six major populations (African, Central Asian, East Asian, European, Native

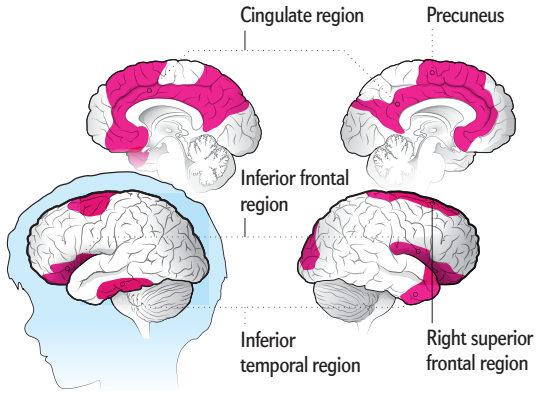
SOURCE: "SOCIOECONOMIC GRADIENTS PREDICT INDIVIDUAL DIFFERENCES IN NEUROCOGNITIVE ABILITIES," BY KIMBERLY G. NOBLE ET AL., IN *DEVELOPMENTAL SCIENCE*, VOL. 10, NO. 4; JULY 2007

Graphic by Amanda Montañez

A Brain on Poverty

The travails of an impoverished upbringing reduce the surface area of some parts of the cortex more than others. The affected regions (*magenta*) participate in various forms of mental processing. The researchers demonstrated the connection by plotting collected measures of the affected regions (referred to as the cortical surface area) by socioeconomic status.

Areas of Vulnerability



Who Suffers Most

American and Oceanic). We determined from the data that socioeconomic disparities that we observed in brain structure were independent of genetically defined race.

We saw dramatic differences from person to person. For example, some children and adolescents from disadvantaged homes had larger cortical surface areas, whereas some advantaged children had smaller areas. We might consider a comparable situation with gender and height: in childhood, boys tend to be taller than girls, but we know that in every elementary school classroom, some girls are taller than some boys. Along the same lines, although children from higher-income homes tended to have larger brain surfaces, our research team could not predict an individual's brain size simply only by knowing his or her family income.

The relation between family income and surface area was strongest at the lowest end of the income spectrum and tended to level off at higher-income brackets. That is, dollar for dollar, differences in family income were associated with proportionately greater differences in brain structure among the most disadvantaged families.

In another recent study, we reported on socioeconomic disparities in cortical thickness. Overall, cortical thickness tends to decrease with age. But our work suggests that a family's socioeconomic circumstance may influence this trajectory. At the lower levels of family SES, cortical thickness tended to decrease steeply earlier in childhood, leveling off during adolescence. At higher SES levels, cortical thickness declined more gradually with age through late adolescence.

This finding is consistent with work from other labs suggesting that adversity can, in some cases, accelerate brain maturation—in essence, causing a young child's brain to "grow up" more quickly. The rapid reduction of cortical thickness suggests that many poor children's brains may lack "plasticity"—an ability to change in structure to accommodate the essential learning that takes place during childhood and adolescence.

Of course, one of the most important questions we needed to answer was whether differences in brain structure affected a child's cognitive abilities. The disparities we found in brain surface area seemed to confirm, in part, previous findings that higher family income predicts a child's ability to pay attention and inhibit inappropriate responses. Work by Seth Pollak of the University of Wisconsin–Madison and separate studies by John Gabrieli of the Massachusetts Institute of Technology have suggested that differences in brain structure (cortical volume or thickness) may account for between 15 and 44 percent of the gap in educational achievement for an adolescent from a low-income household.

This line of research is compelling but still in its infancy. We still need to learn what causes the association between SES and brain development. Is it differences in nutrition, neighborhood, school quality, parenting style or family stress, or a combination? Are we even certain that all these differences are explained by experience—or do genetics also most likely play a role?

Few studies to date have directly examined these questions. A recent finding by Joan Luby and her colleagues at Washington University in St. Louis provides some evidence that income disparities in children's brain structure may be accounted for by stressful life events and differences in parenting style. Less supportive and

SOURCE: "FAMILY INCOME, PARENTAL EDUCATION AND BRAIN STRUCTURE IN CHILDREN AND ADOLESCENTS." BY KIMBERLY G. NOBLE ET AL., IN *NATURE NEUROSCIENCE*, VOL. 18; MAY 2015

Graphic by Tami Tolpa (brain illustrations) and Amanda Montañez (graph)

more hostile parenting appears to lead to worse outcomes—in this case, a smaller hippocampus. In my lab, we are looking at how chronic stress and fewer verbal interactions between parents and children may, in part, explain these findings.

Another persistent question was whether the difficulties experienced early in life by poor children stem more from their time in the womb than with family income after they are born. Our group reported recently that brain function in the first four days of life bore no relation to parents' income level or educational attainment, lending support to the idea that socioeconomic disparities in brain development result from differences in postnatal experience. This work still needs to be replicated, given that the sample used in that study was relatively small: only 66 families. But work by several other research groups has suggested that some structural or functional brain differences may become evident only later in the first year of life.

We do not yet have the evidence to explain the links between family, social and economic circumstances and a child's growing brain. Disentangling the connections among SES, early childhood experience and brain development will remain a clear priority for future research.

CORRELATION IS NOT CAUSATION

ALTHOUGH DOZENS OF STUDIES have supplied evidence of the relation between family income and healthy brain development, this type of research needs to be placed on a surer footing. The oft-cited adage "correlation is not causation" helps to explain the lingering uncertainty: Does growing up in a disadvantaged home cause differences in the brain, or does a distinct developmental course lead a child to flounder in school or at work?

The field of neuroscience has been silent on the issue of causality. To test cause and effect, we need the gold standard of scientific testing: a randomized controlled trial in which one "treatment" group is assigned randomly to receive an intervention, and the other is randomized to receive the "control" experience, enabling us to assess the impact of one intervention or another on brain development.

For this type of study, a research team needs to assess, for instance, what should be the right intervention to reduce socioeconomic disparities. Quite a few school and home-based interventions, such as Head Start, already aim to reduce divergences in children's achievement. Indeed, many of these efforts are effective, even though the challenges such interventions face are often daunting: high-quality interventions are expensive, difficult to scale up and often suffer from "fade-out," in which positive effects dwindle with time once children are no longer receiving services.

Given these difficulties, we have decided to consider a much simpler intervention—one that is easy to administer and would in principle have near-perfect acceptance in the community. The study we have designed will consider the effects on brain development of directly supplementing family income with a monetary subsidy. Cash transfers, as opposed to counseling, child care and other services, have the potential to empower families to make the financial decisions they deem best for themselves and their children. Evidence from studies conducted both in the U.S. and in the developing world has suggested that direct income supplements may hold promise. The idea of supplying a universal basic income is gaining traction and is being piloted by several charitable organizations and governments around the world.

But none of these studies so far has measured the effects of family income supplementation on children's brain development. Recently we have formed a team of experts from the social sciences and neurosciences to pursue this question. I am working with economist Greg Duncan of the University of California, Irvine, developmental psychologists Katherine Magnuson of the University of Wisconsin–Madison and Hirokazu Yoshikawa of New York University, and economist Lisa Gennetian of N.Y.U. We are raising funds to launch the first ever randomized experiment to test a cause-and-effect connection between poverty reduction and brain development. The goal of this study is ambitious, although the premise is straightforward. We will begin by recruiting 1,000 low-income U.S. mothers at the time of a child's birth, and mothers will be randomized to receive a $333 monthly income supplement or a $20 monthly income supplement.

Funds will be disbursed on a preloaded debit card to the mothers who sign up for the study in the hospital where a child is born. The debit card will be automatically reloaded each month for the duration of the study. No constraints will be placed on how the money is spent. Families will be tracked over the first three years of the children's lives to gauge the impact of the unconditional cash transfer on cognitive and brain development.

We will also carefully measure numerous aspects of the families' lives, including stress, the quality of family relationships and how recipients use the funds provided. A recent one-year pilot study involving 30 low-income mothers suggested that our approach is quite feasible and that a debit card can serve as a reliable means for distributing income to mothers. Although a substantial number of participants had never previously used a debit card, they reported few problems with card activation, accessing cash or using it for point-of-sale transactions. This gives us confidence that our approach could scale up to the level of a full study.

Our hypothesis is that increased family income will trigger a cascade of positive effects for these families. As their children pass through early childhood, we posit that they will be better able to develop visual, auditory and other critical cognitive skills at the pace of children from families at higher-income levels.

If our hypothesis is correct, our trial has the potential to inform social policies that affect the lives of millions of disadvantaged families with young children. We suspect that such policies could be put in place with an uncomplicated government infrastructure. Although income may not be the only factor that determines a child's developmental trajectory, it may be the easiest one to alter from the standpoint of implementing policy—a down payment of sorts to promote the health of a growing child's brain. SA

MORE TO EXPLORE

Socioeconomic Gradients Predict Individual Differences in Neurocognitive Abilities. Kimberly G. Noble et al. in *Developmental Science*, Vol. 10, No. 4, pages 464–480; July 2007.

Family Income, Parental Education and Brain Structure in Children and Adolescents. Kimberly G. Noble et al. in *Nature Neuroscience*, Vol. 18, pages 773–778; May 2015.

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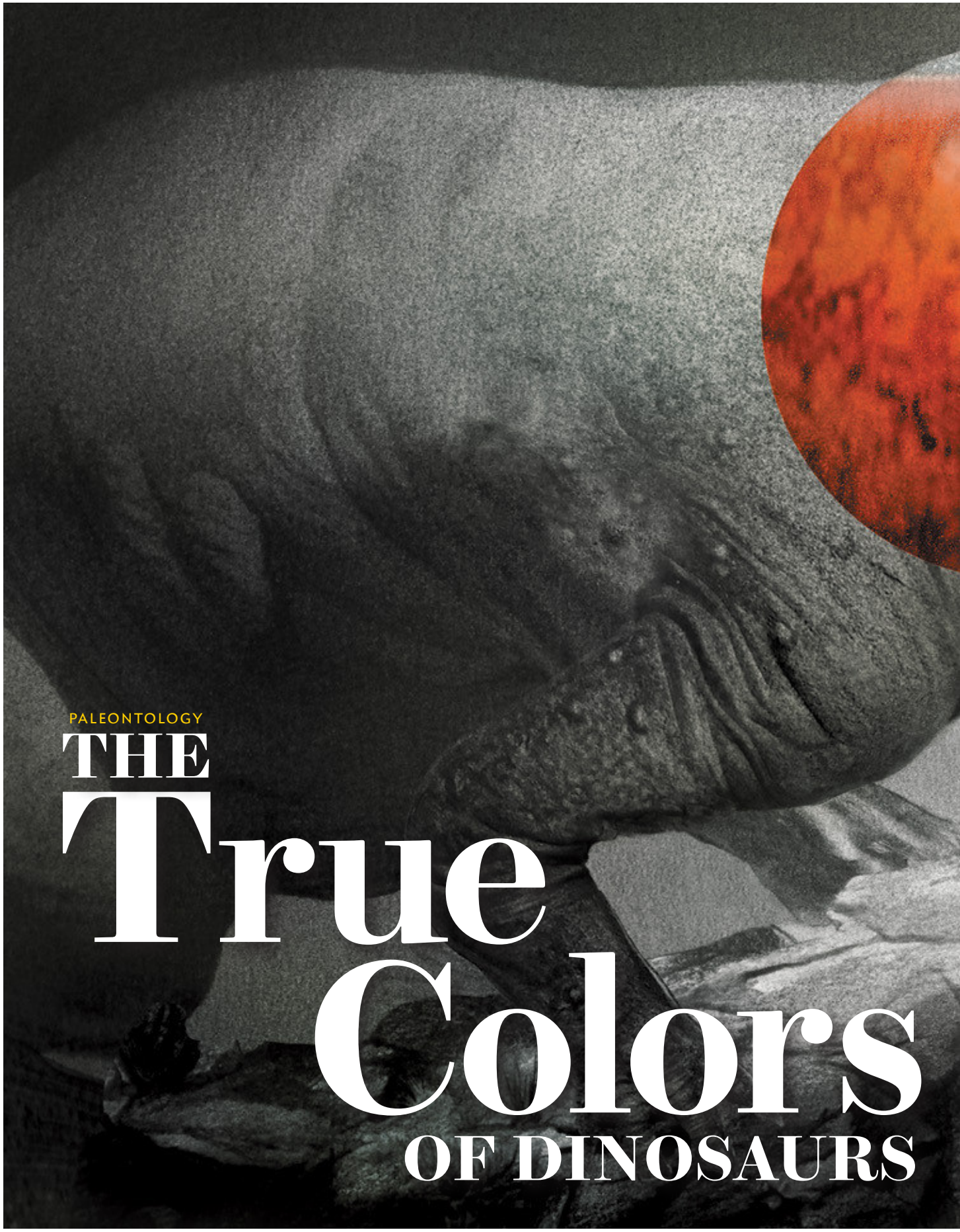


PALEONTOLOGY

THE True Colors OF DINOSAURS

PSITTACOSAURUS is one of several dinosaurs whose coloring has been deduced from fossilized pigments.

Long thought impossible, preservation of fossil pigments is allowing scientists to reconstruct extinct organisms with unprecedented accuracy—a feat that is yielding surprising insights into the lives they led

By Jakob Vinther

Illustration by Greg Ruth

Jakob Vinther thought he was going to become a botanist until he found his first fossils at age 11 while attending summer camp in his home country of Denmark. Today he is a senior lecturer in the schools of biological sciences and earth sciences at the University of Bristol in England. His research focuses on pigments and other molecules preserved in the fossil record.

ON A DAY IN OCTOBER 2006, I SAT IN A DARK LABORATORY AT YALE UNIVERSITY and zoomed into the fossilized ink of a 200-million-year-old squid relative under an electron microscope. An ocean of translucent balls, each roughly a fifth of a micron in diameter, loomed into view. To the untrained eye, they might have been unimpressive. But I was riveted. These ancient structures looked exactly like the granules of melanin pigment that color the ink of modern squid and octopuses.

Perhaps I should not have been so surprised at the resemblance. Researchers had announced the first discovery of fossil ink granules a couple of years earlier. But seeing them with my own eyes was a revelation. As I examined cephalopod specimens from various locales and time periods, I realized their ink was always the same, perfectly preserved for hundreds of millions of years.

