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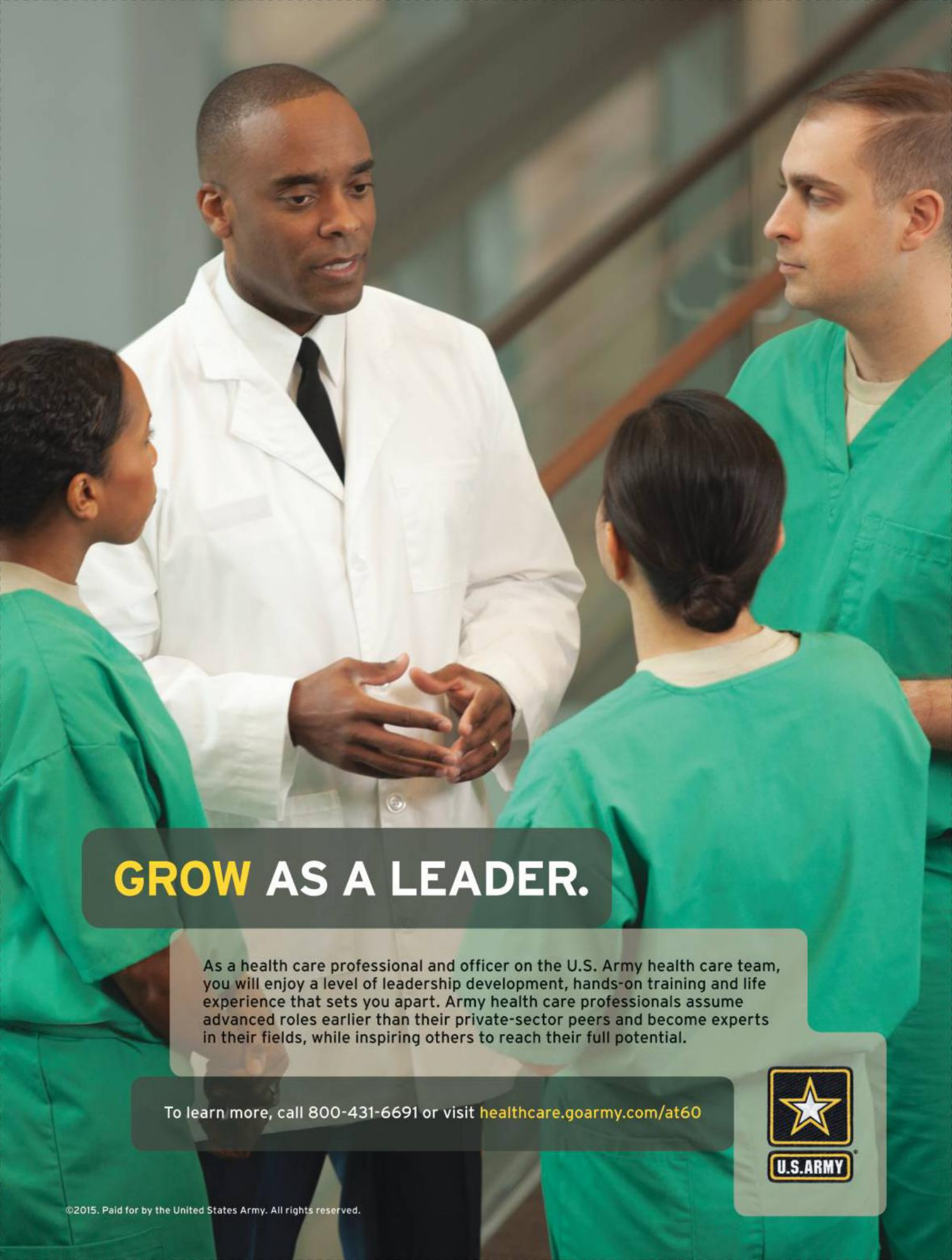
The Amazing Teen Brain

Rapidly changing wiring leads to mental agility—and risky behavior



ON THE COVER

Teenage behavior is all over the map. For years neuroscientists (and parents) have been baffled as to why. Extensive MRI studies are revealing that underneath the triumphs and pitfalls of teen life are sweeping changes in the networking of brain regions. The new knowledge could help teens avoid mental illness and make smart choices for a bright future. Illustration by FOREAL.

SCIENTIFIC AMERICAN

June 2015 Volume 312, Number 6

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FEATURES

Photograph by Jeff Wilson (flame deflector on rocket-engine test stand)

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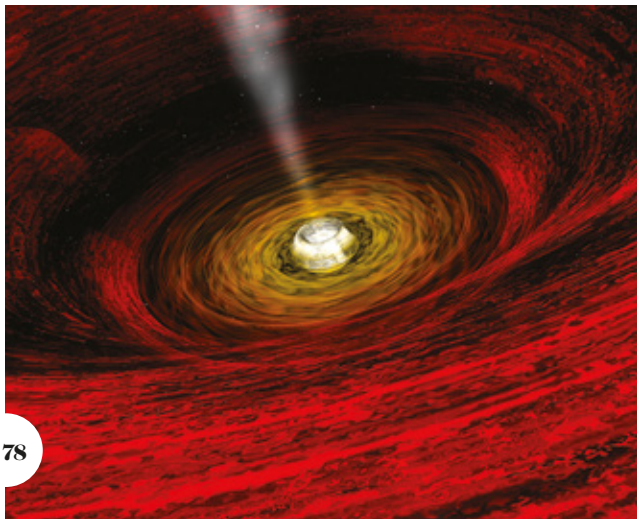

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DEPARTMENTS

ON THE WEB

The Hubble's Quarter of a Century
Our In-Depth Report commemorates the Hubble Space Telescope's unprecedented 25 years in orbit.
Go to www.ScientificAmerican.com/jun2015/hubble-25

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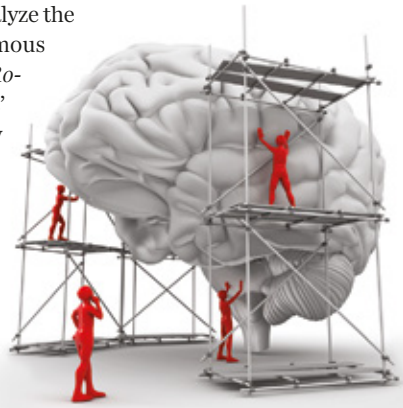
Mariette DiChristina is editor in chief of *Scientific American*. Follow her on Twitter @mdichristina

Promises and Perils

Listening to my 14-year-old daughter explain her writing assignment the other night, I was surprised to learn we both had similar homework. I was about to start this letter to introduce the current issue and its cover story, "The Amazing Teen Brain," by psychiatrist Jay N. Giedd. Her essay was going to analyze the reasons behind the rash behavior of the famous star-crossed young lovers in Shakespeare's *Romeo and Juliet*. As she explained, "Teenagers' brains are not fully developed yet, so they have a problem with impulse control." As she dispassionately talked about the brains of people her own age, I was struck anew by how grown-up teens can seem.



At the same time, as we are reminded painfully and too frequently not only by fictional plays but also by real-world headlines, adolescents are uniquely vulnerable to risky behavior, leading to mishaps or to recruitment to violent ends as soldiers or even terrorists. A key question around the recent trial of Dzhokhar Tsarnaev, who was 19 at the time of the Boston Marathon bombing, for instance, was the degree to which he was under the influence of his 26-year-old brother, Tamerlan.

At root is a developmental mismatch between the mental networks that manage emotion, which shift rapidly at puberty, and those that handle so-called executive function, which mature in a person's 20s. Giedd also describes how an earlier onset of puberty in recent decades has extended this angst-ridden period.

The protracted maturation, however, beneficially creates prolonged plasticity—enabling teenagers' enviable leaps of cognition and adaptability, for example, to today's data-enriched world. Both traits have served our species well in the past. Now, as science provides a better understanding of this powerfully influential developmental window, society—from parents to policy leaders to youngsters themselves—can work together to support teens on their journey. For the full story, turn to page 32.

Rather than soaring into the future, the Space Launch System, a successor to the shuttle, has been called a "rocket to nowhere"—a congressional jobs program with little hope of actually flying to space. But in "Birth of a Rocket," starting on page 56, journalist David H. Freedman takes a look at how the system, which is on time and on budget for a 2018 flight, could actually become the vehicle of choice to reach Mars in about 25 years. Given the sufficient political will—no small hurdle—the teens of today could see humans step onto another planet. SA

GETTY IMAGES (*brain*)

Illustration by Nick Higgins

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February 2015

"It would be wise for us to give up the notion that we are a benevolent and sharing species."

ROBERT E. MARX *UNIVERSITY OF MIAMI MILLER SCHOOL OF MEDICINE*

PRIORITIZING POPULATION

In "A Puzzle for the Planet," Michael E. Webber discusses the need to integrate three key factors (energy, water and food) to make it possible to meet the needs of a growing population. A critical point is that we have to stabilize that population in the first place. As long as it continues to grow, all other efforts are merely stopgaps.

Avi Ornstein
New Britain, Conn.

WEBBER REPLIES: Population growth is indeed important, but it turns out that economic growth is a bigger deal: demand for food, energy and water are growing faster than population because people tend to demand more meat and electricity (both of which are water-intensive) as they are elevated out of poverty. The average Chinese citizen, for instance, consumes about a fourth of the energy of a typical U.S. citizen, and as the former becomes richer, that gap narrows. (Meanwhile urbanization, which reduces birth rates, is increasing.)

Therefore, making sure that people have the energy, water and food they need for a free and prosperous life, without all the environmental and security challenges that plague our old approaches, is the most effective place to start. Plus, the policy levers (investing in new technologies, reinventing markets and pushing for a culture of conservation) for solving this nexus are more straightforward and palatable than population controls, which are objectionable on many levels.

BLACK HOLE BIZARRENESS

I agree with Adam Brown's crazy but fun article—"Can We Mine a Black Hole?"—that it is physically impossible to rapidly mine black holes for energy. There are many other "catches" that he does not mention, however. One is that the more massive a black hole is, the colder it is, and a black hole with a mass greater than about one tenth of that of Earth will have a temperature lower than that of the cosmic microwave background (CMB), which is about 2.73 kelvins. Any black hole with greater mass will therefore gain energy from the CMB and get more massive (and hence, oddly, colder). Only lighter, smaller black holes radiate, getting lighter and hotter as they do so, until they explode in a sudden burst of particles. So find a micron-size black hole but do not go close to it!

Michael Albrow
Fermi National Accelerator Laboratory

BROWN REPLIES: The CMB is indeed much hotter than a solar-mass black hole, but it won't be for long. Because the universe is expanding, the temperature of the CMB is falling; thanks to dark energy, it is falling exponentially, halving every 10 billion years or so, and will soon (relatively speaking!) be much colder than any black hole.

OUR MURDEROUS ANCESTORS

Kate Wong's suppositions about what brought about Neandertals' extinction in "Neandertal Minds" are contrary to the known history of anatomically modern *Homo sapiens* (that is, us). Her assertions that Neandertals were just outcompeted and that the 1.5 to 2.1 percent Neandertal DNA within people outside of Africa is the result of occasional "dalliances" would be historically unlikely.

The most likely scenario would involve waves of immigrating anatomically modern humans taking over land and causing death by plunder and disease, as Europeans discovering the New World did. And it would be naive to think that our Neandertal DNA was the result of consensual dalliances when rape went hand in hand with the pillage of every other civilization.

It would be wise for us to give up the notion that we are, or our ancestors before us were, a benevolent and sharing species.

Robert E. Marx
University of Miami Miller School of Medicine

NEANDERTAL SPELLING

The cover of the issue and Wong's article refer to "Neandertals." So is the spelling for "Neanderthal" now without an "h"?

Steve Larios
via e-mail

THE EDITORS REPLY: German linguistic reforms in the early 1900s changed the spelling of the name of the Neander Valley from "Neander Thal" to "Neander Tal" (the "h" was silent). Today the common name of these extinct humans can be spelled with or without the "h." Scientific American has long favored "Neandertal."

MEMRISTOR NETWORKS

In "Just Add Memory," Massimiliano Di Ventra and Yuriy V. Pershin talk about how a network of memristors—computing components that change electrical resistance in response to the amount of current and retain that change—can solve a maze problem in one step. They fail to mention that to appropriately "wire" the memristors in the maze, so that an input is connected to an output, each square of it would need to be visited and a memristor placed where needed. Doing so may require more of the maze to be visited than a random drunkard's walk solution or the classic right-hand-to-the-wall solution.

Dave Brumley
San Diego

THE AUTHORS REPLY: To create a maze, the only thing you need to know is the maze topology—namely the position of the

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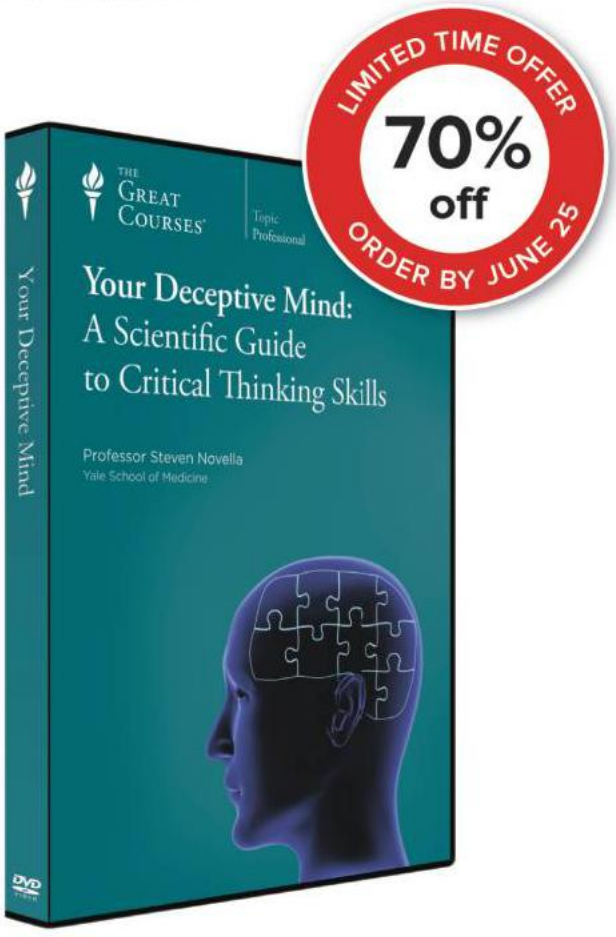

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walls and openings. But the knowledge of the topology does not mean that the maze solution is known or even exists. As an example, let us consider a maze drawing in a magazine. The maze solver knows the topology at the outset but not the maze solution and needs time to find it. The same is true for finding the maze solution with memristor networks.

IS VS. OUGHT

"A Moral Starting Point," by Michael Shermer [Skeptic], reminds us that although science and morality depend on each other, they are distinct. Science is about what "is"; morality is about what "ought" to be. When we make moral arguments, we act as humans equipped with a capacity for empathy toward human and nonhuman life and informed by science. We can contrast science-informed, empathy-based morality with religion-based morality, but science is not what makes us moral human beings; empathy is.

ANNE DENTON
Fargo, N.D.

SHERMER REPLIES: The most controversial section of my book The Moral Arc *is my assertion that science's description of the way something "is" can tell us what we "ought" to do. Ever since the scientific revolution, when scientists such as Copernicus, Kepler, Galileo and Newton discovered that the world is governed by natural laws that can be understood and used to make predictions and test hypotheses, thinkers in other fields have sought to understand the laws and principles that govern political, economic, legal, social and moral systems. They have then used these tenets to make predictions and test hypotheses about how best we should live. I contend that the "is-ought" fallacy is itself a fallacy.*

ERRATA

"Neandertal Minds," by Kate Wong, erroneously describes Gibraltar as the southernmost tip of the Iberian Peninsula. The southernmost part is Cape Tarifa.

"A Weakness in Bacteria's Fortress," by Carl Zimmer [January 2015], incorrectly refers to penicillin grabbing onto a protein that aids in building cell membranes in bacteria. The protein helps to build bacterial cell walls.

LETTERS TO THE EDITOR

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Letters may be edited for length and clarity. We regret that we cannot answer each one. Post a comment on any article at ScientificAmerican.com/jun2015

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A Last Right for Dying Patients

Health care providers do a poor job preparing people for critical decisions

Dying, never easy to confront, has become still more difficult in the era of high-tech medicine. The end of life often comes after repeated surgeries, a retinue of drugs with painful side effects, endless consultations with specialists and being harnessed to life-supporting hospital equipment. We have become so adept at prolonging life that death often arrives after months or years of coping with not just one but several severe ailments.

Many patients would choose not to extend their life this way, but modern medicine does not help them with this crucial decision. The nonprofit Institute of Medicine's report *Dying in America,* published last September, found that the vast majority of people in the U.S. have never had an end-of-life discussion with a health care provider, or even family members, about trade-offs between extra days and extra comfort. Straightforward changes to medical training and incentives would bring a healthy improvement to a sad situation.

Only 6,500 physicians are board-certified in hospice and palliative care, the specialty focused on pain relief and end-of-life care. That number is between 6,000 and 18,000 fewer physicians than we need, according to a 2010 estimate. The best way to fill these gaps is to train a broad swath of health care professionals—generalists, specialists, nurses and physician assistants—in this kind of medicine. At present, medical schools spend too little time on the subject. Every student should receive extensive grounding in how to treat pain, breathing problems and depression and in how to preserve mental faculties. Students should be required to practice interviewing patients and family members about their desires for care—questions that go beyond asking whether patients wish to be kept on a ventilator if their health deteriorates.

It is especially important to learn to have "the conversation"—the careful and honest interaction between doctor and patient to plan the best course when options look bleak. After this discussion, which can also involve the family, a patient might decide to forgo yet another debilitating round of chemotherapy and instead focus on remaining mobile and comfortable enough for a few months to attend a granddaughter's wedding. Or the patient might want to press on with treatment at all costs. Either way, personal values, not technology, should determine these choices.

Skills in helping patients to navigate life's final stages also need to be tested after they are taught. Right now only 2 percent of the board-certification examination for oncologists, for whom palliative medicine is clearly relevant, is devoted to end-of-life care. Before getting a license to practice, any provider, not just cancer physicians, should prove competence in this vital area.

Better education is not the entire answer, however. Money matters, too. Physicians will help more with end-of-life planning when government and private insurers reimburse them for their time. These discussions have not been covered under Medicare, and the Centers for Medicare & Medicaid Services has moved much too slowly on plans to add such reimbursement.

Palliative care has shown its worth. Several studies during the 2000s suggested that such care might increase patient survival compared with standard practice, possibly because it reduces patient depression and high-risk medical procedures.

The upside extends to the health care system's bottom line. Diane E. Meier, a professor of geriatrics and palliative medicine at the Icahn School of Medicine at Mount Sinai, noted in a 2011 paper that palliative care, at its current level of penetration in U.S. hospitals, saves $1.2 billion annually over standard care—a figure that could rise to $4 billion a year if implemented at nearly all hospitals. The savings, in part, come from avoiding unwanted procedures.

Ultimately the reasons for making these changes go beyond any hard-nosed cost-benefit analysis. Careful consultations among doctors, patients and families add compassion that is often missing in medicine. "Technological society has forgotten what scholars call the 'dying role' and its importance to people as life approaches its end," writes Harvard University physician Atul Gawande in *Being Mortal,* his 2014 book that is still high on best-seller lists. "People want to share memories, pass on wisdoms and keepsakes, settle relationships," he adds. "They want to end their stories on their own terms." When health care providers help patients attain this, everyone regains a measure of humanity. SA

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Illustration by Skip Sterling

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Commentary on science in the news from the experts

Barbara J. King, a biological anthropologist at the College of William & Mary, has studied baboons in Kenya and great apes in captivity. Her article "When Animals Mourn" in the July 2013 *Scientific American* was selected for inclusion in *The Best American Science and Nature Writing 2014.* She writes weekly for NPR's 13.7: Cosmos & Culture blog.

Ending a Cruel Legacy

Experiments that separate infant monkeys from their mothers cause profound and unnecessary suffering. They should be stopped

Raised in total or partial social isolation, clinging desperately to wire or cloth "mothers," rhesus monkey infants subjected to American psychologist Harry F. Harlow's maternal-deprivation experiments in the 1950s self-mutilated, rocked, and showed other signs of deep depression and anxiety. Based on the principle that animal models could illuminate issues of maternal care and depression in humans, Harlow's research is still discussed in psychology, anthropology and animal behavior classes. Yet this kind of profound primate suffering is not consigned to the historical record. Today rhesus monkey infants are still forcibly separated by laboratory researchers from their mothers and stressed in ways that leave them physically and emotionally traumatized.

At the Eunice Kennedy Shriver National Institute of Child Health and Human Development's Laboratory of Comparative Ethology (LCE) in Poolesville, Md., headed by psychologist Stephen Suomi, infant monkeys are taken from their mothers often within hours of birth. For 22 hours a day (24 on weekends), these infants have no cage mates with which to interact. As I know from my work with free-ranging infant wild baboons in Kenya—monkeys that have a social organization similar to that of the rhesus—this regimen results in a terrible distortion of the animals' natural way of life. In the wild, these monkey infants live at the secure center of a matriline, a group of related females. They play with peers and explore their world but scamper back to the warmth and protection of the most important being in their lives, the mother.

At the LCE, in contrast, the motherless infants undergo stressors (such as being intentionally frightened while they are alone) in experiments designed to evaluate their reactivity and thus to understand developmental risk factors leading to mental illness in humans. Peer-reviewed literature from the LCE reports that these infants suffer behavioral and biological consequences for the duration of their lives, including poor health, increased stress, maternal incompetence and abnormal aggression.

As a person who watches two beloved family members struggle with mental illness, I know the importance of research in this arena. Yet systematic reviews tell us conclusively that animal models do not translate well to human mental health. To treat mental illness in humans requires direct attention to the real stressors we experience in our own lives—not artificial ones that we make rhesus infants endure. Research of diverse types, including neuroimaging and long-term follow-up of patients' day-to-day lives, is making substantive inroads in this endeavor.

It is no adequate defense to note that this kind of research meets federal and university animal care guidelines. The bar to gain approval to experiment invasively on primates (and other animals) is quite low. As Lawrence Arthur Hansen pointed out two years ago in the *Journal of Medical Ethics,* oversight committees are disproportionately composed of the very people who derive their livelihood from continuing these experiments: animal researchers and institutional veterinarians.

Bringing onboard knowledgeable parties who do not directly benefit from money awarded to these projects—social scientists and bioethicists, for instance—would be a first step in addressing this skew. As Hansen observes, though, equally necessary is a change in institutional culture to ensure that committees more directly consider benefit-harm issues.

I am struck by parallels with the case of biomedical research on chimpanzees at the National Institutes of Health, which in 2011 was deemed "unnecessary" by an independent Institute of Medicine review. Repeatedly, biomedical studies on chimpanzees had been approved by review boards and animal care committees. The oversight process did not ethically protect those lab chimpanzees in the past, and it is not ethically protecting the lab monkeys now.

It is not necessary to be against *all* biomedical research on nonhuman primates to see how outdated and misguided *some* research is. It is time to end Harlow's cruel legacy. SA

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Illustration by Julian Callos

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Key speakers included **Dr. Mason Freeman** of Massachusetts General Hospital and Harvard Medical School, **Dr. Jose-Carlos Gutierrez-Ramos** of Pfizer, Nobel Laureate **Dr. Phillip A. Sharp** of The Massachusetts Institute of Technology, and **Dr. Tadataka "Tachi" Yamada** of Takeda Pharmaceuticals. **Robert K. Coughlin** of MassBio also made remarks.

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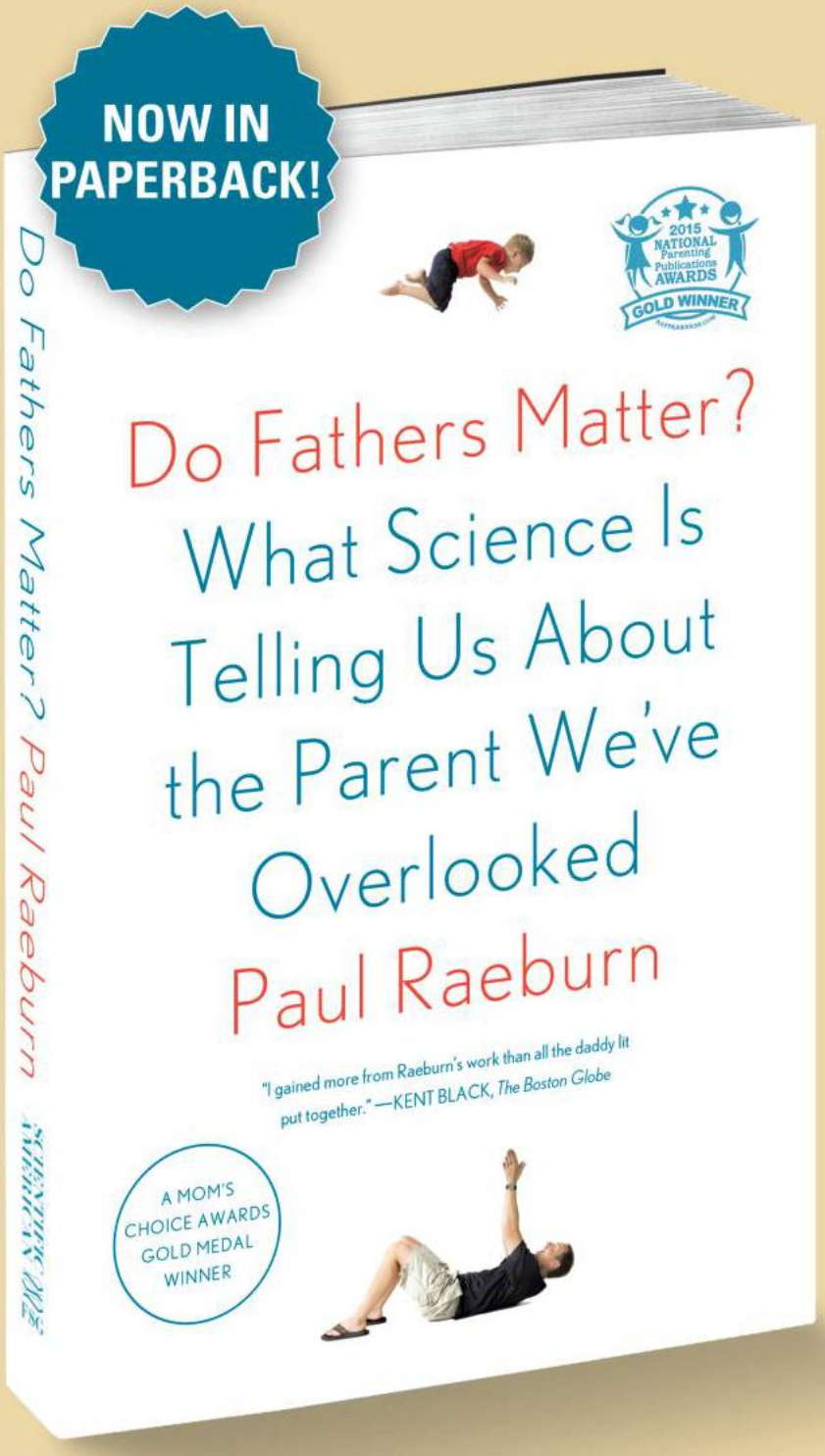

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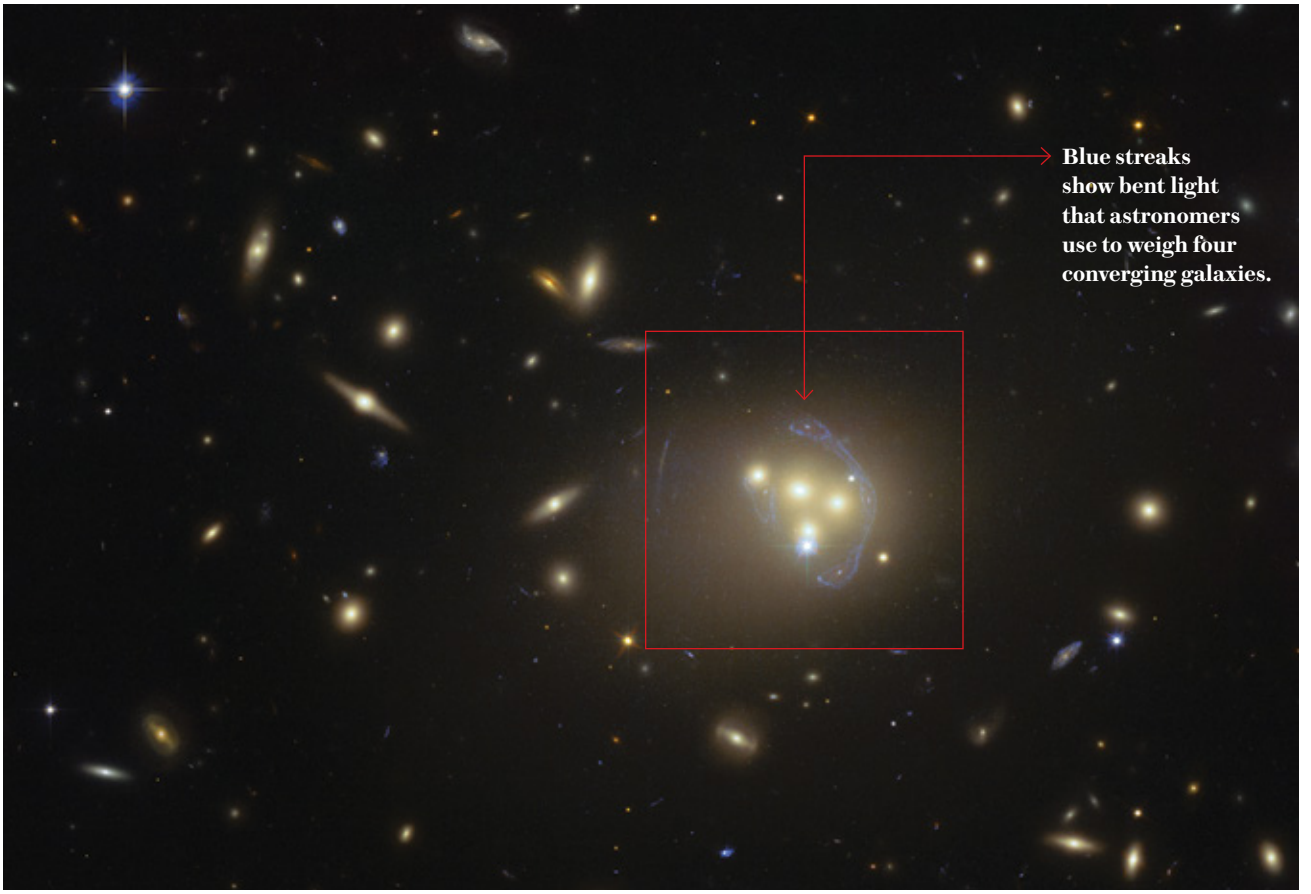

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PHYSICS

Dark Matter Drops a Clue

After decades of negative findings, physicists finally have a lead

Something is out there in the cosmos. We can't see it, we can't touch it and we know it's there only by the gravitational pull it exerts on cosmic objects. For decades the story of dark matter has been one revelation after another about what this mysterious material is *not*, a gradual winnowing of possibilities that has made physicists increasingly nervous. What happens when the last candidate gets crossed off the list? Will we be doomed never to glimpse the nature of the stuff that contributes about 25 percent of all mass in the universe?

This dreary narrative took a turn in a hopeful direction earlier this spring. Researchers uncovered one of the most intriguing clues in years: a hint of a new force that may allow dark matter to "talk" to itself. This insight would help explain what kind of particles dark matter might be made of.