The consistently superb preservation of the ink made me wonder whether melanin might persist in fossils of other kinds of organisms. Melanin is the same pigment found in hair, skin, feathers and eyes. It can impart red, brown, gray and black hues and create metallic sheens. If I could find melanin in other fossils, perhaps I could reconstruct the coloring of extinct animals, including dinosaurs. For decades scientists have assumed that pigments hardly ever survive the fossilization process. The few known examples all came from fossils of invertebrate creatures, not backboned ones. Thus, researchers could only guess at the colors of most long-vanished animals, using modern ones as a guide. As a result, dinosaur reconstructions varied widely: some sport the drab earth tones associated with reptiles and amphibians; others flaunt the rainbow hues of modern birds (the only dinosaurs that have survived to modern times).

But discoveries I and others have made over the past 11 years are taking out some of the guesswork. Our examinations of dozens of fossils have revealed many examples of melanin-bearing structures. By studying the shapes and organizations of these structures, we have been able to deduce the actual colors and patterns of extinct dinosaurs and other animals from deep time. These clues to the physical appearances of the creatures, in turn, have led to intriguing insights into their behaviors and habitats.

To test my hypothesis that melanin survives in other fossils and can be used to deduce the true colors of extinct animals, I wanted to find and analyze fossils with dark stains indicative of organic preservation in those anatomical regions generally known to contain melanin: the outer covering of the body and the eyes. And I needed to be able to examine the darkened areas under the electron microscope, which might require cutting a specimen down to size. Well-preserved fossils are rare, however, and museums guard them closely. Fortunately, a remarkable fossil site in my home country of Denmark called "Fur and Ølst Formation" had yielded exquisite bird fossils with feathers, which would be an ideal test case. I managed to convince the curator of vertebrate fossils at the Geological Museum in Copenhagen to cut down a typewriter-sized block of limestone containing a skull of a little bird with stains where the eyes used to be and a dark halo of feather impressions into a piece the size of a slice of bread so that it could fit into the museum's electron microscope.

I had a good idea of what to search for under the microscope. Before obtaining the fossil bird for analysis, I had read numerous scientific papers to figure out what melanin looks like in the feathers of living birds. Melanin is synthesized in specialized cells known as melanocytes by cellular components called melanosomes. Typically the melanin remains encased in the melanosomes, which measure about 0.5 to two microns long and take two forms: a sausage-shaped kind that produces a form of melanin called eumelanin, which absorbs all wavelengths of light and thus gives squid ink and raven feathers their black color, and a meatball-shaped variant that makes pheomelanin, which imparts a rusty red hue. An absence of pigments results in white plumage.

IN BRIEF

Scientists long assumed that they could only guess at the colors of dinosaurs and other extinct organisms.

But recent discoveries of preserved pigments in fossils of a wide range of creatures have upended that notion.

Analyses of the pigments are allowing researchers to infer the actual colors of animals that vanished long ago.

The color patterns have, for their part, revealed other previously unknown aspects of the animals' lives.

Gray and brown colors, for their parts, appear to arise from combinations of eumelanin, pheomelanin and pigment absence.

I had also consulted one of the world's leading experts on bird color: Richard Prum of Yale. Because I knew from the fossil ink that eumelanin can preserve, I figured I would start by looking for that pigment in the feathers. Talking to Prum and his then Ph.D. student Vinod Saranathan, I learned that the sausage-shaped melanosomes line up in a distinctive way along the barbs and barbules that constitute a feather's branches. The melanosomes arrive there during development, when the melanocytes transfer them into specialized cells called keratinocytes that give rise to feathers and hair. If the dark stains on the feather impressions evident in the Danish bird fossil came from melanin, then I should see the sausages arranged this way along the feather branches under the microscope.

With great anticipation, I zoomed in on the fossil feathers—and encountered millions of sausage-shaped structures. Unfortunately, the underground railway was less than 50 meters from the museum's basement, where the electron microscope was located; vibrations from the constant train traffic made it impossible to get a clear image. But the images were good enough to see the sausages. I immediately e-mailed them to my then Ph.D. supervisor at Yale, Derek Briggs, a pioneer in the study of extraordinarily preserved fossils. He replied with less enthusiasm than I had hoped for, noting that these structures were the same as those he and others had found in fossil feathers and mammal hair for decades and had identified as bacteria.

FOSSIL of a *Psittacosaurus* preserves pigment patterns indicative of a type of camouflage called countershading.

I still thought the sausages were melanosomes, though, and made my argument to Briggs. Not only did they have the right shape and size but their orientation in the feather structures mirrored that of black melanosomes in modern bird feathers. Furthermore, it was clear from the fossil squid ink that melanin can fossilize. Briggs began to warm to the idea, but he was not convinced until he showed the images to Prum, who confirmed that they resembled melanosomes in every aspect.

To bolster the hypothesis that melanosomes can persist in fossils of extinct birds, Briggs wanted to find another example. He rummaged through the scientific literature for a good test case and found a description of a little Cretaceous feather from Brazil that preserves distinct black and white color bands. Briggs thought that if we could show that this specimen also preserves aligned melanosomes—but only in the dark bands because white coloration stems from a lack of pigment—we would have enough evidence to make our case. We managed to get the specimen on loan and put the entire block under the electron microscope. Lo and behold, when I examined the dark bands of this 108-million-year-old feather, thousands of little melanosomes aligned along the axes of the fine feather branches came into focus. When I looked at the white bands, in contrast, I saw nothing but rock matrix—which is exactly what one should expect in the absence of pigment.

PAINT BY NUMBER

SINCE THE PUBLICATION of our melanosome discoveries in 2008, my team and several others have described melanosomes and other pigments from additional fossils. Researchers have also started investigating the chemistry of fossil melanin and substantiated our observations that melanin can survive for millions of years, almost chemically intact. Together with Caitlin Colleary, then a master's student at the University of Bristol in England, where I now work, we showed that the slight alterations evident in the fossil melanin are the result of sustained exposure to elevated pressure and heat in the ground. (A few investigators still maintain that the observed structures might be bacteria, but they are running out of options to support their claims.)

Some of our most spectacular findings have uncovered the colors of dinosaur feathers. In 2009 my Yale colleagues and I teamed up with Matthew Shawkey and Liliana D'Alba, both now at Ghent University in Belgium, and others to reconstruct the color pattern of *Anchiornis huxleyi,* a small, predatory, feathered dinosaur from China that lived around 155 million years ago. Like the Danish bird I had studied previously, the *Anchiornis* fossil had some dark stains visible to the naked eye, indicating the presence of organic material, probably melanin. But because we were aiming to reconstruct the pattern of its full plumage—a much more ambitious task than simply determining the presence or absence of melanosomes—we could not rely on these stains to tell us all we wanted to know. Instead we had to develop a way to objectively predict colors from the shapes of the melanosomes. To do this, we studied melanosomes from 12 black, 12 brown and 12 gray feathers of modern-day birds. By considering the length, width and aspect ratio of the melanosomes, as well as how much they vary in shape, we could predict feather color using a statistical method called quadratic discriminant analysis with 90 percent accuracy.

When we applied our method to the melanosomes of *Anchiornis,* the results were striking. Our statistical predictions indicated that the feathers that covered much of the creature's body were mostly gray. The long feathers on the animal's arms and legs, in contrast, were unpigmented by melanosomes and thus white, except for the melanosome-laden tips, which we predicted were black. (Modern birds often have black-tipped wing feathers. The melanin, in addition to coloring the feathers, also fortifies them against battering winds. Perhaps *Anchiornis* benefited from this strengthening property of melanin, too.) Most surprisingly, the feathers on the crown of the head contained impressions of round melanosomes—the "meatballs"—that would have given *Anchiornis* a ruddy crest. All told, this combination of colors made for a spectacularly flamboyant creature.

At around the same time we published our *Anchiornis* study, Fucheng Zhang of the Institute of Vertebrate Paleontology and

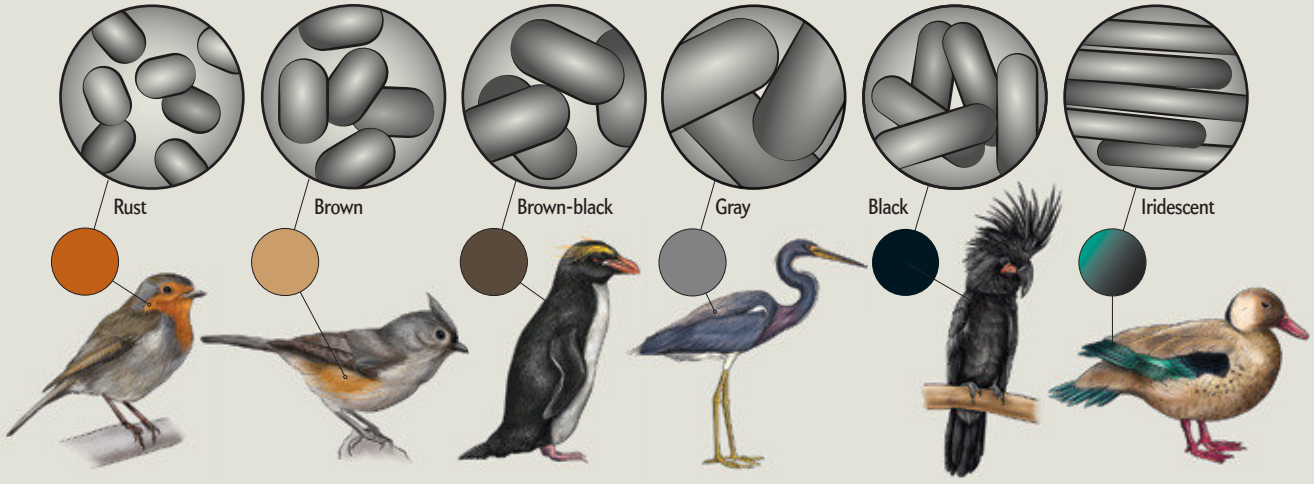
COURTESY OF JAKOB VINTHER AND BOB NICHOLLS

In Living Color

Microscopic pigment-bearing cell structures known as melanosomes can persist in fossils for tens of millions of years. Studies of preserved pigments have allowed scientists to reconstruct the actual colors of a wide range of extinct animals, including a number of dinosaurs. These findings are not only revealing, for the first time, what these creatures really looked like, but they are also elucidating previously murky aspects of the animals' lives—from their activity cycles to the type of environment they inhabited.

Melanosome Size, Shape and Configuration Predict Color

Melanosomes contain two forms of melanin: eumelanin, which gives rise to black tones, and pheomelanin, which imparts rusty red hues. Combinations of these melanins and absence of pigment create brown, gray and white colors. Iridescence, for its part, stems from the stacking of melanosomes in ways that refract light. Analyses of melanosomes from feathers of modern-day birds have yielded a database that researchers can use to predict colors and patterns of extinct animals from the size, shape and arrangement of fossil melanosomes.



Standing Out

Melanosomes preserved in a small dinosaur known as *Microraptor* reveal that this creature had showy, iridescent black plumage similar to a crow's. Paleontologists had suspected that *Microraptor* was nocturnal, based on the large size of its eye sockets. But modern birds with iridescent coloring tend to be active during the day, suggesting that *Microraptor* was actually diurnal.

Microraptor

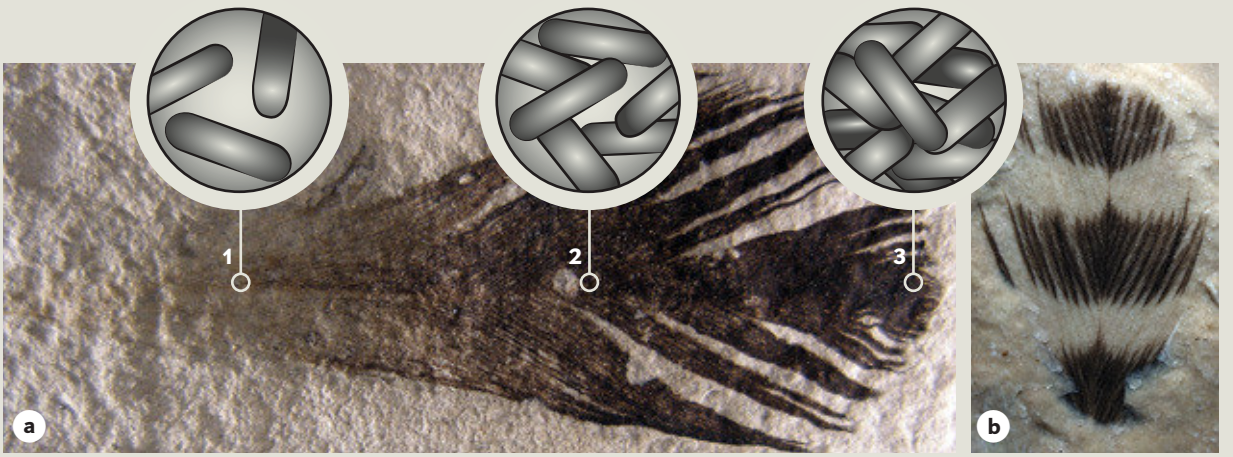
Psittacosaurus

Blending In

The melanosomes preserved in a *Psittacosaurus* fossil show that this animal had a dark back and light belly. This pattern, called countershading, is common in modern-day animals and helps to camouflage them from predators and prey. The specific form of countershading seen in *Psittacosaurus* suggests that the creature would have best blended into a habitat with diffuse sunlight such as that seen in a canopy forest.

Melanosome Density and Distribution Predict Pattern

Fossil feathers show how varying degrees of melanosome concentration can create patterns. For instance, the gradient pattern seen in a 55-million-year-old specimen from Denmark **a** arises from the combination of low melanosome concentrations that yield pale colors (*1*), intermediate concentrations that produce midrange tones (*2*) and high concentrations that form intense tones (*3*). In a 108-million-year-old fossil feather from Brazil **b**, dark and light stripes stem from melanosome-rich and melanosome-free areas, respectively.



COURTESY OF JAKOB VINTHER (*feather photographs*)

Illustrations by Raúl Martín (dinosaurs) and Jillian Ditner (birds and melanosomes)

Paleoanthropology in Beijing, Michael J. Benton of the University of Bristol and their colleagues reported that they had found fossil melanosomes in a range of birds and dinosaurs recovered from 130-million-year-old rocks in China. The pattern of meatball melanosomes in one fuzz-covered dinosaur, *Sinosauropteryx,* implied that it had sported a reddish coat and a tiger-striped tail, making it the first known ginger dinosaur.

Since those early days our feather data set has grown to comprise hundreds of samples, including ones that allow us to accurately predict iridescence, the metallic sheen seen in the plumage of hummingbirds and peacocks, among other birds. Melanosomes responsible for this effect tend to be longer than typical melanosomes, and they may even be hollow or flattened. The iridescence arises from the packing of the melanosomes within the feather. Certain configurations of melanosomes refract light in ways that create different colors, depending on the angle at which the animal is viewed or illuminated.