The clue turned up in observations of a corner of the universe called the Abell 3827 cluster. Astronomers recently tracked dark matter's location within four colliding galaxies in this cluster by using a phenomenon known as gravitational lensing (the bending of light as it passes near massive objects). Observations made with the Hubble Space Telescope and the Very Large Telescope in Chile revealed that the dark matter surrounding at least one of the galaxies significantly lagged behind the ordinary matter there, suggesting dark matter particles were interacting with one another and slowing themselves down—a phenomenon never seen before.

Astronomers led by Richard Massey of Durham University in England surmise that because the interactions did not affect the normal matter, they must have occurred through some force other than gravity that influences only dark matter. An exchange of "dark photons" may create the force, for example. Such a situation potentially parallels the way regular protons interact with one another through the electromagnetic force: when two protons approach one another, each releases a photon—the force carrier

FURTHER READINGS AND CITATIONS ScientificAmerican.com/jun2015/advances

ADVANCES

The Hubble Space Telescope spied dark matter acting strangely in colliding galaxies.

of electromagnetism—and the other absorbs it. This exchange transfers momentum, causing both protons to separate.

The news has galvanized physicists in search of answers. "If this holds up, it is beyond a big deal," says physicist Neal Weiner of New York University, who was not involved in the study. A scenario with dark photons is a change from the most basic and popular conception of dark matter as a single type of particle, commonly called a weakly interacting massive particle, or WIMP. But the idea that dark matter involves dark photons as well as exotic interactions might help explain some problems with the single-particle WIMP explanation for dark matter, such as why the centers of galaxies are less dense than expected.

This concept would also help physicists considerably narrow down the list of dark matter contenders. "Although we have evidence of dark matter from a huge variety of sources," Weiner says, "we have so far no clear indication of anything other than its gravitational interaction. If it is shown to have self-interactions at this level, it will eliminate a huge number of models" for what dark matter could be. In particular, the finding, released online in April and published in June in *Monthly Notices of the Royal Astronomical Society,* may conflict with many popular versions of a hypothesis that dark matter is a particle predicted by supersymmetry theory. Supersymmetry—an appealing idea that attempts to explain many mysteries of physics, such as why the Higgs boson's mass is as low as it is—posits more particles in the universe than those that have so far been found. Yet if one of these particles (which could be a WIMP) were responsible for dark matter, most versions of the theory would not predict self-interactions.

The study's co-authors say it is too early to rule out a more mundane explanation for their observations. For instance, dark matter outside the colliding galaxies but along Earth's line of sight might be contributing to the gravitational lensing. "One caveat with this new study is that it's only one object," says team member David Harvey of the Swiss Federal Institute of Technology in Lausanne. "There are unknown unknowns that may be changing the result." And previous searches in other clusters have not seen signs of self-interacting dark matter, including a March *Science* study led by Harvey that analyzed 72 collisions of galaxy clusters rather than individual galaxies. Because clusters collide faster

COURTESY OF ESA/HUBBLE SPACE TELESCOPE

COMMENT AT ScientificAmerican.com/jun2015

than galaxies, however, there is less time for dark matter to interact and drag behind, so the two findings are not contradictory.

If the recent observations turn out not to reflect new forces or dark matter interactions, Abell 3827 will become yet one more example of what dark matter isn't. Meanwhile searches for its particles in underground detectors continue to come up empty, and dark matter has so far failed to appear in CERN's Large Hadron Collider. Scientists hope these trends could soon change: the collider restarted in April at its highest energy levels yet, and the detectors are now extremely sensitive. "Dark matter has been so elusive, but we've never had the data we're going to have," Harvey says. "I feel like it's now or never."

—*Clara Moskowitz*

BY THE NUMBERS

Sewage Is a Gold Mine (Literally)

0.3

Grams of gold Arizona State University researchers extracted from one metric ton of sewage

28,600

Dry tons of sewage produced by one million Americans a year

$13 million

Projected value of metals, including gold, silver and platinum, in that sewage

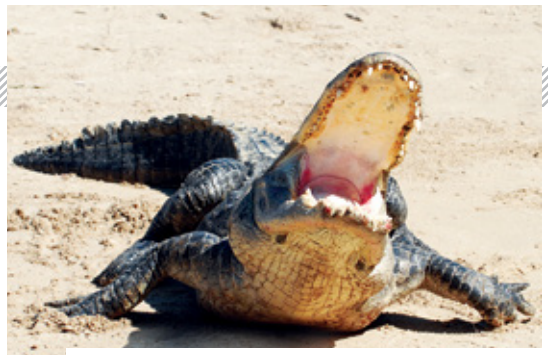
For more sewage moneymaking schemes, see Steve Mirsky's Anti Gravity column "Gold Flush," on page 81.

ISTOCKPHOTO (*toilet*); SOURCE: "CHARACTERIZATION, RECOVERY OPPORTUNITIES, AND VALUATION OF METALS IN MUNICIPAL SLUDGES FROM U.S. WASTEWATER TREATMENT PLANTS NATIONWIDE," BY PAUL WESTERHOFF ET AL., IN *ENVIRONMENTAL SCIENCE & TECHNOLOGY*; PUBLISHED ONLINE JANUARY 12, 2015

BIOMECHANICS

Prehistoric Swagger

Modern-day alligators may illustrate how dinosaurs went from two-legged to four



Alligators hyperextend their digits when they walk with their body raised from the ground.

ISTOCKPHOTO

All dinosaurs once pranced, strolled or lumbered about on two legs. But some took to occasionally resting or running on all fours for greater stability and over time evolved into quadrupeds. During the transition, the forelimbs were shorter than the hind limbs, raising the question of how the intermediate animals leveled out the tilted stance from those stubby appendages: Did they walk on their "fingertips" or their palms? New research suggests the latter—some early dinosaurs and their close relatives may have stepped straight down on the front of their palms.

Dinosaurs are closely related to alligators' ancestors and consequently share many structural features with gators. So biologist Joel Hutson and geologist Kelda Hutson compared the forelimb mechanics of alligators with fossils from *Postosuchus*—a relative of early dinosaurs and an ancestor of alligators and crocodiles—to learn more about joint mobility. The Hutsons measured movement of each joint in alligator specimens in multiple states: intact, without scales, without muscles and tendons, without ligaments and, finally, without cartilage. The team found that the ability of bone-on-bone specimens to hyperextend matched that of the fossils. They also verified that with cartilage in place, the alligator digits easily hyperextended backward, suggesting that *Postosuchus* would have been capable of hyperextension as well. Thus, perhaps dinosaurs making the transition from bipedalism walked in such a way, too—walking on their palms with hyperextended fingers. The results were published online in March in the *Journal of Zoology*.

Range-of-motion comparisons among dinosaur fossils and fresh, intact tissues have rarely been performed, says Mason Meers, a biologist at the University of Tampa who researches the evolution of crocodile locomotion. "The work's 100 years overdue," he adds. And although the study is small, the results shed more light on exactly how strange early dinosaurs would have looked as they stalked about, Joel Hutson says. For instance, while in the process of developing four legs dedicated to locomotion, dinosaurs might have used their wrists and palms as if they were stilts. —*Sarah Lewin*

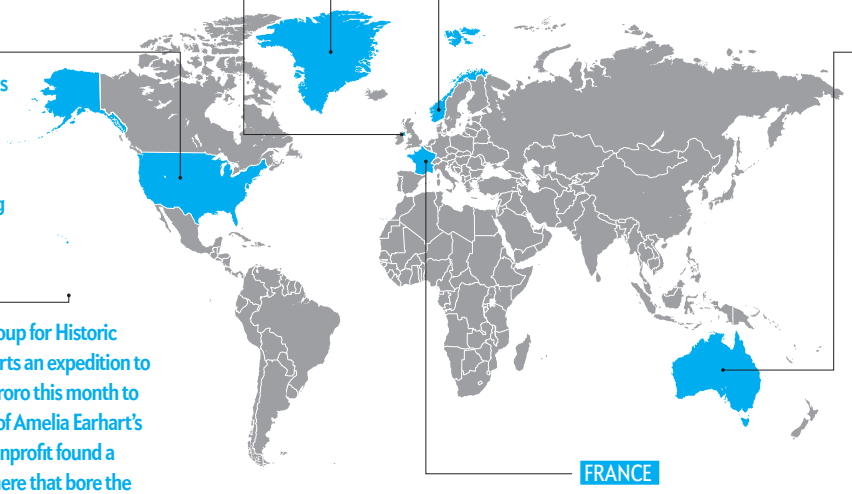
IN THE NEWS

Quick Hits

NORTHERN IRELAND
Every secondary school will receive access to an educational version of the popular video game Minecraft to help teach science and computer coding, among other subjects.

NORWAY/GREENLAND
Polar bears venture off the ice during summer months, more than they have in past years, to eat seabird eggs—a change in behavior that is devastating bird populations, according to a new study based on a decade of data.

U.S.
On June 5 and 6, finalists in the DARPA Robotics Challenge put their robots to the test in disaster scenarios, vying for a $2-million prize.



AUSTRALIA
One of the biggest asteroid-impact zones ever found was uncovered deep in the earth's crust, measuring 400 kilometers wide. The space rock split in two just before striking the planet some 300 million to 600 million years ago.

KIRIBATI
The International Group for Historic Aircraft Recovery starts an expedition to the island of Nikumaroro this month to search for remnants of Amelia Earhart's plane; in 2014 the nonprofit found a piece of aluminum there that bore the plane's signature pattern of rivets.

FRANCE
The International Earth Rotation and Reference Systems Service, based at the Paris Observatory, adds an official leap second to June 30 to compensate for the earth's rotation; four leap seconds have been added since 1999.

For more details, visit www.ScientificAmerican.com/jun2015/advances

MEDICINE

The Doctor Will See You Now

Three innovative eyeglasses give physicians superhuman vision

The standard safety goggles that surgeons and other doctors often wear have a single important purpose: to protect the eyes from spurts and splashes of blood and other bodily fluids. Now health care professionals are welcoming a new generation of medical spectacles that not only shield the eyes but also enhance them.

INJURY

NAME: O2Amp
MAKER: 2AI Labs
PURPOSE: The glasses reveal bruises, rashes and internal injuries invisible to the naked eye. Idaho-based nurse Jake Youren used them to detect hidden bruising on a woman who had recently been in a car crash. Other doctors find the glasses useful for spotting blood clots.
HOW IT WORKS: The human eye naturally tunes to very subtle shifts in skin coloration that correspond to changes in blood flow. 2AI's spectacles, which come in shades of green, pink and violet, unlock the full potential of this innate sensitivity. Dyes in the polycarbonate glasses block particular wavelengths of light that ordinarily interfere with our perception of either red oxygenated blood—the kind that accumulates with injury—or blue unoxygenated blood running through veins.
PRICE: Starting at $127
STAGE: In use

VEINS

NAME: Eyes-On Glasses
MAKER: Evena Medical
PURPOSE: These specs help nurses locate veins when inserting needles, IVs and catheters, saving time and minimizing pain, injury and costs.
HOW IT WORKS: Eyes-On Glasses are like an x-ray for blood vessels. They emit four benign beams of near-infrared light at just the right wavelengths to be absorbed by veins while bouncing off tissue. Two mounted cameras detect where light has been reflected and absorbed. An onboard processor uses those data to generate a vein road map, which a projector then displays on a transparent visor.
PRICE: Around $10,000
STAGE: Debuting in November

CANCER

NAME: Fluorescent goggles
MAKER: Samuel Achilefu and his colleagues, Washington University School of Medicine in St. Louis
PURPOSE: In many cases, it is extremely difficult for a surgeon to be sure that the entirety of a tumor has been excised because microscopic bits and pieces can stay behind undetected. These goggles help doctors notice lingering cancer cells, which could increase the likelihood of a recurrence if not removed.
HOW IT WORKS: While operating, surgeons inject tissue with a fluorescent dye that binds only to cancer cells and glows green under near-infrared light. A camera fixed to a visor picks up the fluorescence while a small computer and fiber-optic cable use that information to overlay glowing dots on the wearer's field of view that indicate where a tumor still remains.
PRICE: Less than $10,000
STAGE: Still in development

—Ferris Jabr

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COMMENT AT ScientificAmerican.com/jun2015

JOEL SARTORE National Geographic

LANGUAGE

From Babbling Bats to Baby Talk

Flying mammals offer a new way to study human chatter

In 1970 child welfare authorities in Los Angeles discovered that a 14-year-old girl referred to as "Genie" had been living in nearly total social isolation from birth. An unfortunate participant in an unintended experiment, Genie proved interesting to psychologists and linguists, who wondered whether she could still acquire language despite her lack of exposure to it.

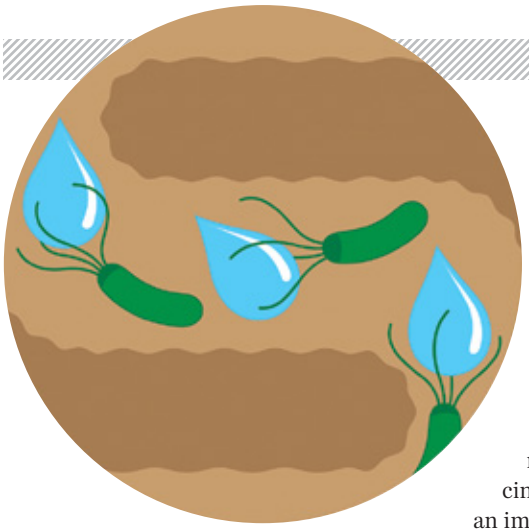
Genie did help researchers better define the critical period for learning speech—she quickly acquired a vocabulary but did not gain proficiency with grammar—but thankfully, that kind of case study comes along rarely. So scientists have turned to surrogates for isolation experiments. The approach is used extensively with parrots, songbirds and hummingbirds, which, like us, learn how to verbally communicate over time; those abilities are not innate.

Studying most vocal-learning mammals—for example, elephants, whales, sea lions—is not practical, so Tel Aviv University zoologists Yosef Prat, Mor Taub and Yossi Yovel turned to the Egyptian fruit bat, a vocal-learning species that babbles before mastering communication, as a child does. The results of their study, the first to raise bats in a vocal vacuum, were published this spring in the journal *Science Advances*.

Five bat pups were reared by their respective mothers in isolation, so the pups heard no adult conversations. After weaning, the juveniles were grouped together and exposed to adult bat chatter through a speaker. A second group of five bats was raised in a colony, hearing their species' vocal interactions from birth. Whereas the group-raised bats eventually swapped early babbling for adult communication, the isolated bats stuck with their immature vocalizations well into adolescence. They figured out how to produce adult vocalizations but could not discriminate infantile sounds from mature acoustics. Once the two groups of adolescents were combined, the secluded bats caught up with their peers. Yovel points out that bat communication is more comparable to human language than is birdsong. "Fruit bat vocalizations are emitted in a conversational context," he says. "They are not singing to advertise their status, as birds do. This is much more similar to the context in which humans use speech."

Duke University neurobiologist Erich Jarvis, who studies vocal learning in birds, agrees that bats are poised as our fellow mammals to reveal more of the details of human language acquisition. But he also notes that the study's bats might have received nonauditory feedback from their mothers, possibly affecting their vocal learning. For now the researchers want to understand just what the bats are talking about, both in the laboratory and in the wild. Perhaps insights from their vocabulary will echo through our own language arts.

—Jason G. Goldman



HEALTH

Our Personal Vaccine Helpers

A fact of early childhood the world over, vaccines are a mainstay of global public health. But not all prove equally effective in all kids. Why? Gut microbes may be a big reason

Rotavirus used to infect most youngsters until a widely available oral vaccine came out in 2006. The virus, which causes severe diarrhea and thus life-threatening dehydration, still kills more than 450,000 kids globally every year, largely in Asia and Africa, because the vaccine is not always effective. Vanessa Harris of the University of Amsterdam wanted to find out why infants in those regions have such high rates of so-called nonresponders. Perhaps, she reasoned, the microbes that live in a child's large intestine played a role.

Harris and her colleagues, including collaborators in South Asia, studied 66 Pakistani infants and 66 matched Dutch control subjects, all of whom received the oral rotavirus vaccine. Most of the children in the Netherlands mounted the expected immune response, but only 10 of those in Pakistan did the same. A genetic scan of fecal samples taken from each infant before the vaccine revealed that the responders harbored a higher diversity of microbes in their intestinal tract. They also carried more organisms from the group Proteobacteria.

Many Proteobacteria propel themselves with the help of tail-like flagella. Those tails contain flagellin, a protein known to bolster immune cell activity. An abundance of such bacteria in the body could act as a natural immunity—and thus vaccine—booster, says Bali Pulendran, an immunologist at the Emory University School of Medicine, who was not involved in the study, which was presented in March at a Keystone Symposia meeting in Colorado.

Last year Pulendran and his colleagues demonstrated the role of flagellated bacteria in the success of the influenza vaccine. Mice living in a sterile environment that had no intestinal bacteria, as well as those inoculated with only nonflagellated bacteria, failed to raise antibodies after receiving the shot, rendering it useless. Normal mice and those inoculated with only flagellated bacteria, however, launched the typical, strong immune activity. A small follow-up human study by the team could soon reveal whether the same pattern shows up among people who have received three types of different broad-spectrum antibiotics.

Other microbial factors might also be at play. Research published in 2014 in *Pediatrics* showed that varying compositions of gut bacteria in Bangladeshi infants correlated with reactions to the tetanus, tuberculosis and oral polio vaccines. Taken together, these lines of research indicate that our body's native bacteria may help determine our individual immune response to vaccines. Whether the findings will eventually lead to microbiome screens or specially formulated probiotic supplements for ingestion prior to vaccination remains to be seen.

Still, a more thorough account of all the tiny organisms that live within us could help scientists make significant improvements in vaccine efficacy. And those small steps could save many thousands of lives.

—Katherine Harmon Courage

Illustrations by Thomas Fuchs

SPACE

Flying Saucers for Mars

NASA's disk-shaped landing technology signals progress for human flight to the Red Planet

COURTESY OF NASA/JPL-CALTECH

Landing is the toughest part of any trip to Mars. The planet's atmosphere is too thin for parachutes alone to bleed off a spacecraft's blistering entry speeds, and landing solely via retro-rockets requires more fuel than any near-future mission to Mars is likely to have. NASA uses both techniques together for most of its Mars missions, and even its high-tech Curiosity rover used a vintage 1970s parachute apparatus during its landing in 2012. That technology limits landings to 1.5-ton probes. Anything heavier will yield only a smoking crater. For more robust robotic missions—or eventual human ones—a new approach is required.

This month the space agency plans to test the full conception of a new lander, the Low-Density Supersonic Decelerator (LDSD), which could deposit twice as much mass across a wide variety of Martian terrain. The LDSD consists of a six-meter Kevlar-insulated inflatable disk and a 30-meter parachute capable of withstanding supersonic speeds—the largest ever deployed. An eight-meter disk suitable for human landings is also under development. Together the relatively lightweight inflatable disk and giant parachute could deliver bulkier payloads to Mars, without requiring large amounts of extra fuel or very heavy atmospheric-entry heat shields.

To test the LDSD, NASA will use Earth's upper stratosphere as a stand-in for the thin Martian atmosphere. First, a giant, football-stadium-sized balloon will hoist a mock lander 37 kilometers high over the Pacific Ocean near Hawaii. Then the LDSD will separate from the balloon and fire rockets to reach higher altitudes and speeds. At a height of 55 kilometers and a velocity nearly four times the speed of sound, its disk will inflate, slowing the vehicle so that the parachute can deploy. This will be the critical moment—aerodynamic forces shredded the parachute during an early flight demonstration in 2014.

If all goes well this time around, about three hours after launch the saucer will splash down in the Pacific, clearing the way for bigger, more sophisticated missions to Mars and other destinations in the solar system. And even if there are hiccups, says Ian Clark, the LDSD lead at the NASA Jet Propulsion Laboratory, "we would much rather learn these items now than learn them at Mars." —*Lee Billings*

ENVIRONMENT

Rain-Forest Threats Resume

Until recently, Brazil stood out as a hopeful outlier in the plague of deforestation. Between 1990 and 2010 clearing of tropical forests increased 62 percent worldwide, but in Brazil, such destruction plummeted from 2004 to 2011, in part because of tough environmental regulations and a ban on the sale of soybeans grown on rain-forest-cleared land. Since August 2014, however, tree cutting more than doubled in the country compared with the same period a year earlier, according to a satellite analysis released this spring by the independent research institution Imazon.

The report may signal a new round of challenges facing the world's largest rain forest. Most of the land cleared in the uptick will serve as cattle pasture, spurred by higher global prices for beef. (Cutting the forest for ranches is the largest driver of deforestation in the Brazilian Amazon, accounting for nearly 70 percent of clearing.) And Brazil's recently reelected president, Dilma Rousseff, has called for several new hydroelectric dams and a major highway that, if built, will slice through the pristine heart of the Amazon.

Her administration also supports legislation that weakens environmental protections and offers amnesty to those who illegally cut down trees, citing the need for economic growth.

A 2014 study by Brazil's National Institute for Space Research found that deforestation, especially extensive cutting along the southern edge of Amazonia, has decreased the movement of atmospheric moisture to the south. Climate scientists at the institute say the change is a possible factor in a severe drought that has necessitated rationing of water in Brazil's largest metropolis, São Paulo. And if clearing of the Amazon continues, says Phillip Fearnside, a biologist at Brazil's Amazon research institute INPA, "you will end up with a permanent drought, not just a one-year thing."

Tree loss in the Amazon reverberates beyond Brazil's boundaries. It reshuffles the climate deck for the entire Western Hemisphere: the rain forest pumps 20 billion tons of water vapor daily into the atmosphere through leaf transpiration, an influx that has ripple effects in weather systems a continent away. The Amazon is currently nearly 20 percent deforested, which may be close to a tipping point in terms of its ability to maintain the climate system and rains that it helps to support, says pioneering Amazon researcher Thomas Lovejoy. A perfect storm of deforestation, fire and climate change, he fears, could potentially transform vast swaths of the southern and eastern Amazon into savanna.

One 2013 study, for example, predicts that a fully deforested Amazon would mean 50 percent less snowfall in California's Sierra Nevada, quashing spring runoff vital to the region's agriculture. (Whether the present level of deforestation factors in the current West Coast drought is unknown.) To avoid further damage, many players will need to come together, but Brazil now appears to be moving in the opposite direction. —*Richard Schiffman*

ANTONIO SCORZA *Getty Images (top)*; RICARDO FUNARI *Getty Images (middle)*; RAPHAEL ALVES *Getty Images (bottom)*

COMMENT AT ScientificAmerican.com/jun2015

PSYCHOLOGY

Kiddo Knows Best

Unrealistically positive views of children may promote narcissism

Sometimes it's cute when kids act self-centered. Yet parenting styles can make the difference between a confident child and a narcissistic nightmare, psychologists at the University of Amsterdam and Utrecht University in the Netherlands concluded from the first longitudinal study on the origins of intense feelings of superiority in children.

Two prominent but nearly opposing schools of thought address how narcissism develops. The first attributes extreme self-love to a lack of affection from parents; the other implicates moms and dads who place their children on a pedestal by lavishing them with praise. Over the course of 18 months, 565 kids aged seven through 11 took multiple surveys designed to measure self-esteem, narcissism and their parents' warmth, answering questions about how much they identify with statements such as "kids like me deserve something extra." The parents filled out reciprocal surveys about their approach to child rearing.

In a March issue of *Proceedings of the National Academy of Sciences USA*, the Dutch researchers report that children of excessively praising parents were more likely to score high on narcissistic qualities but not on self-esteem. They also found that lack of parental warmth showed no such link to narcissism.

The correlation shows that positive feedback should be tied to good behavior in a child rather than piled on indiscriminately, says psychologist Luke Hyde of the University of Michigan, who did not participate in the work. A 2008 meta-analysis of 85 studies showed that narcissism is on the rise in young adults in the West, which could stem in part from a cultural emphasis on praise, with the goal of boosting high self-esteem, notes Eddie Brummelman, lead author of the *PNAS* paper. "It might be well intended," he adds, "but it actually backfires."

Such results support the praise-centric school of thought on narcissistic origins, although other scientists in the field point out that controversy still remains over the definition of narcissism itself. Brummelman and his colleagues considered narcissistic personality traits (such as the desire for admiration), not narcissistic personality disorder (characterized by an impairment of daily functioning), in their study because clinicians are discouraged from diagnosing the disorder in youth—no one knows at what age the full-blown psychiatric condition sets in. —*Andrea Alfano*

Q&A

An Apocalypse Think Tank

Martin Rees co-founded the Center for the Study of Existential Risk.

This year the Doomsday Clock moved forward for the first time since 2012. The theoretical countdown to catastrophe was devised 67 years ago by the *Bulletin of the Atomic Scientists,* a watchdog group created in 1945 by scientists who worked on the Manhattan Project. Its contemporary caretakers have inched the clock three minutes closer to midnight based on the threats of climate change and a slowdown in disarmament.

But global warming and nuclear malaise are not the only threats facing humanity. One organization is looking at the potential threats posed by emerging technologies—dangers no one has even considered yet. The Center for the Study of Existential Risk (CSER) at the University of Cambridge, founded in 2012, develops scientific methodologies for evaluating new global risks—to determine, for example, if a scenario in which robots take over the earth represents science fiction or a real-life possibility. Some of the world's greatest minds, including Stephen Hawking, Jaan Tallinn (a founding engineer of Skype) and philosopher Huw Price, contribute to the endeavor.

Scientific American sat down with one of the center's co-founders, astrophysicist Lord Martin Rees, to ponder the possible end of life as we know it. Edited excerpts follow.

—Interview by Erin Biba

Why start a group that delves into the threat of new technologies?

Throughout history our ancestors have confronted risks: pestilence, storms, earthquakes and human-induced disasters. But this century is different. It's the first when one species, ours, can determine the planet's future, threaten our civilization and jeopardize the existence of future generations.

What types of scenarios do you examine?

At the moment, there is a wide divergence among experts about both the probabilities and the impacts. Climate scientists differ on whether there are tipping points that could lead to catastrophe. There is a huge range of views among artificial-intelligence experts: some think that human-level AI with a mind of its own (and goals orthogonal to those of humans) could develop before midcentury; others deem this prospect very remote and argue that we should focus our concern on the ethics and safety of dumb autonomous robots (military drones, for instance). And there is already a lively debate on the frontiers of biotech. I hope that CSER will help forge a firmer consensus about which risks are most real and help to raise these on the agenda.

What are the major risks to humanity as you see them and how serious are they?

I'm personally pessimistic about the community's capacity to handle advances in biotech. In the 1970s the pioneers of molecular biology famously formulated guidelines for recombinant DNA at the Asilomar conference. Such issues arise even more starkly today. There is current debate and anxiety about the ethics and prudence of new techniques: "gain of function" experiments on viruses and the use of so-called CRISPR gene-editing technology. As compared with the 1970s, the community is now more global, more competitive and more subject to commercial pressures. I'd fear that whatever can be done will be done somewhere by someone. Even if there are formally agreed protocols and regulations, they'll be as hard to enforce as the drug laws. Bioerror and bioterror rank highest on my personal risk register for the medium term (10 to 20 years).

Is there anything people worry about that they shouldn't?

Many who live in the developed world fret too much about minor risks (carcinogens in food, low-radiation doses, plane crashes, and so forth). Some worry too much about asteroid impacts, which are among the natural risks that are best understood and easiest to quantify. Moreover, it will soon be possible to reduce that risk by deflecting the path of asteroids heading for the earth. That's why I support the B612 Sentinel project.

What should worry us more are threats that are newly emergent. They surely merit more attention, and they are what CSER aims to study. It's an important maxim that the unfamiliar is not the same as the improbable. The stakes are so high that even if we can reduce the probability of catastrophe by one part in a million, we'll have earned our keep.

CHARLIE FORGHAM-BAILEY *Redux Pictures*

COMMENT AT ScientificAmerican.com/jun2015

David Noonan, a science writer in New Jersey, wrote about medical marijuana in the February 2015 issue.

The Not So Silent Epidemic

Snoring can signal life-threatening apnea. New remedies such as a jolt to a nerve may help

Every night, before he goes to sleep, Al Pierce, whose thunderous snoring used to drive his wife out of their bedroom, uses a small remote control to turn on an electronic sensor implanted in his chest. The sensor detects small changes in his breathing pattern—early signs that Pierce's airway is beginning to collapse on itself. When the device senses these changes, it triggers a mild jolt of electricity that travels through a wire going up his neck. The wire ends at a tiny electrode wrapped around a nerve that controls muscles in his tongue. The nerve, stimulated by the charge, activates muscles that thrust Pierce's tongue forward in his mouth, which pulls his airway open.

Throughout the night the 65-year-old plumber in Florence, S.C., gets hundreds of little jolts, yet he sleeps quietly. In the morning, rested and refreshed, Pierce uses the remote to turn off the device.

This new technology, called upper-airway electronic stimulation and approved by the U.S. Food and Drug Administration last summer, offers much more than relief from an annoying noise. Pierce's loud snoring was the most obvious symptom of obstructive sleep apnea, a drastically underdiagnosed disorder shared by an estimated 25 million Americans. It can lead to high blood pressure, heart disease, diabetes, depression and an impaired ability to think clearly. Overall, people with severe sleep apnea have triple the risk of death from all causes as compared with those without the disorder.

Yet help has not been easy for sufferers to find. One very effective option, a strap-on mask that gently pushes air into the throat to hold it open, is rejected by a great many of the people who try it because the device is uncomfortable. Other alternatives offer only mixed results. So a surgical implant and nerve stimulation, as extreme as it may sound, could be the answer for many. In a study published last January in the *New England Journal of Medicine,* the technique reduced episodes of severe apnea by about two thirds. The FDA approval opens the door to insurance coverage for the treatment.

Doctors, for several reasons, have not been pushing to find apnea therapies. Patients tend not to bring serious apnea up with physicians as a problem, for one thing. And doctors may have their own reasons for treating the disorder lightly. "Sleep apnea is not on a death certificate," says Patrick J. Strollo, Jr., a sleep specialist at the University of Pittsburgh Medical Center. "While it may contribute to death, it's not really a direct cause." So, he says, "there is less urgency from primary care doctors and other doctors to address this problem."

Pierce found out that he had apnea only because his wife,

Illustration by Massimiliano di Lauro

Gail, asked her doctor for a prescription for sleeping pills. He asked why, and Gail explained that she needed them because of her husband's snoring. About half of the people who snore loudly have sleep apnea, according to the National Sleep Foundation. The doctor told her that if things were that bad, her husband should come in for a sleep study: an overnight observation period during which various sensors are attached to a patient. The study revealed that Pierce was having as many as 30 apnea episodes an hour. Despite years of feeling tired all the time, he was stunned that he had an actual medical problem. "I thought that was the way everyone lived. I didn't know any different," Pierce recalls.

Obstructive sleep apnea often develops when people age or put on extra weight. Fat narrows the tube of the airway, and the muscles in the mouth and throat also can lose their tone. When these muscles further relax during sleep, the airway becomes constricted and blocks the flow of air to the lungs. Some people with severe apnea stop breathing altogether, for up to a minute or two, as many as 600 times a night. This oxygen deprivation forces the heart to work harder and creates surges of adrenaline, which in turn cause blood pressure to spike. In addition, fluctuating oxygen levels can cause cell and tissue damage in the lungs and other organs.

Major interventions such as reconstructive throat surgery have often been ineffective. Physicians frequently recommend lifestyle-based changes such as losing weight and sometimes even playing the didgeridoo, a large Australian wind instrument that strengthens and tones the muscles of the tongue. Nose strips and generic mouthpieces, readily available over the counter, target snoring, the symptom, rather than sleep apnea, the underlying problem. The trouble is, what helps one patient may fail another completely. Plus, anything designed to go into the mouth or throat during sleep, to prop the airway open, can bother the patient and actually disrupt sleep. Any treatment has to be comfortable, easy to use and reliable.