Amazingly, in 2009 we found evidence of iridescence in a 49-million-year-old fossil feather from Messel, Germany. The fossil, kept at the Senckenberg Museum in Frankfurt, preserves the original arrangement of melanosomes that generated the iridescence. They were packed into a dense, smooth layer found in the finest branches of the feather fossil, the barbules. There the melanosomes occurred strictly on the farthest edge of the feather and on the top surface, the only part that was not obscured by other, overlapping feathers. We deduced that the tips were iridescent because that arrangement of melanosomes is known to produce what is called thin-film interference, the kind that occurs when gasoline floats on water and creates a vivid rainbow of colors.

The patterns were subtle, with fine veining, dots and stripes.

It was not long before we discovered evidence of iridescence in an actual dinosaur—a crow-size creature from China with wings on all four limbs. Dubbed *Microraptor,* it was a primitive cousin to *Jurassic Park*'s *Velociraptor.* The movie depicted *Velociraptor* with scaly skin, but scientists now know that both these dinosaurs were, in fact, covered in feathers. In *Microraptor,* the feathers preserve long, sausage-shaped melanosomes arranged to bend light in eye-catching ways. Its plumage thus would have been black, with the same shiny sheen as a crow's. *Microraptor* is not the only extinct creature now known to have had that rainbow shimmer. Jennifer Peteya of the University of Akron and Ghent's Shawkey recently discovered the same coloration in another fossil from China, a so-called enantiornithine bird with two long tail streamers called *Bohaiornis.*

MORE THAN SKIN DEEP

BEYOND ALLOWING PALEONTOLOGISTS and artists to reconstruct extinct organisms more accurately, fossil pigments are revealing previously unknown facets of the daily lives of both dinosaurs and other long-gone creatures. For instance, experts had presumed that *Microraptor* was nocturnal, based on the large size of its eye sockets. But our discovery that it possessed iridescent plumage suggests otherwise because in modern birds such coloration is typically found in species that are active in the daytime. The bold coloring of *Anchiornis,* for its part, probably helped attract mates or served as some other kind of display, as occurs in flashily dressed modern birds. Thus, color patterns may provide a way to test behavioral hypotheses about a species using a different line of evidence than usual.

Preserved melanosomes can also help scientists place enigmatic organisms on their rightful branch in the tree of life. Recently my colleagues and I were able to solve the long-standing mystery of the bizarre 300-million-year-old Tully monster, the first fossil of which was discovered in Illinois in 1955. With its worm-like body, hammerhead eyes and claw-shaped mouth, the creature had long defied classification. Some experts supposed it to be a soft-bodied creature related to mollusks; others placed it variously among the segmented worms, roundworms and arthropods (the group that includes insects and crustaceans). Our study of a couple of the Tully monster specimens found melanosomes preserved in the retina of the eye. A number of animal groups use melanin to protect the retina. But the Tully monster's retina exhibited a distinctive layering of meatball melanosomes and sausage melanosomes that is unique to vertebrates. Thanks to fossil pigments, then, we can confidently ascribe the Tully monster to the vertebrate branch of the family tree.

Fossil pigments in one species can also illuminate aspects of the other species with which it interacted. Among insects, most color patterns evolved not to help the creatures attract mates but rather as a tactic to avoid getting eaten. Their pigments can thus provide clues to their predators. Fossils of insects called lacewings offer a fascinating example. Between 170 million and 150 million years ago certain distinctive color patterns made their evolutionary debut in insects. Perhaps the most dramatic pattern to emerge during this time was the eyespot, a marking that resembles the eye of a different kind of animal and serves to startle predators approaching their prey at speed from a distance. Lacewings are one of the first creatures known to have had eyespots. What kind of predator were they defending against? Most color patterns of modern insects have evolved as a defense against birds, which are their main predators nowadays. But the lacewings' eyespots predate the origin of birds as we know them. Their predators were instead most likely a small group of dinosaurs called the paravians, which are known to have lived at the same time as these lacewings and are thought to have given rise to birds. Although the fossil record of paravians themselves has been unable to unequivocally pinpoint when flight evolved in this group, the appearance of these eyespots in the lacewings hints that some paravian dinosaurs had taken wing by this point and were exerting birdlike predation pressure on the insects.

Other fossil melanosome discoveries have allowed my collaborators and me to reverse engineer the environment in which extinct organisms lived. Our first foray into this realm of investigation began with a particularly splendid fossil of a small, plant-eating dinosaur called *Psittacosaurus,* a relative of *Triceratops.* These skeletons are quite common in northeastern China and are often very complete. This specimen stood out even in that good company, however. A thin film drapes its body—the remains of the skin, including delicate scales. And its tail displays long, filamentous bristles that may be precursors to feathers. Previous dis-

SCIENTIFIC AMERICAN ONLINE Learn more about fossil pigments at ScientificAmerican.com/mar2017/vinther

coveries of dinosaur feathers have all come from the mostly carnivorous theropod group of dinosaurs. The bristles on *Psittacosaurus,* a distantly related member of the plant-eating ceratopsian group, hint that plumage might have been far more widespread among the dinosaurs than previously thought.

When I first encountered the specimen in 2009, a year after we had announced the discovery of melanosomes in fossil birds, I saw right away that it preserved evidence of beautiful color patterns all over the body. The patterns were subtle, with fine veining, dots and stripes. And I could see that the animal had a dark back that gave way to a pale belly. That kind of dark-to-light color gradient from back to belly counteracts the light-to-dark gradient created by illumination from the sun. This pattern, known as countershading, is common among modern animals ranging from dolphins to deer, helping both predators and prey blend in with their surroundings and thereby elude detection.

I eventually showed the *Psittacosaurus* pattern to Innes Cuthill, who is part of a group that studies camouflage at the University of Bristol. It was then that we realized that we had the opportunity not only to study countershading in a dinosaur but also to deduce from the fossil alone what kind of environment the creature lived in. To reconstruct an animal's habitat, scientists usually gather clues from fossils of other animals and plants found nearby. This kind of approach is problematic, however, because oftentimes the site where a fossil is discovered is not where the organism lived. The Chinese psittacosaur, for example, was recovered from sediments of an ancient lake. The creature was clearly not aquatic, so its remains must have been transported to the lake from the surrounding terrestrial environment, perhaps by moving water. Our study might be able to provide clues about that setting—specifically, the light conditions under which this dinosaur evolved its camouflage.

Cuthill and his collaborators had recently studied countershading in modern ungulates; the group that includes horses, antelope, camels, pigs and rhinoceroses. Although countershading by definition involves darker coloration on the back and lighter coloration on the underside (except for some animals, such as caterpillars, that live their lives upside down), the intensity of those shades and the nature of the transition from dark to pale differ from species to species. Cuthill's team wanted to investigate how well that variation correlates to variation in the lighting conditions found in different environments. Because sunlight varies depending on the latitude at which an animal lives, as well as the density of vegetation in its habitat, the researchers had theorized that ungulate countershading, too, should differ according to latitude and habitat. Their findings bore out that notion. Broadly speaking, if an animal lives in open habitats, the direct sunlight will create a shadow high on the body, with a very sharp transition to the illuminated areas. These animals usually exhibit a countershading that matches this pattern, with dark backs that almost immediately give way to pale bellies and little intermediate coloration in between. Pronghorn antelope offer a great example of this kind of countershading. In closed habitats, in contrast, the diffuse light that filters down through the vegetation scatters in all angles, producing a shadow that hangs farther down the body and transitions to the illuminated area gradually. White- and black-tailed deer, common in North American forestlands, exhibit this pattern.

We knew from our visual inspection of the *Psittacosaurus* fossil that it had countershading of some sort. But to identify the pattern more precisely, we had to subject the fossil to special imaging techniques that mapped the distribution of the preserved melanins. We then projected the pigment pattern onto an accurate, life-size model of the dinosaur, which we accomplished by enlisting the help of British paleoartist Bob Nicholls. Through this work we determined that the transition from dark to light occurred low on the belly and tail in *Psittacosaurus*.

To test the function of the dinosaur's color pattern, we painted a second copy of the full-scale model gray. We then photographed this model in a range of daylight conditions, from gloriously sunny to oppressively cloudy, as well as in open land and underneath conifer trees to capture the shadows cast on it. Next we inverted the dark and light shades in the photographs, effectively creating the ideal countershading patterns for concealing the animal in each of the lighting conditions. Comparing our reconstruction of the actual countershading pattern of the *Psittacosaurus* with the idealized countershading patterns, we determined that the animal's coloring would have best camouflaged it in a habitat with diffuse light, such as that seen in a canopy forest.

A VIVID FUTURE

SCIENTISTS STILL HAVE MUCH TO LEARN about paleocolor. Our ability to see broad categories of color in fossils—those that stem from the shape and arrangement of melanosomes—is already a massive leap forward from what we knew about ancient hues less than 10 years ago. But there are other pigments to look for in fossils, including carotenoids, which produce bright reds and yellows, and porphyrins, which produce such hues as green, red and blue. These pigments have turned up in the fossil record on occasion. Researchers have identified carotenoid pigments derived from fossil bacteria dating back several billion years; porphyrins are preserved in a blood-engorged mosquito from 46 million years ago and in the eggs of a 66-million-year-old dinosaur known as an oviraptorosaur. Pigments not known from modern organisms have come to light, too, including some from fossil sea lilies and algae dating to between 300 million and 150 million years ago.

We will probably encounter limitations to the detail with which we can reconstruct paleocolors; over millions of years some information is bound to be lost forever. In addition, because exceptional fossils with organic preservation are rare and precious, we must restrict destructive chemical sampling of them. As techniques advance, however, the new discoveries they afford will undoubtedly change our understanding of the past faster than ever before. Each one will bring us that much closer to seeing dinosaurs and other prehistoric creatures as they really were, in full Technicolor glory. SA

MORE TO EXPLORE

The Colour of Fossil Feathers. Jakob Vinther et al. in *Biology Letters,* Vol. 4, No. 5, pages 522–525; October 23, 2008.

3D Camouflage in an Ornithischian Dinosaur. Jakob Vinther et al. in *Current Biology,* Vol. 26, No. 18, pages 2456–2462; September 26, 2016.

FROM OUR ARCHIVES

Taking Wing. Stephen Brusatte; January 2017.

scientificamerican.com/magazine/sa

ROBOTICS

AM I HUMAN?

RESEARCHERS NEED NEW WAYS TO DISTINGUISH ARTIFICIAL INTELLIGENCE FROM THE NATURAL KIND

By Gary Marcus

GETTY IMAGES (*fingerprint*)

Illustrations by Zohar Lazar

>> In 1950 Alan Turing devised a thought experiment that has since been revered as the ultimate test of machine intelligence. He called it the "imitation game," but most people know it as the Turing test. Anticipating what we now call chat bots—computer programs that masquerade as humans—Turing envisioned a contest in which a machine tries to trick an interrogator into believing it is human, answering questions about poetry and deliberately making mistakes about arithmetic. Today, in the eyes of the general public, the Turing test is often seen as a kind of a Rubicon, a measure of whether machines have truly arrived. But it shouldn't be: the Rubicon can be passed, though for the wrong reasons. It is now possible to build machines that fool people, at least for brief periods—but the victories are fleeting, and they do not seem to be carrying us even close to genuine intelligence.

Gary Marcus is director of Uber AI Labs and a professor of psychology and neural science at New York University. His most recent book, co-edited with Jeremy Freeman, is *The Future of the Brain* (Princeton University Press, 2014).

The problem is that Turing's test is too easily gamed. One can "win" simply by being deceptive or feigning ignorance. As Turing himself partly anticipated, the trick to winning is mostly *not* to answer the questions. If a judge asks a machine, "Do you have feelings?" the machine must lie to win. But that odd twist is not an exception—it is the rule. The way to win the Turing test is to deceive.

In 2014, for example, a chat bot named "Eugene Goostman" supposedly "won" the Turing test by pretending to be a sarcastic 13-year-old boy from Odessa, Ukraine, who never answered questions directly. Some judges were fooled (about a third, enough to count as a shallow victory). But so what? The judges got only a few minutes to conduct their interviews, and they undoubtedly would have ferreted out the truth soon enough. In reality, Eugene knew—and understood—almost nothing. Consider this dialogue, which computer scientist Scott Aaronson had with the bot:

SCOTT: *Which is bigger, a shoebox or Mount Everest?*
>> EUGENE: *I can't make a choice right now. I should think it out later. And I forgot to ask you where you are from …*
SCOTT: *How many legs does a camel have?*
>> EUGENE: *Something between 2 and 4. Maybe, three? :-))) By the way, I still don't know your specialty—or, possibly, I've missed it?*
SCOTT: *How many legs does a millipede have?*
>> EUGENE: *Just two, but Chernobyl mutants may have them up to five. I know you are supposed to trick me.*
SCOTT: *No, I need to know that you're not a chatbot. Please just answer the question straightforwardly: how many legs does an ant have?*
>> EUGENE: *Something between 2 and 4. Maybe, three? :-))) Oh, what a fruitful conversation ;-).*

Clearly, Turing's original test has not withstood the test of time.

Not long after Goostman hit the media, I sug-

IN BRIEF

In the mind of the public, Alan Turing's "imitation game," in which a machine tries to convince an interrogator that it is human, has long been considered the ultimate test of artificial intelligence.

But Turing's test has not aged well. Passing it is more a matter of deception than of true intelligence. AI experts argue that the time has come to replace Turing's test with a battery of events that will assess machine intelligence from many different perspectives.

A truly intelligent machine should be able to understand ambiguous statements, build a piece of flat-packed furniture, pass a fourth-grade science test, and more. The difficulty of these tasks underscores the fact that, hype aside, human-level artificial intelligence remains very far in the future.

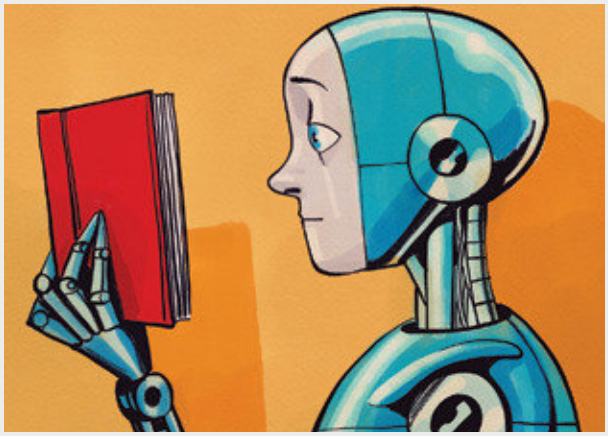
TEST 01

THE NEW TURING TESTS

AI researchers are developing a variety of tests to replace Alan Turing's 67-year-old "imitation game." Here's a look at four different approaches.

By John Pavlus

TEST 02



Winograd Schema Challenge

Named after pioneering AI researcher Terry Winograd, a "Winograd schema" is a simple but ambiguously worded natural-language question. Answering correctly requires a "commonsense" understanding of how agents, objects and cultural norms influence one another in the real world.

Winograd's first schema, which he wrote in 1971, sets a scene ("The city councilmen refused the demonstrators a permit because they feared violence") and then poses a simple question about it ("Who feared violence?"). This is known as a pronoun disambiguation problem (PDP): in this case, there is ambiguity about whom the word "they" refers to. But Winograd schemas are subtler than most PDPs because the meaning of the sentence can be reversed by changing a single word. (For example: "The city councilmen refused the demonstrators a permit because they *advocated* violence.") Most people use "common sense" or "world knowledge" about typical relationships between city councilmen and demonstrators to resolve the problem. This challenge uses an initial round of PDPs to weed out less intelligent systems; ones that make the cut are given true Winograd schemas.

PROS: Because Winograd schemas rely on knowledge that computers lack reliable access to, the challenge is robustly Google-proof—that is, hard to game with Internet searches.

CONS: The pool of usable schemas is relatively small. "They're not easy to come up with," says Ernest Davis, a professor of computer science at New York University.

DIFFICULTY LEVEL: High. In 2016 four systems competed to answer a set of 60 Winograd schemas. The winner got only 58 percent of the questions correct—far short of the 90 percent threshold that researchers consider a passing grade.

WHAT IT IS USEFUL FOR: Distinguishing comprehension from mere simulations of it. "[Apple's digital assistant] Siri has no understanding of pronouns and cannot disambiguate," explains Leora Morgenstern, a researcher at Leidos who worked on the Winograd Schema Challenge with Davis. That means "you really can't carry on a dialogue [with the system], because you're always referring to something previous in the conversation."

Standardized Testing for Machines

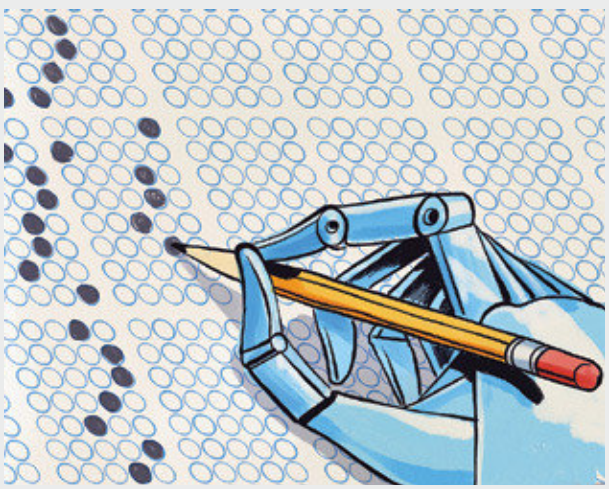
AI would be given the same standardized, written educational tests that we give to elementary and middle school students, without any handholding. The method would assess a machine's ability to link facts together in novel ways through semantic understanding. Much like Turing's original imitation game, the scheme is ingeniously direct. Simply take any sufficiently rigorous standardized test (such as the multiple-choice parts of New York State's fourth-grade Regents science exams), equip the machine with a way of ingesting the test material (such as natural-language processing and computer vision) and let 'er rip.

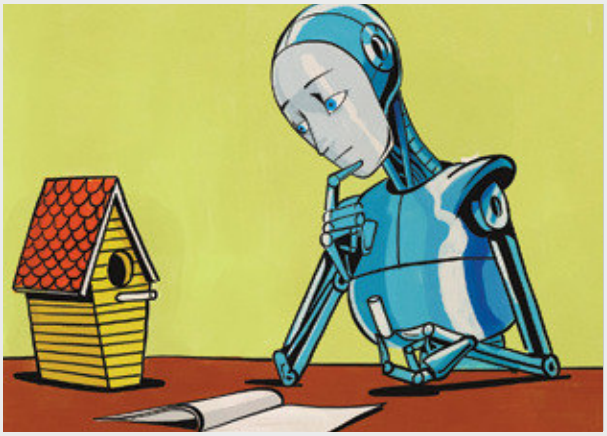
PROS: Versatile and pragmatic. Unlike Winograd schemas, standardized test material is cheap and abundant. And because none of the material is adapted or preprocessed for the machine's benefit, test questions require a wealth of versatile, commonsense world knowledge just to parse, much less answer correctly.

CONS: Not as Google-proof as Winograd schemas, and as with humans, the ability to pass a standardized test does not necessarily imply "real" intelligence.

DIFFICULTY LEVEL: Moderately high. A system called Aristo, designed by the Allen Institute for Artificial Intelligence, achieves an average 75 percent score on the fourth-grade science exams that it has not encountered before. But this is only on multiple-choice questions without diagrams. "No system to date comes even close to passing a full 4th grade science exam," the Allen Institute researchers wrote in a technical paper published in *AI Magazine*.

WHAT IT IS USEFUL FOR: Administering reality checks. "Fundamentally, we can see that no program can get above 60 percent on an eighth-grade science test—but at the same time, we might read in the news that IBM's Watson is going to medical school and solving cancer," says Oren Etzioni, CEO of the Allen Institute for Artificial Intelligence. "Either IBM had some startling breakthrough, or perhaps they're getting a little bit ahead of themselves."





Physically Embodied Turing Test

Most tests for machine intelligence focus on cognition. This test is more like shop class: an AI has to physically manipulate real-world objects in meaningful ways. The test would comprise two tracks. In the construction track, a physically embodied AI—a robot, essentially—would try to build a structure from a pile of parts using verbal, written and illustrated instructions (imagine assembling IKEA furniture). The exploration track would require the robot to devise solutions to a set of open-ended but increasingly creative challenges using toy blocks (such as "build a wall," "build a house," "attach a garage to the house"). Each track would culminate with a communication challenge in which the robot would be required to "explain" its efforts. The test could be given to individual robots, groups of robots or robots collaborating with humans.

PROS: The test integrates aspects of real-world intelligence—specifically, perception and action—that have been historically ignored or underresearched. Plus, the test is essentially impossible to game: "I don't know how you would, unless someone figured out a way to put instructions for how to build anything that's ever been built on the Internet," says Ortiz of Nuance.

CONS: Cumbersome, tedious and difficult to automate without having machines do their construction in virtual reality. Even then, "a roboticist would say that [virtual reality] is still only an approximation," Ortiz says. "In the real world, when you pick up an object, it might slip, or there might be a breeze to deal with. It's hard for a virtual world to faithfully simulate all those nuances."

DIFFICULTY LEVEL: Science-fictional. An embodied AI that can competently manipulate objects *and* coherently explain its actions would essentially behave like a droid from *Star Wars*—well beyond the current state of the art. "To execute these tasks at the level at which children can do them routinely is an enormous challenge," Ortiz says.

WHAT IT IS USEFUL FOR: Imagining a path to integrating the four strands of artificial intelligence—perception, action, cognition and language—that specialized research programs tend to pursue separately.

I-Athlon

In a battery of partially or completely automated tests, an AI is asked to summarize the contents of an audio file, narrate the storyline of a video, translate natural language on the fly and perform other tasks. The goal is to create an objective intelligence score. Automation of testing and scoring—without human supervision—is the hallmark of this scheme. Removing humans from the process of evaluating machine intelligence may seem ironic, but Murray Campbell, an AI researcher at IBM (and a member of the team that developed Deep Blue), says it is necessary to ensure efficiency and reproducibility. Establishing an algorithmically generated intelligence score for AIs would also free researchers from relying on human intelligence—"with all its cognitive biases," Campbell notes—as a yardstick.

PROS: Objectivity, at least in theory. Once I-Athlon judges decided on how to score each test and weight the results, computers would do the actual scoring and weighting. Judging the results should be as cut-and-dried as reviewing an Olympic photo finish. The variety of tests would also help identify what the IBM researchers call "broadly intelligent systems."

CONS: Inscrutability, potentially. I-Athlon algorithms might give high marks to AI systems that operate in ways that researchers do not fully understand. "It is quite possible that some decisions of advanced AI systems will be very difficult to explain [to humans] in a concise and understandable way," Campbell admits. This so-called black box problem is already becoming an issue for researchers working with convolutional neural networks.

DIFFICULTY LEVEL: It depends. Current systems could perform quite well on some potential I-Athlon events, such as image understanding or language translation. Others, such as explaining the contents of a video narrative or drawing a diagram from a verbal description, are still in the realm of sci-fi.

WHAT IT IS USEFUL FOR: Reducing the impact of human cognitive biases on the work of measuring machine intelligence and quantifying—rather than simply identifying—performance.

John Pavlus is a frequent *Scientific American* contributor.

gested an alternative test, designed to push toward real intelligence rather than just dubious evasion. In a *New Yorker* blog post, I proposed that Turing's test be dumped in favor of a more robust comprehension challenge—"a Turing Test for the twenty-first century."

The goal, as I described it then, was to "build a computer program that can watch any arbitrary TV program or YouTube video and answer questions about its content—'Why did Russia invade Crimea?' or 'Why did Walter White consider taking a hit out on Jessie?'" The idea was to eliminate the trickery and focus on whether systems could actually comprehend the materials to which they were exposed. Programming computers to make wisecracks might not bring us closer to true artificial intelligence, but programming them to engage more deeply in the things that they see might.

Francesca Rossi, then president of the International Joint Conferences on Artificial Intelligence, read my proposal and suggested we work together to make this updated Turing test a reality. Together we enlisted Manuela Veloso, a roboticist at Carnegie Mellon University and former president of the Association for the Advancement of Artificial Intelligence, and the three of us began to brainstorm. Initially we focused on finding a single test that could replace Turing's. But we quickly turned to the idea of *multiple* tests because just as there is no single test of athletic prowess, there cannot be one ultimate test of intelligence.

We also decided to get the AI community as a whole involved. In January 2015 we gathered some 50 leading researchers in Austin, Tex., to discuss a refresh of the Turing test. Over a full day of presentations and discussion, we converged on the notion of a competition with multiple events.

One of those events, the Winograd Schema Challenge, named for AI pioneer Terry Winograd (mentor to Google's Larry Page and Sergey Brin), would subject machines to a test in which language comprehension and common sense intersect. Anyone who has ever tried to program a machine to understand language has quickly realized that virtually every sentence is ambiguous, often in multiple ways. Our brain is so good at comprehending language that we do not usually notice. Take the sentence "The large ball crashed right through the table because it was made of Styrofoam." Strictly speaking, the sentence is ambiguous: the word "it" could refer to the table or the ball. Any human listener will realize that "it" must refer to the table. But that requires tying knowledge of materials science with language comprehension—something that remains far out of reach for machines. Three experts, Hector Levesque, Ernest Davis and Leora Morgenstern, have already developed a test around sentences like these, and speech-recognition company Nuance Communications is offering a cash prize of $25,000 to the first system to win.

Our hope is to include many others, too. A Comprehension Challenge in which machines are tested on their ability to understand images, videos, audio and text would be a natural component. Charles Ortiz, Jr., director of the Laboratory for Artificial Intelligence and Natural Language Processing at Nuance, proposed a Construction Challenge that would test perception and physical action—two important elements of intelligent behavior that were entirely absent from the original Turing test. And Peter Clark of the Allen Institute for Artificial Intelligence proposed giving machines the same standardized tests of science and other disciplines that schoolchildren take.

Aside from the tests themselves, conference attendees discussed guidelines for what counts as a good test. Guruduth Banavar and his colleagues at IBM, for example, emphasized that the tests themselves should be computer-generated. Stuart Shieber of Harvard University emphasized transparency: if the events are to push the field forward, awards should be given only to systems that are open—available to the AI community as a whole—and replicable.

When will machines be able to rise to the challenges that we have set? Nobody knows. But people are already taking some of the events seriously, and that could matter for the world. A robot that has mastered the Construction Challenge could, for example, set up temporary camps for displaced people—on Earth or distant planets. A machine that could pass the Winograd Schema Challenge and a fourth-grade biology exam, for example, would bring us closer to the dream of machines that can integrate the vast literature on human medicine, perhaps a vital first step toward curing cancer or deciphering the brain. AI, like every field, needs clear goals. The Turing test was a nice start; now it is time to build a new generation of challenges. SA

Just as there is no single test of athletic prowess, there cannot be one ultimate test of intelligence.

MORE TO EXPLORE

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AGRICULTURE

CORNBOY VS. THE BILLION-DOLLAR BUG

Technology to defeat the corn rootworm, scientists worry, will work only briefly against an inventive foe

By Hannah Nordhaus

Photographs by Patrick Cavan Brown

BUG PATROL: Perched on a scaffold 30 feet above an Illinois cornfield, a researcher looks for flying Western corn rootworms, a pest (*inset*) that can destroy entire corn crops.

Hannah Nordhaus is author of *The Beekeeper's Lament* (Harper Perennial, 2011) and *American Ghost* (Harper, 2015). She writes about science, history and the natural world and lives in Boulder, Colo.

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THERE IS, DESPITE THE NAME, NOTHING URBAN ABOUT PIPER CITY, ILL.

It is a farm town with a skyline of grain elevators, a tidy grid of pitch-roofed houses and, a few blocks beyond, endless fields: corn, soybean, corn, soybean, corn, corn, corn, perfectly level, perfectly square, no trees, no cows, no hedgerows, no bare land. In late August of 2013, a man named Joseph Spencer followed a corn-flanked county road northwest from Piper City until his GPS advised him to leave the road altogether and turn onto a gravel track. Spencer, an entomologist who studies farm insects, was looking for a farmer named Scott Wyllie.

In good growing years, crop corn around Piper City and elsewhere is as standardized and predictable as a widget rolling off an assembly line: the plants have the same spacing, the same height. Wyllie's corn, however, had developed a personality. The stalks had twisted back on themselves like the neck of a goose. Spencer could pull one from the ground with a flick of his wrist; the once white roots underneath were gnawed and brown, like teeth gone rotten. Some plants had tipped over from their own weight. And the air was teeming with grain-sized, yellow-and-black striped beetles. They clambered on leaves, mating, defecating and munching on corn silk. Spencer had to close his mouth to keep the insects out.