Difficulty meeting all those criteria is what bedevils the strap-on mask, called CPAP, for continuous positive airway pressure. The oxygen mask covers the nose (or the nose and mouth) and is held in place by straps that wrap around the head. A small bedside pump delivers a steady flow of pressurized air to the mask through plastic tubing. The therapy, available since the early 1980s, almost guarantees relief from obstructive sleep apnea symptoms, and research shows that it lower rates of cardiovascular disease and death in patients who use it.

Use is the key: fully half of the people who try the mask abandon it. Pierce is one of them. "I was miserable," he says. Like so many others, Pierce could not sleep easily while wearing something over his face, and he did not like the way the tubing restricted his movements in bed.

Strollo is a strong CPAP advocate but has long recognized the need for an alternative. Upper-airway electronic stimulation could be that option, he says. Strollo led a large study of the new treatment, a yearlong safety and efficacy trial involving 126 people with moderate to severe obstructive apnea. The participants all had a body mass index (BMI) of 32 or less (a man who is five feet, 10 inches in height and 223 pounds in weight has a BMI of 32), had tried CPAP first and had no history of cardiovascular disease. In last January's *New England Journal of Medicine* study, Strollo and his colleagues reported that the therapy, with a device made by Inspire Medical Systems, reduced subjects' sleep apnea events by 68 percent, from a median of 29.3 events an hour to nine an hour, basically turning severe apnea into a mild case. (CPAP, after adjustment, can do even better. It can cut the number of severe apnea events to fewer than five an hour, on average, but only in patients who stick with it.)

Nose strips and generic mouthpieces, readily available over the counter, target snoring, the symptom, rather than sleep apnea, the underlying problem.

Alan R. Schwartz, a sleep specialist at Johns Hopkins University who did much of the early work on nerve stimulation—he showed in animals that jolting the tongue-controlling nerve would open their airway—says he is pleased but cautious. "We've still got a lot to learn," he notes, pointing out that overweight and obese people, who make up a significant percentage of the obstructive apnea population, are not considered good candidates for the procedure because of their excess airway tissue.

What is more, stimulation involves an invasive procedure. The surgery to implant the device takes about two hours. A head and neck surgeon, working through an incision in the side of the neck, under the patient's jaw, places an electrode on the hypoglossal nerve, which controls the muscles of the tongue. The surgeon also puts a battery pack and a sensor in the chest and connects them to the electrode with a wire lead. The patient usually can go home a day later; the device is turned on and adjusted after a month.

Researchers are investigating more alternatives, such as medication. In a six-week trial involving 120 patients, David W. Carley, a physician at the University of Illinois at Chicago, is testing a drug called dronabinol, which is a synthetic version of an active compound in marijuana. He is comparing people who get the drug with those who do not. Dronabinol may prevent or reduce sleep apnea episodes by stimulating certain neurotransmitter activity in the brain. Other researchers are looking at the role played by leptin, a hormone that suppresses appetite and may improve respiratory function. A small study of 26 obese subjects with BMIs greater than 45 suggests that certain levels of leptin may minimize upper-airway collapse.

Schwartz is also trying to modify the stimulation technique, testing a device that eliminates the sensor. Instead it sends a repeated charge to the nerve in the tongue during the night to keep the airway open. This refinement should simplify the surgery and reduce parts that could fail, Schwartz says.

Pierce, however, is quite happy with the system he has. When he is awake—or quietly sleeping—he does not even notice it. SA

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

The Upgrade Game

Why feature-clogged tech upgrades keep selling—and why we keep buying

Usually once you pay for something, you own it, and the transaction is complete. That's how it works with, for example, sneakers, pretzels or dog shampoo.

But in technology, you're never really finished paying. Buying Microsoft Word, or Quicken, or an iPhone may feel like a one-time transaction, but it's not. Every year you'll be offered the chance to buy a newer, updated version.

Since Word debuted in the 1980s, upgraded versions have been offered 14 times. Since Photoshop 1.0 in 1990: 20 times. If you'd bought Photoshop in 1990 and stayed current by buying each annual upgrade, you'd have paid more than $4,000 by now.

Something similar happens in the hardware world. You might have purchased that first 2007 iPhone or Samsung Galaxy phone, but you've almost certainly bought a new version by now.

Clearly, this business model works well for tech companies. But how well does it work for us? At first, you might answer, "We keep upgrading, don't we? Obviously, we're happy!"

The problem is that the tech companies have only one big tool to entice you to upgrade each year: *piling on new features*. More, more features. Microsoft Word was once a word processor. Today it's a database, and a Web-layout program, and a floor wax.

Eventually these companies have no choice but to add features that nobody asked for. Meanwhile bloated, overwhelming technology has a very real emotional effect on us; we feel like idiots when we can't master it.

Then, as the software becomes increasingly weighed down with features, the interface must be redesigned to accommodate them all. (Such a redesign is then, of course, marketed as a new feature.) And each time you lose a few days of productivity as you learn the new layout.

Nobody's *forcing* us to keep up with the upgrades. If we don't like the upgrade ritual, we can just get off the treadmill. Right?

Well, no. Sooner or later the product we currently own is no longer "supported" (the company won't help you with problems and won't update that version for newer operating systems). Microsoft, for example, has cut off mainstream support for Windows XP, Vista and even 7. It abandons each version of Office as soon as five years after its release.

In the end, your unsupported program won't run on the latest computers and operating systems. You may not even be able to *open* the documents created by a program's earlier version.

It's not all the industry's fault, though. We *like* surrounding ourselves with unnecessary features. It's the SUV syndrome: people who are nonfarmers, in nonmountainous areas, buy far more car than they need—you know, in case there's a flash flood on the drive to Whole Foods.

Back in the 1980s, Microsoft responded to complaints that Word for the Mac was too complex by offering a stripped-down program called Microsoft Write. It could open and save Word documents, but it was *only* a word processor. And guess what? It bombed. Nobody wants Standard; we all want Deluxe.

In other words, both the software companies and their customers struggle with the challenge of perpetual feature bloat—but neither party shows any sign of considering other arrangements. No tech company on earth, for example, would create a product just once, designed perfectly for its task, and just sell that version forever, making only compatibility tweaks as necessary. That would be unthinkable.

Adobe abandoned the upgrade model in 2013, in favor of an annual subscription plan. Longtime customers were furious at first—what incentive would Adobe now have to keep improving its programs?—but the new model was ultimately a financial coup for the company. Other developers are flirting with the same.

So far few other consumer software firms have followed suit. And why should they? When you step back and consider the way the annual upgrade cycle really works, you realize we've all been on subscription plans all along. SA

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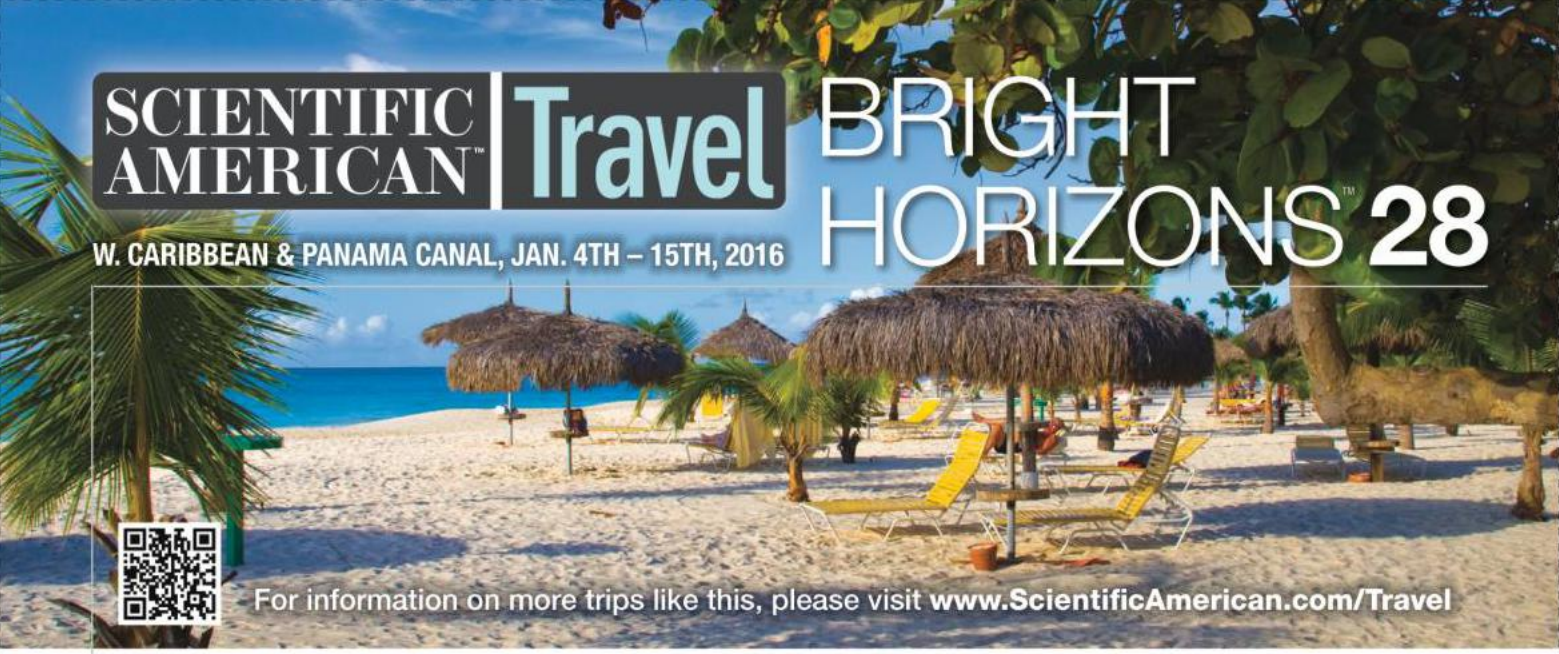
Illustration by Fredrik Rättzén



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Psychology

Speaker: Monisha Pasupathi, Ph.D.

Your Memories Are Not Your Own

Learn how personal memory is shaped by important people in our lives and by the culture and society we live in, and why memory's malleability is useful. We'll look at emerging psychological and neuroscience work relating our capacities to recall the past to our abilities to simulate the future.

Rationality Needs Feelings

The idea that feelings make us irrational is widely held, but untrue. In fact, emotions have important functions for directing our attention, readying us for challenges, and expanding our thinking. Explore how emotions operate, the purposes they serve, and the ways that people seek to control them.

Personality Matters

People are diverse in many ways — from basic traits to the kinds of life stories that they create. Learn what personality research tells us about how these differences arise, what they mean for our lives, and why diversity of personality may be useful for humanity.

Moral Reasoning and Moral Identity

Researchers once thought moral reasoning arose during adolescence, but contemporary work suggests that in some respects, even young children have notions of fairness and welfare. We'll discuss reconciling our understanding of morality with our sometimes imperfect behaviors and how to develop a sense of ourselves and others as moral agents.

Achieving the Good Life

Research has explored three different facets of a good life: happiness, purpose, and wisdom. The paths to these three facets may overlap but are also distinct. Explore what we know about these three features of the good life and learn how you can cultivate happiness, purpose, and wisdom.

Anthropology

Speaker: Chris Stringer, Ph.D.

Human Evolution: the Big Picture

Get an introduction to 7 million years of human evolution, from the time of our divergence from the African apes to the emergence of humans. The fact that we walk on two legs distinguishes us from our primate relatives, which Darwin attempted to explain in evolutionary terms. We'll look at how Darwin's ideas have fared in the face of the latest discoveries.

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The First Humans

About 2 million years ago the first humans appeared in Africa. Discover what drove their evolution and led to a spread from their homeland to Asia and Europe. Could a controversial find on the far-away island of Flores, in Indonesia, be a relic of these early stages of human evolution? Find out.

The Neanderthals: Another Kind of Human

Our close relatives the Neanderthals evolved in parallel with our own species. They are often depicted as bestial ape-men, but in reality they walked upright as well as we do, and their brains were as large as ours. Track the evolution of the Neanderthals in light of the latest discoveries — and be open to surprises.

The Rise of Homo Sapiens

Modern humans are characterized by large brains and creativity. How did our species arise and spread across the world and how did we interact with other human species? Delve into the origins of human behavioral traits such as complex technology, symbolism and burial of the dead for insights into essential humanness.

Astrophysics

Speaker: Glenn Starkman, Ph.D.

The State of the Universe Report

The universe is big and getting bigger at an accelerating rate. Hear the latest thoughts on cosmic microwave background radiation, supernovae and other phenomena that give us information on the early universe, cosmic expansion, and the large-scale structure of the universe.

In the Beginning

First there was something, then there was much, much more. What was that something, and how did it become everything we see in the universe? Explore these deep questions and lay the groundwork for our subsequent sessions delving into dark matter and inflation.

Oh Dear, What Could Dark Matter Be?

Physicists thought they were going to make dark matter at CERN's Large Hadron Collider, but it's nowhere to be seen. Others have been hoping to make it by shining lasers on concrete, but nothing gets through. So what is dark matter anyway? Get up to speed on current theories and the quest to detect dark matter.

Dissonance in the Cosmic Symphony

The Standard Model of Cosmology is awfully good at explaining a lot about the universe — but not everything. For example, we don't know what's causing the dark energy that's pulling space apart. Hear about prospects for addressing these mysteries and how they are presenting new areas of research for the undaunted physicist.

Mathematics

Speaker: Michael Starbird, Ph.D.

The Five Elements of Effective Thinking

A romantic belief is that brilliant thinkers magically produce brilliant ideas. In truth, however, brilliant innovators practice habits of thinking that inevitably carry them step by step to works of genius. Learn to hone your skills in effective thinking to create new insights, ideas and solutions.

To Infinity … and Beyond

People once thought infinity was incomprehensible — an idea so vast that understanding it was beyond the scope of our finite minds. But we'll create a framework to study infinity and use models from a child's method of sharing to take us to a new understanding of infinity and beyond.

The Fourth Dimension

Untying knots, stealing gold bricks from closed iron safes, and unfolding hypercubes are all part of a journey in the fourth dimension. By applying the basic principles of mathematical thinking to the fourth dimension, we'll explore how deep understanding of the simple and familiar is the key to investigating the complex and mysterious.

Expect the Unexpected

Whether we flip a coin, look at data or ask for birthdays, we find that our intuition about what to expect from random chance is often far from what actually happens. Deepen your understanding of the nature and workings of probability and randomness so you can leverage them as reasoning tools.

Jay N. Giedd is chair of the division of child and adolescent psychiatry at the University of California, San Diego, and a professor at the Johns Hopkins Bloomberg School of Public Health. He is also editor in chief of the journal *Mind, Brain, and Education*.

NEUROSCIENCE

the amazing teen brain

A mismatch in the maturation of brain networks leaves adolescents open to risky behavior but also allows for leaps in cognition and adaptability

By Jay N. Giedd

IN BRIEF

MRI studies show that the teenage brain is not an old child brain or a half-baked adult brain; it is a unique entity characterized by changeability and an increase in networking among brain regions.

The limbic system, which drives emotions, intensifies at puberty, but the prefrontal cortex, which controls impulses, does not mature until the 20s. This mismatch makes teens prone to risk taking but also allows them to adapt readily to their environment.

Earlier onset of puberty in children worldwide is expanding the years during which the mismatch occurs.

Greater understanding of the teen brain should help parents and society better distinguish typical behavior from mental illness while helping teens become the people they want to be.

Illustration by Harry Campbell, Photograph by Ethan Hill

The "teen brain" is often ridiculed as an oxymoron—an example of biology gone wrong.

Neuroscientists have explained the risky, aggressive or just plain baffling behavior of teenagers as the product of a brain that is somehow compromised. Groundbreaking research in the past 10 years, however, shows that this view is wrong. The teen brain is not defective. It is not a half-baked adult brain, either. It has been forged by evolution to function differently from that of a child or an adult.

Foremost among the teen brain's features is its ability to change in response to the environment by modifying the communications networks that connect brain regions. This special changeability, or plasticity, is a double-edged sword. It allows teenagers to make enormous strides in thinking and socialization. But the morphing landscape also makes them vulnerable to dangerous behaviors and serious mental disorders.

The most recent studies indicate that the riskiest behaviors arise from a mismatch between the maturation of networks in the limbic system, which drives emotions and becomes turbo-boosted in puberty, and the maturation of networks in the prefrontal cortex, which occurs later and promotes sound judgment and the control of impulses. Indeed, we now know that the prefrontal cortex continues to change prominently until well into a person's 20s. And yet puberty seems to be starting earlier, extending the "mismatch years."

The plasticity of networks linking brain regions—and not the growth of those regions, as previously thought—is key to eventually behaving like an adult. Understanding that, and knowing that a widening gap between the development of emotional and judgment networks is happening in young people today, can help parents, teachers, counselors and teenagers themselves. People will better see that behaviors such as risk taking, sensation seeking, and turning away from parents and toward peers are not signs of cognitive or emotional problems. They are a natural result of brain development, a normal part of adolescents learning how to negotiate a complex world.

The same understanding can also help adults decide when to intervene. A 15-year-old girl's departure from her parents' tastes in clothing, music or politics may be a source of consternation for Mom and Dad but does not indicate mental illness. A 16-year-old boy's propensity to skateboard without a helmet or to accept risky dares from friends is not trivial but is more likely a manifestation of short-range thinking and peer pressure than a desire to hurt himself. Other exploratory and aggressive actions might be red flags, however. Knowing more about the unique teen brain will help all of us learn how to separate unusual behavior that is age-appropriate from that which might indicate illness. Such awareness could help society reduce the rates of teen addiction, sexually transmitted diseases, motor vehicle accidents, unwanted pregnancy, homicide, depression and suicide.

GREATER CONNECTIVITY

FEW PARENTS OF A TEENAGER will be surprised to hear that the brain of a 16-year-old is different from the brain of an eight-year-old. Yet researchers have had difficulty pinning down these differences in a scientific way. Wrapped in a tough, leathery membrane, surrounded by a protective moat of fluid and completely encased in bone, the brain is well protected from falls, attacks from predators—and the curiosity of scientists.

The invention of imaging technologies such as computerized tomography and positron-emission tomography has offered some progress, but because these techniques emit ionizing radiation, it was unethical to use them for exhaustive studies of youth. The advent of magnetic resonance imaging (MRI) finally provided a way to lift the veil, offering a safe and accurate way to study the anatomy and physiology of the brain in people of all ages. Ongoing studies are tracking thousands of twins and single individuals throughout their lives. The consistent theme that is emerging is that the adolescent brain does not mature by getting larger; it matures by having its different components become more interconnected and by becoming more specialized.

In MRI scans, the increase in connectivity among brain regions is indicated as greater volumes of white matter. The "white" in white matter comes from a fatty substance called myelin, which wraps and insulates the long wire, or axon, that extends from a neuron's body. Myelination—the formation of this fatty sheath—takes place from childhood through adulthood and significantly speeds up the conduction of nerve impulses among neurons. Myelinated axons transmit signals up to 100 times faster than unmyelinated ones.

Myelination also accelerates the brain's information processing by helping axons recover quickly after they fire so that they are ready to send another message. Quicker recovery time allows up to a 30-fold increase in the frequency with which a given neuron can transmit information. The combination of faster transmission and shorter recovery time provides a 3,000-fold increase in the brain's computational bandwidth between infancy and adulthood, permitting extensive and elaborate networking among brain regions.

Recent investigations are revealing another, more nuanced

PAGE 32: GROOMING BY TINNA EMPERA *Couture/Remix*; STYLING BY MONICA COTTO; PHOTOGRAPH FOR ILLUSTRATION PURPOSES ONLY

role for myelin. Neurons integrate information from other neurons but only fire to pass it on if the incoming input exceeds a certain electrical threshold. If the neuron fires, that action initiates a series of molecular changes that strengthens the synapses, or connections, between that neuron and the input neurons.

This strengthening of connections forms the basis for learning. What researchers themselves are now learning is that for input from nearby and distant neurons to arrive simultaneously at a given neuron, the transmission must be exquisitely timed, and myelin is intimately involved in the fine-tuning of this timing. As children become teenagers, the rapid expansion of myelin increasingly joins and coordinates activities in different parts of the brain on a variety of cognitive tasks.

Scientists can now measure this changing interconnectivity by applying graph theory, a type of mathematics that quantifies the relation between "nodes" and "edges" in a network. Nodes can be any object or detectable entity, such as a neuron or a brain structure like the hippocampus or a larger region such as the prefrontal cortex. Edges can be any connections among nodes, from a physical connection such as a synapse between neurons to a statistical correlation such as when two parts of the brain are activated similarly during a cognitive task.

Graph theory has helped me and others to measure how different brain regions develop and become interconnected to one another and to correlate such features with changes in behavior and cognition. Brain changes are not confined to adolescence. Most brain circuits develop in the womb, and many continue to change throughout life, well beyond the teen years. It turns out, however, that during that period there is a dramatic increase in connectivity among brain regions involved in judgment, getting along with others and long-range planning—abilities that profoundly influence the remainder of a person's life.

TIME TO SPECIALIZE

AS THE WHITE MATTER along neurons is developing with age in adolescents, another change is taking place. Brain development, like other complex processes in nature, proceeds by a one-two punch of overproduction, followed by selective elimination. Like Michelangelo's *David* emerging from a block of marble, many cognitive advances arise during a sculpting process in which unused or maladaptive brain cell connections are pruned away. Frequently used connections, meanwhile, are strengthened. Although pruning and strengthening occur throughout our lives, during adolescence the balance shifts to elimination, as the brain tailors itself to the demands of its environment.

Specialization arises as unused connections among neurons are eliminated, decreasing the brain's gray matter. Gray matter consists largely of unmyelinated structures such as neuron cell bodies, dendrites (antennalike projections from the cells that receive information from other neurons) and certain axons. Overall, gray matter increases during childhood, reaches a maximum around age 10 and declines through adolescence. It levels off during adulthood and declines somewhat further in senescence. The pattern also holds for the density of receptor cells on neurons that respond to neurotransmitters—molecules such as dopamine, serotonin and glutamate that modulate communication among brain cells.

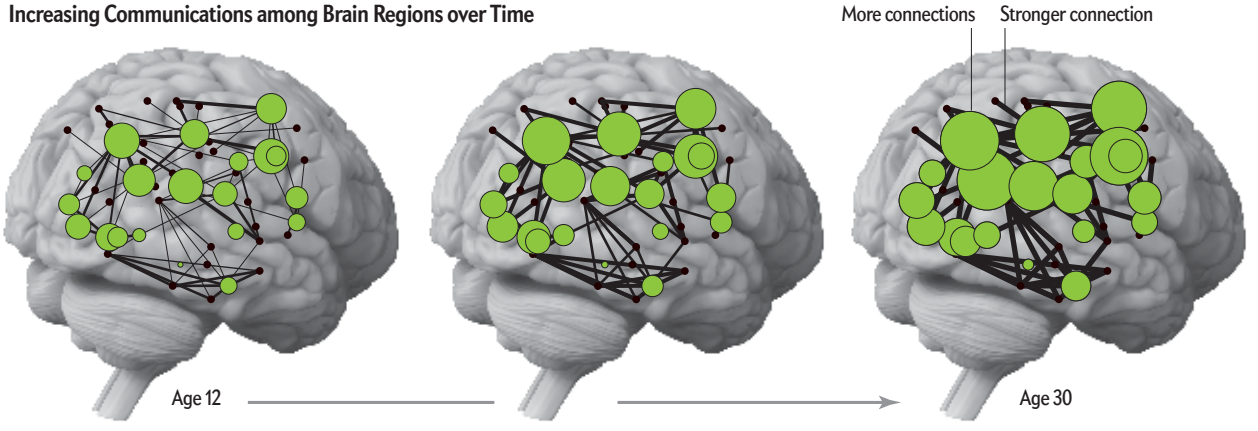
Although the raw amount of gray matter tops out around puberty, full development of different brain regions occurs at different times. Gray matter, it turns out, peaks earliest in what are called primary sensorimotor areas devoted to sensing and responding to sight, sound, smell, taste and touch. It peaks latest in the prefrontal cortex, crucial to executive functioning, a term that encompasses a broad array of abilities, including organization, decision making and planning, along with the regulation of emotion.

A NEW VIEW

Greater Networking Brings Maturity

The most significant change taking place in an adolescent brain is not the growth of brain regions but the increase in communications among groups of neurons. When an analytical technique called graph theory is applied to data from MRI scans, it shows that from ages 12 to 30, connections between certain brain regions or neuron groups become stronger (*black lines that get thicker*). The analysis also shows that certain regions and groups become more widely connected (*green circles that get larger*). These changes ultimately help the brain to specialize in everything from complex thinking to being socially adept.

Increasing Communications among Brain Regions over Time



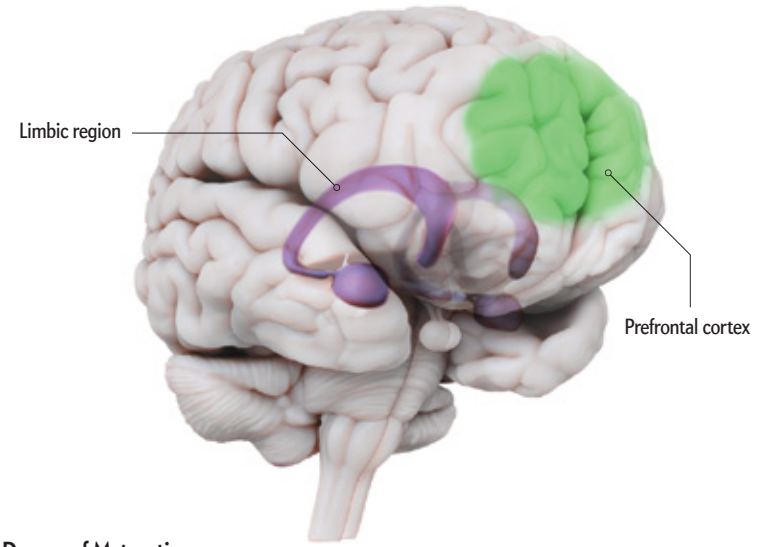
SOURCE: "DEVELOPMENT OF BRAIN STRUCTURAL CONNECTIVITY BETWEEN AGES 12 AND 30." BY EMILY L. DENNIS ET AL., IN *NEUROIMAGE*, VOL. 64; JANUARY 1, 2013 (SUPPLEMENTARY VIDEO 2)

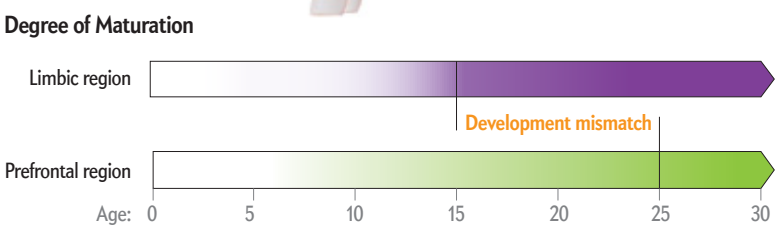
Illustration by David Killpack (brains) and Jen Christiansen (nodal diagrams)

ROOTS OF RISK TAKING

Emotion vs. Control

Teenagers are more likely than children or adults to engage in risky behavior, in part because of a mismatch between two major brain regions. Development of the hormone-fueled limbic system (*purple*), which drives emotions, intensifies as puberty begins (typically between ages 10 to 12), and the system matures over the next several years. But the prefrontal cortex (*green*), which keeps a lid on impulsive actions, does not approach full development until a decade later, leaving an imbalance during the interim years. Puberty is starting earlier, too, boosting hormones when the prefrontal cortex is even less mature.





An important feature of the prefrontal cortex is the ability to create hypothetical what-ifs by mental time travel—to consider past, present and possible future outcomes by running simulations in our mind instead of subjecting ourselves to potentially dangerous reality. As philosopher Karl Popper phrased it, instead of putting ourselves in harm's way, "our theories die in our stead." As we mature cognitively, our executive functioning also makes us more likely to choose larger, longer-term rewards over smaller, shorter-term ones.

The prefrontal cortex is also a key component of circuitry involved in social cognition—our ability to navigate complex social relationships, discern friend from foe, find protection within groups and carry out the prime directive of adolescence: to attract a mate.

Adolescence is therefore marked by changes in gray matter and in white matter that together transform the networking among brain regions as the adult brain takes shape. The prefrontal cortex functions are not absent in teenagers; they are just not as good as they are going to get. Because they do not fully mature until a person's 20s, teens may have trouble controlling impulses or judging risks and rewards.

A MISMATCH IN MATURATION

UNLIKE THE PREFRONTAL CORTEX, the hormone-fueled limbic system undergoes dramatic changes at the time of puberty, which traditionally begins between ages 10 and 12. The system regulates emotion and feelings of reward. It also interacts with the prefrontal cortex during adolescence to promote novelty seeking, risk taking and a shift toward interacting with peers. These behaviors, deeply rooted in biology and found in all social mammals, encourage tweens and young teens to separate from the comfort and safety of their families to explore new environments and seek outside relationships. These behaviors diminish the likelihood of inbreeding, creating a healthier genetic population, but they can also pose substantial dangers, especially when mixed with modern temptations such as easy access to drugs, firearms and high-speed motor vehicles, unchecked by sound judgment.

What most determines teen behavior, then, is not so much the late development of executive functioning or the early onset of emotional behavior but a mismatch in the timing of the two developments. If young teens are emotionally propelled by the limbic system, yet prefrontal control is not as good as it is going to get until, say, age 25, that leaves a decade of time during which imbalances between emotional and contemplative thinking can reign. Furthermore, puberty starting at an earlier age, as is the case worldwide, lengthens the gap of time between the onset of increased risk taking and sensation seeking and the rise of a strong, stabilizing prefrontal cortex.

The lengthening mismatch supports the growing notion that the teen years are no longer synonymous with adolescence. Adolescence, which society defines as the transition from childhood to adulthood, begins in biology with the onset of puberty but ends in a social construct when a person achieves independence and assumes adult roles. In the U.S., attainment of an adult role—often characterized by such events as getting married, having a child and owning a home—is occurring approximately five years later than in the 1970s.

The large influence of social factors in determining what constitutes an adult has led some psychologists to suggest that adolescence is less of a biological reality than a product of changes in child rearing since the industrial revolution. Yet twin studies, which examine the relative effects of genes and environment by following twins who have different experiences, refute the view that social factors can substantially override the biology. They show that the pace of biological maturation of white

SOURCE: JAY N. GIEDD

Illustration by David Killpack (brain) and Jen Christiansen (graphic)

and gray matter can be influenced somewhat by the environment but that the fundamental timing is under biological control. Sociologists see this, too; risk taking, sensation seeking and a move toward peers happen in all cultures, although the degree can vary.

VULNERABILITY AND OPPORTUNITY

THE GRAY MATTER, white matter and networking developments detected by MRI underscore the observation that the most striking feature in teen brain development is the extensive changes that occur. In general, this plasticity decreases throughout adulthood, and yet we humans still retain a level of plasticity far longer than any other species.

Protracted maturation and prolonged plasticity allow us to "keep our options open" in the course of our own development, as well as the entire species' evolution. We can thrive everywhere from the frigid North Pole to hot islands on the equator. With technologies developed by our brain, we can even live in vessels orbiting our planet. Back 10,000 years ago—a blink of an eye in evolutionary terms—we spent much of our time securing food and shelter. Today many of us spend most of our waking hours dealing with words and symbols—which is particularly noteworthy, given that reading is only 5,000 years old.

Prolonged plasticity has served our species well but creates vulnerabilities in addition to opportunities. Adolescence is the peak time of emergence for several types of mental illnesses, including anxiety disorders, bipolar disorder, depression, eating disorders, psychosis and substance abuse. Surprisingly, 50 percent of the mental illnesses people experience emerge by age 14, and 75 percent start by age 24.

The relation between typical adolescent brain changes and the onset of psychopathology is complicated, but one underlying theme may be that "moving parts get broken." The idea is that the extensive changes in white matter, gray matter and networking increase the chance for problems to arise. For example, almost all the abnormal brain findings in adult schizophrenia resemble the typical changes of adolescent brain development gone too far.