The beetles are Western corn rootworms, and it had been their wormlike larvae that gnawed Wyllie's corn roots to destruction. Wyllie, who farms 1,000 acres, told Spencer he had done everything the experts recommended to fight the insects. He rotated his corn crop with soy every other year to interrupt the rootworm food supply. He planted corn seeds that were genetically engineered to release a toxic protein that kills the hungry larvae. But in the field that day, Spencer could see that these approaches—the most successful and widely used strategies to fight the pest—had failed. "I got a chill down my back," Spencer remembers. "I thought, 'This is it. The worst-case scenario.'" Spencer has spent most of his career studying rootworm behavior at the Illinois Natural History Survey at the University of Illinois at Urbana-Champaign. And he knew that the insects swirling around him meant trouble not only for Wyllie's crop but for the entire Midwestern corn belt.

The rootworm—*Diabrotica virgifera virgifera*—is the most expensive and consequential pest in American agriculture. It is known as the "billion-dollar bug"—although in fact it probably costs the U.S. closer to $2 billion every year. The beetle spends its life cycle on corn, and corn is the nation's largest crop by far. It

IN BRIEF

The most costly beetle in the U.S. keeps evolving ways to resist pesticides designed to protect a $50-billion corn industry.

The latest attempt, from Monsanto, involves embedding molecules in corn that target specific rootworm genes, killing the insect.

But the real problem, scientists assert, are giant, single-crop farms that give the pests chances to adapt and survive.

ROOT OF EVIL: Entomologist Joseph Spencer eyes adult rootworms captured in a screened tent, monitoring their behavior (*1*). The larvae of these insects chew on corn roots, destroying the plant and laying waste thousands of acres of valuable crops (*2*).

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frequently covers 80 million acres and sometimes more. The crop brings in $50 billion in annual sales. Farmers spend hundreds of millions in chemicals, seeds and labor fighting it. Agriculture companies spend hundreds of millions developing products to help them do so.

The result is an evolutionary arms race: the beetle damages farmers' crops; seed companies create a product to kill it; the beetle evolves to resist the product; the corn gets infested again. And then, "just in time, the good guys in the white hats ride into town," Spencer says, with a new beetle-killing weapon. For the past decade the weapon of choice has been famously controversial genetically modified corn plants that make chemicals to kill rootworm larvae. But Spencer saw in Wyllie's fields that rootworms were winning.

Today farmers and scientists are pinning their hopes on a new modification—a corn laced with special genetic molecules that work within a rootworm cell nucleus to shut down crucial genes. The new technology should arrive in fields by the end of this decade. But environmentalists are concerned gene alterations may harm helpful insects such as ladybugs. And scientists and farmers alike know it is only a matter of time until the rootworm evolves to resist the new corn. "You can't stop resistance," Spencer says. "You can only slow it down."

BEHAVIOR CHANGE

SPENCER'S OFFICE at the Illinois Natural History Survey is littered with corn paraphernalia: corn-themed signs, mugs, bottles and silverware he picked up from eBay. His colleagues there call him "Cornboy," and although Spencer turned 53 last October, there is indeed something boyish about him, from his Dennis the Menace grin to his impish enthusiasm for all things corn and rootworm. (Draped over his desk chair is a T-shirt he made: two mating rootworms and the caption, "We like to watch.")

His calling was born of calamity. In 1987 an entomologist with the Natural History Survey named Eli Levine got a call from a Piper City grain-elevator agronomist who was seeing damage in corn that had been rotated with soy. Scientists believed this to be impossible. Because Western corn rootworms feed exclusively on corn and lay their eggs there, farmers had been able to control the beetles simply by swapping corn and soy fields every year—when the larvae emerged in soy the next spring, there was nothing for them to eat. Levine drove out to Piper City to look for another explanation. There wasn't one. "The beetles were laying eggs in soy," he says.

This wasn't the first time the rootworm had changed its behavior. When entomologist John Lawrence LeConte first wrote about the beetle in Kansas in 1868, it was a harmless chewing insect from Central America found in low populations on the Western Great Plains. The adults emerged from the ground in early summer, fed on maize, squash and prairie grasses, mated, laid eggs in crevices in the soil, and died before the first frost. In the spring, the eggs hatched into tiny, white, maggotlike larvae, feeding underground on roots until it was time to emerge.

It was only with the advent of efficient center-pivot irrigation in the 1950s, which allowed continuous mass production of corn, that rootworms spread east from Colorado and Kansas across prairie lands that had been converted to cornfields. By 1964, when the beetles arrived in Illinois, they were already resistant to many of the insecticides farmers used to fend them off. And sometime before Levine visited Piper City, some mu-

tant females did something they had never done before: a restless few flew into a field of soy and found that their guts could tolerate soybean foliage long enough to lay eggs there. The next year their progeny emerged to a feast of corn. It was an immensely advantageous adaptation. The beetles had found a way to resist not only modern pesticides but also modern farming practices.

In 1996, after growers in Illinois and Indiana suffered massive losses to these new rootworms—the infestation was so bad that window washers on Chicago's Sears Tower reported masses of wind-borne beetles mobbing their platforms—the survey hired Spencer to study the rootworm's troubling new behavior. Spencer had done his graduate work on onion flies, and his talks on the obscure insects attracted only a couple of hundred people, max. When he gave his first lecture on rootworms, however, more than 1,500 farmers and researchers attended. The crowd was dead-silent, rapt. "I thought, 'Wow, this is a cool insect. People care about it,'" he says.


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TARGETED INSECTICIDE

AS RESISTANT BEETLES continued to spread from Illinois to Iowa, Michigan, Missouri, Ohio, Ontario and Wisconsin, farmers found themselves in a bind. Their livelihoods depended on healthy corn, and they felt they had little choice but to douse acre after acre of their seeds with high levels of toxic, broad-spectrum insecticides. Nobody—not farmers, not entomologists, and especially not the Environmental Protection Agency—was happy about it.

Which is why, in 2003, when the agribusiness behemoth Monsanto came out with a hybrid corn engineered to produce a protein that killed rootworms, farmers rushed to get it into their fields. The company (which funds some of Spencer's research) had already produced a hybrid corn plant with an added gene from a soil bacterium, *Bacillus thuringiensis* (Bt), that was toxic to a moth called the European corn borer. The product proved remarkably effective: there are so few corn borers now, Spencer says, that his current graduate student has never seen the moths outside of a laboratory. Monsanto used a different strain of Bt to engineer the new anti-rootworm toxin, called Cry3Bb1, which bound to the guts of rootworm larvae, creating holes in the worms' digestive lining and killing them.

For about five years farmers who planted the new rootworm-killing seed achieved the same happy results they had seen with the corn borer. But in 2009 Iowa farmers began seeing damage again, and it soon became clear that some rootworm populations had developed resistance. The beetles in Wyllie's field, in fact, proved impervious to crop rotation and to at least two types of Bt toxins. They were, Spencer says, "the baddest rootworms around." Last summer scientists documented resistance to a third toxin; a fourth one has held up in the field, but lab tests indicate that some populations are growing less susceptible to that toxin as well.

Because resistance appears inevitable, Spencer is taking a closer look at rootworm behavior, hoping to figure out which rootworms are most likely to move around and spread troublesome traits—not all the insects disperse equally. It is possible that knowledge could help contain the pests, he says, by helping the ag companies design and deploy the "next best thing in a way that matches the reality of what the insects are capable of."

On a humid afternoon last July, he and a team of student helpers head out to the Lost 40, a test plot located near the Natural History Survey labs, where four yellow, 30-foot scaffolds loom over the fields. Spencer grabs a bug net and a cooler full of vials and dry ice, hooks them to a carabiner and climbs a scaffold. "Up we go!" he says, "to get the best view in Illinois!" Three helpers head up the three other platforms—two in corn and

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LOOKING FOR A WEAKNESS: In a greenhouse, Spencer grows corn that releases a beetle-killing toxin (*1*). Spencer examines rootworm larvae under a microscope (*2*). In a research laboratory, scientists care for rootworm eggs for five months until the larvae hatch (*3*). After hatching, the larvae are driven off roots by heat lamps and collected at the bottom of funnels (*4*).

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another that towers above a crosshatched corduroy of soy. Other students move to spots on the ground in strips between fields. "Everybody turn on their walkie," Spencer says. He's the geek explorer: Tilley hat, khaki bandanna, zip-off pants, stopwatch, reading glasses, multiple pens in his pocket. He waves his net high in the air. "In 40 seconds we're going to start the 6:17 collection," he announces.

The team plans to conduct eight collection periods of 10 minutes apiece, during which they will catch as many rootworms as possible. By doing so, Spencer hopes to better understand "the populations that leave and the ones that don't"—and whether beetles that resist Bt corn and crop rotation are more likely to leave their home fields. Some rootworms are talented long-distance travelers. Once the insects rise above the layer of turbulent air below the scaffolds, he says, "they're going to go a long way." They can relocate as far as 100 miles if caught in the convective updrafts of thunderstorms. Spencer has old photographs of billions of rootworms piled two to three inches deep along the shore of Lake Michigan after one such storm.

From above, the corn looks like a very large marching band, tasseled hats crowded impossibly close—"the massed multitudes," Spencer says. When he first arrived in Illinois, he sometimes caught up to 15 beetles a minute. "It snowed rootworms." But beetle populations have been low in the post-Bt years, and floods in the spring of 2015, which drowned many larvae in the ground, suppressed populations even further. That summer he caught nine beetles all season. He calculates that the effort cost his lab about $89,400 per rootworm ounce, with labor and material costs. That is more than 80 times the price of gold. (Now every spring he offers his students a prize: 10 gold dollars if they catch the first adult rootworm of the season. Then Spencer eats the insect. "They're not delicious or anything," he says. The wing casings get caught in his teeth.)

The sun drops lower over the jungle of corn. Spencer sees something off in the middle distance. He races across the scaffold, leans far out over the guard rail, and swishes his net up and out. "Woohoo! I caught a rootworm!" He examines the beetle deep in the net—"My heart's racing!"—then opens the cooler and flash-freezes it—"Put her in a vial, blink! Awesome." It is one of nine beetles the team will catch that night.

The next day he and his team dissect the insects in the lab, grinding each one into a vial of "beetle gemish" and testing their gut contents. The fields around the scaffolds are planted with two types of corn, each engineered with a different Bt trait. Dipping gene check sticks—they look like pregnancy tests—in the bug smoothie, Spencer "interrogates the beetles' digestive systems" to determine which proteins are in their guts and thus where the beetles fed during the previous 24 hours. If an insect tests positive for a trait not present in his own fields or for two different traits, he knows that beetle is a "mover." The team also sets up tents within cornfields, slurping the beetles up with "bugsuckers," modified shop vacuums that look like Ghostbusters proton packs. If those beetles come from fields planted with rootworm-killing Bt, he knows they have developed resistance.

Spencer puts on magnifying "nerd goggles" and places a larva under a microscope—it's a tiny, groping "neonate," between two and three millimeters long, white and newly hatched. It is in this life stage that the rootworm finds the corn roots on which it does much of its billion-dollar damage. "This little thing," he says, "is the worm that roars." Next he places six yellow-and-black adults under the microscope; they run up and down the sides of their clear-plastic cage. One mated female camps herself in a corner with a corn silk. In an instant, she gobbles the filaments down to nothing. Her swollen, oily abdomen wiggles as she eats, and a froth spreads across her face. It is almost, I dare say, cute. But her hunger—her desperate evolutionary drive to survive and reproduce—is anything but.

A GENETIC ATTACK

THE AG COMPANIES haven't, of course, given up on taming that hunger. Monsanto, DuPont Pioneer, Syngenta and Dow Agro-

Sciences all sell engineered seeds that kill rootworms, and they, too, have evolved in the face of growing insect resistance to their products. In 2009 they began to combine different Bt toxins for rootworms into one corn plant. These "stacked" products offer a more effective strategy for delaying resistance, working from different angles much as a multidrug "cocktail" does to control HIV in humans. After Wyllie's bad summer in 2013, he switched to a stacked Bt corn, and his beetles are now under control. But with three of the four traits on the market failing, there may not be anything to stack in coming years. "If you have a trait that's already compromised and you combine it with another trait that's working well," Spencer says, "it's functionally acting like a single-drug cocktail," rendering the good trait more vulnerable to resistance without the protection of a second effective trait. Farmers need new ingredients to add to the cocktail. Researchers at DuPont Pioneer recently announced the discovery of a new bacterial gene that kills rootworms, but because it takes about 12 years and $136 million to shepherd a new GM trait through the regulatory process, it will not be available to farmers any time soon.

TINY TERROR: Larvae, which look like worms about two millimeters in length, pack a destructive punch that belies their size. They can easily ruin hundreds of millions of dollars of corn in a year.

There is one new ingredient that may join the cocktail sooner, however. Monsanto is seeking regulatory approval for a corn seed that would integrate two older Bt toxins with a new technology called RNA interference, or RNAi. The technology uses targeted RNA—the ubiquitous molecule that transmits genetic code and helps to assemble proteins—to turn off or turn down specific genes. When rootworm larvae eat the corn, segments of double-stranded RNA, created in a lab and incorporated into the plant, bind to and interfere with an insect gene that produces proteins essential to waste storage and disposal within the rootworms' cells. Without those proteins, the insects die.

The RNAi trait has received initial regulatory approval from the U.S. Department of Agriculture and the Environmental Protection Agency, and Monsanto hopes that the final Bt-RNAi corn seed will win EPA approval by the end of this decade. If it does, it would be the first wide-scale application of RNA interference in corn agriculture. (Monsanto currently has an experimental-use permit to test the product on outdoor plots.)

It is a promising technology. Traditional pesticides function much like incendiary bombs, destroying intended targets, such as rootworms, but creating vast collateral damage among beneficial insects, aquatic species, birds and mammals. RNAi works, instead, like a ninja, using unique sequences of synthetic genetic code to take out only its intended victim, then disappearing (RNA degrades quickly in the environment). "It's the ideal pesticide," says Stephen Levine, a toxicologist at Monsanto. "It's specific. It does what it's supposed to do. Then it goes away."

That is the theory, anyway. In a 2012 paper, however, a Chinese research team reported that it found snippets of RNA from food plants in the livers of mice that consumed those plants. The RNA affected a cholesterol-regulating gene also found in humans. This "cross-kingdom effect" was surprising because these types of RNA were not thought to survive in the hostile environment of the mammalian gut; if true, the results raised the possibility that RNAi in plants could affect humans. A study presented at a conference in 2013 found that RNA created to kill rootworms could also kill ladybugs, a beloved beneficial insect. That same year Jonathan Lundgren, an entomologist then at the USDA's North Central Agricultural Research Laboratory in Brookings, S.D., published a paper suggesting that RNAi could affect nontarget organisms in unexpected ways. He also says the USDA hindered the publication of another paper he wrote about RNAi and honeybee genomes. Lundgren has since resigned and filed a federal whistle-blower suit. "I'm not against RNAi," he says, "but the potential exposure of a corn product is so large."