In many other ways, adolescence is the healthiest time of life. The immune system, resistance to cancer, tolerance to heat and cold, and other traits are at their greatest. Despite physical robustness, however, serious illness and death are 200 to 300 percent higher for teens than for children. Motor vehicle accidents, the number-one cause, account for about half of teen deaths. Homicide and suicide rank second and third. Unwanted teen pregnancy, sexually transmitted diseases and behavior leading to incarceration are also high, imposing tough, lifelong consequences.

So what can doctors, parents, teachers and teens themselves do about these pitfalls? For clinicians, the paucity of novel medications in psychiatry and the propensity of the adolescent brain to respond to environmental challenges suggest that nonmedication interventions may be most fruitful—especially early in teen development, when white matter, gray matter and networking are changing fast. Treatment of obsessive-compulsive disorder is one example; behavioral interventions that trigger the obsessive impulse but gradually modify a person's response may be highly effective and could prevent a lifetime of disability. Appreciating that the brain is changeable throughout the teen years obliterates the notion that a youth is a "lost cause." It offers optimism that interventions can change a teenager's life course.

More study will help, too. The infrastructure for adolescent research is not well developed, funding for this work is meager and few neuroscientists specialize in this age group. The good news is that as researchers clarify the mechanisms and influences of adolescent brain developments, more resources and scientists are being drawn into the field, eager to minimize risks for teenagers and harness the incredible plasticity of the teen brain.

Understanding that the adolescent brain is unique and rapidly changing can help parents, society and teens themselves to better manage the risks and grasp the opportunities of the teenage years. Knowing that prefrontal executive functions are still under construction, for example, may help parents to not overreact when their daughter suddenly dyes her hair orange and instead take solace in the notion that there is hope for better judgment in the future. Plasticity also suggests that constructive dialogue between parents and teens about issues such as freedoms and responsibilities can influence development.

Adolescents' inherent capacity to adapt raises questions about the impact of one of the biggest environmental changes in history: the digital revolution. Computers, video games, cell phones and apps have in the past 20 years profoundly affected the way teens learn, play and interact. Voluminous information is available, but the quality varies greatly. The skill of the future will not be to remember facts but to critically evaluate a vast expanse of data, to discern signal from noise, to synthesize content and to apply that synthesis to real-world problem solving. Educators should challenge the adolescent brain with these tasks, to train its plasticity on the demands of the digital age.

Greater society has some compelling opportunities as well. For one thing, it could be more focused on harnessing the passion, creativity and skills of the unique adolescent development period. Society should also realize that the teen years are a turning point for a life of peaceful citizenship, aggression or, in rare cases, radicalization. Across all cultures, adolescents are the most vulnerable to being recruited as soldiers and terrorists, as well as the most likely to be influenced to become teachers and engineers. Greater understanding of the teen brain could also help judges and jurors reach decisions in criminal trials.

For teens themselves, the new insights of adolescent neuroscience should encourage them to challenge their brain with the kinds of skills that they want to excel at for the remainder of their lives. They have a marvelous opportunity to craft their own identity and to optimize their brain according to their choosing for a data-rich future that will be dramatically different from the present lives of their parents. SA

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ASTRONOMY

All the Light There Ever Was

Galaxies in every corner of the universe have been sending out photons, or light particles, since nearly the beginning of time. Astronomers are now beginning to read this extragalactic background light

By Alberto Domínguez, Joel R. Primack and Trudy E. Bell

IN BRIEF

The night sky may look dark, but it is actually filled with the accumulated light of all the galaxies that have shone in the universe's history.

This extragalactic background light is difficult to detect because it has spread out throughout the expanding cosmos and because it is outshone by brighter nearby sources of light.

Astronomers have finally been able to measure this light by observing how gamma rays from distant bright galaxies called blazars are dimmed when they collide with photons of the extragalactic background light.

Studying the background in this way allows scientists to examine the record of cosmic history that the light preserves.

CALEB CHARLAND

Why is the night sky dark?

Alberto Domínguez is a postdoctoral fellow in the department of physics and astronomy at Clemson University, where he studies galaxy evolution and cosmology.

Joel R. Primack is Distinguished Professor Emeritus of Physics at the University of California, Santa Cruz. He is one of the main developers of the modern theory of cosmology, dark matter and galaxies.

Trudy E. Bell is a former editor of *Scientific American* and *IEEE Spectrum* and author of a dozen books.

After all, if the universe is filled with billions of galaxies, every one of them swirling with billions of stars that have been emitting photons of light for billions of years, why would the universe not be awash with light? German astronomer Wilhelm Olbers pondered that question in the 1820s, and the riddle became known as Olbers's paradox. By then, astronomers and philosophers had wondered for centuries why the sky was dark and what the darkness implied about the nature of the universe. It turns out that these scholars were on to something truly profound.

More light is out there than we can easily see. Even from deep space, far away from the lights of Earth and the stars of the Milky Way, the sky of intergalactic space is *not* absolutely black. It glows with what is called the extragalactic background light (EBL). The EBL consists of all the photons of light radiated by all the stars and galaxies that have ever existed, at all wavelengths from the ultraviolet through the far infrared, during all of cosmic history to the present. The EBL from distant galaxies is faint because extragalactic space is vast compared with the number of galaxies that glow (or have ever done so). Because the universe is expanding, the photons emitted by galaxies over the history of the cosmos have spread throughout the cavernous volume of space and become dilute. And because of the expansion, light from distant galaxies undergoes a "redshift"—wavelength increases, pushing the light toward the red side of the electromagnetic spectrum, outside the visible realm.

Astronomers have realized for a while that this extragalactic background light should exist but were unable to measure it accurately. Between 2012 and 2013, for the first time, researchers (including two of us, Domínguez and Primack) were able to unambiguously quantify the extragalactic background light using gamma-ray data from the Fermi Gamma-ray Space Telescope and ground-based very high energy gamma-ray detectors called atmospheric Cherenkov telescopes. Intriguingly, because stars contribute most of the EBL either directly as starlight or through heating dust that radiates at longer wavelengths, the background preserves the "memory" of star formation at different epochs throughout the history of the universe. Indeed, measurements of the EBL are allowing us to explore the evolution of galaxies from ancient times to the present. Eventually it may let us study the very first generation of galaxies from more than 13 billion years ago, whose light is too faint to see directly with current telescopes.

THE COSMIC BACKGROUNDS

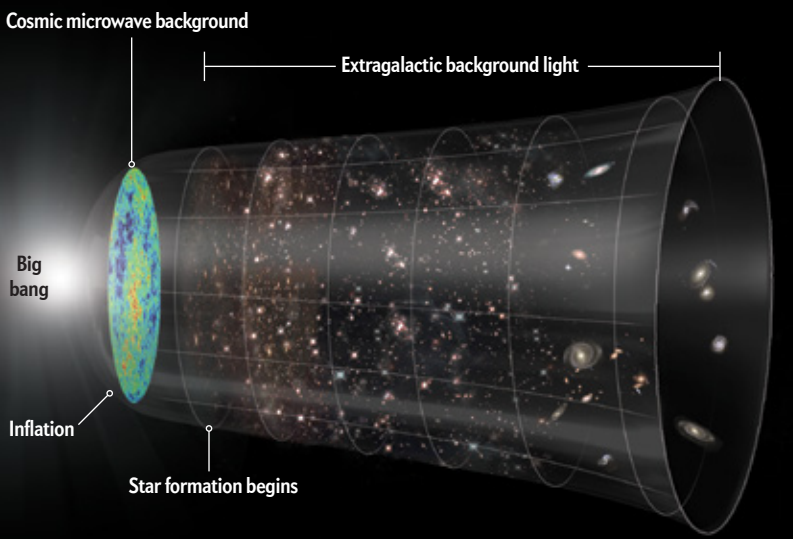
OLBERS'S PARADOX was primarily a philosophical question until the 1960s, when phenomenal astronomical discoveries across the entire electromagnetic spectrum were transforming cosmology from speculation to a hard observational science. Researchers were beginning to discover a menagerie of bizarre galactic and extragalactic objects. The universe, it was becoming clear, is filled with a rarefied "gas" of photons zooming every which way through extragalactic space. These photons come in many wavelengths—and equivalently, in many energy ranges (shorter wavelengths correspond to waves with higher frequencies and thus greater energies; long wavelengths have lower frequencies and thus smaller energies). That gas includes the EBL, as well as several other radiation fields seen in all directions. The brightest is the cosmic microwave background (CMB), which originated from the explosive big bang. In 1965 Arno Penzias and Robert W. Wilson discovered the CMB while at AT&T Bell Laboratories, for which they received the 1978 Nobel Prize in Physics. Another radiation field, an extragalactic diffuse x-ray background, was discovered in the 1960s with sounding rockets. In the late 1960s an orbiting solar observatory found yet another background of more energetic gamma rays.

The EBL—the cosmic background encompassing the near-ultraviolet, visible and infrared wavelengths—is second in energy and intensity to the CMB. Unlike the CMB, however, the EBL was not produced all at once. Instead it has been growing over billions of years, beginning with the formation of the first stars in the first galaxies roughly 200 million years after the big bang. Indeed, the EBL is still being added to today as new stars are born and begin to shine.

Directly measuring the EBL by collecting its photons with a telescope is akin to trying to observe the dim band of the Milky Way at night from among the brightly lit theaters and skyscrapers in New York City's Times Square. The EBL has a lot of competition at the same visible and infrared wavelengths. Earth is inside an extremely bright galaxy with billions of stars and immense clouds of glowing gas that outshine the extragalactic background light. Even worse for directly measuring the EBL, Earth resides in a very well-lit solar system: sunlight scattered by all the dust near Earth's orbit around the sun creates the zodiacal light—sometimes so luminous that from a dark site at the right time of year it

Extragalactic Background Light

The extragalactic background light (EBL) includes all the light from all the galaxies that have ever shined. It began to accumulate when the first stars and galaxies formed, roughly 200 million years after the big bang, and new galaxies add their light all the time. Still, because space is so vast (and expanding), this light is dim and diffuse. The cosmic microwave background (CMB) is another radiation field that also pervades the universe. The CMB, however, does not grow with time; rather it was formed all at once, about 400,000 years after the big bang.



can be mistaken for early dawn—that shines in similar wavelengths to the EBL.

How could astronomers ever hope to isolate, capture and identify faint EBL photons when they are swamped by a much brighter glow from the solar system and Milky Way? They cannot. Ground- and space-based telescopes have not succeeded in reliably measuring the EBL directly. In 2000 Piero Madau of the University of California, Santa Cruz, and Lucia Pozzetti of the Bologna Astronomical Observatory added up the light from galaxies detected by the Hubble Space Telescope. (Remember, the EBL is *all* the light emitted from near-ultraviolet through infrared wavelengths, including all the light from bright galaxies, which is easy to measure, plus galaxies too faint for telescopes to see.) But that count did not include faint galaxies or other possible sources of light, which means it gave only a lower limit for how bright the EBL could be at various wavelengths.

In 2011 Domínguez and Primack and our observational collaborators placed stronger lower limits on the EBL by adding up the amount of infrared and visible light observed from ground- and space-based telescopes from nearby galaxies out to about eight billion years ago—what astronomers call a redshift of 1, a little more than halfway back in time to the big bang. (Looking great distances out into space is equivalent to looking eons back in time because one sees objects as they looked when the light now reaching telescopes first departed on its journey—billions of years ago, in the case of truly distant galaxies.) We measured the changing patterns of wavelengths emitted by galaxies at different distances—that is, at various cosmic eras. This method allowed the best EBL determination yet based on observations. We calculated upper and lower estimates for the EBL from even more distant, older galaxies at redshifts greater than 1.

To move beyond limits, however—to truly measure the brightness of the extragalactic background light—astronomers would need to take another tack.

COLLIDING LIGHT

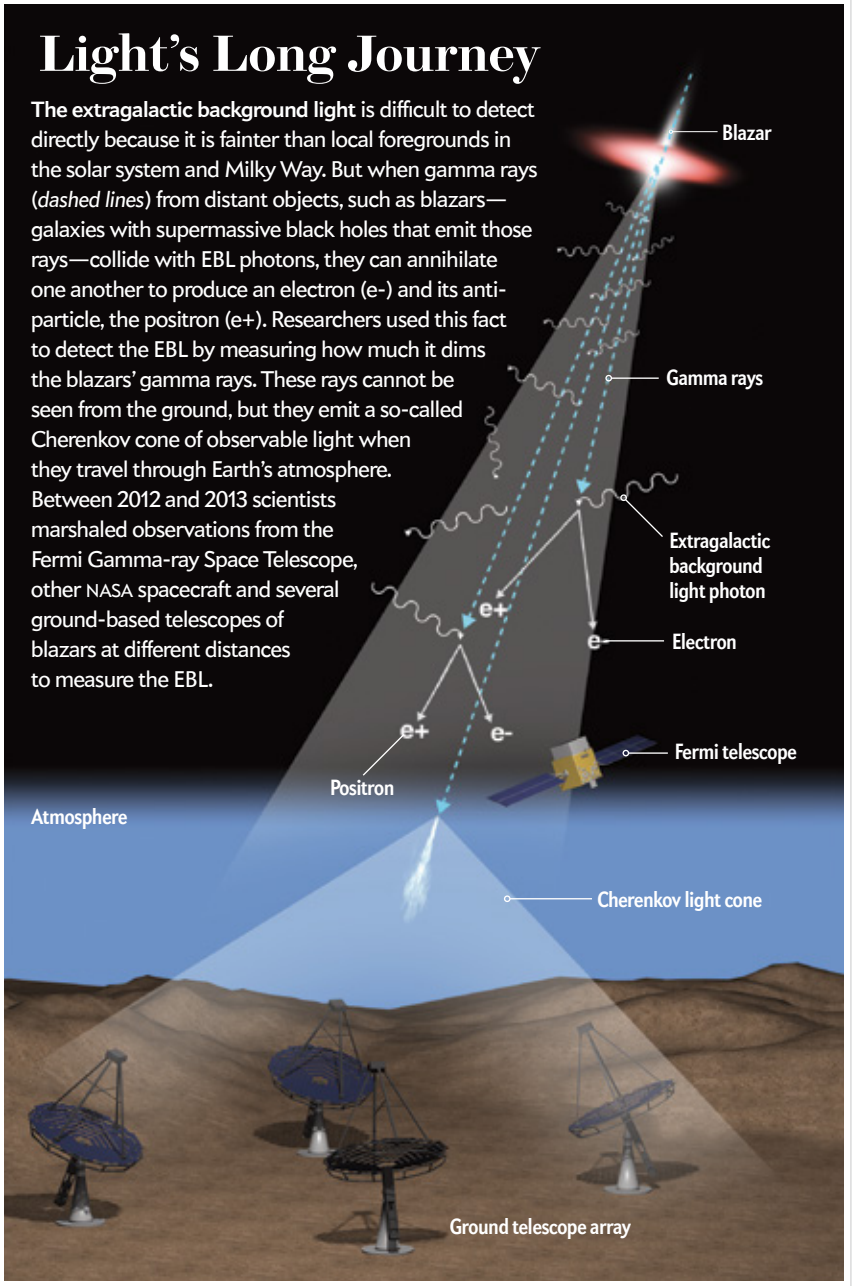
AS FAR BACK AS THE 1960S, researchers started thinking about looking for the EBL through its interactions with other, more easily visible, forms of light.

Photons, it turns out, can collide with other photons. Specifically, high-energy gamma rays may collide with lower-energy photons, such as visible starlight, and mutually annihilate to create an electron and its antiparticle, the positron. Several astronomers began to wonder: What might happen if high-energy gamma rays from a distant cosmological source heading toward Earth collided with lower-energy EBL photons along the way? Would the EBL photons effectively waylay gamma rays, weakening the apparent brightness of the gamma-ray source as seen from Earth? If scientists could detect this attenuation of gamma rays, they reasoned, it might reveal the composition of the EBL.

That question remained purely a matter of theoretical speculation until 1992, when NASA's EGRET (Energetic Gamma Ray Experiment Telescope) detector onboard the orbiting Compton Gamma Ray Observatory discovered the first of a new class of gamma-ray sources that came to be called blazars: galaxies with central supermassive black holes emitting gamma rays in strong jets that happen to be pointed toward Earth like flashlight beams. The gamma rays in such jets have phenomenal energies of billions of electron volts—that is, giga-electron volts (abbreviated GeV). Indeed, some blazars, such as Markarian 421 (Mrk 421 for short), are emitting gamma rays at mind-boggling energies as high as 20 trillion electron volts (TeV), or about 100 million times as much energy as medical x-rays.

At about 400 million light-years away, the blazar Mrk 421 is relatively nearby as extragalactic distances go. But finding such a powerful gamma-ray source in the 1990s made Primack wonder whether similar TeV-energy blazars might exist at far greater distances—and thus be useful for detecting the EBL. Indeed, over the following years other TeV-energy gamma-ray blazars were discovered at increasingly greater distances. And figuring out how to harness blazars to measure the EBL began to occupy Domínguez in 2006, when he started Ph.D. research at the University of Seville in Spain, where he studied blazars with the MAGIC gamma-ray observatory.

Illustrations by Don Foley



In 2012 Domínguez was among nearly 150 co-authors led by Marco Ajello, now at Clemson University, who made the first measurement of how much blazar light gets absorbed by the EBL. The team pored over data from NASA's orbiting Fermi Gamma-ray Space Telescope, analyzing observations of 150 blazars at different distances to measure how much their gamma rays were attenuated with increasing distance—that is, after traveling through greater thicknesses of the EBL. The observations extended out to a redshift of 1.6, corresponding to light emitted almost 10 billion years ago.

To improve on that measurement, astronomers needed a way to better understand blazars' intrinsic nature and thus to know how many gamma rays of various energies a blazar actually produced *before* some of those gamma rays were absorbed by collisions with EBL photons across billions of light-years of extragalactic space.

The best way of estimating a blazar's initial output is to combine theoretical models of how blazars work—especially how they generate higher-energy gamma rays—with telescope observations of blazar's lower-energy gamma rays and x-rays, which are not absorbed by the EBL as often. The high-energy gamma rays in many blazars are thought to originate in a process called synchrotron self-Compton (SSC) scattering. In the blazar jet, an energetic beam of electrons and positrons interacting with magnetic fields emits x-rays. Some of those x-rays are then hit—Compton-scattered is the technical term—by the same energetic electrons, kicking them to much higher energies to become gamma rays. The SSC models allow us to predict the unattenuated intensity of the high-energy gamma rays by comparing them with the low-energy gamma-rays we can observe.

Finally, in 2013, Domínguez, Primack, Justin Finke of the Naval Research Laboratory, Francisco Prada of the Institute of Astrophysics of Andalusia, and three others collated nearly simultaneous observations of 15 blazars at different cosmological distances made by half a dozen NASA spacecraft and several ground-based telescopes operating at different wavelengths. We compared the Fermi Gamma-ray Space Telescope findings with the intensity of x-rays from the same blazars measured by the x-ray satellites Chandra X-ray Observatory, Swift, the Rossi X-ray Timing Explorer and XMM-Newton, plus optical and radio wavelengths measured by ground-based observatories.

By comparing these observations in various wavelengths with SSC models of the blazars' output, we were able to calculate the original *unattenuated* gamma-ray brightness emitted at the highest TeV energies by nine of the blazars. We then compared those calculations with direct measurements by ground-based telescopes of the actual *attenuated* gamma-ray light received at Earth from those same blazars. Thus, at long last, we measured the EBL through its imprint on the gamma rays of various energies received from blazars located at different redshifts.

WINDOW TO THE PAST

THE DETECTION OF THE EBL was one of the toughest measurement challenges in observational astronomy—perceiving such a faint and diffuse signal required coordinating telescopes and re-

SOURCE: NINA McCURDY AND JOEL R. PRIMACK *University of California High-Performance AstroComputing Center*; FRAME FROM A CONCEPTUAL ANIMATION OF 3C 120 CREATED BY WOLFGANG STEFFEN *National Autonomous University of Mexico (blazar)*

searchers around the world to make simultaneous observations of extremely distant objects. It has given us a powerful new tool for studying cosmic history. Almost as soon as astronomers realized that blazars might be useful for studying the EBL, back in the 1990s, Primack and Donn MacMinn—then a brilliant college senior at the University of California, Santa Cruz—began to explore whether such measurements might reveal something about the evolution of galaxies. We still have many basic questions about galaxy formation, such as how common massive stars were in galaxies at various stages of development, how dust absorbed starlight and reemitted the energy at longer wavelengths, and how the number of stars that formed in galaxies varied during different epochs in the universe. MacMinn and Primack wondered whether studying gamma rays from blazars at different distances—gamma rays that traveled through different amounts of the EBL—might help answer some of those fundamental questions by providing windows on different eras of star formation in the universe.

For example, we know that distant galaxies in the early universe look significantly different from nearby galaxies: instead of being smooth spheroids or magnificent spirals, they are compact and distorted. Their distorted shapes were partly caused by collisions among these early galaxies because the young universe was much denser than it is today. The early galaxies also emit much more of their light at long infrared wavelengths than nearby galaxies do. That fact means that the EBL light created by long-ago galaxies at great distances has a different wavelength spectrum than the EBL light emitted by recent galaxies at closer range.

Thus, the pattern of gamma-ray energy absorbed by EBL photons from great distances out in space—that is, far back in time—should also differ from the pattern of gamma-ray energy absorbed by EBL photons nearby. Indeed, by 1994 MacMinn and Primack had done enough preliminary theoretical modeling to assert that the *dominant* factor influencing the characteristics of the EBL would be the epoch of galaxy formation at which the photons were emitted. We predicted how the gamma-ray attenuation by the EBL would have evolved over time based on several different cosmological assumptions. Eventually we showed that it would be possible to use measurements of the absorption by EBL photons of gamma rays from TeV sources at different distances to distinguish among competing theories of galaxy evolution.

Now that we have the first measurements of the EBL from blazar attenuation, we are starting to dig into our data to build a picture of star and galaxy formation throughout the cosmic timeline. For example, the wavelength spectrum of our EBL measurements gives a view of what was happening during the peak of star formation—a "cosmic high noon"—between eight billion and 12 billion years ago. The EBL spectrum shows two bumps: one representing ultraviolet and visible light shining from stars and another, larger bump in longer-wavelength far-infrared light. This second bump appears to come from dust. We know that exploding stars produce dust (made of heavier elements such as carbon, oxygen and iron) that envelops and obscures star-forming regions and that during cosmic high noon, dust absorbed much of the starlight and reradiated it in the infrared. The EBL gives us a way to study just how common such dust-obscured galaxies (nicknamed "DOGs") were during this era—an important factor in understanding how rocky planets such as Earth formed because these planets contain large quantities of cosmic dust.

LOOKING INTO THE FUTURE

WHAT A SATISFYING EXPERIENCE, to realize a dream extending back more than two decades, where observations from many instruments confirm predictions. Moreover, how exciting it is to explore these new data—indeed, this brand-new cosmological instrument—to begin to discern what the evolution of the EBL reveals about the evolution of the universe.

Future EBL research could likewise tell us about earlier periods in the universe's history. If we could extend our observations of the EBL to include a few additional gamma-ray sources at higher redshift, astronomers could study how the universe was reionized (when ultraviolet light from the first stars knocked the electrons off hydrogen atoms) during the first billion years after the big bang. That goal is a major motivation for the huge new international Cherenkov Telescope Array now being designed with installations in both the Northern and Southern Hemispheres, which will consist of different instruments tailored to be sensitive to gamma rays from low to very high energies. And once we better understand and quantify the EBL, we can subtract its attenuation from the observations of blazars and gamma ray bursts to more fully describe the nature of those exotic objects themselves.

Meanwhile the EBL intensity measured indirectly by our gamma-ray attenuation technique is compatible with the EBL intensity estimated independently from observed galaxies over earlier cosmic epochs. This agreement means that the light emitted from galaxies at optical and near-infrared wavelengths appears to explain the EBL observations via gamma-ray attenuation, and it helps us close the accounting books.

As observations improve, agreement between these different types of measurement will either get tighter—powerfully constraining alternative sources of light in the universe (for example, the decay of hypothetical relic particles in the early universe)—or else discrepancies will emerge that will point toward new astrophysical phenomena (for example, exotic hypothetical particles converting to gamma rays). Better gamma-ray observations should come from continued use of existing facilities and the planned Cherenkov Telescope Array. Additionally, improved galaxy observations—including from future observatories such as the James Webb Space Telescope, the Large Synoptic Survey Telescope and 30-meter-class ground-based telescopes—will help scientists understand galaxy formation better.

We now know the answer to Olbers's paradox: the night sky is not dark; rather it *is* filled with the glow of all the galaxies that ever existed, even if that glow is difficult to detect. And all the time, supernovae are going off, gas clouds are glowing and new stars are being born to add their light to the pervading background that fills every cubic inch of the cosmos. SA

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scientificamerican.com/magazine/sa

Wajahat Z. Mehal divides his time between directing research programs on inflammation and providing care to patients with liver disease both at the West Haven Department of Veterans Affairs Medical Center in Connecticut and at Yale University.

MEDICINE

CELLS ON FIRE

A newly discovered structure in cells underlies inflammation wherever it occurs—an insight that may lead to new treatments for ailments as diverse as atherosclerosis, Alzheimer's and fatty liver disease

By Wajahat Z. Mehal

IN BRIEF

Redness, swelling, warmth and pain have long been recognized as hallmarks of inflammation, which can be caused by infection or tissue damage.

In the past several years scientists determined that cells produce certain molecular complexes, known as inflammasomes, to launch the process.

Surprisingly, many seemingly unrelated conditions—such as Alzheimer's, gout and heart disease—share the same inflammasomes.

Investigators hope to use this insight to develop new drugs that will one day treat a wide range of chronic illnesses more effectively.

Illustration by Brian Stauffer

ANYONE WHO HAS EVER HAD A PIMPLE IS FAMILIAR WITH THE TISSUE REDNESS, swelling, warmth and pain that mark an infection. This response, known as inflammation, has been recognized since ancient times. But the process, which is often set in motion by cells of the immune system, can also occur whenever tissue is damaged—even in the absence of a pathogenic organism—as, for example, when you stub your toe or, more seriously, suffer a heart attack. This second condition is called sterile inflammation, and when it goes awry, it contributes to a wide range of seemingly unrelated medical conditions, from Alzheimer's disease to diabetes to various liver conditions.

Although prolonged inflammation and its role in disease have been known for decades, research over the past few years has yielded surprising and important insights into its origins. Among the most intriguing: inflammation is not an automatic reaction but requires the active assembly of molecular structures before it can be launched. Cells involved in inflammation build the structures—called inflammasomes—quickly and then quickly disassemble them, usually within a day of the injury. (Imagine assembling a factory in a few minutes when a product is needed and then breaking it down once the need has passed, and you get the picture.) Presumably the rapid disassembly helps the body to avoid excessive damage. Some inflammation is helpful; it kills pathogens and blocks their spread in the body. But too much can harm nearby healthy tissues and thus extend any initial injury.

Discovery of the inflammasome is interesting to biologists in its own right, but it also has profound implications for medicine. Researchers have learned that disturbances in the assembly and disassembly cycle can fuel ongoing, destructive inflammation. Right now many medicines that fight pain and swelling block the activity of certain proteins that fan the inflammatory flame. But the new work suggests that medicines able to block creation of the inflammasome or prompt its breakdown might impede the downstream production of those problematic proteins and thereby reduce tissue injury in a wholly new way. Such drugs, alone or in combination with existing ones, should help fight inflammation that currently does not respond well to therapy.

Indeed, recent discoveries about how inflammasomes sometimes go into overdrive are forcing me and other medical investigators to radically change the way we think about human disease. Rather than classifying diseases on the basis of the specific organs (heart or liver) involved, we are thinking more in terms of the cellular machinery that may be at fault: so far scientists have characterized four different versions of inflammasomes, with more likely to come. One advantage of this change in approach is that researchers can start testing whether drugs that work for, say, gout—in which one particular inflammasome is activated—may also benefit individuals with heart disease, which is triggered by the same inflammasome.

STRANGER VS. DANGER

THE INFLAMMATORY RESPONSE is part of the so-called innate branch of the immune system, typically thought of as the first line of defense against germs that invade the body. In it, white blood cells called macrophages or their relatives home to the site and then spit out proteins that induce the swelling and heat needed to immobilize and weaken microbes; the secretions also recruit still more immune cells to the area. (The pus you see in infected wounds is composed of such white cells.)

For years researchers believed that the innate system initiated this cascade solely by distinguishing "self" from "nonself." Macrophages recognize particular molecules that are common to multiple pathogens but are not present in people or other vertebrates. After making contact with these foreign molecules, the macrophages release the proteins that unleash the rest of the inflammatory response. The foreign, pathogen-only, nonself molecules are colloquially termed "stranger signals." Charles Janeway, Jr., and Ruslan M. Medzhitov, both at Yale University, laid the groundwork for this research in the late 1980s and mid-1990s.

It eventually became apparent, however, that macrophages are exquisitely reactive to certain self molecules made by the body, such as ATP (which serves as a kind of rechargeable chemical battery for cells) and the hereditary substances DNA and RNA. These molecules are usually locked securely away inside various compartments of the cell, far from the tentaclelike protrusions of any macrophages. But if self molecules spill out into the spaces between cells—which might happen when, for example, you accidentally hit your thumb with a hammer—they become detectable by proteins known as the toll-like receptors and certain other molecules on immune cells. Our body does not take a chance, and it responds to these danger signals with the assumption that strangers (pathogens) are also around; it sets off the same inflammatory response that is evoked by microbes.

This chain reaction has major consequences, the most important of which is that the inflammatory response to cellular damage can increase the amount of injury in the tissue if it fails to shut down when it is no longer needed.

GROWING EXCITEMENT

ALTHOUGH THE BROAD OUTLINE of the inflammatory response was established more than 15 years ago, excitement started building in the past decade as investigators uncovered more of the details about what exactly happens inside a macrophage before it launches such a powerful defensive reaction. Before then, investigators thought that to get to the bottom of how inflammation develops they would need to trace hundreds of molecular signals affecting dozens of different kinds of cells (including macro-

How to Light a Fire in the Body

Much to researchers' surprise, all cells in the body trigger inflammation in much the same way—by building a molecular structure, called an inflammasome, which spews out compounds called cytokines. Typically these cytokines provoke a standard, short-lived inflammatory response of redness, swelling, pain and warmth. But various ailments (such as Alzheimer's disease and gout) may result if an inflammasome remains active for too long—depending on such factors as the amount of cytokines produced and the reaction in different tissues to those cytokines. Activating substances include so-called stranger signals (produced by microbes) and danger signals (produced when the body itself becomes damaged). The discovery of a common molecular pathway may allow drug firms to develop new medications for illnesses that were previously thought to be unrelated.