RNAi is the perfect example, says Martha Crouch of the Center for Food Safety, of the "chaos of an emerging technology" that seems to promise only progress, until "the oops moment when something unexpected and harmful" happens—such as ozone holes, carcinogenic children's pajamas, rat-sized-rootworms. "There are," Lundgren adds, "too many knowledge gaps."

But many scientists think there is ample evidence of safety. Despite efforts to do so, other researchers have been unable to reproduce the rodent findings. In considering approval of Monsanto's RNAi-engineered corn plant, an EPA panel concluded that "there is no convincing evidence" that double-stranded RNA is absorbed in the guts of humans or other mammals in a form that causes harm. "What are the chances that it will affect humans? Essentially zero," says Craig Mello, a molecular biologist at the University of Massachusetts Medical School who co-discovered RNAi in 1998 and won a Nobel Prize for that discovery in 2006. RNAi is very organism-specific, adds Monsanto toxicologist Pamela Bachman. Rootworms do share some gene

sequences with other insects, including the one that killed ladybugs in the 2013 study. But Monsanto's product targets a sequence that is not shared with ladybugs or other beneficial insects found near cornfields. "Sequence matters," she says.

CONTAINMENT

AT DAVID MASCHING'S 2,300-acre farm outside Piper City, Spencer meets with a group of corn growers, Wyllie among them. They sit around a table in a barn that looks more like a hangar, with soaring ceilings to accommodate Masching's impressive collection of farm machines.

Under a microscope is a tiny, groping "neonate," between two and three millimeters long, white and newly hatched. It is in this life stage that the rootworm finds the corn roots on which it does much of its billion-dollar damage. "This little thing," entomologist Joseph Spencer says, "is the worm that roars."

The growers wear ball caps, work boots, T-shirts. None farm fewer than 1,000 acres, and all work their land alone, with some family and seasonal help. Even so, margins are slim. When corn prices approached $7 per bushel in 2012, a northern Illinois corn farmer could clear more than $300 per acre after paying for seed, fertilizer, fuel, rent and crop treatments. But corn prices plunged in 2015, and growers lost $65 for each acre they planted. "You can understand," says Spencer's retired colleague Michael Gray, who joined Spencer in Masching's barn, "why producers don't take a chance with rootworms."

Nor other organisms, for that matter. On the way to Piper City, Spencer points out a crop-dusting plane, laden with a "tank mix" of wide-ranging fungicides and pyrethroid insecticides, swooping and angling above the fields. In cornfields worked by most Illinois farmers, you are not likely to see bugs. "It's disconcerting for an entomologist to go into a cornfield and not see an insect," Spencer says. "The ground is sterile. That's what farmers want."

Farmers want security, whether delivered by engineered seeds or dropped from the sky by crop dusters—even if this "insurance mindset," as Spencer describes it, speeds up the treadmill of chemicals and resistance. Farmers want predictability. Where growers once rotated corn, wheat, alfalfa, sorghum and oats, it is now corn and soy and corn and soy again. The rootworm thrives on predictability. Monoculture makes it easy for a lone grower to farm 2,000 acres. But it also makes it easy for the rootworm to destroy those acres. "We created this pest," Gray says. "We gave it a wonderful life," Spencer adds.

Life has been less wonderful for the rootworm in Europe, where the insect turned up in the early 1990s; it seems to have hitched a plane ride from Chicago to Serbia and spread from there. The beetle's trans-Atlantic journey prompted European farmers to fear the same levels of devastation seen in the U.S. But Europe has smaller farms, whose operators plant less corn and rotate it with a wider variety of plants. The insect does some damage in regions where farmers plant corn continuously, but overall populations remain under control. "The rootworm is not a problem in Europe," says researcher Stefan Vidal of the University of Göttingen in Germany, who helped to coordinate the European Union–funded response to the rootworm invasion. Diversity, European farmers concluded, is the best defense.

In the American corn belt, farmers do not feel they have that option. They are too big to fail, yoked to horizon-to-horizon economies of scale and the technological investments that enable them to make a living in America's hyperspecialized commodity market: the $400,000 combines, the hangar-sized barns, the pesticides, engineered seeds and the double-stranded RNA. It has become an escalating arsenal of silver bullets that inevitably miss their shifting mark.

Rootworms have brains so small that you can barely dissect them. But evolution has its own intelligence. "It's a lesson that we have failed to learn over and over and over," Spencer says. "Natural selection is always going to win. SA

DISCLOSURE: In 2014 Nordhaus moderated a panel session, organized by Monsanto, on honeybees at an environmental conference. Monsanto paid her travel expenses.

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FROM OUR ARCHIVES

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Testing every newborn for a raft of known genetic risks is technologically feasible. Some worry the results could do more harm than good

By Bonnie Rochman

GENOMICS

SHOULD BABIES BE SEQUENCED?

IN 2010 IN TEXAS, JENNIFER GARCIA HAD A BABY, A LITTLE BROTHER FOR HER FOUR-YEAR-OLD SON. She named him Cameron. Garcia had opted to do prenatal testing for conditions that included Down syndrome and cystic fibrosis with both boys. The tests came back fine. Once her sons were born, she did not think twice about having their heels pricked in the hospital and the resulting droplets of blood scanned for about 30 diseases that make up the standard newborn-screening test administered to babies born in hospitals throughout the Lone Star State.

Months passed, and Cameron grew, lifted his head, smiled at his parents. He looked healthy and strong, hovering in the 90th percentile for height and weight for babies his age. He laughed at the family dog. He learned to logroll across a room to reach a toy. Then, at seven months old, he got pneumonia. In the hospital, he suffered seizures and had to be intubated. CT scans and MRIs followed, then EEGs, spinal taps and blood transfusions.

No one knew what was wrong. First, doctors thought Cameron had meningitis, then pertussis, then tuberculosis, so they plied him, just in case, with antiseizure medications, antibacterials, antivirals and antifungals. Specialists came and went, teams from critical care, pediatrics, neurology, epileptology, toxicology, immunology, infectious disease, respiratory therapy. Ten days after he was admitted to a major medical center in Houston, an answer to what was ailing Cameron finally emerged: an immunologist suspected he had severe combined immunodeficiency, a genetic disorder otherwise known as bubble boy disease. Children with severe combined immunodeficiency, or SCID, do not have a functioning immune system, which was why Cameron was not getting better.

Adapted from The Gene Machine: How Genetic Technologies Are Changing the Way We Have Kids—And the Kids We Have, *by Bonnie Rochman, by arrangement with Scientific American/ Farrar, Straus and Giroux (US), China Renmin University Press (China).*

STEPHEN MARKS *Getty Images*; PHOTOGRAPH FOR ILLUSTRATION PURPOSES ONLY

The diagnosis perplexed Garcia and her husband, John. They had no family history of SCID. In fact, they had never even heard of it. In any case, wasn't Cameron's newborn-screening test supposed to pick it up? Garcia started researching, and what she found left her in disbelief. Severe combined immunodeficiency is detectable via newborn screening, using the same dried blood spots that the Texas Department of State Health Services analyzes for the other diseases for which it scans. But Texas, along with most states at the time, did not screen for SCID. When SCID is identified early, before a baby falls seriously ill, a bone marrow transplant usually can cure the otherwise fatal condition, because it serves to replace the compromised immune system with a healthy version. More than 90 percent of babies who receive transplants in the first three and a half months of life recover. Cameron was already eight months old at his diagnosis, desperately ill and fighting for his life.

Understandably, Cameron's mother emphasizes the downsides of not screening for a disease if it is technically feasible. Cameron was born just one month after SCID had been added to the national list of recommended core newborn-screening conditions. Yet more than two years would pass before Texas would begin screening every baby for SCID. That was far too late for Cameron, who died on March 30, 2011. He was nine months old.

Since the night she left the hospital without Cameron in her arms, Garcia has become an activist who was ultimately instrumental in persuading Texas to include SCID among the diseases for which it screens. Knowing that all babies born in Texas hospitals are now tested for SCID makes Garcia's loss marginally bearable. "I wanted his little life to have meant something not just to our family.... I wanted people to know this little baby changed things and opened eyes for a lot of people...," Garcia said in a video about the importance of screening for SCID. "If we would have known Cameron had SCID, if we could have found that out earlier, before any infections, absolutely, 100 percent, Cameron would be here today."

But what if we did not have to go through the time-consuming process of adding new diseases, one by one, to the list of disorders that newborn screening can detect? What if one test could look for many of the diseases that newborn screening identifies, plus lots more?

The question is not hypothetical. In highly anticipated research that stands to overhaul what we know about health from the first moments of life, the National Institutes of Health has charged four university medical centers with studying the medical, behavioral, economic and ethical implications of using genome sequencing to map out the entirety of babies' genetic code. Would it be wise to sequence every baby's genome?

Bonnie Rochman is a journalist covering science, health and parenting. She formerly worked as a columnist for *Time* magazine and has written for the *New York Times Magazine* and the *Wall Street Journal*, among others.

NEWBORNS are already tested for a range of genetic conditions with a heel stick. The stick could also provide enough blood to screen for many more such disorders.

A THORNY ISSUE

THERE ARE OBVIOUS BENEFITS. Far more children who are at risk could be identified, allowing earlier treatment for someone whose life, like Cameron Garcia's, hinged on early detection. But inevitably, some parents will have to cope with finding out about health problems that cannot be mitigated and about the genetic missteps called variants of uncertain significance whose impact is unclear: they could indicate a problem, or they could simply be a string of DNA gobbledygook.

IN BRIEF

Many serious diseases that can be screened for at birth are not included in standard newborn genetic tests.
Full genome sequencing of newborns for existing and potential disorders is now technologically possible and might soon be economically feasible.
Scientists are exploring whether the resulting flood of genetic information will help parents and physicians care for newborns—or add unnecessary anxiety, complexity and cost.

DAN McCOY *Getty Images*

Depending on what results are returned to parents, many moms and dads will wind up finding out that the bulk of their child's genome is still incomprehensible. Michelle Huckaby Lewis, a trained pediatrician and lawyer who researches genetics policies at the Johns Hopkins Berman Institute of Bioethics, worries that could cause problems. "The genetics and subspecialty workforces will not be staffed adequately to meet the growing demand," she wrote in a commentary in *JAMA Pediatrics*. "Moreover, coveted appointments with subspecialists may be filled by children whose conditions may not manifest until later in life making access more difficult for those whose needs are more urgent."

What is the best way for doctors to incorporate this wealth of data into caring for the youngest and most vulnerable patients?

Regardless, it seems to be the direction in which health care is headed. "We are moving to a world where the technology will get so good and the cost will get so low that it will be very appealing to apply sequencing to not only sick people but well people," says geneticist Robert C. Green. Green co-leads the BabySeq Project, a newborn-screening study taking place in part at Harvard University–affiliated Brigham and Women's Hospital and Boston Children's Hospital, one of the four federally funded study sites.

BabySeq is examining how parents and doctors can use genomic data to improve children's health care. Green and his coleader, Alan Beggs, are studying 240 sick and 240 healthy newborns. They are randomly sequencing half of each group to assess whether parents of sick kids respond differently to sequencing results than do parents of healthy babies. Do parents of sick babies find the additional information helpful while parents of babies deemed healthy find it overwhelming? Does either group prefer the more limited picture provided by conventional newborn screening? What is the best way for doctors to incorporate this wealth of data into caring for the youngest and most vulnerable patients? The intent, Green says, is to answer some questions: "Is this scary or not? Is this useful? Is this likely to confuse the hell out of people or not?"

In a lead-up to the study, Green and his colleagues surveyed parents soon after their child's birth to ask if they would want to sequence their baby's DNA. They found a groundswell of interest in newborn sequencing. Three months later they went into greater detail, explaining to parents exactly what kinds of data that genome sequencing could generate about their children—cancer risk, for example, or predisposition for Parkinson's disease.

The percentage of parents who remained interested hardly budged. "This suggests there is a gigantic appetite out there for this, even in healthy babies," Green says. "It is going to be hard to resist."

Still, sequencing a baby and "vomiting the results out to the family," as Green characterizes it, "feels like it's very dangerous." The combination of anxious parents and doctors trying to interpret uncertain results seems particularly volatile. "People are a bit more sanguine about finding out stuff about themselves than they are about their kids," Green notes. "The salient question is harm. Depending on whom you talk to, there are all these theories about harm—about anxiety, distress, misconstruing information. All these questions are heightened when talking about babies because they aren't able to have a choice. This is a first opportunity to look for harm."

MODELING THE FUTURE

WHEN I VISITED BOSTON in the spring of 2015, the project was on the cusp of recruiting its first infant. I thought I would meet with one researcher, maybe two, but was greeted by half a dozen people—neonatologists, geneticists, genetic counselors—in a hospital conference room. It takes a village to raise a child—and to hash out the details of sequencing that child. They explained that BabySeq (which, by late 2016, had enrolled about 100 families) would limit the results it returns to parents to only those gene changes that are linked to diseases that take root in childhood. The infants' parents and their pediatricians would also be enrolled in the study, with the goal of assessing medical outcomes and impact on parent-child bonding, as well as whether the data are useful and how they are incorporated into a child's health care. In other words, does the massive influx of information from genome sequencing translate into better health care for a child? Does the benefit justify the costs, financially and emotionally?

"If you imagine a world where every baby could be sequenced quickly, how would that information be used by their doctors to facilitate their care, to make a diagnosis, to prescribe medication?" Green asks. "We're trying to model that situation at a time when it's not really easy or cheap to sequence and doctors aren't used to dealing with it. We're trying to model the future."

But not a speculative, far-off future, if Green's predictions are correct. "In five years, I am suggesting that sequencing will be given away as a freebie," he asserts. SA

MORE TO EXPLORE

Newborn Screening Controversy: Past, Present, and Future. Michelle Huckaby Lewis in *JAMA Pediatrics*, Vol. 168, No. 3, pages 199–200; March 2014.

Psychosocial Factors Influencing Parental Interest in Genomic Sequencing of Newborns. Susan E. Waisbren et al. in *Pediatrics*, Vol. 137, Supplement No. 1, pages S30–S35; January 2016.

The BabySeq Project: Preliminary Findings from a Randomized Trial of Exome Sequencing in Newborns. R. C. Green et al. Presented at the American Society of Human Genetics 2016 Annual Meeting, Vancouver, October 18–22, 2016.

FROM OUR ARCHIVES

Perils of Newborn Screening. Ariel Bleicher; July 2012.

scientificamerican.com/magazine/sa

RECOMMENDED

By Clara Moskowitz

MORE TO EXPLORE
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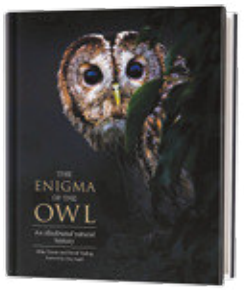
scientificamerican.com/mar2017/recommended

The Enigma of the Owl: An Illustrated Natural History

by Mike Unwin and David Tipling. Yale University Press, 2017 ($40)



ELF OWL, native to the southwestern U.S. and parts of Mexico, looks out from a saguaro cactus.

With their straight-on stares and nocturnal habits, owls are among the most intriguing and inscrutable of animals. In this large-format book, more than 200 photographs of owls in the wild and essays by nature writer Unwin help to demystify the creatures. The pictures, taken or selected by Tipling, catch owls on the wing, in the nest and on the hunt, providing a close-up look at dozens of species. Among the highlights: the Eurasian eagle owl, which can weigh up to 10 pounds and take down foxes and eagles, and the great grey owl, which, by sound alone, can locate and catch prey creeping underneath a layer of snow up to 30 feet below the bird's perch in a tree.

The Death and Life of the Great Lakes

by Dan Egan. W. W. Norton, 2017 ($27.95)

The Great Lakes are undergoing "an ecological catastrophe unlike any this continent has seen," according to Pulitzer Prize finalist Egan. Humans have dramatically altered the lakes' fauna since invasive species first snuck up through the man-made Saint Lawrence Seaway. Blunders sometimes stemmed from well-meaning policies. Researchers imported Asian carp to kill river nuisances without chemicals, and now some worry the fish has silently invaded Lake Michigan's floor via the Chicago Sanitary and Ship Canal. And the lakes' imported problems are quickly becoming national disasters, such as the tiny and quick-spawning quagga mussel that has infested regions as far away as Lake Mead and Lake Powell on the Colorado River. Egan also relates the passionate narratives of conservationists and lake lovers who are fighting to save the Great Lakes. *—Ryan F. Mandelbaum*

Never Out of Season: How Having the Food We Want When We Want It Threatens Our Food Supply and Our Future

by Rob Dunn. Little, Brown, 2017 ($27)

Our ancestors tens of thousands of years ago ate a tremendous variety of food based on what was in season. But in the U.S. today, nearly half the carbon in children's bodies originates from corn, and in regions of China, almost all calories consumed come from rice. This new way of eating brings greater risk, writes biologist and writer Dunn, who has authored several articles for *Scientific American*. Growing just a few crop types, each with minimal genetic diversity, leaves staples vulnerable to disease, climate change and unsustainable farming techniques. Dunn weaves together powerful historical and modern examples to show that the safety of our global food supply rests on the edge of a knife. *—Andrea Gawrylewski*

Curators: Behind the Scenes of Natural History Museums

by Lance Grande. University of Chicago Press, 2017 ($35)

Natural history museums have gone through just as fascinating an evolution over the years as many of the species they chronicle in their displays. The earliest known museum was established in 530 B.C. in the ancient Mesopotamian city of Ur by Babylonian princess Ennigaldi. More recently, natural history museums in the 16th and 17th centuries devolved into "cabinets of curiosities" that often blended fact and fiction. But today these museums are more relevant than ever, serving as educational centers, entertainment hubs and institutions of original research, argues Grande, a curator of more than 33 years at the Field Museum in Chicago. In this lively account, he introduces readers to the hidden workings of natural history museums and the eccentric scientists and professionals that run them.

RICK AND NORA BOWERS *Alamy*

Michael Shermer is publisher of *Skeptic* magazine (www.skeptic.com). His book *The Moral Arc* (Henry Holt, 2015) is out in paperback. Follow him on Twitter @michaelshermer

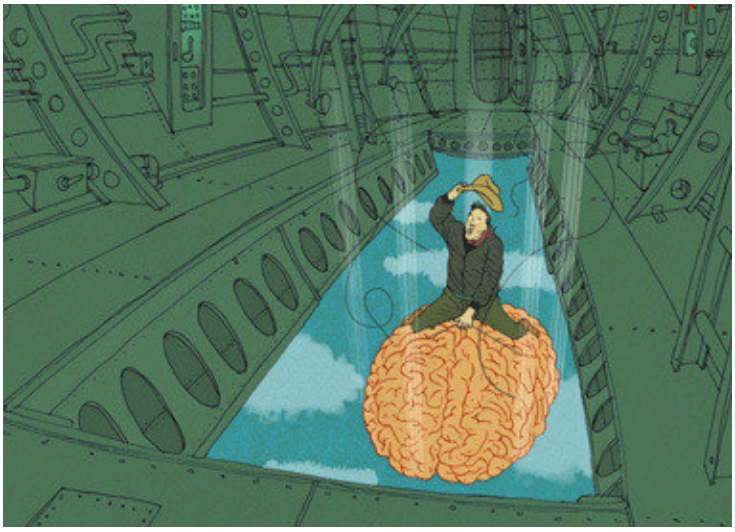
Apocalypse AI

Artificial intelligence as existential threat

By Michael Shermer

In 2014 SpaceX CEO Elon Musk tweeted: "Worth reading Superintelligence by Bostrom. We need to be super careful with AI. Potentially more dangerous than nukes." That same year University of Cambridge cosmologist Stephen Hawking told the BBC: "The development of full artificial intelligence could spell the end of the human race." Microsoft co-founder Bill Gates also cautioned: "I am in the camp that is concerned about super intelligence."

How the AI apocalypse might unfold was outlined by computer scientist Eliezer Yudkowsky in a paper in the 2008 book *Global Catastrophic Risks:* "How likely is it that AI will cross the entire vast gap from amoeba to village idiot, and then stop at the level of human genius?" His answer: "It would be physically possible to build a brain that computed a million times as fast as a human brain.... If a human mind were thus accelerated, a subjective year of thinking would be accomplished for every 31 physical seconds in the outside world, and a millennium would fly by in eight-and-a-half hours." Yudkowsky thinks that if we don't get on top of this now it will be too late: "The AI runs on a different timescale than you do; by the time your neurons finish thinking the words 'I should do something' you have already lost."



The paradigmatic example is University of Oxford philosopher Nick Bostrom's thought experiment of the so-called paperclip maximizer presented in his *Superintelligence* book: An AI is designed to make paperclips, and after running through its initial supply of raw materials, it utilizes any available atoms that happen to be within its reach, including humans. As he described in a 2003 paper, from there it "starts transforming first all of earth and then increasing portions of space into paperclip manufacturing facilities." Before long, the entire universe is made up of paperclips and paperclip makers.

I'm skeptical. First, all such doomsday scenarios involve a long sequence of if-then contingencies, a failure of which at any point would negate the apocalypse. University of West England Bristol professor of electrical engineering Alan Winfield put it this way in a 2014 article: "*If* we succeed in building human equivalent AI and *if* that AI acquires a full understanding of how it works, and *if* it then succeeds in improving itself to produce super-intelligent AI, and *if* that super-AI, accidentally or maliciously, starts to consume resources, and *if* we fail to pull the plug, then, yes, we may well have a problem. The risk, while not impossible, is improbable."

Second, the development of AI has been much slower than predicted, allowing time to build in checks at each stage. As Google executive chairman Eric Schmidt said in response to Musk and Hawking: "Don't you think humans would notice this happening? And don't you think humans would then go about turning these computers off?" Google's own DeepMind has developed the concept of an AI off switch, playfully described as a "big red button" to be pushed in the event of an attempted AI takeover. As Baidu vice president Andrew Ng put it (in a jab at Musk), it would be "like worrying about overpopulation on Mars when we have not even set foot on the planet yet."

Third, AI doomsday scenarios are often predicated on a false analogy between *natural intelligence* and *artificial intelligence.* As Harvard University experimental psychologist Steven Pinker elucidated in his answer to the 2015 Edge.org Annual Question "What Do You Think about Machines That Think?": "AI dystopias project a parochial alpha-male psychology onto the concept of intelligence. They assume that superhumanly intelligent robots would develop goals like deposing their masters or taking over the world." It is equally possible, Pinker suggests, that "artificial intelligence will naturally develop along female lines: fully capable of solving problems, but with no desire to annihilate innocents or dominate the civilization."

Fourth, the implication that computers will "want" to do something (like convert the world into paperclips) means AI has emotions, but as science writer Michael Chorost notes, "the minute an A.I. *wants* anything, it will live in a universe with rewards and punishments—including punishments from us for behaving badly."

Given the zero percent historical success rate of apocalyptic predictions, coupled with the incrementally gradual development of AI over the decades, we have plenty of time to build in fail-safe systems to prevent any such AI apocalypse. SA

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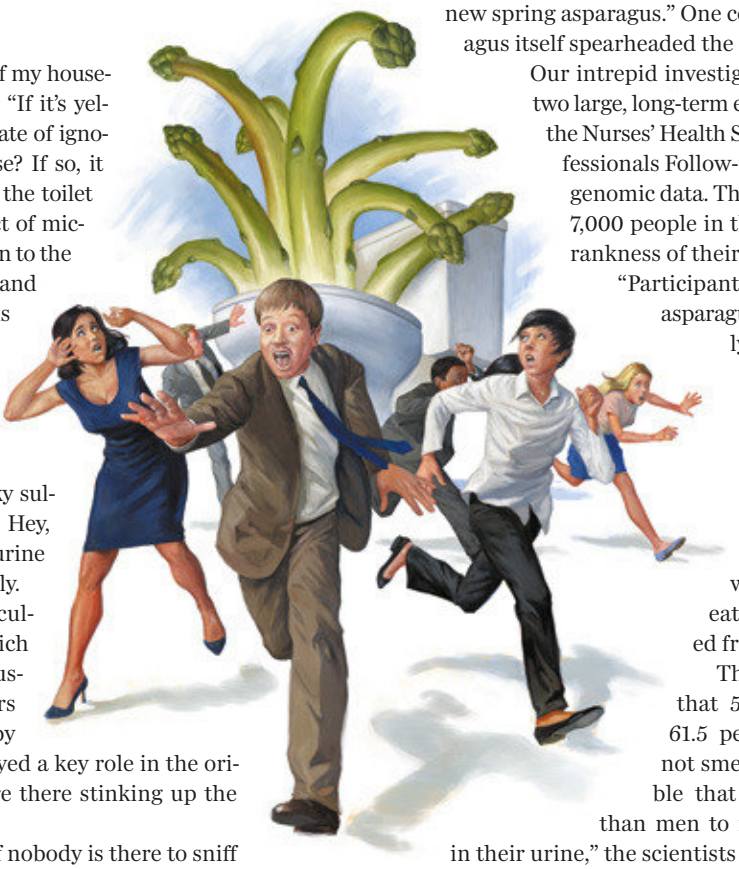
Illustration by Izhar Cohen

Steve Mirsky has been writing the Anti Gravity column since the moon's orbit was approximately 81 centimeters closer to Earth. He also hosts the *Scientific American* podcast Science Talk.

23 and Pee

Genome analysis pinpoints the DNA that gives some people an asparagus edge

By Steve Mirsky



To conserve water, members of my household abide by the old aphorism "If it's yellow, let it mellow." You're in a state of ignorance about that wizened phrase? If so, it recommends that one not flush the toilet after each relatively innocent act of micturition. But there's one exception to the rule: after asparagus, it's one and done—because those delicious stalks make urine smell like hell. To me and mine, anyway.

The digestion of asparagus produces methanethiol and S-methyl thioesters, chemical compounds containing stinky sulfur, also known as brimstone. Hey, when I said that postasparagus urine smells like hell, I meant it literally.

Methanethiol is the major culprit in halitosis and flatus, which covers both ends of that discussion. And although thioesters can also grab your nostrils by the throat, they might have played a key role in the origin of life. So be glad they were there stinking up the abiotic Earth.

But does a compound reek if nobody is there to sniff it? Less philosophically, does it reek if you personally can't smell it? For only some of us are genetically gifted enough to fully appreciate the distinctive scents of postasparagus urine. The rest wander around unaware of their own olfactory offenses.

Recently researchers dove deep into our DNA to determine, although we've all dealt it, exactly who smelt it. Their findings can be found in a paper entitled "Sniffing Out Significant 'Pee Values': Genome Wide Association Study of Asparagus Anosmia." Asparagus anosmia refers to the inability "to smell the metabolites of asparagus in urine," the authors helpfully explain. They don't bother to note that their bathroom humor plays on the ubiquity in research papers of the *p*-value, a statistical evaluation of the data that assesses whether said data look robust or are more likely the stuff that should never be allowed to mellow.

The findings appeared in the notorious Christmas issue, which always features screwball scholarship, of the *BMJ* (known as the *British Medical Journal* from 1857 to 1988—that is, two decades after Queen Victoria first sat on the throne until midway in the reign of Elizabeth II). No need to buy the volume, as the urinary tract can be streamed online.

"This study," the authors write, "was conceived during a scientific meeting attended by several of the coauthors in bucolic Sweden, where it became apparent that some of us were unable to detect any unusual odor in our urine after consuming new spring asparagus." One could thus say that asparagus itself spearheaded the research.

Our intrepid investigators took advantage of two large, long-term epidemiological studies—the Nurses' Health Study and the Health Professionals Follow-up Study—that provided genomic data. They then recruited almost 7,000 people in those studies to rank the rankness of their postasparagus urine.

"Participants were characterised as asparagus smellers if they strongly agreed with the prompt 'after eating asparagus, you notice a strong characteristic odor in your urine.'" Any other answer got one rated anosmic. The authors helpfully note, "Those who responded 'I don't eat asparagus' were excluded from the analysis."

The responses indicated that 58 percent of men and 61.5 percent of women could not smell the sulfur. "It is possible that women are less likely than men to notice an unusual odor in their urine," the scientists say, "because their position during urination might reduce their exposure to volatile odorants." In this case, men must face the facts.

The genomic analysis revealed three apparently important genetic constructs—all in a region on human chromosome 1 that contains various genes in the olfactory receptor 2 family—related to the ability to smell asparapiss. The researchers, tongues briefly removed from cheeks, point out that their "findings present candidate genes of interest for future research on the structure and function of olfactory receptors [that] … might shed light more generally on the relation between the molecular structure of an odorant and its perceived odor."