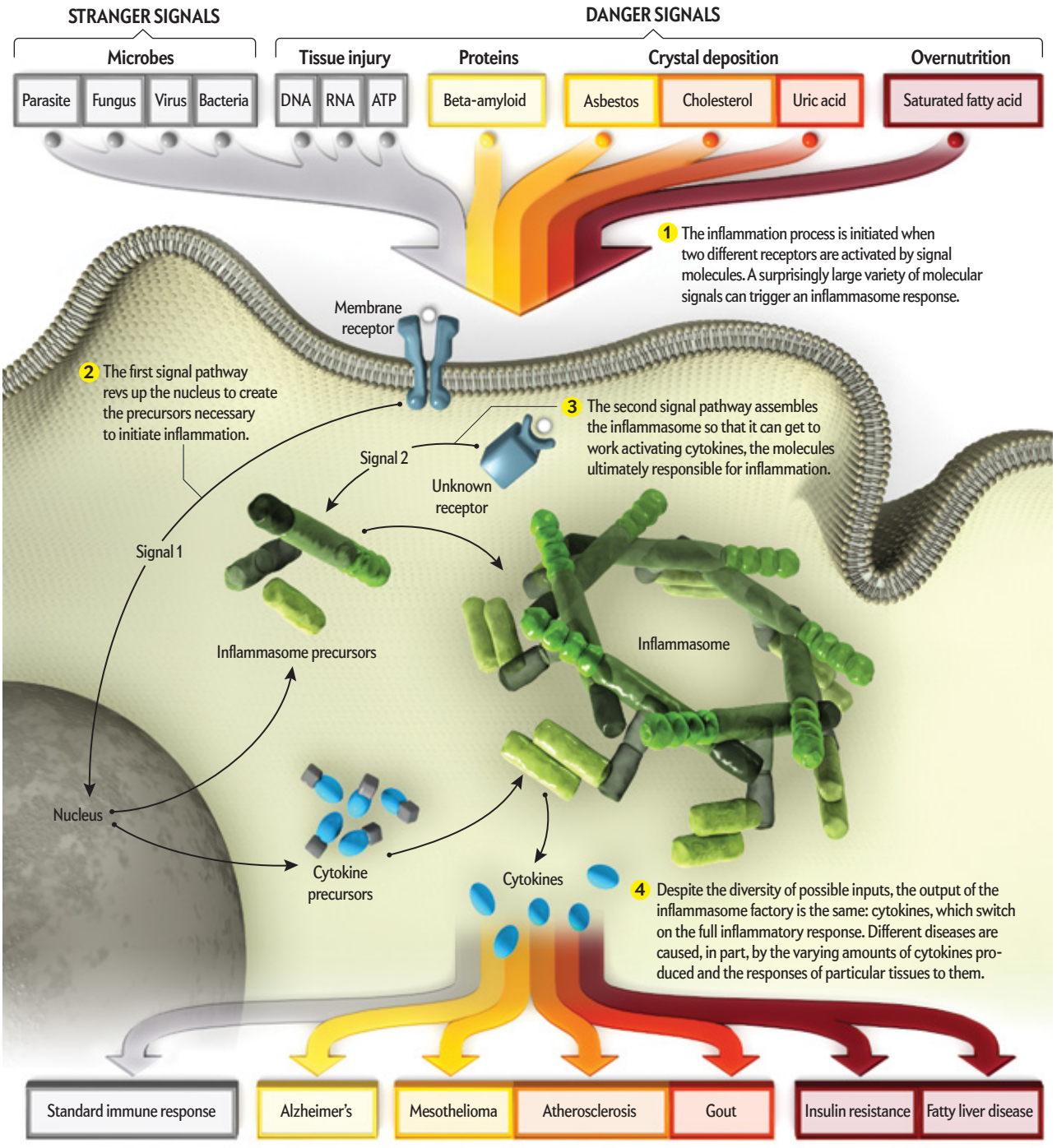

Illustration by Emily Cooper

phages). By focusing on macrophages, however, they soon realized that just a few sequences of molecular interactions, or "pathways," were needed to sound the initial alarm. Moreover, other cells used those same pathways. With just a few pathways to investigate, researchers hope to develop a handful of medications that either block the production of inflammasomes altogether or promote their disassembly in a wide variety of ailments.

So what happens inside macrophages? For starters, any macrophages near damaged cells get bathed in broken bits of DNA, RNA and other danger signals (also known as DAMPs, or danger-associated molecular patterns). Some of these danger signals bind to one particular protein on the outer surface of the macrophage cell, and others lock onto a different substance, whose identity and location are still being worked out. Once bound, these receptors activate one or the other of two different cellular processes: the first (which researchers call the signal 1 pathway) revs up the production of certain molecules needed to initiate inflammation, and the second (the signal 2 pathway) assembles an inflammasome. The fully formed inflammasome processes the newly produced inflammatory molecules in a way that activates them and then, in a process that researchers have not yet identified, releases them outside of the macrophage.

Somewhat unexpectedly, the output of an inflammasome after it gets built is quite limited—no matter whether danger signals or stranger signals get the ball rolling. Each of the four inflammatory structures that researchers have so far described ultimately produces and releases mainly two substances—specifically interleukin-1 beta (IL-1β) and interleukin-18 (IL-18). These substances, which belong to a group of signaling molecules known as cytokines, had been known to affect inflammation. But no one—before the discovery of inflammasomes—knew how they were produced. Once these interleukins are released, they spread throughout the tissue, triggering the production of yet more cytokines, which stimulate increased local blood flow, recruitment of other immune cells and a constellation of changes that collectively make up the full inflammatory response.

But more surprises were yet to come. Study after study began showing that inflammasomes are at the heart of a wide range of diseases and disorders for which inflammation was thought to play, at best, a secondary role. Indeed, inflammasomes can be constructed in all manner of cells, not just macrophages and other immune cells. (For example, certain cells in the intestine build inflammasomes whose release of cytokines triggers the production of mucus in response to danger or stranger signals.) In addition, formation of microscopic particles was found to spur a variety of diseases in different parts of the body. As it turned out, one inflammasome in particular, known as NLRP3, found in many different cells, appears to be responsible for most of the inflammation caused by these deposits—whether asbestos in the lungs (mesothelioma) or uric acid in the joints (gout). In fact, research now suggests that it is not cholesterol per se but rather the tendency of cholesterol to aggregate into crystals in blood vessel walls under certain circumstances that drives the atherosclerotic changes in the arteries that result in heart attack and stroke. Similarly in Alzheimer's, the accumulation of the protein complex beta-amyloid in the space between the neurons activates the NLRP3 inflammasome in cells known as microglia, which are the brain's equivalent of macrophages, resulting in the death of neurons. Thus, a diverse range of substances—uric acid, cholesterol, beta-amyloid, asbestos and others—results in a spectrum of diseases that affect different organs and behave in different ways but all depend on the inflammasome machinery.

FOOD SHOCK

THE TRUE STUNNER of the field, in my opinion, however, was the discovery that eating can trigger an inflammatory response. More specifically, eating too much in one sitting will trigger an acute episode of inflammation that eventually resolves itself, and routinely eating so many calories that the body has to store them as fat triggers chronic inflammation. Biologists had little reason to suspect such a relation. After all, nutrients are not bacteria-specific molecules or particulates, nor are they sequestered inside cells (which would make them obvious candidates for danger signals). And yet several studies conducted in the past few years in animals have determined that certain nutrients, such as saturated fatty acids (found in meat and cheese and also manufactured by our body), can in high amounts act as danger signals and directly activate the NLRP3 inflammasome in macrophages and other cells. This finding has opened up a whole new area of research looking at the effects of specific metabolites (products of digestion) on inflammasome activity. For example, investigators have learned that consuming too many carbohydrates or other nutrients causes inflammation indirectly; the body must first convert the excess into fatty acid molecules.

The differences between diseases are caused by the type of initiating signal as well as the site of inflammasome activation and its duration.

Although many organs are affected by inflammation related to overeating, the strongest response has been seen in the liver, probably in part because that organ takes up a lot of fatty acids. In addition, the healthy liver contains many immune cells that are primed to undergo activation and can induce liver injury even after a mild stimulus. Together these processes can result in the liver becoming swollen and inflamed, resulting in what physicians call fatty liver disease. Though reversible, this condition is often indistinguishable from what is frequently seen in the liver of people who drink a lot of alcohol. (For reasons that are not entirely understood, fatty liver disease may sometimes progress to cirrhosis—which is a potentially fatal condition.)

That finding is disturbing enough, but adding to the concern

SCIENTIFIC AMERICAN ONLINE See research pictures of inflammasomes in action at ScientificAmerican.com/jun2015/mehal

is the realization that as much as a third of obese children now have fatty liver disease. This pattern raises the possibility that at least some of them will fall ill with cirrhosis in early adulthood. It is as though large numbers of preteens were suffering from alcoholic liver disease, except the offending agent is excess calories, not alcohol. If, as animal research suggests, the NLRP3 inflammasome mediates the food-related inflammation, then it seems likely that a treatment able to prevent construction of the inflammasome could limit liver inflammation and injury in people who are overweight or obese. In support of this idea, researchers have shown that obese mice lacking inflammasome components have a healthier liver—although they are prone to infection.

Given that overnutrition can cause inflammation, my colleagues and I at Yale University decided to pursue the reverse question: whether undernutrition results in metabolites that can reduce inflammasome activation. The anti-inflammatory effects of fasting and exercise are well known, so we examined two molecules that are increased throughout the body during these states: beta-hydroxybutyrate and lactic acid. We found that the molecules interact with particular, distinct receptors on macrophages; together these interactions initiate a series of biochemical reactions in the cells that ultimately turn off the genes involved in triggering inflammasome production. Our next challenge is to figure how to harness these moderating pathways to deactivate inflammation in various diseases.

CHRONIC INFLAMMATION

THE FIRST STEP in learning how to disarm the inflammasome is to figure out how the body does it naturally—a process that normally kicks in 18 to 24 hours after an inflammasome is constructed. At the same time, researchers hope to decipher the molecular pathways that allow inflammasomes to function longer than they should during various ailments. That knowledge should suggest ways to shut down abnormally persistent inflammasomes.

For example, studies indicate that all the known danger signals—whether they trip the signal 1 or signal 2 pathway—result in a limited burst of inflammation even if the danger signals persist in the intercellular environment. After a while, immune cells simply stop responding to the long-term presence of the pathway 1 signals (the ones that rev up production) in a process called tolerance. In contrast, the pathway 2 danger signals (the ones that trigger the production of the inflammasome itself) induce the death of immune cells if they stick around too long. The result in either case is the shutting down of the inflammatory process.

Clearly then, additional signals are required to keep an inflammasome activated for a long time, as occurs in diabetes and fatty liver disease. My group, in collaboration with others, has determined that adenosine—a substance that is produced by the body whenever it breaks down ATP molecules for energy—seems to delay the dismantling of the NLRP3 inflammasome. Ironically, adenosine has long been considered an anti-inflammatory molecule because it counteracts later products of the inflammatory process.

THERAPIES TO COME

THE DISCOVERIES OUTLINED throughout this article have profoundly changed the way we view inflammation. In addition to understanding the individual steps, researchers now generally agree that many different stimuli—stranger signals, danger signals and even many of the normal breakdown products of food—converge on a single inflammatory factory (the inflammasome), which has relatively few outputs. The differences between diseases are caused by the type of the initiating signal, as well as the site of inflammasome activation and its duration. For example, uric acid crystals in joints trigger episodes of acute inflammation (gout), which resolve despite persistence of the crystals (at least until the next flare-up), but silica crystals in the lung result in chronic inflammation, followed by scarring.

This new information provides possible molecular targets against which pharmaceutical companies can try to develop new drugs. Such therapies are directed toward blocking the inflammasome at different steps in its construction, including the binding of danger signals to their receptors. Several companies have already begun experiments with different compounds that work directly on the inflammasome. But it will likely take at least a decade before these potential drug candidates can be fully tested and determined to be safe and effective.

In the meantime, many researchers have begun trying out treatments that are already effective (and have been approved by the U.S. Food and Drug Administration) for one disease on individuals with different diseases that share the same inflammasome. For example, because the drug anakinra, which has long been used to treat rheumatoid arthritis, blocks the receptor to which IL-1β binds after it leaves the inflammasome, the medication is now being tested in a wide range of NLRP3-driven diseases, including a few rare but debilitating inflammatory syndromes in children.

My group is also investigating whether the common drug digoxin, which is used to treat certain heartbeat disorders, might decrease inflammation in neurological disorders such as Alzheimer's. Other researchers recently demonstrated that digoxin inhibits a molecule called HIF-1α. My group at Yale then determined that HIF-1α is required for sustained activation of the NLRP3 inflammasome. Because NLRP3 appears to be active in the brain of Alzheimer's patients, our combined results suggest that digoxin might be a potential Alzheimer's treatment—although much further study is needed. Too much digoxin has been shown to cause confusion and other symptoms that mimic dementia, and it can have other side effects as well.

The past few years have seen an explosion of research into the basic biology of the inflammasome. The next few years will produce insights and possibly new therapies in ways that cannot be entirely predicted. But the rich and complex organization of this astonishing cellular factory makes it clear that tackling inflammation at its source could relieve more of the suffering and disability that currently makes life so difficult for so many people. SA

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ETHOLOGY

the networked animal

In a wide variety of species, who befriends whom strongly influences how individuals and the larger group behave

By Lee Alan Dugatkin and Matthew Hasenjager

IN BRIEF

Like we humans, members of many animal species spend their lives in complex social networks that influence their and the group's behavior.
Researchers are using techniques developed for the study of human social networks to analyze these animal systems.
The structures of animal networks can play a large part in mating opportunities, the spread of disease and information, and the teaching of survival skills.
Analyses of these networks show that certain individuals play outsize roles in maintaining the overall well-being of the community.

SO MUCH OF OUR LIFE IS INFLUENCED BY WHO is in our social networks: we rely on extended families, friends of friends of friends, co-workers and their connections to gain intelligence on everything from what books to read to how to vote to which jobs to pursue. But we are by no means alone in this reliance: social networks also affect the daily experiences and, indeed, survival of individuals in many animal species. That chimpanzees and other primates have complex social lives has been well known for decades. More recent studies have revealed that the actions of single birds, dolphins and other creatures make complete sense only in their social context. These findings could affect everything from conservation efforts to understanding our own social networks.

Illustration by Mark Allen Miller

And the research on animals—which often uses techniques developed to study human group behavior—may provide feedback to inform further investigations by us and about us.

Lee Alan Dugatkin is a professor of biology at the University of Louisville, with some 150 journal articles to his credit, as well as the popular books *The Altruism Equation: Seven Scientists Search for the Origins of Goodness* and *Mr. Jefferson and the Giant Moose: Natural History in Early America.*

Matthew Hasenjager is a doctoral candidate in Dugatkin's laboratory. His dissertation examines animal social networks.

WHY NETWORK ANALYSIS IS NEEDED

IT TOOK BOTH TIME and new ways of thinking for students of animal behavior—ethologists—to realize just how important social networks can be in the animal kingdom.

In the 1930s future Nobel laureate Konrad Lorenz published his now famous studies describing imprinting in geese—the instinctive emotional attachment of a newborn to the first caretakers it encounters during a critical period in development. Soon the idea that most creatures are basically robots, engaging in hardwired, programmed behavior (that is, under the control of genes) became dogma.

Quickly, however, researchers realized that external factors interacted with the underlying genetic programming. Nature (genes) plus nurture (environment) drove animal behavior. Although that statement may seem comprehensive, it is actually not terribly useful—nature plus nurture includes virtually every possible influence one can imagine.

Investigators thus began to examine how trial-and-error learning also shaped behavior. Along with the observations of field researchers, these studies forced the recognition that animals were much smarter than we gave them credit for: chimps and crows make and use tools; parrots solve problems using logic; elephants disable electric fences by dropping large rocks on them. In the course of studying such obvious intelligence, researchers also began to observe that some animals in groups learned behaviors by copying their group mates. And a particular group member might notice that it was being watched by others trying to glean information.

Of course, as physicists know, once you get beyond a two-body problem, things can get exceedingly complicated. Early attempts to study the ways that individuals in a social group interact thus tended to concentrate on interplay involving two or three individuals. Scores of studies focused on an animal copying the mate choice of another, on a group member spying on the fighting abilities of a potential competitor or on a scrounger stealing food from a more productive group member. But the more that ethologists studied such behavior, the more they realized that these interactions among a few individuals were just a hint of the intricate set of relationships among all the members of a group.

What was needed for a fuller understanding of the social life of animals was the recognition that many animals, just like we humans, are embedded within complex social networks—the relationships that connect each individual to every other group member.

HOW IT IS DONE

MODERN APPLICATION of this approach began in earnest about 15 years ago, when ethologists started to freely adopt methods long used by social scientists for the study of human social networks—first in workplaces or neighborhoods, later in virtual communities such as Facebook and Twitter.

Social networks in animals range from simple associations involving only a few individuals, such as a loose shoal of fish traveling together, to far more complicated configurations, such as might be found in a troop of baboons, where individuals are embedded in multiple overlapping affiliations (such as mating, dominance or grooming networks) that can influence group members both directly and indirectly. Networks can change frequently: members may come or go, and individuals can change their position and connections in response to disease, acquisition of knowledge and previous interactions.

In both simple and complex animal societies, interactions among network members have important implications for survival and reproduction. Accuracy of information about food, predators and mates, as well as the speed at which that information travels in a group, depends on a social network's structure. Who plays with, fights with or helps whom also depends on network structure. And diseases and parasites can be transmitted from one individual to another, without the two ever meeting, by passing the pathogen through intermediates.

As part of their overall assessments, researchers specifically identify several features of animal networks: the keystone individuals (those that have many connections and whose removal disrupts the social network); nodes (any individual that is included within the network); density of the network (a ratio of the number of actual ties to the number of all possible ties); degree (the number of ties between each individual and all others); reach (the number of friends of the friends of an individual); and centrality (the percentage of all connections among individuals that include a given individual). For example, most people in the U.S. have low centrality at the scale of country, but with almost everyone aware of the president and connected to him by their local officials, his centrality approaches 100 percent.

To get a feel for how social networks operate in nature—and how they may be the key driver of the ways that everyone in the group ultimately behaves—let us peek into the not so private lives of three nonhuman species that have been examined in this way.

MACAQUE POLICE KEEP THE NETWORK INTACT

PIG-TAILED MACAQUES (*Macaca nemestrina*) create multiple networks, such as ones composed of playmates or grooming partners. Networks differ in size, and a monkey might have different favorite partners in different networks. A particular macaque may also play a stronger role in one network than in another. But the various networks share a common feature: they operate under the watchful eye of a few authority figures that keep the peace. These macaque "police," some of the group's highest-rank-

ing males, spend time and energy breaking up fights between other individuals in their social networks.

Jessica Flack of the Sante Fe Institute and her colleagues (including renowned Emory University primatologist Frans de Waal) studied the role of the police in a troop of 84 macaques at the Yerkes National Primate Research Center at Emory in the early to mid-2000s. Geneticists often decipher the role of a single gene in a cell or an organism by disabling the gene and observing the consequences of its absence. Flack's team adapted this "knockout" approach to the macaques by removing three policing males. They then watched and waited.

The loss of a low-ranking group member did little to the social networks. But as might be expected, the absence of police led to increased aggression and decreased reconciliation after fights in the population. Less predictably, without the police to swim freely in their environment—might severely disrupt the killer whale social network and weaken the prospects for survival of the entire group. This understanding could, at the very least, inform policies to minimize the impact of our actions on these amazing creatures.

THE BIRD SONG-AND-DANCE NETWORK

WILD POPULATIONS OF BIRDS in their natural habitats have also been the subject of social network analyses. One such species is Central America's long-tailed manakin (*Chiroxiphia linearis*). Males are strikingly handsome, distinguished by their indigo feathers, red cap and, as the name indicates, long, thin tails. Find the right pair of males together on a perch, and a bird-watcher can witness one sweet song-and-dance routine. Female manakins watch, too, assessing these performances when se-

SOCIAL NETWORK strength and reach influence everything from mating chances in long-tailed manakins (*left*), to grooming in macaques (*center*), to the propensity of some bottlenose dolphins (*right*) in Brazil to work with human fishers to catch mullet.

present, the play and grooming networks also underwent complex restructuring.

With police gone, for instance, group members played with and groomed fewer partners; that is, the "degree" of their play and grooming networks decreased. And the "reach" of the remaining monkeys—the number of friends of the friends of an individual—went down in those networks. At the same time, the cohesion of the entire society weakened; the population underwent a kind of balkanization, dividing into smaller, more homogeneous groups that rarely interacted with outsiders. These observations led Flack and her colleagues to hypothesize that the presence of police allowed for a healthier and denser network, where members had more and friendlier contacts with larger numbers of their fellows.

This kind of knockout experiment, which revealed that some individuals in a network are especially valuable to its structure, suggests that an understanding of animal social networks may be important to conservation biology. Take the case of killer whales (*Orcinus orca*). Individual juvenile females and clusters of related females appear to be key hubs for the transmission of information about foraging opportunities and other aspects of life in the sea. Anything people do that disturbs such individuals or group information hubs—from hunting to polluting the oceans to constructing barriers that impede the ability of whales lecting mates. For males, the chance to perform matters—a lot. Unfortunately for them, competition for the chance at a spot in a duet is high and often quite aggressive.

David McDonald of the University of Wyoming spent more than 10 years in Costa Rica, totaling 9,288 hours observing the birds. He discovered, using social network analysis techniques, that it is males with a high degree of connectedness during their early lives that get the privilege of performing at this avian open-mic night.

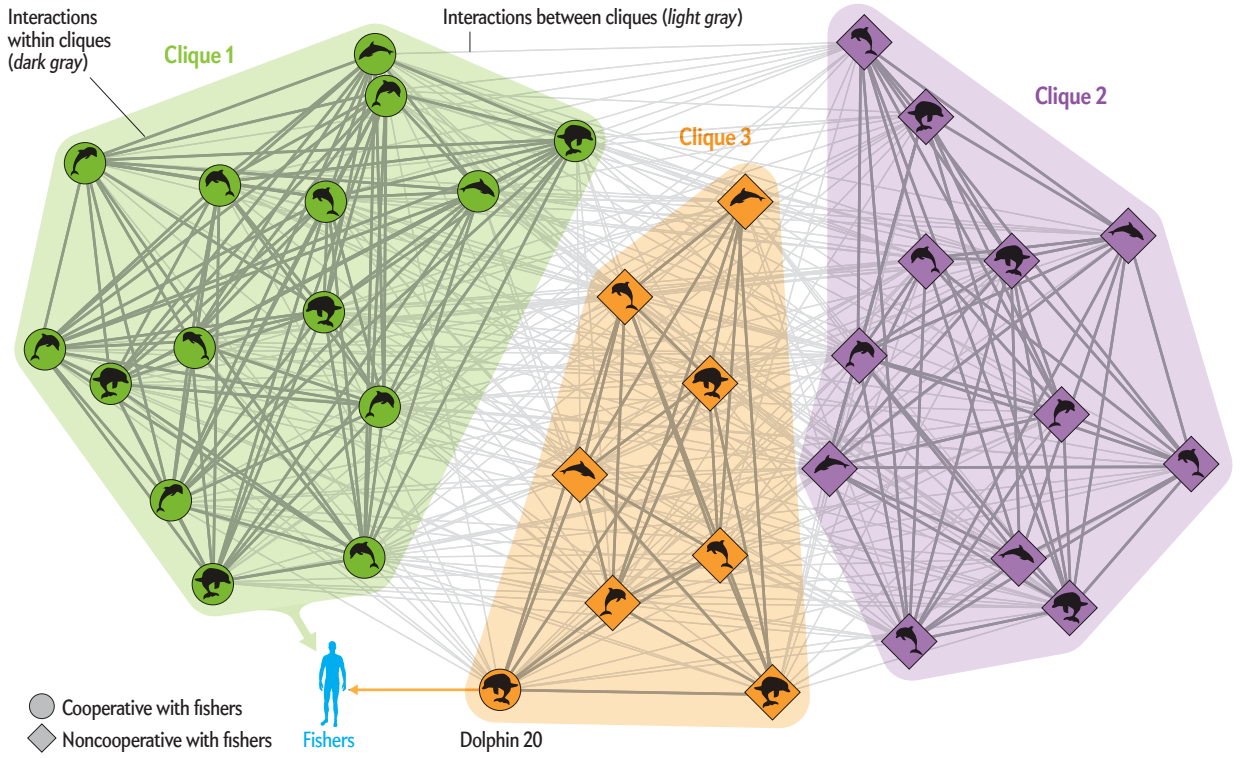
Like any dance battle, it is all quite complicated, but what happens is something like this: Clusters of eight to 15 males spend their time in "perch zones," areas that contain one to several perches, where the birds will ultimately perform. Any male in a cluster can practice singing and dancing on a perch outside the breeding season (late February to early September) or even during the breeding season as long as females are nowhere around. But with females present during the breeding season, only the two highest-ranking males—labeled alpha and beta—can sing and dance on perches. The competing performers actually become a team to aggressively dismiss all other males from the area.

The alpha male wins almost all matings in a perch zone. The payoff for the beta male is succession to the coveted top position once the reigning alpha male dies. This system creates a huge

MARIE READ *Science Source (birds)*; JOE McDONALD *Getty Images (monkeys)*; STEPHEN FRINK *Getty Images (dolphins)*

Dolphins and Humans Team Up to Bag Fish

Some—but only some—members of a community of dolphins in the Laguna region of southern Brazil formed a unique alliance with local artisanal fishers attempting to net mullet. The dolphins formed three cliques. All members of clique 1 (*green*) were cooperative (*indicated by circles*) with the fishers and highly interactive (*lines joining individuals*) with one another. Clique 2 (*purple*) members interacted less with one another than did clique 1 animals and had no contact with fishers (*indicated by squares*). Clique 3 (*orange*) dolphins were also uninterested in the fishers, with the notable exception of one member, known as dolphin "20" (*orange circle*). This individual aided the humans and liaised between its clique and the cooperative clique 1—and may yet teach clique 3 to work with humans. The collaboration of dolphins with fishers is known to enhance dolphin foraging success and human catch size.



benefit for both alpha and beta males, one that all males want but that few get.

As young males mature between ages one and six, they often move between perch zones, establishing relationships with many other males. The average age of a successful breeding male is 10 years, meaning that any given male has many other males in his social network as he matures. In his nearly 10,000 hours of fieldwork, McDonald tracked which males interacted with one another each year for more than 10 years. He built a social network map from his data to see if the structure of the network would reveal which males ended up as successful duet singers.

His network metrics took account of both short pathways that connected one individual directly to another and indirect pathways that could include interactions between birds several links removed from the first individual. ("I don't know Bert personally, but I know Kermit, who knows Ernie, who knows Bert.") McDonald ultimately determined that centrality was the secret: central males were much more likely than less well-connected ones to rise up in the breeding hierarchy, sometimes achieving the alpha and beta statuses that would allow them onstage to sing and dance their way into females' hearts.

It is important to note at this point that this kind of research identifies network structures and associates such structures with observed behavior. A direct causal connection between the structure and behavior is assumed—but not proved. Conceivably, alpha and beta males, rather than gaining power because of their many connections, could have gained many connections because of some features that made them popular among their peers.

THE DOLPHIN FISHING NETWORK

AS WE PREVIOUSLY MENTIONED, many tools of social network theory were imported from the social sciences. It is unsurprising, then, that some of the first subjects of detailed nonhuman social network analysis were bottlenose dolphins, already recognized as big-brained, intelligent, highly social animals, like us (on our good days).

SOURCE: "THE STRUCTURE OF A BOTTLENOSE DOLPHIN SOCIETY IS COUPLED TO A UNIQUE FORAGING COOPERATION WITH ARTISANAL FISHERMEN," BY F. G. DAURA-JORGE ET AL., IN *BIOLOGY LETTERS*, VOL. 8, NO. 5; OCTOBER 23, 2012

SCIENTIFIC AMERICAN ONLINE Listen to an interview with Dugatkin at ScientificAmerican.com/jun2015/dugatkin

Graphic by Jen Christiansen

In the late 1990s then graduate student David Lusseau fell in love with the common bottlenose dolphins (*Tursiops truncatus*) of Doubtful Sound, a gorgeous fjord in southern New Zealand, more than 200 miles west of the University of Otago, where Lusseau, now at the University of Aberdeen in Scotland, was working on his doctoral dissertation. For seven years Lusseau tracked these beautiful animals. One of his tools was photography, which helped him methodically identify the natural markings on each of the 64 dolphins in Doubtful Sound and to better follow those individuals.

After observing more than 1,000 pods of various sizes that contained subsets of these 64 animals, Lusseau determined that the dolphins were part of one large social network linking virtually all of them. Furthermore, he found that individual dolphins clearly preferred the company of only some other specific group members. But he could not put his finger on why. What did dolphin networking accomplish, and what manner of information or benefits might be shared among associates?

To investigate those questions further, Lusseau joined forces with Paulo C. Simões-Lopes of the Laboratory of Aquatic Mammals at the Federal University of Santa Catarina in Brazil. They studied a population of 55 bottlenose dolphins that were living on the other side of the planet and engaging in a unique behavior that Simões-Lopes had identified a few years earlier—a mutually beneficial interaction with the local artisan fishers (*Homo sapiens*).

Each spring, from April to June, fishers in the Laguna region of Brazil use a technique introduced to the area by settlers from Portugal's Azores more than 200 years ago. They cast long nets into the water to catch schools of mullet (*Mugil platanus*) migrating from the cooler waters off of Argentina. In recent years they have received help: some—but only some—of the bottlenose dolphins in the lagoons actually herd schools of mullet toward the fishers. At the right time, the dolphins slap the water with their head or tail. The slaps tell their human partners when and where to cast their nets. The upshot of this remarkable interplay is that both species of mammals catch more fish than they otherwise would.

Lusseau's previous experience made him consider social network analysis as a way to scrutinize the details of this rather incredible behavior. From September 2007 to September 2009, Lusseau, Simões-Lopes and some of their colleagues went out on boats in the lagoon system, dolphin photographs in hand, and gathered data on which dolphins were swimming together. The research team was able to collect reliable data on 35 of the 55 individuals in this population. Even this incomplete data set made it clear that these dolphins had established a highly structured social network.

A statistical analysis found that the Laguna dolphins could be subdivided into three cliques within which individuals spent most of their time. Although all the dolphins in any one clique had some tenuous interactions with the dolphins of the other cliques, animals within these cliques tended to swim together and interact mostly with the other individuals in their clique. Such close-knit associations could serve to facilitate information transmission among members.

Clique 1 consisted of 15 dolphins, every one of which cooperated with the local fishers. This clique was highly interconnected, with all its dolphins often associating with one another, both during the autumn mullet fishing season and during the remainder of the year. Information flow was therefore easy. Not surprisingly, clique 1 benefited from its relationship with the fishers, whereas the other cliques lost out on this opportunity.

Cliques 2 and 3 differed greatly from clique 1. None of the dozen dolphins that formed clique 2 cooperated with the fishers. And although clique 2 dolphins were often found together, both in and out of fishing season, their social relationships were weaker than those seen for individuals in clique 1.

Of the eight clique 3 animals, seven did not cooperate with fishers—but one dolphin, labeled "20"—did. And of all the dolphins in the Laguna population, dolphin 20 spent the most time interacting across cliques. It appears that dolphin 20 acted as a liaison between its clique and cooperative clique 1 [*see box on opposite page*]. Determining the influence of such liaisons in highly complex networks should be a fertile area for future study. The findings already suggest, though, that having a tight network, as clique 1 did, can help animals overcome challenges that individuals cannot solve alone—in this case, devising a way to communicate effectively with members of another species: human fishers.

The researchers do not yet know whether some key clique 1 individuals—perhaps older, experienced dolphins—teach other group members how to cooperate with the fishers. But given that teaching has been found for other complex feeding behaviors observed in dolphins, it would not be surprising to find similar instruction going on here. Indeed, such socially learned traditions form the basis of animal culture and are strongly facilitated by social networks.

Attitudes toward animals have evolved greatly since the early conception of them as robots mindlessly carrying out genetic programs. Ethologists now know that many animals are much smarter, more behaviorally flexible and better able to learn than the pioneers of the field could have dreamed. We anticipate that more studies of social networks, along with greater exposure to those studies, will further change the way that people think about animals. Hardly preprogrammed automatons, many nonhuman creatures spend their lives, as we do, within a complex social milieu—in networks where both direct and indirect interactions with other individuals drive so much of what matters to survival and success. SA

MORE TO EXPLORE

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BIRTH OF

Is NASA's Space Launch System a flying piece of congressional

TECHNOLOGY

A ROCKET

pork or our best shot at getting humans to deep space?

By David H. Freedman

AEROJET ROCKETDYNE RS-25 engines powered the space shuttle, and soon they will power NASA's next deep-space exploration vehicle, the Space Launch System (SLS).

Photographs by Jeff Wilson

David H. Freedman is a contributing editor at *The Atlantic* and author of five books, most recently *Wrong*, which is about problems with the published findings of medical scientists and other experts.

Deep inside a giant but little known NASA facility,

crews have for years been staging elaborately faked space missions. This is not a conspiracy theory. It is the sad tale of NASA's Michoud Assembly Facility, the sprawling New Orleans complex where the space agency had for decades built its biggest rockets.

After the space shuttle's last flight in 2011, Michoud's massive hangar-like facilities were rented out to Hollywood studios, housing some of the production for *Ender's Game* and other science-fiction movies.

But lately a growing cadre of NASA engineers and other workers have been engaged on an important new production here—a sequel to the agency's greatest days of human spaceflight. Michoud is back in the rocket-making business, serving as a factory for the biggest, most ambitious space vehicle ever to undergo construction: the Space Launch System, often called by its acronym, SLS.

The SLS is the rocket in which NASA hopes to thunder a crew of astronauts skyward from Cape Canaveral, Fla., for roughly a year's journey to the surface of Mars while hauling the living quarters, vehicles and supplies they will need to spend at least

IN BRIEF

After the cancellation of the Constellation program, NASA's successor to the space shuttle, the U.S. decided to rely on private contractors for access to low-Earth orbit while building its own rocket—the Space Launch System (SLS)—to get crew and cargo to deep space.

Based on shuttle components and backed most enthusiastically by politicians with home districts that would benefit, the SLS has been called a "rocket to nowhere," a congressional jobs program with no mission and little chance of actually flying.

Yet so far the SLS is on time and on budget. Mission planning is under way, with a first flight scheduled for 2018. Like any multidecade program, the SLS's survival depends on future politics—but could this piece of flying pork be our best shot at getting to Mars?

AS EARLY AS NEXT YEAR, engineers at the NASA Stennis Space Center in Mississippi (*left*) will test-fire the 212-foot-tall core stage of the SLS.

a few weeks shuffling through the rusty dust there. That mission is still about 25 years away. But between now and then, the SLS could carry people to Earth's moon and an asteroid and send a probe to search for life on Europa, one of Jupiter's moons. It is an interplanetarily groundbreaking project, one of the most audacious NASA has ever undertaken.

Why, then, do so many people seem to hate it?

REPLACING THE SHUTTLE

AFTER THE GIDDY TRIUMPH of the Apollo moon exploration program in the 1960s and early 1970s, the space shuttle was supposed to make Earth-orbit access relatively cheap and routine. Instead the shuttle averaged more than $1 billion a trip, flew only a few times a year and was twice afflicted by catastrophe. In 2004, a year after the *Columbia* disintegrated on reentry, killing seven people, President George W. Bush charged NASA with replacing the shuttle with a more Apollo-like program that would bring us back to the moon and then to Mars. The resulting effort, called Constellation, led to the design of two new Ares rockets, a crew launch vehicle and a giant, Saturn V–like version intended to haul cargo. But by 2011, after having burned through some $9 billion, all Constellation had produced was an *Orion* crew capsule that was being constructed by Lockheed Martin and a rocket that had been launched once as a test. President Barack Obama canceled the program, directing NASA to refocus its energy on a mission to an asteroid. The agency was to turn to the private sector for an orbital ferry service to get cargo and crew to the International Space Station (ISS).

Still, many in Congress pushed hard to continue the quest for a new heavy-lift rocket capable of getting humans to the moon and Mars. The resulting compromise was the SLS, a single big rocket for both crew and cargo that would eschew much of the new technology planned for Ares and instead rely on space shuttle engines, boosters and tanks for most of its kick. The SLS was Ares on the cheap.

From the beginning, the SLS has been dogged by the perception that Congress cooked it up to protect jobs at NASA and its major contractors. "This vehicle has the distinction of being the first rocket designed by a committee of politicians rather than by scientists and engineers," wrote the editors of the *Economist* last December. Some critics deride the SLS as the "Pork Rocket" or "Senate Launch System." Southern senators whose states are home to large NASA or contractor facilities have indeed been the SLS's loudest proponents in Congress. Supporters include, for example, Senator Richard Shelby of Alabama—some 6,000 people are employed at the NASA Marshall Space Flight Center in Huntsville, Ala., where the SLS is managed—and Senator David Vitter of Louisiana, home to NASA's Michoud facility, where SLS core-stage prime contractor Boeing is deploying many of the 1,500 people it already has working on the program.

And a big program—and rocket—it is. The SLS will initially have a bottom core stage powered by four RS-25 space shuttle engines that use standard liquid hydrogen and oxygen fuel. Attached to each side of the core stage will be solid rocket boosters, which provide the extra push needed to get the heavy rocket airborne [*see illustration on next page*]. A second stage, atop the

first, will take over at an altitude of about 50 kilometers to push the rocket into orbit, and the *Orion* crew capsule will sit on top of the entire structure. At 98 meters, the rocket will be slightly shorter but more powerful than a Saturn V, which powered every manned mission to the moon, and will carry three times the payload of the shuttle. None of the components are designed to be reusable. Over the next decade, SLS upgrades will include more powerful engines and boosters. The eventual Mars-capable SLS would get even more power in its upper stage, giving it twice the thrust of the first version.

Critics charge that by specifying that the SLS rely on shuttle components, Congress ensured that the shuttle's big aerospace contractors would profit. "Once again, Boeing is making out like a bandit," says Peter Wilson, senior defense research analyst at RAND Corporation. Others contend that the shuttle-recycling approach will leave the SLS a troubled Franken-rocket with stitched-together parts from a dead program. The use of the shuttle boosters has already led to a problem with gaps in heat insulation, for example.

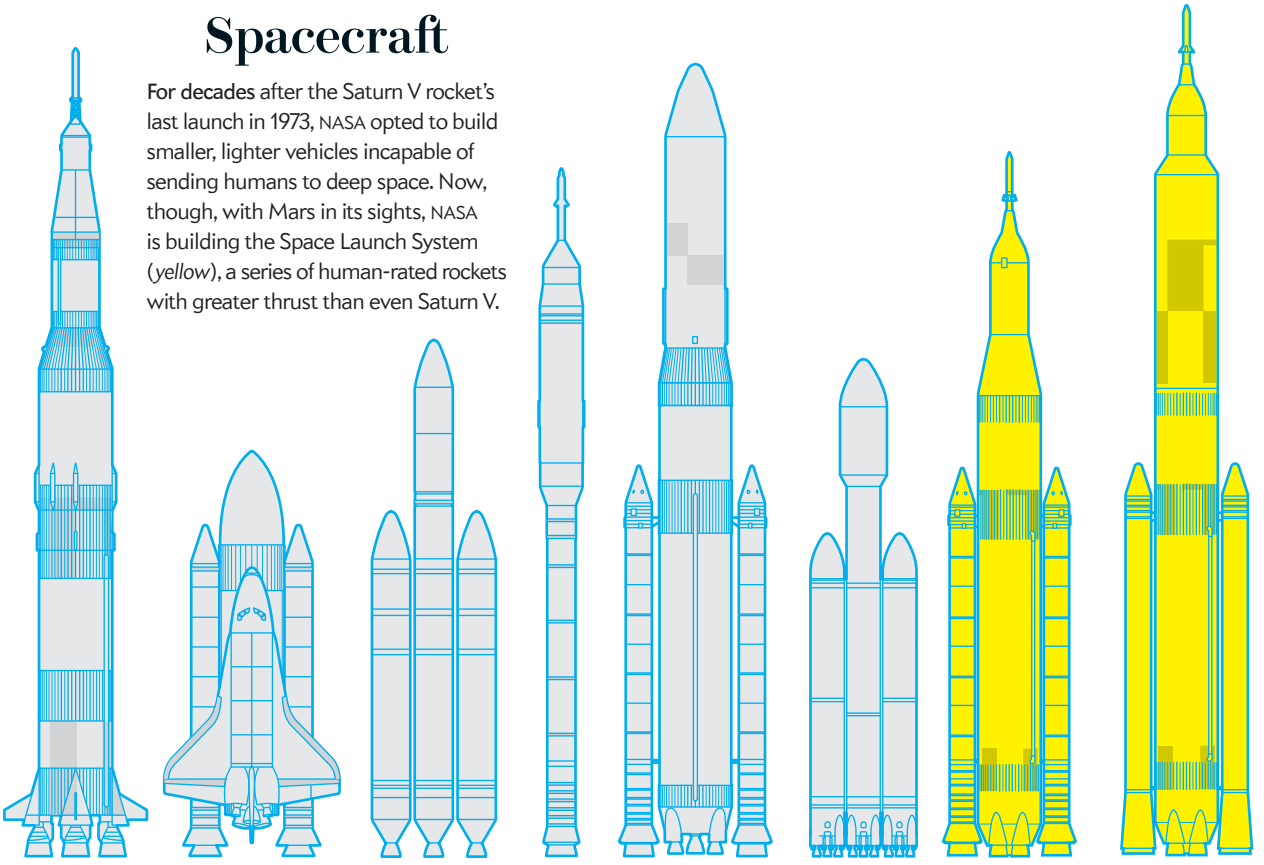
Estimates of the SLS's final cost vary wildly. NASA has publicly projected that it will take $18 billion to get the SLS to first launch—$10 billion for the rocket itself, $6 billion for the *Orion* crew capsule and $2 billion to get Cape Canaveral fitted to handle SLS launches. (Incidentally, Senator Bill Nelson of Florida is another big supporter of the SLS.) But a leaked internal study came up with a cost of more than $60 billion over the next 10 years. Others predict that delivering a crew to Mars will cost up to $1 trillion. NASA's stated target is $500 million per launch, but others have put it as high as $14 billion when all program costs are figured in.

Critics insist that the government and public will never back their enthusiasm for space exploration with the many hundreds of billions of dollars the SLS's grandest missions will require. Several analyses, including one internal study performed by NASA, have suggested that we can get to deep space and Mars without a heavy-lift rocket. It might be cheaper, some argue, to rely on smaller rockets akin to the Delta IV, used for about a decade to launch satellites, to heft into low-Earth orbit the fuel, components and materials needed to construct deep-space vehicles and then build the big craft there. And if it turns out we do need a giant rocket, many say, why not turn the job over to so-called new space? SpaceX, the company founded by Silicon Val-

TIMELINE

Once and Future Spacecraft

For decades after the Saturn V rocket's last launch in 1973, NASA opted to build smaller, lighter vehicles incapable of sending humans to deep space. Now, though, with Mars in its sights, NASA is building the Space Launch System (*yellow*), a series of human-rated rockets with greater thrust than even Saturn V.



Saturn V
First flight: 1967

Space shuttle
First flight: 1981

Delta IV heavy
First flight: 2004

Ares I
Ares V
Canceled 2010

Falcon heavy
In development

SLS 70t
(crew configuration)
In development

SLS 130t
(crew configuration)
In development

Illustration by George Retseck

BARREL SEGMENTS stacked and welded together to form a tall cylinder will serve as the shell of the SLS's core stage. Inside that shell, a tank each of liquid hydrogen and liquid oxygen will carry the rocket's fuel. At NASA's Michoud Assembly Facility, engineers are now producing "confidence" barrels to test the strength of the components.

ley icon Elon Musk, has already won orbital ferry contracts with NASA using its well-regarded Falcon 9 rockets. The "SLS is only adding small incremental improvements to technology developed 40 years ago," says James Pura, president of the Space Frontier Foundation, an advocacy group dedicated to advancing space exploration. "NASA ought to tell private industry what sort of payload it wants to get into deep space, offer a set amount of money for the job and let companies like SpaceX build it." SpaceX is developing a 27-engine, SLS-class heavy-lift rocket and is working on new, more powerful engines that, if successful, would allow that rocket to outpull even the largest envisioned SLS. And SpaceX is designing all its major components to be reusable; the SLS, in contrast, is entirely disposable.

Despite these objections, SLS mission planning is under way. A 2018 first flight will send a crewless SLS and *Orion* out well past the moon, and a second, not yet formally scheduled flight will do much the same with a crew perhaps a few years later, taking humans farther from Earth than ever before. What happens after that will ultimately be up to Congress and a new president, but right now a crewed asteroid visit is tentatively planned for the mid-2020s, with a human mission to Mars to follow in the 2030s.

THE ROCKET FACTORY

NASA TESTS ITS BIGGEST ROCKETS at Stennis Space Center, which lies in a web of lakes, rivers, bayous and canals near the southernmost tip of Mississippi. As we gear up in hard hats and safety vests, Tom Byrd, who until his retirement in January was a NASA deputy manager here, tells me there are three reasons for the center's proximity to water: the activities at Stennis require access to large barges, to marine construction expertise and to a ready way to cool giant slabs of metal exposed to temperatures approaching those found on the surface of the sun.

Each test stand here is a huge metal-and-concrete structure that looks something like a cross-sectional slab taken from the middle of a mega ocean freighter. We climb up through one of the stands, and along the way I am shown a control room that would not look out of place in a circa 1950s Soviet power plant—mostly steam gauges and big, clunky dials. I ask why they have not been upgraded to digital panels. The answer is one that will prove to be a sort of mantra for the SLS program: it has taken decades to get this stuff to work well despite unfathomable forces and innumerable glitches, so why mess with it?

From the top of the stand, however, I can see that Stennis is actually awash in upgrades. Canals and roads are being reworked to handle larger loads, and the test stands themselves are getting renovations and reinforcements because the SLS is going to subject them to greater stresses than any previous rocket. "The forces generated here are bigger than during actual launches because a rocket in the test stand can't escape its own plume," explains Byrd. Throughout an approximately nine-minute test-firing, thousands of nozzles will shoot high-pressure jets of water at the stand's walls—not for cooling but to tamp down ferocious vibrations that could otherwise rip the stand apart. Even before the SLS, no private structure was allowed within 13 kilometers of the stands because the sound waves alone from a test could shake it

IN A HYDROSTATIC TEST CELL at Michoud, engineers pump water into the liquid-oxygen tank to check for leaks. In the fully assembled rocket, the oxygen tank will sit above a much larger liquid-hydrogen tank, the two separated by an "intertank" section.

apart. And the SLS engines will generate the most powerful rocket thrust ever produced on Earth.

Just across the Mississippi-Louisiana border, a few hours away via canal (or, in my case, 45 minutes by car), sits Michoud, which I visit the next day. In contrast to the isolation of Stennis, Michoud is in the middle of an industrial area on the outskirts of New Orleans. In some ways, Michoud is a factory like any other, with welding stations, forklifts, cranes and parts bins. It is just all done on a much larger scale.

Inside, Michoud is gleaming. To tour the complex is to watch it fill up, minute by minute, with new gear—towering robot arms that can move at blinding speed, wheeled platforms and cranelike handlers that whisk components weighing tens of metric tons from one station to another, parts-organizing systems that ensure that an engine consisting of hundreds of thousands of parts does not end up with one too many or few. When you build a machine as powerful as an SLS rocket engine, you must have a very low tolerance for assembly deviation. "If our parts-tracking system told us that one of these tiny washers here is left over, all work would stop until we found it," says Patrick Whipps, one of NASA's managers at Michoud.

When it comes to zipping a crew of heroes into deep space on the wings of a barely controlled explosion, a certain level of conservatism is not necessarily a bad thing.

Many of the components that will go into the rockets built here originated in other vehicles. "We're not going to have many one-of-a-kind components on the SLS," says William Gerstenmaier, the NASA associate administrator who heads up the agency's human space exploration efforts. Yet new manufacturing equipment and methods should make the those components much less expensive to build than they have been in the past, Whipps adds. Upgrades include a friction-stir welding machine the size of a municipal water tower tank. Massive aluminum-alloy rocket sections can be dropped whole into this leviathan, where drills will meld the two sections together. It is the largest machine of its type in the world.

The SLS goes beyond shuttle technology in many other ways as well. To analyze the stresses on the SLS from buffeting and other aerodynamic instabilities during its climb through the atmosphere, NASA turned to state-of-the-art fluid dynamics software. Without it, the engineers would have had to redesign the rocket to provide more stress resistance to cover a much bigger margin for error. In addition, new avionics and digital controllers relying on computer chips that are several generations ahead of those used in the space shuttle will enable automated flight and engine controls to react many times faster to sudden changes and dangerous conditions.

Leftover shuttle engines will get the SLS airborne for the first four flights, but new versions will be needed starting in the 2020s. For those, NASA is using machines that will produce the thousands of required coin-sized turbine blades by laser-welding powdered metal into the right shapes instead of individually machining them, cutting production time for an engine's worth of blades from a year to a single month. "We're using computer control everywhere to minimize labor costs and improve precision," Gerstenmaier says.

THE CASE FOR THE SLS

WHEN THE SLS PROGRAM is in full swing, the aim will be to turn out at least two rockets a year—possibly as many as four. In the rocket world, that is mass production. But it will grind to a halt if NASA cannot convince the American public that the SLS is worth building.

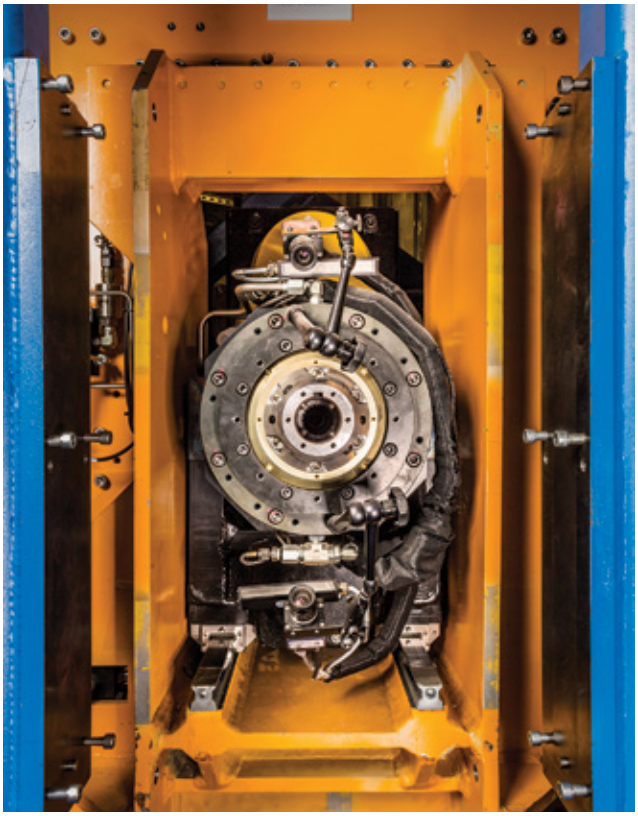
The two broadest objections—that $18 billion is too much to spend on a rocket and that we should focus on sending probes and robots, not humans, into space to do science—can be addressed as matters of perspective. Eighteen billion dollars is not all that much for the capability of sending humans to another planet and back; it cost a third more than that to improve traffic flow in Boston via the "Big Dig." It is easy to claim there are cheaper ways of doing it, but NASA's success and safety records have set the bar high, and it is unlikely that the American public would put up with higher chances of a catastrophic failure in order to shave off what amounts to a few thousandths of the federal budget.

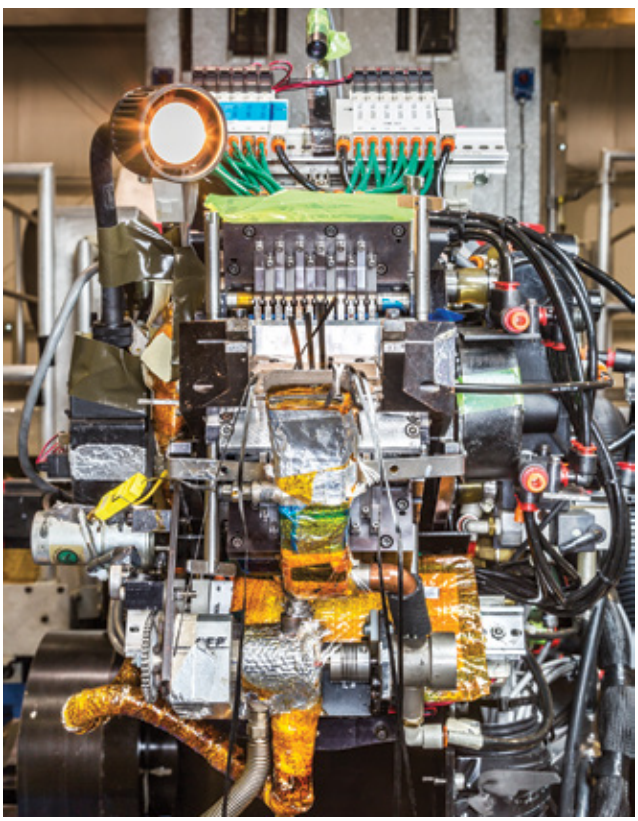
As for sticking with probes and robots, the case is often made that the science haul from a human-crewed mission is likely to be bigger than what a probe or rover can deliver. But the real justification for human spaceflight is to take steps toward expanding the human race's stomping grounds.

The SLS does have many fans. These supporters include NASA's current leadership and rank and file, a number of space experts and a growing chunk of the American public, much of which was thrilled last December by the flawless orbital flight of the *Orion* crew capsule that will be sitting atop the SLS when it heads into deep space. The experts among them can easily argue, point by point, with the critics.

Use smaller rockets to heft components and fuel into space for orbital assembly? Some 500 metric tons of materiel will be needed for a crewed Mars mission, Gerstenmaier calculates. That is a feat that the SLS could manage in four launches but that would take at least two dozen launches of a maxed-out Delta IV. Gerstenmaier contends that every one of those launches raises program risk a bit because the worst things are most likely to happen in the first minute of a mission. The approach is also more vulnerable to delays, with the effect of stretching out individual launches cumulatively across all the launches. "We used the many-launches approach with the space shuttle to build the space station, and it ended up taking decades," he says.

But the most significant potential drawback to a lift-it-in-small-chunks approach, Gerstenmaier says, is the massive amount





MICHOUD WORKERS use the segmented ring tool (*top left*) to make rings that connect domes and barrels. The "beer can" (*top right*) holds barrel segments in place for testing. Workers lift an aluminum panel onto the tool used to assemble the dome-shaped cap of the core stage (*bottom right*). At the bottom left is the machine that fabricates the carbon-fiber skin of the *Orion* capsule the SLS will carry to space.

SCIENTIFIC AMERICAN ONLINE See a video of SLS engine tests at ScientificAmerican.com/jun2015/rocket

of in-orbit construction that would be required, including of habitats, interplanetary vehicles and fuel depots. That is a daunting task, given our limited experience with the very tricky craft of in-space assembly. "You'd have a huge number of dockings; you'd be fabricating in space," he says. "Inevitably some of the pieces wouldn't work right and would be difficult to fix there. It adds an enormous amount of complexity and risk." The SLS's sheer girth will also allow packing in bulkier, ungainly payload shapes up to 10 meters across, such as those with solar panel and antenna arrays, that otherwise would have to be complexly folded and thus more vulnerable to damage or malfunction.

Another big advantage to the heavy-lift route: some of an outsize rocket's extra thrust can be converted into higher speeds that get spacecraft to their destinations more quickly. That is a critical consideration for crewed flight to Mars, where radiation exposure and supply requirements set tight upper limits on mission duration. Distant robotic missions benefit, too, because planning for follow-up missions has to wait for data to come in from predecessors to maximize the scientific returns. Because of its sheer power, the SLS can send missions into deep space using its own fuel, as opposed to gravitationally slingshotting around planets as the Voyager and Galileo missions did.

The "SLS will cut the time for a Europa visit from six-plus years to 2.5 years," says Scott Hubbard, a consulting professor of aeronautics and astronautics at Stanford University. "It would be an enabler for a very compelling scientific mission." Add these shorter transit times to the higher payload masses and packaging flexibility, and you have a powerful case for a heavy-lift rocket. That helps to explain why both China and Russia are working on SLS-class designs.

The same goes for SpaceX. Yet new space is not as natural a source for deep-space rockets as it is for transport to the ISS and back. There is no existing market, and none envisioned, for deep-space exploration beyond the handful of missions NASA has tentatively planned for the SLS. That eliminates the opportunity for SpaceX to leverage development costs for a heavy-lift rocket over various commercial customers, as it has with its smaller rockets. Stripped of that advantage, SpaceX is no better positioned than Boeing, Lockheed Martin and other conventional aerospace contractors, says former NASA astronaut Scott Parazynski, a veteran of five shuttle missions who is now at Arizona State University. "Those are very capable contractors, and I don't see SpaceX in a dramatically different light," he explains.

Hewing to the tried and tested instead of innovating might be a recipe for failure in the automobile, cell phone or software industries, but when it comes to zipping a crew of heroes into deep space on the wings of a barely controlled explosion, a certain level of conservatism is not necessarily a bad thing. SpaceX suffered several explosions and losses of control in its earlier rockets—par for the course in the development of new designs. Last October a crew member was killed in the explosion of a prototype rocket that Virgin Galactic built to bring tourists into suborbital space—just three days after the explosion of a crewless rocket built by private company Orbital Sciences, one that was headed to the ISS.

These accidents serve as reminders that in spite of decades of experience, rocketry is hard. It carries a high risk of pure catastrophe. That is one reason leaders at the Inspiration Mars Foundation, a privately funded organization that has been trying to facilitate a mission to Mars, are among those who have, after initial skepticism, been lining up behind the SLS. Other Mars experts agree. The "SLS has been criticized from day one as a rocket to nowhere," Hubbard says. "But it now has clear-cut, defensible missions, and it's time for everyone to get behind thinking about how we can make sure it all comes together."

ESCAPE VELOCITY

FOR 500 SECONDS ON A COOL NIGHT this past January, one of the Stennis Space Center's hulking engine tests turned into a fireball. It was the first test of an R-25 shuttle engine since 2009, and it went perfectly. If the successful tests keep coming, time may be on the SLS's side. The longer the program lasts—if it remains on budget and on time—the more it will stand as its own proof of concept. In its first three years, the program has achieved smooth and rapid progress, gliding through design reviews and entering into early manufacturing steps. That is blindingly fast for a major new human-rated rocket. Only a few glitches have cropped up; those insulation gaps were just about the worst of them, and the problem was quickly fixed with a layer of adhesive.

Anything could happen in the years ahead, under new presidents and congresses, contends Joan Johnson-Freese, a professor at the U.S. Naval War College who specializes in space. Maybe the consensus in government will become that we should abandon Mars for now and focus on setting up a base a little closer to home. "Some in Washington have an almost criminal nostalgia for the moon," she says. Others think NASA should forget both the moon and Mars for now and concentrate on asteroids, not only because they may contain answers to important questions about the origins of the solar system but also because we might learn how to divert or destroy any that end up heading toward Earth.

But the allure of Mars remains widespread. Lately that allure has been building, as it dawns on more people that we could reach the Red Planet within their lifetime. "We'd all like to see us go there," Parazynski says. "Other missions would be a distraction." He has concerns about the SLS, but not because he thinks it is a lousy way to get to Mars. He worries that because it will not be cheap or immediate, we will abandon the SLS before we get there.

At the moment, there are no showstoppers in sight for the SLS. That claim alone, which cannot be made for any alternative Mars rocket proposal, may ensure that the project stays the course. Sure, it was cobbled together from congressional mandates. Yes, it lacks the innovative verve of rival schemes. But there is every indication it will work as planned, and it is funded for the foreseeable future. That should be good enough to make the SLS the rocket that takes us to Mars. And if it does, the criticisms will be quickly forgotten. SA

MORE TO EXPLORE

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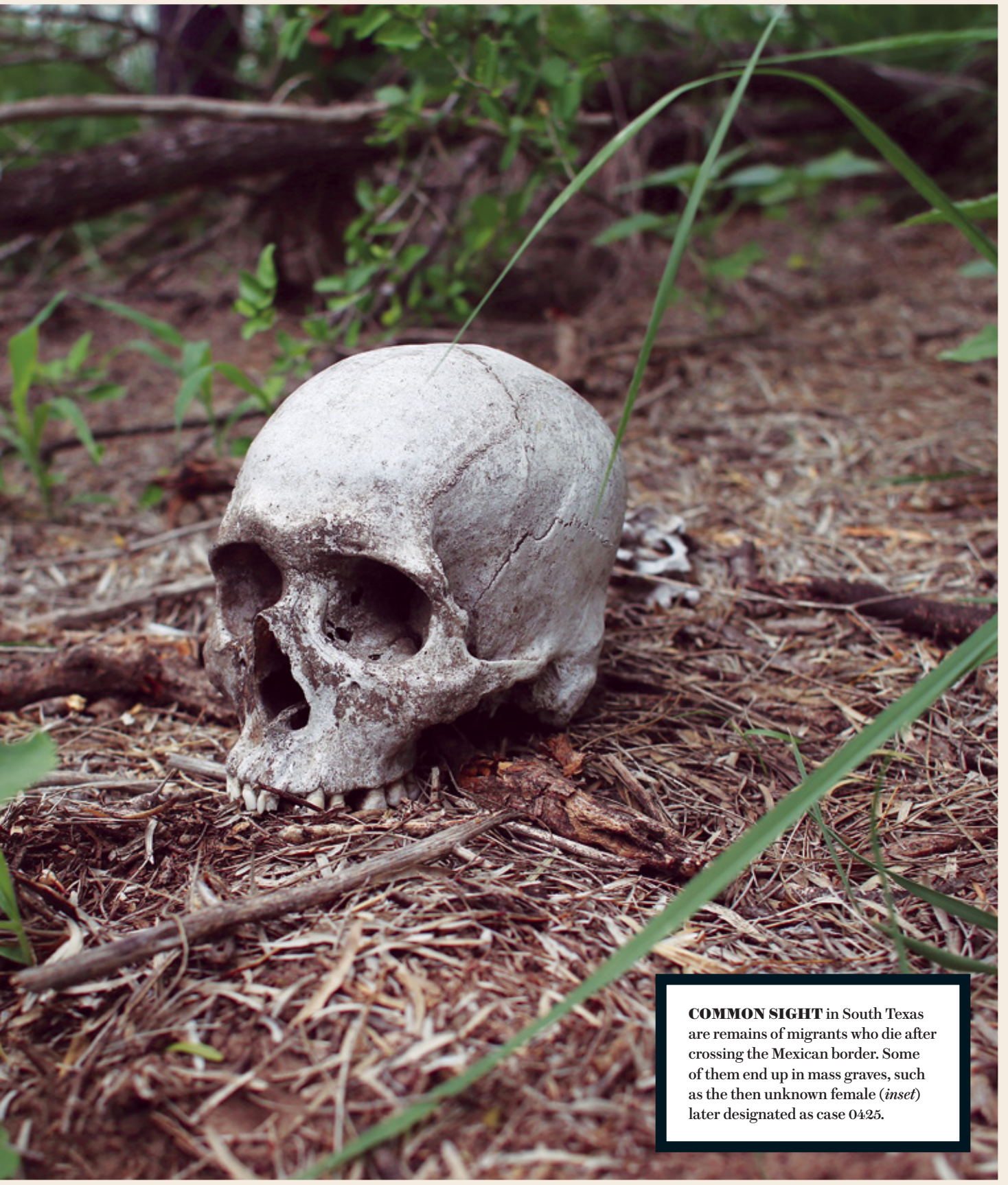
FORENSIC SCIENCE

THE MYSTERY OF CASE 0425

Scientists are identifying the remains of undocumented migrants who died crossing the Mexican border—people whose names would otherwise have been lost forever

By Ananda Rose



COMMON SIGHT in South Texas are remains of migrants who die after crossing the Mexican border. Some of them end up in mass graves, such as the then unknown female (*inset*) later designated as case 0425.

Ananda Rose is author of *Showdown in the Sonoran Desert: Religion, Law, and the Immigration Controversy* (Oxford University Press, 2012). She is writing her second book, which is about migrant deaths in Texas.

On June 28, 2012, a worker at La Cantina Ranch in Brooks County, Texas, was tending wild game feeders. On the ground, he found what he thought were bones scattered in an eight-foot-diameter area of mesquite-laden brush.