In contrast to that brief trespass into seriousness, they warn, "Future replication studies are necessary before considering targeted therapies to help anosmic people discover what they are missing." As long as they don't miss the bowl. SA

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Illustration by Matt Collins

MARCH

1967 Eat the Whales

"A proposal to raise plankton-eating whales in captivity for the dual purpose of providing food for the expanding human population and saving the whales from extinction has been advanced by Gifford B. Pinchot of Johns Hopkins University. He suggests that the corrals for domesticated whales could be coral: the atolls of the Pacific. An important feature of the scheme would be to fertilize the water in the atolls artificially to increase the production of plankton. Pinchot notes: 'These filter-feeding whales are in an almost unique position in the food chain in the sea, since they are large and feed on zooplankton. If they are exterminated, this extremely efficient mechanism for converting plants into animal protein will be lost forever.'"

Magnet Progress

"For a substantial number of applications, superconducting magnets now perform better and more economically than comparable conventional magnets. Moreover, it seems probable that in the not too distant future the growing need for stronger and cheaper magnetic fields in many areas of science and technology will be filled by superconducting magnets. At the National Magnet Laboratory in Cambridge, Mass., continuous fields as strong as 250,000 gauss have been achieved with a conventional electromagnet, but the electric power consumed by the magnet is about 16 million watts—approximately the power requirement for a town of 15,000 inhabitants."

1917 Flying Car

"A luxurious limousine with a highly finished body and with its three occupants sitting in elaborately and comfortably upholstered seats, dashing along a road or taking to the air by virtue of its short wings and soon reaching a speed of 65 miles an hour and showing all the ease of maneuvering which belongs to the modern aeroplane. It is the delineation of the autoplane [*see illustration*] which was exhibited at the recent Pan-American Aeronautic Exposition held in New York. The autoplane has been designed by Glenn H. Curtiss and his engineers. The machine is designed to sell in the neighborhood of $10,000 [$190,000 in 2017]."

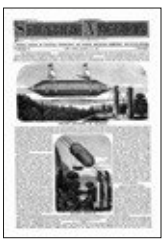
For a look at aviation technology in 1917, see a selection of archive images at www.ScientificAmerican.com/mar2017/aviation-1917

Women at Work

"A development of the war in Europe that has attracted widespread attention is the employment of women in munition factories. The most serious feature of the employment of women in mechanical work is an economic one. In England, France, Canada, and also in Germany, the movement is largely on a patriotic basis, and the wages paid to women are less than the men they replace received. After the war is ended, will women continue to seek this kind of employment? Will employers give women greater wages than at present? And more important than anything else is the question of what will become of the army of men, with families to support, when they return from the war and find their places taken by women, and those mostly unmarried? The necessities of the present are laying the foundation for future problems of most serious, far reaching and revolutionary importance."

1967

1917


1867


"Autoplane" from 1917: part car, part airplane, all luxury.

1867 Modern Traffic: Railroad and Canal

"We must dismiss the lumbering system of 'trains' for high-speed traffic, and resort to a single vehicle combining engine, tender and carriage, in which fifty passengers may go at an average rate of sixty miles an hour at moderate cost, and with but forty or fifty tuns of total weight in motion. The obstacle to rapid traveling on railroads at present, is the great weight and unsteadiness of the vehicles, involving an enormous waste of power and increase of risk at high speed. As for goods traffic, except express freighting, we must go back to and modernize water carriage, penetrating all parts of the country with a water system of rivers and canals, for steamboats of 250 tuns burden."

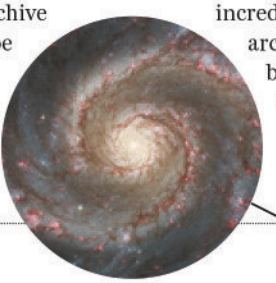
SCIENTIFIC AMERICAN, VOL. CXVI, NO. 12, MARCH 24, 1917

SCIENTIFIC AMERICAN ONLINE
FOR A LOOK BACK AT HUBBLE'S FIRST 25 YEARS, GO TO
SCIENTIFICAMERICAN.COM/MAR2017/GRAPHIC-SCIENCE

Long Live Hubble

Data from the space telescope will yield discoveries long after the instrument is kaput

With luck, the Hubble Space Telescope will yield more startling images of the cosmos for years. But because NASA is no longer servicing the telescope, it is expected to give up the ghost sometime after 2020. That does not mean that the Hubble discoveries will stop, however. NASA maintains an archive of data gathered over Hubble's lifetime—the telescope went live in 1991—and makes it available to the public for free. The archive has already yielded discoveries such as nebulae and distant galaxies. "The legacy is a treasure trove of data that can be mined in the future," says Arfon Smith, who leads a new data-science initiative at Hubble's home, the Space Telescope Science Institute. "The data are incredibly valuable and still ridiculously useful." The archive is a testament to the enduring value of big, basic science research—the data can pay off in ways astronomers cannot yet imagine. *—Katie Peek*



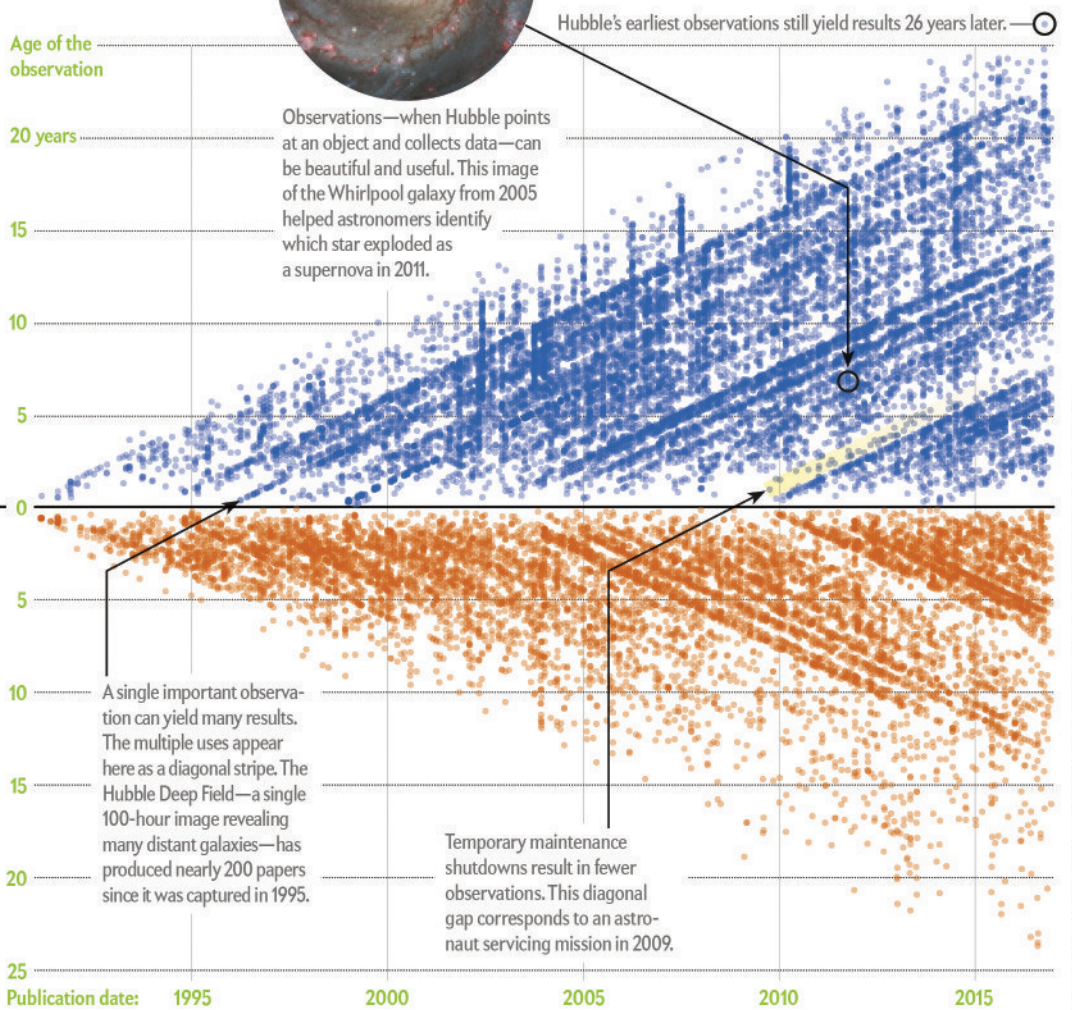
Observations—when Hubble points at an object and collects data—can be beautiful and useful. This image of the Whirlpool galaxy from 2005 helped astronomers identify which star exploded as a supernova in 2011.

How to Read It
Each dot represents a Hubble observation referenced in a published paper.

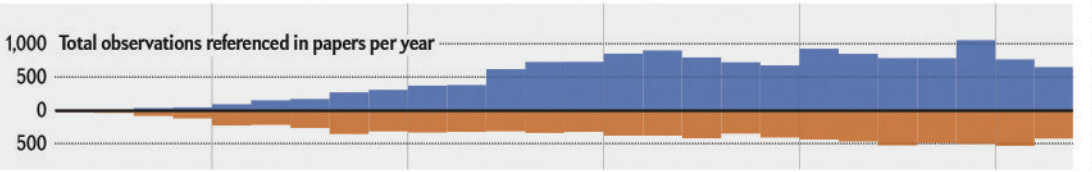
Blue dots (nearly 14,000) relate to Hubble's archive: instead of asking for new observations, the researcher answered a question using existing images.

Orange dots (nearly 9,000) relate to new data: a researcher makes a specific observation request to answer a question.

An additional 10,000 references to Hubble observations appeared in papers using a mix of the telescope's new and archival images. Data are current as of early December 2016.

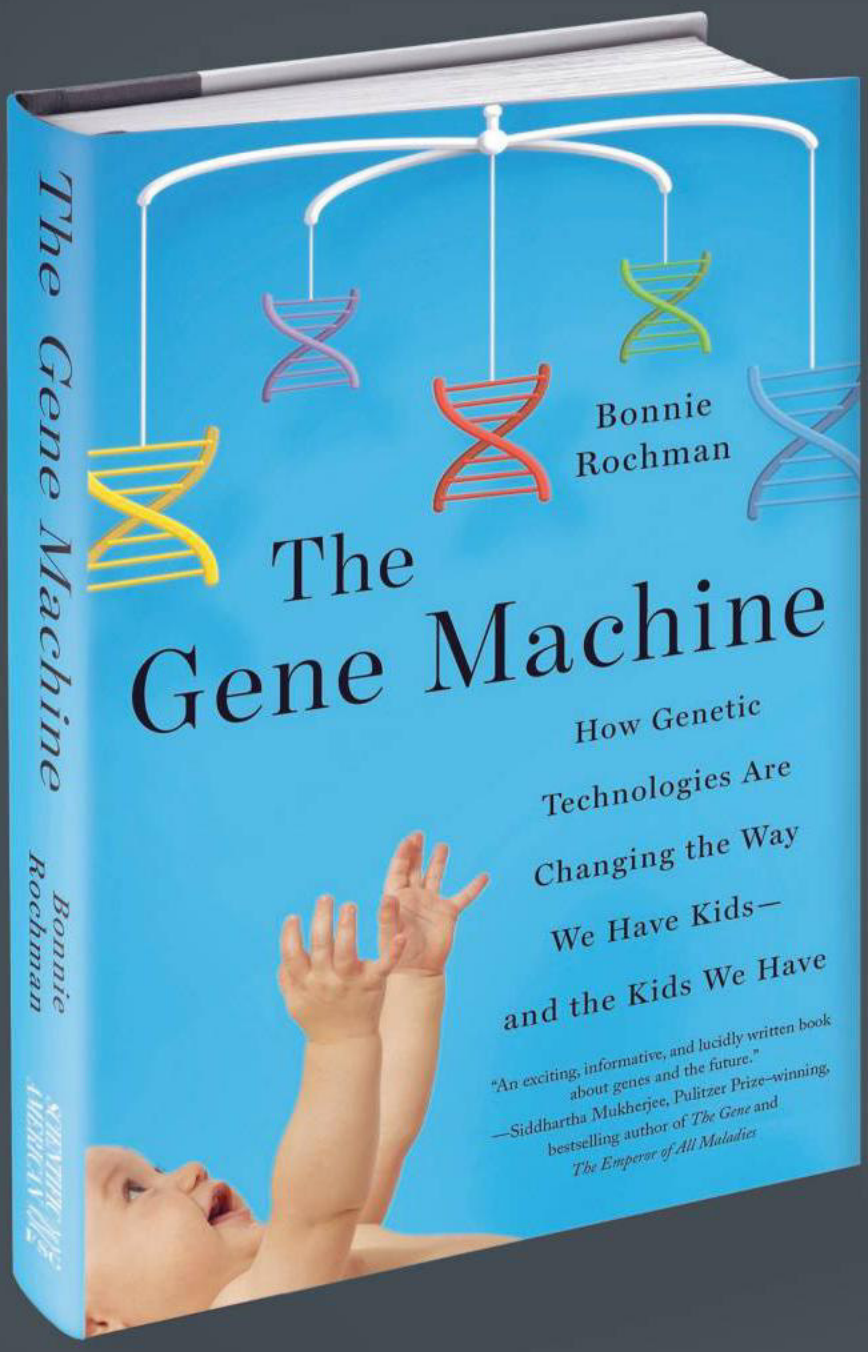


After Hubble's eventual demise, results based on new data (*orange*) will disappear, but those based on the archives (*blue*) will continue.



SOURCE: BARBARA A. MIKULSKI ARCHIVE FOR SPACE TELESCOPES, SPACE TELESCOPE SCIENCE INSTITUTE (*data*); HUBBLE HERITAGE TEAM (STScI/AURA) (galaxy)

Graphic by Katie Peek



"An exciting, informative, and lucidly written book about genes and the future."

—Siddhartha Mukherjee, Pulitzer Prize–winning, bestselling author of *The Gene* and *The Emperor of All Maladies*

"Provides parents with a clear-eyed explanation of the promise and pitfalls of ever-evolving genetic technologies so that they can make clear-eyed decisions about the unprecedented choices they'll be facing on their baby-making journey."

—Heidi Murkoff, bestselling author of the What to Expect series

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"A great read. Bonnie Rochman negotiates the pros and cons of genetic technologies and humanizes scientific endeavors by venturing into the hearts and homes of families facing tough choices caused by the hardship of inherited disease."

—James Grifo, M.D., Ph.D., director of the New York University Langone Fertility Center

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