A deputy from the Brooks County Sheriff's Office showed up later in the day. According to the report, animals had already been there and left teeth marks in the bones. There were tangled clumps of black hair, torn items of clothing and a few personal effects—a backpack, four chicken-flavored Ramen packages, bug spray, a toothbrush and an unopened bag of Salsa Verde Doritos.

A pauper's burial took place soon afterward in the Sacred Heart Burial Park in the county seat of Falfurrias, about 10 miles away from where the body was discovered. The remains and personal items were transferred to a local funeral home and assigned a state death record number: 0425.

The remains appeared to be those of a migrant who had crossed the border illegally via Mexico. Along this 2,000-mile divide, the U.S. Border Patrol arrests hundreds of thousands of migrants every year, some of them children traveling alone. Many more than the numbers in the official record attempt the trip. They are fleeing chaos in their home countries—gang violence, drug trafficking, collapsed economies, and ineffectual and corrupt governments. In the flat, featureless terrain where the thermometer reaches triple digits in summer months, migrants often succumb to dehydration, exhaustion, sickness or injury, or else they often simply get lost in endless miles of scrub after being abandoned by human smugglers.

If 0425 had died in Arizona, authorities would have performed an autopsy, submitted a DNA sample to various government databases and, if a match were found, they would have passed along the identity to the consulate of the deceased's presumed country of origin, which would then be responsible for notifying the family. Texas, however, has had trouble coping with the influx. As other states tighten controls, undocumented migrants have flocked to Texas. Between October 2011 and October 2014, about 685 perished in Texas, compared with some 540 in California, Arizona and New Mexico combined.

In Brooks County, where the body was found, one in three residents lives below the poverty line. The county has neither the infrastructure nor the financial resources to handle the inundation along the border. As a result, remains are often just thrown into the ground at Sacred Heart and other burial grounds without any attempt to figure out who the deceased were.

When Lori E. Baker, a forensic anthropologist at Baylor University, first heard about the haphazard way that burials were

IN BRIEF

More undocumented migrants died crossing into Texas in recent years than in any other state along the Mexican border. Overwhelmed county governments have at times put the remains in mass graves.

A team of three forensic scientists, along with a cadre of their students, have started to look for remains in cemeteries in South Texas to identify the deceased and return them to their families.

Case 0425, a migrant who died after reaching Texas, illustrates the challenges the scientists face in making a determination of sex, height, age and nationality from skeletal remains.

PRECEDING PAGES: ISTOCKPHOTO (*folder*); JOHN MOORE *Getty Images* (*skull*); COURTESY OF KRISTA LATHAM *University of Indianapolis* (*grave marker*); THIS PAGE: JOHN MOORE *Getty Images*

WOMAN known as 0425 (*above*) died in South Texas in 2012 before her remains (*center*) were exhumed by straw-hatted Lori E. Baker and her students from Baylor University (*left*) in 2013.

being carried out at Sacred Heart, she was appalled. Baker, who, in 2001, helped in Peru's investigation of that country's human-rights abuses, assembled a small team of forensic scientists and students to exhume the remains of border crossers at Sacred Heart and identify them.

The group set to work as though they were conducting an archaeological dig. Instead of excavating ruins, they started the precise and tedious task of digging up and documenting remains and personal effects.

One of the first cases they took up was 0425.

CONSTRUCTING A BIOLOGICAL PROFILE

AFTER WEEKS OF DIGGING in the late spring of 2013, the scientists had unearthed around 70 migrants, far more than expected. Some turned up in milk crates; others were commingled in a single body bag. Still others had no grave markers at all—even simple signs that might have read "unknown female" were missing. "We know that we must always expect the unexpected," wrote Krista Latham of the group's informal motto in a 2014 post on a blog called Beyond Borders. Latham directs the University of Indianapolis Molecular Anthropology Laboratory and had volunteered to be one of the team leaders.

Latham brought four graduate students with her to Brooks County. The working conditions were challenging. In addition to the heat and humidity—and the spiders, scorpions, snakes and fire ants—there was a complete absence of maps or notes of any kind documenting the number and nature of the burials. "We did not know if they were buried in a wooden box that would protect them or just in plastic," Latham says. "So we had to go very slowly and use small hand tools in order to not potentially damage the remains."

The team created a grid system at the cemetery using string. The scientists measured the distance from any point where excavations were taking place, aboveground or belowground, to a fixed point on the grid. In that way, they could make a record of everything that turned up in the various subsurface layers and eventually compile a comprehensive map of the site.

The remains of 0425 were assigned in July 2013 to Kate Spradley, a biological anthropologist at the Forensic Anthropology Center at Texas State University. Spradley, a youthful 42-year-old with a serious demeanor, says she was motivated to take on this work part-time because she felt it would imbue her teaching and research with a vital service mission.

In the initial cataloguing of the remains, 0425 looked like a relatively straightforward case. The official report on file linked the remains to Arely Noemy Blanco Sosa, a 39-year-old Salvadoran woman. The name came from a national ID card that lay not far from the skeleton scattered at La Cantina Ranch, which the Sheriff's Office assumed was Blanco Sosa's. Unlike others in which only a small number of bones could be found, the skeleton was nearly intact [*see box on next page*].

The Forensic Anthropology Center has rows of steel tables, one stacked atop another. Each one holds a skeleton laid out carefully to preserve the proper anatomical placement of bones—a radius must lie just next to the ulna on each table. Spradley began her work on 0425 by creating a photographic inventory of the skeleton and accompanying personal effects. Even with a nearly complete skeleton and cutting-edge forensic tools, a positive identification of 0425 became a surprisingly difficult endeavor.

During the inventory, Spradley's team discovered another national identity card underneath the insole of the right shoe. It belonged to a 37-year-old woman of Honduran nationality, casting doubt on whether 0425 was really Blanco Sosa.

The forensic team then began to compile a biological profile of 0425—an analysis of sex, ancestry, age and stature and a dental record. The researchers proceeded to soak the remains in hot water and detergent—a process called maceration that speeds up natural decay by loosening cartilage, ligaments, tendons and other soft tissue. The skeleton was left to dry, invento-

COURTESY OF KRISTA LATHAM *University of Indianapolis (body bag)*; COURTESY OF THE FAMILY OF MARIA ALBERTINA IRAHETA GUARDADO *(portrait)*

ried and boxed—and held in a container for months.

Perhaps the biggest challenge in this line of work is finding sufficient funds to carry out a forensic analysis. Neither federal nor local governments provide money for identifying desperately poor migrants who are not U.S. citizens. The lack of money meant the various laboratory procedures required for a biological profile had to wait. The situation these volunteer scientists faced was captured in a grant proposal drafted by Spradley that read like an impassioned plea for help. She compared the number of migrant remains recovered in Brooks County in 2012 with the passenger capacity of a Boeing 737. "If a 737 crashes, it is considered a mass disaster and state funding is spent to facilitate recovery and identification of the passengers," she wrote. "Because these migrant deaths accumulate slowly, albeit in the same geographic location, they are not considered a mass disaster and no funding has been released to adequately process this particular mass fatality."

A year and almost nine months after 0425's bones were found, on March 20, 2014, Spradley and her students were able to return to their analysis of 0425's profile. Preliminary identification of the most basic details of a person's identity—sex and stature—is not always a simple matter in these cases, because the remains have degraded and critical bones are missing. The relatively intact skeleton meant that Spradley was able to perform a complete evaluation of the pelvis. The set of pelvic bones, including the ventral arc, the subpubic concavity and the medial ischiopubic of the left os coxa, enabled her team to confirm with "a probability of 100%," that 0425 was female, according to a report Spradley co-authored.

The scientists used another technique to estimate 0425's stature. Known as the Fully anatomical method, it measures bones down the midline of the body from heel to head. The method was first developed for gauging the height of Frenchmen killed during World War II at the Mauthausen concentration camp in Austria. It showed that 0425 stood between four feet, eight inches, and five feet.

Estimating 0425's age posed more of a difficulty. Some experts say it is virtually impossible to establish an individual's exact age at the time of death by relying only on skeletal remains because some people experience more wear and tear to their bones than others. Spradley and her team looked at the structure of the bones to determine how old the deceased was. The analysis showed that 0425's epiphyses—the end parts of the body's longer bones—had not fully fused, suggesting that she had led a life with a high degree of physical stress or nutritional deprivation that could have retarded her growth as a child. "As individuals grow older," Spradley explains, "the epiphyses fuse, so you know you are dealing with an adult at least in their mid-20s." The unfused bones from 0425 yielded estimates ranging from 20 to 35 years in age.

WHERE WAS SHE FROM?

SPRADLEY NEXT TRIED TO DETERMINE ancestry by analyzing 0425's skull. She gained her expertise in what is known as craniometric analysis as a graduate student, when she studied the skulls of individuals of African ancestry, finding that physical stresses during childhood could bring about changes in bone structure. The team gathered data needed for the analysis by using a digitizer to create a three-dimensional computer model of the skull. This information then went into a program called FORDISC 3.1. The program enabled a comparison of 0425's skull with existing digital reference data about skull shape for a group of a particular ancestry.

For Latin Americans, making these comparisons is arduous. No well-established collections of Hispanic bones exist as a refer-

COLD CASES

Bones That Keep Their Secrets

An all-volunteer team of forensic anthropologists has identified only two of the more than 110 sets of remains it has encountered since beginning work at Sacred Heart Burial Park in Brooks County, Texas, in the spring of 2013. The members hoped to have identified more by now. But many of these cases are cold: only a few skeletal fragments exist, making the task virtually impossible.

The forensic team leader who knows this best is Krista Latham. She directs the University of Indianapolis Molecular Anthropology Laboratory and specializes in piecing together an identity from inspection of the most degraded and fragmented skeletons.

One case the forensic team in Texas encountered demonstrates the near futility of these undertakings. Ranch hands had recovered skeletal fragments on December 26, 2011, at Hornsby Ranch in Brooks County and transferred them to Sacred Heart. The remains for case number 0402 were interred with a simple marker that read "unknown female remains." Later analysis showed that they turned out to be those of a male, despite the labeling on the grave marker.

Lifting of the coffin lid revealed two additional sets of human remains, not an uncommon occurrence. At the time of the burial, the coffin had been rotated 180 degrees, so the grave markers did not correspond to the bones buried there. Inside the coffin, there was a small bundle wrapped in white plastic. A laboratory analysis showed that only 2 percent of 0402's skeleton was present for making a forensic analysis. The team found the cranium, the left and right os coxae (hip joints), and the left femoral shaft. Even the teeth were missing.

The sparseness of 0402's remains is not unusual. "Bones may not be recognized as bones and therefore not collected or [those who recover the remains] may not have realized the extent to which scavengers can scatter the remains and may not have expanded their search," Latham explains. "So it is very possible that remains [of 0402] are still on the ranch in that location."

She draws parallels between forensic anthropology work in Chile and what is happening in Texas. "We see a similar phenomenon at the border," Latham says. "These are the disappeared and the invisible, the silent. No one is working to give them a voice, and they deserve it." She and others do what they can, even if sometimes it is not enough. Case 0402 has yet to be identified—and probably never will be. —*A.R.*

SCIENTIFIC AMERICAN ONLINE Watch a video by Pilar Timpane about forensic anthropology in Texas at ScientificAmerican.com/jun2015/forensic-anthro

ence source. Most of the data come from late 19th- and early 20th-century skeleton collections of European-Americans and African-Americans from the U.S. The lack of data means that the ancestry of Hispanics often stays a mystery in forensic investigations. In the worst cases, attempts to determine ancestry can lead to utter confusion. "Methods for a person considered white, when applied to an individual considered [a male] Hispanic, will usually provide a sex assessment of female," Spradley says. "If sex isn't right, no one will be identified."

Whereas skull measurements Spradley took for 0425 revealed her ancestry as "probable Hispanic," that designation failed to pin down whether the woman came from Mexico, Guatemala, El Salvador or Chile—or whether in the case of, say, a Mexican, her home was in Oaxaca or Veracruz. Also missing was any means of classifying ethnic or tribal groups—Maya, Zapotec, Xinca, Lenca, Afro-Colombian, and so on. Spradley has been trying to address the need for better comparative data by documenting differences in bone structure and genetic markers of ancestry for immigrants of Central American origin who make up most of the fatalities in South Texas. She is bringing together records on border-crossing fatalities from the Pima County Office of the Medical Examiner in Tucson, Ariz., two documented cemetery collections from Mexico and records on victims of human-rights violations during Guatemala's civil war.

Spradley uses this information to classify differences in skull size and shape—say, between Mexicans and Guatemalans. These specifics then go into the Forensic Anthropology Data Bank (FDB), co-founded in the 1980s by Spradley's graduate adviser, Richard Jantz of the University of Tennessee Knoxville. The data will ultimately help make it easier to pin down where migrants such as 0425 began their journey.

A CHEEK SWAB, A POSITIVE ID

WITH THE BIOLOGICAL PROFILE COMPLETE, Spradley and her team tried to identify the remains by matching the profile with a database of missing person reports. Spradley contacted the Tucson-based Colibrí Center for Human Rights, which has been building a repository of missing persons who are not U.S. citizens. The database is needed because the National Missing and Unidentified Persons System (NamUs) in the U.S. has significant gaps in information on foreign nationals.

In the Colibrí database, the biological profile for 0425 generated a possible match with a missing person document that had been filed in Honduras. As it turned out, a Honduran family had submitted the report to Colibrí. The information matched some of the details in the biological profile, including the sex, ancestry, stature and personal effects compiled during the investigation. It also corresponded to the name that had appeared on the identity card found in the shoe: Maria Albertina Iraheta Guardado. Now Spradley had to confirm it. Colibrí's executive director, Robin Reineke, referred the Texas State researchers to the Argentine Forensic Anthropology Team, a human-rights group that had been collecting DNA samples of family members of missing migrants—family reference samples—to help confirm the identity of those who had died during border crossings.

DNA tests are performed only after the biological profile that has been meticulously compiled can be matched with a specific missing person report. The Texas State lab took a sample from the metatarsal bone in the foot and dispatched it to the lab used by the Argentine group for comparison with the family reference samples on file. The DNA from the metatarsal bone matched that of the family reference sample. On April 25, 2014, the scientists finally had the confirmation they needed. It took two years from the time Iraheta Guardado's remains were found to establish her identity.

WAITING FOR CLOSURE

MARIA ALBERTINA IRAHETA GUARDADO was 37 when she decided to leave the Dos Bocas community in Santa Rosa de Aguán, Honduras, and emigrate to the Bronx to meet up with her sister, who works as a house cleaner. She wanted to send money back to her mother and help support her six children. Some of them are already adults. But two—a nine-year-old and a 14-year-old—still live with Iraheta Guardado's mother.

According to the mother and sister, who spoke with me on the phone, Iraheta Guardado also wanted to leave because of a growing weariness with the violence that plagues Honduras, the country with the highest murder rate in the world, as of 2012. Several years ago her husband was fatally shot by stray bullets in a cross fire, says Iraheta Guardado's mother, Maria Amelia Guardado: "Like everyone else here, he was just murdered, because that's what happens here."

The mother learned from the Argentine Forensic Anthropology Team that her daughter crossed the border near Brownsville, Tex., on June 15, 2012, along with a group of other migrants and a human smuggler. She had walked for two days before fainting and being left behind near Falfurrias.

Identifying Iraheta Guardado took the combined efforts of forensic anthropologists, human-rights organizations, foreign consulates and law-enforcement agencies. Her mother then waited anxiously for her daughter's remains to be returned; they had been delayed because of a bureaucratic snafu over a death certificate. Finally, in early April 2015, they arrived and were returned to the family for burial.

For the team who identified Iraheta Guardado, a positive outcome was a complicated victory. Team members were thrilled with their success, but the grueling effort exacted an emotional cost. As Latham geared up to travel back to Falfurrias for another two-week exhumation in June 2014, she wrote in a blog post: "I won't be able to read [my son] bedtime stories for 13 nights or get his hugs and kisses for 14 days. But the thought that keeps me going is that I am temporarily leaving my family to reunite other families. I will get to hug and kiss my son again, but there are hundreds of mothers whose children are buried unidentified in the Sacred Heart Burial Park who cannot say the same thing." SA

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PUBLIC HEALTH

THE DENGUE STOPPER

Scientists are immunizing mosquitoes against disease with the help of a common microbe

By Scott O'Neill

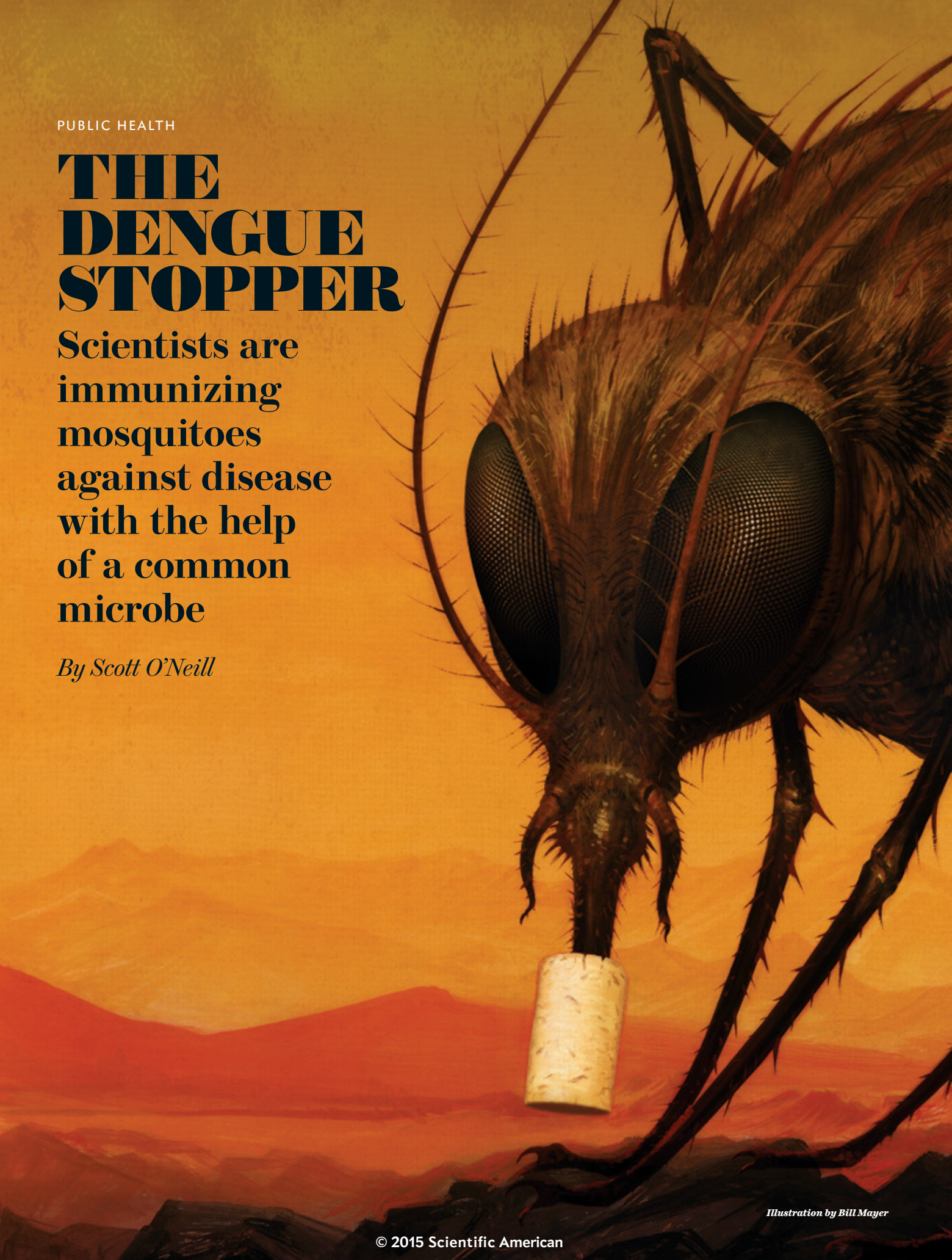


Illustration by Bill Mayer

Scott O'Neill is dean of science at Monash University in Australia and head of Eliminate Dengue, an international *Wolbachia* research collaboration.

THE BEST TIME OF DAY TO RELEASE MOSQUITOES IN NORTHERN AUSTRALIA IS midmorning. Later in the day, winds might sweep the insects away and dash any hope that they will find a mate. Earlier than that, the workers who drive around and release containers full of mosquitoes would have to get overtime pay. And so, on a sweltering January morning at the height of the Australian summer, I climbed into my white van with thousands of mosquitoes stowed in Tupperware cups on the backseat.

Once a week, for about three months in 2011, we made trips like this to release mosquitoes. We concentrated on two communities in the city of Cairns, a popular tourism spot near the Great Barrier Reef. At every fourth house, where residents had agreed to participate in our study, we would grab a cup of mosquitoes from the van, peel off the lid, and set 50 or so insects free.

These were not your garden-variety mosquitoes. Each one was infected with a microbe called *Wolbachia,* a common bacterium that lives in insect cells. For our purposes, the most interesting characteristic of *Wolbachia* is that it appears to block the dengue virus from replicating in the tissues of mosquitoes. Because the virus cannot replicate, the insects do not transmit it to their victims, and the disease does not spread.

Infecting mosquitoes with a bacterium is a roundabout way to fight dengue, but we do it because otherwise the options are few. Dengue, nicknamed "breakbone fever" for the crippling pain it causes, infects 390 million people every year. Because there is no cure or treatment, the chief strategy has been to attack *Aedes aegypti,* the mosquito that transmits the virus. Yet common insecticides such as temephos have lost much of their effectiveness as mosquitoes have developed resistance. Bed nets are almost useless, too, because *A. aegypti* typically feed during the day. At present, one of the most promising tools for halting the spread of dengue—and perhaps malaria and other mosquito-borne illnesses—appears to be spreading *Wolbachia* among wild mosquitoes.

Wolbachia is not an obvious choice as a dengue fighter. It does not naturally occur in the mosquitoes that most often transmit dengue. We actually have had to infect those mosquitoes artificially, in the laboratory. In other words, we use *Wolbachia* to immunize the mosquitoes against dengue and then set them loose in the wild, where (we hope) those mosquitoes will pass the bacterium to their offspring. *Wolbachia* is largely benign for mosquitoes and the environment, although it may reduce the insects' egg production. But the potential benefits for humans are clear: if mosquitoes infected with *Wolbachia* become predominant in the wild, we expect dengue infection rates among people to drop.

PEST CONTROL

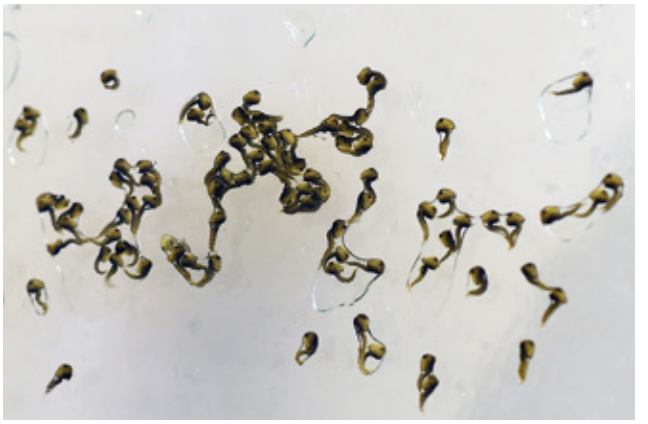
MOSQUITOES ARE AMONG the deadliest creatures on earth. Yellow fever, also transmitted by *A. aegypti,* took out more U.S. troops than enemy fire during the Spanish-American War in 1898. Malaria, transmitted by a parasite harbored in mosquitoes, killed approximately 627,000 people in 2012 alone. Now *A. aegypti* is rapidly spreading dengue around the globe. About half of the world's population is at risk of contracting the disease, according to the World Health Organization. *A. aegypti,* which is recognizable by the white stripes on its legs and the lyre pattern on its thorax, can breed in any pool of standing water, which makes it particularly hard to control. The mosquito is found in tropical and subtropical climates around the world—in Africa, the Americas, the Eastern Mediterranean, Southeast Asia and the Western Pacific. Dengue, however, does not naturally occur in these creatures: the mosquitoes get dengue from us.

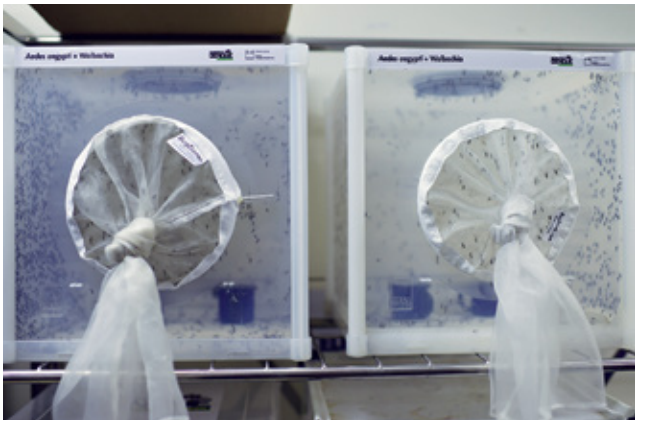
The mechanism of dengue infection is simple. Female mos-

IN BRIEF

Scientists are fighting dengue fever with the help of *Wolbachia,* a common bacterium that stops the virus from replicating inside the mosquitoes that transmit the disease. Without it, we have few weapons against dengue. **Although the bacterium** is common among insects, it does not infect *Aedes aegypti,* a species of mosquito that is a major carrier of dengue. Instead researchers infect the mosquito with *Wolbachia* in the laboratory and then release *A. aegypti* into the wild. **The goal is to reduce** infections in humans by getting *Wolbachia*-infected mosquitoes to mate and pass the bacterium to future generations. If the method works, vast numbers of wild mosquitoes will eventually carry *Wolbachia* and thus be unable to transmit dengue.

***AEDES AEGYPTI* MOSQUITO** (*below*) **is the most common vector for dengue worldwide, but mosquitoes infected with the bacterium *Wolbachia* cannot transmit the virus. Scientists are growing these mosquitoes in the laboratory and releasing them into the wild (*bottom right*), where they could displace *Wolbachia*-free mosquitoes and stop the spread of dengue.**





quitoes bite humans because they need the protein found in our blood to produce eggs. (Male mosquitoes do not bite.) If the mosquito bites someone with dengue—and then, after the virus's roughly eight- to 12-day replication period, bites someone else—it passes dengue into its next victim's bloodstream. *Wolbachia,* however, disrupts this process by preventing replication from ever taking place.

Wolbachia was first identified in 1924 during dissections of household mosquitoes. Interest in the bacterium waned until the 1970s, when researchers noticed that under certain circumstances, it could prevent mosquito eggs from hatching, which suggested the bacterium could be used for insect control. In the 1990s scientists learned that some strains of *Wolbachia* could also shorten insect life span, which presented another way to limit disease transmission by insects.

I was introduced to *Wolbachia* as a Ph.D. student in the mid-1980s. Back then I wondered if we could use it to stop mosquitoes from transmitting human diseases. If we could reduce the life spans of mosquitoes by even a modest amount, it could seriously reduce the ability of the insects to spread disease among humans.

The catch, of course, was *Wolbachia*'s lack of affinity for *A. aegypti*. The bacterium is common in up to 60 percent of insect species—including some mosquitoes that bite humans—but the infection does not easily pass between species. The challenge was finding a way to transfer different strains of *Wolbachia* from another insect—the fruit fly—into this dengue-carrying mosquito. It was a tedious process that took us more than a decade.

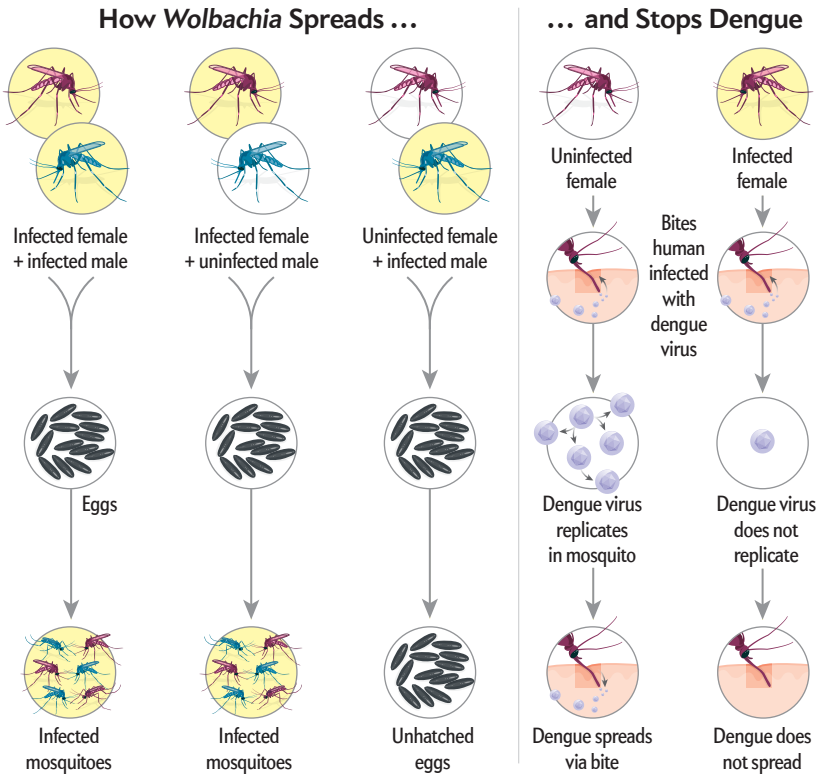
JAMES GATHANY *Getty Images (red mosquito);* CHRISTOPHE SIMON *Getty Images (larvae, net cages and release)*

HOW TO INFECT MOSQUITOES

IMAGINE TAKING a knitting needle and poking it into a balloon. Next, you have to remove the needle without popping the balloon. That pretty well sums up the process of infecting mosquito eggs with *Wolbachia*. In the lab, my team uses microscopic needles to take the microbe from the fruit fly and inject it directly into young mosquito eggs. At first, like balloons pierced with knitting needles, the eggs would burst. We tried with many thousands of eggs before we were successful.

Secrets of *Wolbachia*'s Success

There is no vaccine against dengue, but infecting mosquitoes with a natural bacterium called *Wolbachia* blocks the insects' ability to pass the disease to humans. The microbe spreads among both male and female mosquitoes: infected females lay eggs that harbor the bacterium, and when *Wolbachia*-free females mate with infected males, their eggs simply do not hatch. Researchers are now releasing *Wolbachia*-infected females into the wild in Australia, Vietnam, Indonesia and Brazil.



Once we managed to infect mosquito eggs without destroying them, we had other problems to solve. *Wolbachia* would often disappear after a generation or two of mosquito breeding, which meant there was no way the bacterium would spread in the wild the way we wanted it to. We eventually found that we had to condition the microbes before injecting them into mosquitoes—to get these bacteria, which were used to living in fruit flies, accustomed to their new hosts. To do so, we extracted *Wolbachia* from fruit flies and then grew it in mosquito cell lines. In 2005 we finally prevailed: we infected mosquitoes with *Wolbachia* and watched them pass the bacterium from generation to generation—13 in all. Since then, *Wolbachia* has flourished in all subsequent generations. As we expected, at least one strain of *Wolbachia* shortens the life of *A. aegypti*.

Yet it turns out that *Wolbachia* is even better at fighting dengue than we thought. For reasons we do not fully understand, the dengue virus has trouble growing in *Wolbachia*-infected mosquitoes. We figured this out a few years after successfully transplanting *Wolbachia* into *A. aegypti,* when separate work I had been part of revealed that in fruit flies the bacterium also blocks replication of the *Drosophila* C virus, which is deadly to flies. My team injected dengue directly into our *Wolbachia* mosquitoes, and to our delight, dengue no longer replicated in their bodies. We repeated the experiment a number of times—each time with dozens of mosquitoes—and discovered that our results were consistent.

These days we use a strain of *Wolbachia* that blocks dengue transmission but does nothing to shorten the mosquitoes' lives. After all, we want our mosquitoes to live as long as possible and lay as many *Wolbachia*-infected eggs as they can. We have known since my time as a graduate student that female mosquitoes infected with *Wolbachia* pass the bacterium on to nearly all of their offspring. It takes only a few generations after the introduction of *Wolbachia* before almost every mosquito in a population carries the bacterium.

One of our experiments in northern Australia showed that after releasing approximately 10 mosquitoes per house per week for 10 weeks, more than 80 percent of the wild mosquitoes in the area had *Wolbachia*—and they still had it when we tested them two months after we had stopped releasing mosquitoes. Because *Wolbachia* passes so well through successive generations, we should not have to do any repeat releases. *Wolbachia* should spread on its own.

INTO THE WILD

BEFORE WE COULD RELEASE *Wolbachia* mosquitoes into the wild, we had to address a lot of concerns in the community. We spent months going door-to-door to ask permission to release mosquitoes near people's homes. We conducted formal informational meetings as well as impromptu chats outside shopping centers. Australian federal officials also checked our method for safety before approving the release of the infected mosquitoes.

To humans, *Wolbachia* poses no apparent threat. Our own lab experiments have found that the bacterium cannot be passed on to humans, because it is too big to travel down the mosquitoes' salivary duct and into the human bloodstream. We have also conducted safety tests looking for antibodies in human volunteers, but after three years of letting mosquitoes bite volunteers, the humans still have no sign of the microbe. Our lab staff and volunteers have frequently rolled up their sleeves and spent 15 minutes in the mosquito cages, allowing the insects to drink their fill.

There has been no sign that *Wolbachia* harms the environment, either. Since we started releasing mosquitoes with *Wolbachia* in 2011, we have been studying the animals and insects that encounter them, and our work has reaffirmed that the

SCIENTIFIC AMERICAN ONLINE See a video on bacteria-based dengue prevention at ScientificAmerican.com/jun2015/dengue

Illustration by Lucy Reading-Ikkanda

bacterium resides solely within the cells of insects and other arthropods. Moreover, we do not think that *Wolbachia* would survive even if it were to find a way into the bloodstream of humans or other mammals. Indeed, *Wolbachia* is already found in many other mosquito species, including a number that regularly bite people. Tests conducted on spiders and geckos that have eaten *Wolbachia* mosquitoes showed no ill effects from the exposure and no sign of the bacterium in the tissues of those animals.

Our lab staff and volunteers have frequently rolled up their sleeves and spent 15 minutes in the mosquito cages, allowing the insects to drink their fill.

Before the first *Wolbachia* mosquito releases in 2011, we commissioned an independent risk assessment by the Commonwealth Scientific and Industrial Research Organization (CSIRO), Australia's national science agency. Teams of experts identified and evaluated potential hazards associated with the release of *Wolbachia* mosquitoes, ranging from possible ecological impacts to effects on communities. That agency scrutinized existing studies and interviewed experts in evolutionary biology. Tough issues were involved: changes in mosquito density, the possibility of evolution of the dengue virus, the nuisance of increasing numbers of biting mosquitoes and changes in the community's perceptions of the risks associated with dengue. But CSIRO's final report concluded that the release of *Wolbachia* mosquitoes would have negligible risk to people and the environment—the lowest possible rating.

WOLBACHIA GOES GLOBAL

IN ADDITION TO THE FIELD TRIALS we have been doing in Australia for the past four years, trials are under way in Vietnam and Indonesia. Last September we also started releasing the mosquitoes in Brazil. We have found that *Wolbachia* can establish itself in wild mosquito populations within small communities. Now we are going to attempt to do the same over larger areas. Scaling up our operations may require some tweaks in our methods. Rearing enough adult *Wolbachia* mosquitoes, for example, will be too labor-intensive. In Cairns, we are instead testing the effectiveness of putting *Wolbachia* mosquito eggs into the environment.

Meanwhile other researchers are developing alternative approaches to mosquito control. One entails releasing male mosquitoes that have been genetically modified so that the sperm cells of males carry a lethal gene. When those mosquitoes mate with females in the wild, their offspring die. This approach is innovative and potentially powerful, but it could also be costly. To be effective on a large scale, it could be necessary to constantly release modified mosquitoes; otherwise, unmodified mosquitoes from surrounding areas would move into the area and replenish the population. The use of transgenic mosquitoes also faces strong opposition from critics of genetic modification.

In contrast, the costs of *Wolbachia*-based dengue control are front-loaded: after the initial investment in bacterium-infected mosquitoes, the process takes care of itself. It could be a relatively inexpensive way to tackle dengue, which is especially important in the poor tropical countries where the disease is most prevalent. Another benefit of our approach is that it involves no gene modification—although it still took years to get off the ground because of the work necessary to assure communities of its safety.

We still have a significant hurdle ahead of us: measuring the reduction in dengue that occurs when we introduce *Wolbachia* into communities. This step will be difficult for several reasons. In the areas where we work, reliable data on dengue cases are largely nonexistent, and infection rates can vary widely from year to year. To firmly establish the effectiveness of our method, we will need to compare dengue rates in areas where we have released *Wolbachia* mosquitoes against those where we have not. Doing so will require taking lots of blood samples, which will be laborious.

Yet we believe the work will be worthwhile and not only for fighting dengue. These mosquitoes—or rather the microbes inside them—show promise against other diseases as well. We have seen evidence that *Wolbachia* may also reduce the ability of mosquitoes to transmit chikungunya, which first appeared in the mainland U.S. last July, and yellow fever. Researchers are also attempting to use *Wolbachia*-infected mosquitoes to slow the transmission of malaria and lymphatic filariasis, a profoundly disfiguring disease caused by worms.

The new observations are exciting. For the time being, however, our group will remain focused on evaluating the method against dengue. It is where we first started our research and where we are closest to seeing a real-world impact. One day, we hope, a mosquito bite will leave nothing more consequential than an itchy bump. SA

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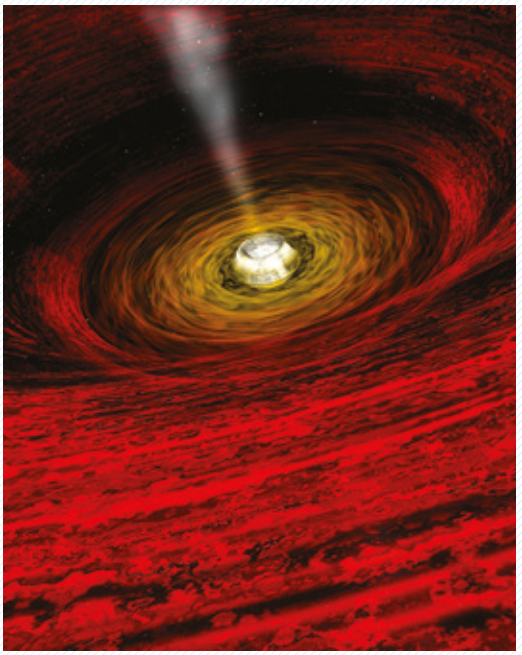

Black Hole: How an Idea Abandoned by Newtonians, Hated by Einstein, and Gambled on by Hawking Became Loved

by Marcia Bartusiak. Yale University Press, 2015 ($27.50)

The concept of black holes arose from general relativity, yet Albert Einstein himself assumed that they could not exist in nature: he postulated that some unknown aspect of stellar physics would keep matter from condensing to a state so extreme that even light could not escape its gravitational pull once drawn in. Yet scientists now accept that such deformations of spacetime actually exist. Science writer Bartusiak's book traces the crooked path black holes took through the history of science, from their first quasi incarnation within Newton's laws, through general relativity, to today's understanding that black holes inhabit the cores of nearly all galaxies. The narrative features intriguing cameos from many of history's well-known physicists, including J. Robert Oppenheimer, who advised graduate students that general relativity was a dead end years after writing the first, largely ignored, modern description of a black hole in 1939. *—Sarah Lewin*

How to Bake π: An Edible Exploration of the Mathematics of Mathematics

by Eugenia Cheng. Basic Books, 2015 ($27.50)

"The world of math is more weird and wonderful than some people want to tell you," writes Cheng, a mathematician at the University of Sheffield in England. Invoking plenty of examples from cooking and baking, as well as other everyday-life situations such as calculating a taxi fare, searching for love through online dating services and training for a marathon, she explains abstract mathematical ideas—including topology and logic—in understandable ways. Cheng's specialty is category theory, which she describes as "the mathematics of mathematics"—a way to organize and understand the many rules and processes that govern math. Her lively, accessible book demonstrates how important and intriguing such a pursuit can be.

The Strange Case of the Rickety Cossack: And Other Cautionary Tales from Human Evolution

by Ian Tattersall. Palgrave Macmillan,* 2015 ($27)

Around when Charles Darwin's theory of evolution was published, scientists were puzzled by ancient human bones discovered in 1856 Germany that featured a prominent browridge. Rather than considering that the remains belonged to a species separate from modern humans, some researchers at the time attributed the skeleton to a Cossack horseman with a painful condition of rickets that caused him to furrow his brow until the bone above his eyes grew. The incident demonstrates how scientists' own biases have often influenced their interpretation of what the fossil record was telling them. "Received wisdoms about human evolution have always conditioned what we have believed about our own origins, often in the face of compelling evidence to the contrary," writes Tattersall, an emeritus curator of anthropology at the American Museum of Natural History in New York City. In this book, he highlights the controversial ideas and colorful personalities that have shaped paleoanthropology and given rise to our current understanding of how we became human.

American Genius

National Geographic Channel. Premiering June 1

Behind many historic inventions—flight, electricity, personal computers—are tales of heated rivalries that spurred the inventors on. This television miniseries profiles the competitions of such geniuses as the Wright brothers and Glenn Curtiss, Nikola Tesla and Thomas Edison, and Steve Jobs and Bill Gates. Actors convey the intensity of the feuds, and interviews with experts illuminate the characters and the science that made the innovations possible. The eight-part docudrama reminds us that sometimes the brightest minds need a competitive nudge to reach greatness.

NASA/CHANDRA X-RAY CENTER/APRIL HOBART

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

Scientia Humanitatis

Reason, empiricism and skepticism are not virtues of science alone

In the late 20th century the humanities took a turn toward postmodern deconstruction and the belief that there is no objective reality to be discovered. To believe in such quaint notions as scientific progress was to be guilty of "scientism," properly said with a snarl. In 1996 New York University physicist Alan Sokal punctured these pretensions with his now famous article "Transgressing the Boundaries: Toward a Transformative Hermeneutics of Quantum Gravity," chockablock full of postmodern phrases and deconstructionist tropes interspersed with scientific jargon, which he subsequently admitted were nonsensical gibberish.

I subsequently gave up on the humanities but am now reconsidering my position after an encounter this past March with University of Amsterdam humanities professor Rens Bod during a European book tour for *The Moral Arc*. In our dialogue, Bod pointed out that my definition of science—a set of methods that describes and interprets observed or inferred phenomena, past or present, aimed at testing hypotheses and building theories—applies to such humanities fields as philology, art history, musicology, linguistics, archaeology, historiography and literary studies.

Indeed, I had forgotten the story he recounted of Italian philologist Lorenzo Valla, who in 1440 exposed the Latin document *Donatio Constantini—the Donation of Constantine,* which was used by the Catholic Church to legitimize its land grab of the Western Roman Empire—as a fake. "Valla used historical, linguistic and philological evidence, including counterfactual reasoning, to rebut the document," Bod explained. "One of the strongest pieces of evidence he came up with was lexical and grammatical: Valla found words and constructions in the document that could not possibly have been used by anyone from the time of Emperor Constantine I, at the beginning of the fourth century A.D. The late Latin word *Feudum,* for example, referred to the feudal system. But this was a medieval invention, which did not exist before the seventh century A.D." Valla's methods were those of science, Bod emphasized: "He was skeptical, he was empirical, he drew a hypothesis, he was rational, he used very abstract reasoning (even counterfactual reasoning), he used textual phenomena as evidence, and he laid the foundations for one of the most successful theories: stemmatic philology, which can derive the original archetype text from extant copies (in fact, the much later DNA analysis was based on stemmatic philology)."

Inspired by Valla's philological analysis of the Bible, Dutch humanist Erasmus employed these same empirical techniques to demonstrate that, for example, the concept of the Trinity did not appear in bibles before the 11th century. In 1606 Leiden University professor Joseph Justus Scaliger published a philological reconstruction of the ancient Egyptian dynasties, finding that the earliest one, dating to 5285 B.C., predated the Bible's chronology for the creation of the world by nearly 1,300 years. This led later scholars such as Baruch Spinoza to reject the Bible as a reliable historical document. "Thus, abstract reasoning, rationality, empiricism and skepticism are not just virtues of science," Bod concluded. "They had all been invented by the humanities."

Why does this distinction matter? Because at a time when students and funding are fleeing humanities departments, the argument that they are at least good for "self-cultivation" misses their real value, which Bod has forcefully articulated in his recent book *A New History of the Humanities* (Oxford University Press, 2014). The transdisciplinary connection between the sciences and humanities is well captured in the German word *Geisteswissenschaften,* which means "human sciences." This concept embraces everything humans do, including the scientific theories we generate about the natural world. "Too often humanities scholars believe that they are moving toward science when they use empirical methods," Bod reflected. "They are wrong: humanities scholars using empirical methods are returning to their own historical roots in the *studia humanitatis* of the 15th century, when the empirical approach was first invented."

Regardless of which university building scholars inhabit, we are all working toward the same goal of improving our understanding of the true nature of things, and that is the way of both the sciences and the humanities, a *scientia humanitatis*. SA

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Illustration by Izhar Cohen

The ongoing search for fundamental farces

Steve Mirsky has been writing the Anti Gravity column since a typical tectonic plate was about 34 inches from its current location. He also hosts the *Scientific American* podcast Science Talk.

Gold Flush

A cloud with a silver lining pales next to solid waste laced with gold

You can't make a silk purse out of a sow's ear. You can't make chicken salad out of chicken—shall we agree we know what word goes at the end of that saying? It's also been thought impossible to, as the Yiddish expression has it, *makhn gold fun drek:* make gold from—sure enough, it's that same word again.

It remains true that you can't *make* gold from feces. But it turns out you can extract enough gold from solid waste to possibly make the effort pay. This excremental explication was performed by one Kathleen Smith, a researcher with the U.S. Geological Survey, at an American Chemical Society meeting held in late March in Denver. The meeting was billed as "Chemistry of Natural Resources," which includes the stuff produced when nature calls.

Smith has had what appears to be, based on her authorship of nearly 100 scientific publications, a long and distinguished career. She has now discovered that papers with titles such as her "Trace-Metal Sources and Their Release from Mine Wastes: Examples from Humidity Cell Tests of Hard-Rock Mine Waste and from Warrior Basin Coal" garner far less media attention than do press releases headlined "Sewage—Yes, Poop—Could Be a Source of Valuable Metals and Critical Elements." (Smith's conference presentation was called "Metal Occurrence in and Potential Recovery from Municipal Biosolids," which we journalist types would probably have ignored, too, to be honest.)

Before we talk about getting the gold out, let's consider how it got in. Most of us are not dining on gold-leaf-covered ice cream, like the kind in the $1,000 sundaes at the New York City restaurant Serendipity 3 (the wealthy customer being the serene dip). Nor are most of us spending more than $400 on a pill filled with shards of gold leaf, the sole purpose of which is to eventually make one's bowel movement, no joke, glitter. A commenter to the online news article discussing this pill helpfully wrote, "You don't need to pay that much. My kid has glittery poos every time he does arts and crafts … just eat regular glitter, it works just fine."

Geophagy—snacking on small amounts of dirt—is a common practice in some regions. But a 2014 paper in the journal *BMC Pregnancy and Childbirth* did not find any gold in soil preferred by pregnant women in Tanzania, where eating earth is believed to alleviate morning sickness—even though the study was done in a gold-mining community. (The samples sadly did contain mercury and other toxic metals used in gold mining.) And whereas a dental patient's gold filling may on occasion pop out of a molar and wind up circling the former chewer's drain, that scenario is rarer than hen's teeth.

Seems that the gold winds up in the solid waste well after said waste is originally produced. "There are metals everywhere," Smith explains in the aforementioned press release, "in your hair care products, detergents, even nanoparticles that are put in socks to prevent bad odors." When you wash your clothes or yourself, incredibly tiny amounts of these metals, including precious or useful ones such as gold, palladium, vanadium, platinum and silver, get sent to the sewer. And the processing procedures at treatment plants, designed to recover usable water, meld metal with manure—about seven million tons annually.

With that much material, even minimal ingredients can add up to a small fortune. A 2015 study in the journal *Environmental Science & Technology* estimated that a community of a million people could make a pile of sludge every year with an extracted mineral value of $13 million. When Smith and her colleagues examined treated solid waste, they found gold "at the level of a minimal mineral deposit." Which means that soon it just may be worth trying to separate the wheat from the chaff. Although anything that started as actual wheat will in this analogy become chaff. Eh, it'll all pan out in the end. SA

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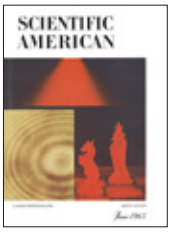
Illustration by Matt Collins



June 1965

Interior of the Earth

"Our experiments with the 90:10 iron-nickel alloy and extrapolations from these results indicate that under the assumed high pressures and temperatures of the earth's core the density of the alloy is about 10 percent less than that of pure iron. Our density values for this alloy agree with the density of the core, as estimated by K. E. Bullen of the University of Sydney and Francis Birch of Harvard University on the basis of seismic data, the moment of inertia and the earth's mass. We conclude, therefore, that the earth's core probably consists of iron-nickel alloys and is similar in composition to the iron-nickel meteorites."

June 1915

The Greatest Invention?

"The most significant event in the annals of human achievement was the invention of the steam engine. Its introduction divided recorded time into two distinctly defined eras, and it may well be said that the entire history of man's material endeavors counts forward or backward from that comparatively recent event. The jump from manual to power operations, which typifies the two eras, was nothing short of cataclysmic, and profoundly affected and stirred mankind in all its relations to an extent inconceivably greater than any political change or decision in battle that is ordinarily cited by the historian to mark the beginning of a new epoch."

Our 70th Anniversary

"When we think that at the time the SCIENTIFIC AMERICAN was started it took three weeks to send a message from New York to Liverpool and three months to Calcutta; when we think that only yesterday we marveled at the application of ether and chloroform to surgery, at the feat of telegraphing across the ocean without wires, at the bigness of the Panama Canal, at the opportunity of viewing the skeleton beneath the living flesh with the X-rays, and the spectacle of a man flying in the air swifter than any bird; when we think that it has been our privilege not merely to see these and many other miracles but to translate them into print, who can blame us if we contemplate our future task with a feeling almost akin to awe?"

More from this special issue from 1915 on the history of invention is online at www.ScientificAmerican.com/jun2015/inventions-1915

June 1865

Interior of the Earth

"Messrs Editors—For my own part I have quite a 'golden' idea—that the interior of the earth is abundantly supplied with, if not mainly composed of, gold, platinum and other precious metals. If we suppose but for an instant that the earth was once in a gaseous or fluid state, is it not quite evident that those substances most difficult of fusion, and possessing the greatest specific gravity, would be first to find their way to the center? Now gold, platinum and a few other of the precious metals possess these properties in a high degree above all other known substances, and though we know them to be scarce on the surface of the earth, we have no assurance but that they are abundant in nature.—John Calvin Moss"

The writer invented the first successful photo-engraving process for printing.

A VIEW OF CIVILIZATION
after 70 years of invention, 1915

Plowing with Steam Engines

"Difficulties have been met with in applying steam power to cultivation. To attach the moving power direct to the implement, as is done in the case of the horse, was found not suitable with a steam engine, from the loss of power in moving such a heavy weight over inequalities of the ground, and from the compression caused by its travelling over the soil to be cultivated. Hence the use of a rope driven by the engine became requisite for working the implement."

Varnish Ingredient

"The purest and best gum copal in the world is found on the mainland of Africa, near Zanzibar. It is, without doubt, a fossil gum. It is dug from the earth by Africans, and by them carried to the Banian [Indian] trader, in small quantities, for sale. When it reaches Zanzibar, it is in a very dirty state, and requires much sifting and garbling before it is merchantable; it is then cleansed with a solution of soda-ash and lime, put up carefully in boxes, when it is ready for the home market. That it is a gum may be proved from the fact of its rough or 'goose-skin' surface, which no doubt is an impression of the sand or earth when it ran down from the tree in a soft state. Pieces, too, are found with sticks, leaves, and insects preserved in them in the most perfect state."

SCIENTIFIC AMERICAN, VOL. CXII, NO. 23, JUNE 5, 1915

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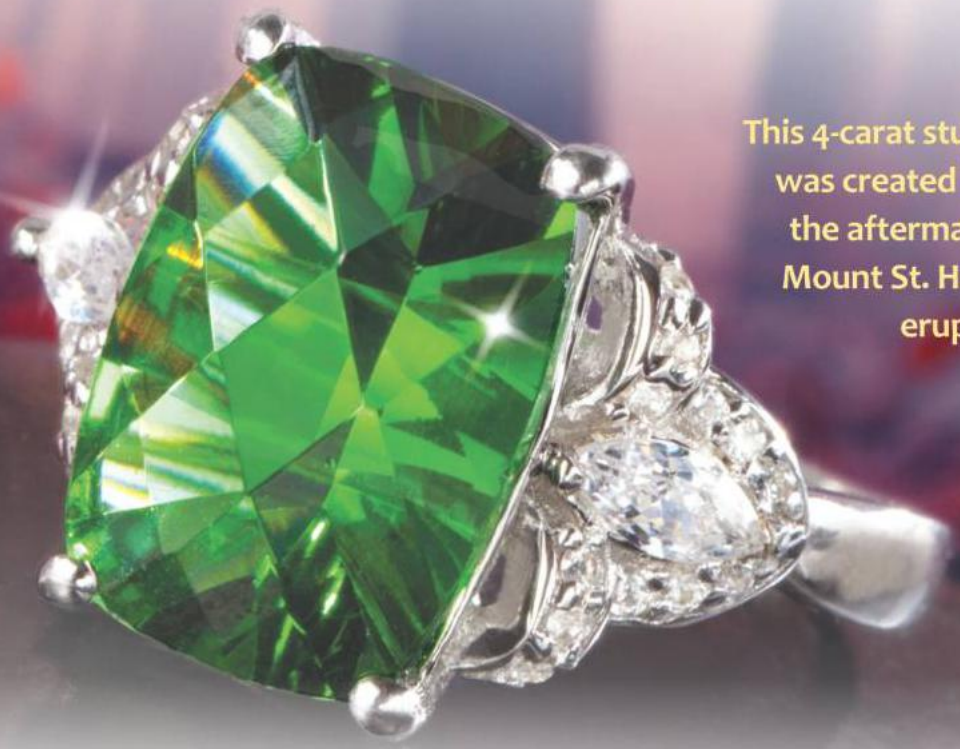

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Twists of Fate

Genes, traits and disease are linked in complex and surprising ways

Our genes are not the last word on disease risk or other traits. Myriad control switches help to arbitrate how genes get expressed in different cells and tissues, and those switches are often triggered by maternal diet, toxic exposures and many other environmental factors. To begin to understand what drives these complex epigenetic effects, scientists analyzed 150 billion bits of genomic data from more than 100 human tissues and cells—brain, heart, bone, and so forth.

The first step was to locate the switches by analyzing specific chemical modifications on the DNA and the proteins that it wraps around. Then researchers took data comparing individuals who have specific biological traits with those who do not to see which traits are associated with which switches. The result is an epigenomic road map that links diseases and traits (*red dots*) with the locations in the body (*white dots*) of the switches most correlated with those features; thicker lines correspond to more robust links. This blueprint should come in handy in sussing out the molecular basis of human variation and disease and in discovering potential new treatments. —*Dina Fine Maron*

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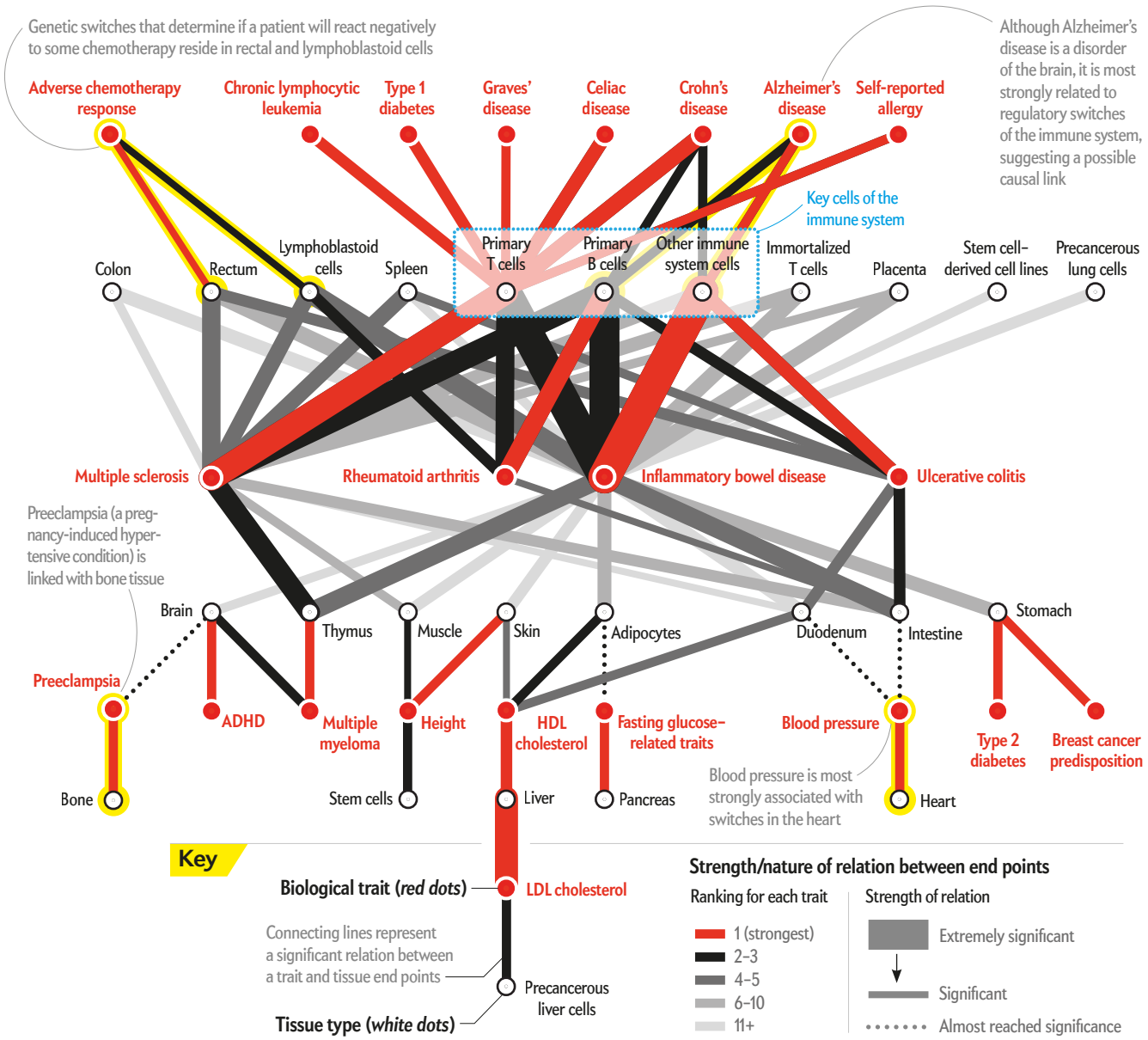
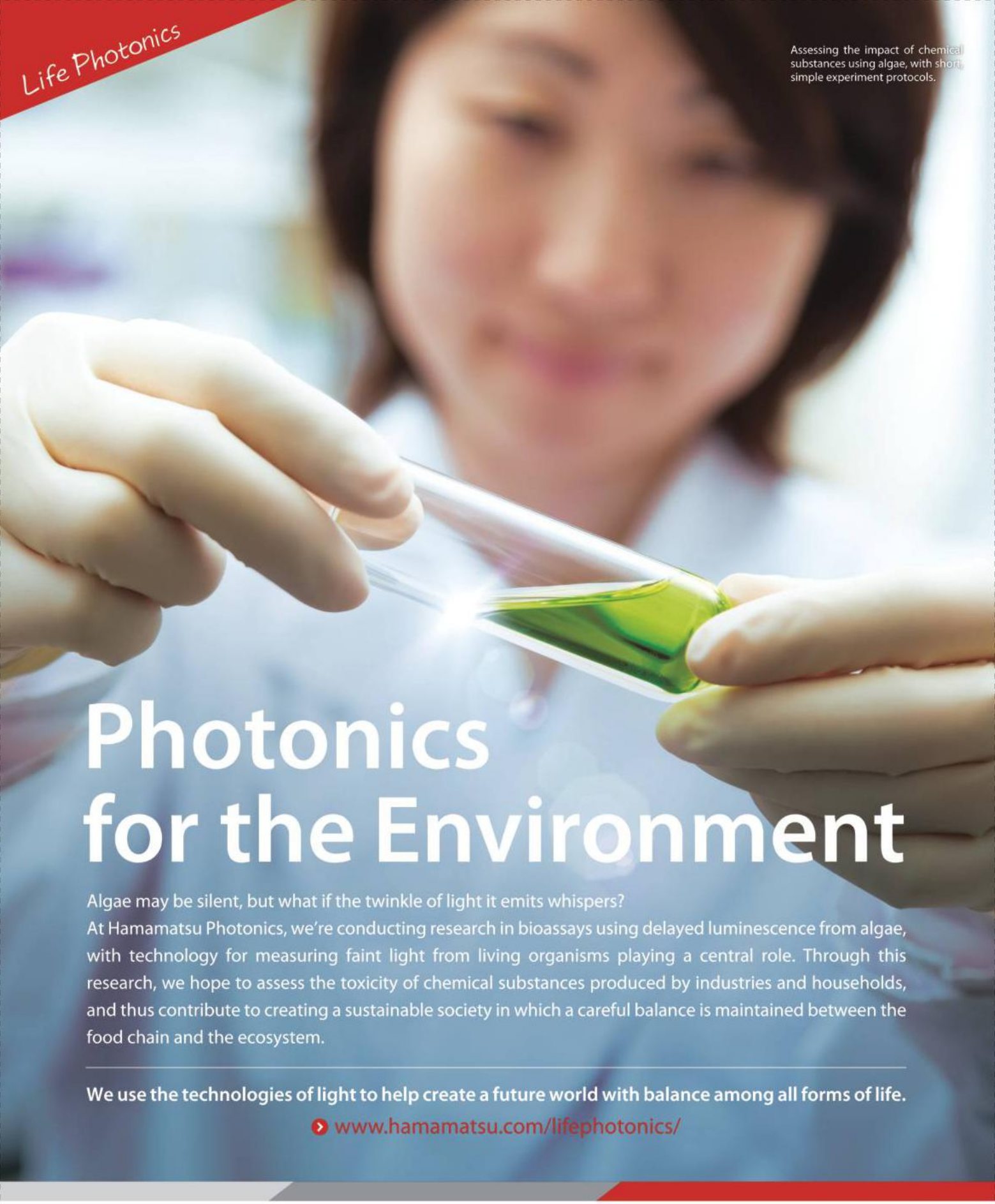
For more graphics about human genetics, see ScientificAmerican.com/jun2015/graphic-science



SOURCE: "INTEGRATIVE ANALYSIS OF 111 REFERENCE HUMAN EPIGENOMES," BY ROADMAP EPIGENOMICS CONSORTIUM ET AL., IN *NATURE*, VOL. 518; FEBRUARY 19, 2015

Graphic by Martin Krzywinski



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