MEDICINE
Dangerous Drug Combinations

HEALTH
A Gene for Obesity

ANIMALS
Complex Lives of Wild Horses

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THE POWER OF SLEEP

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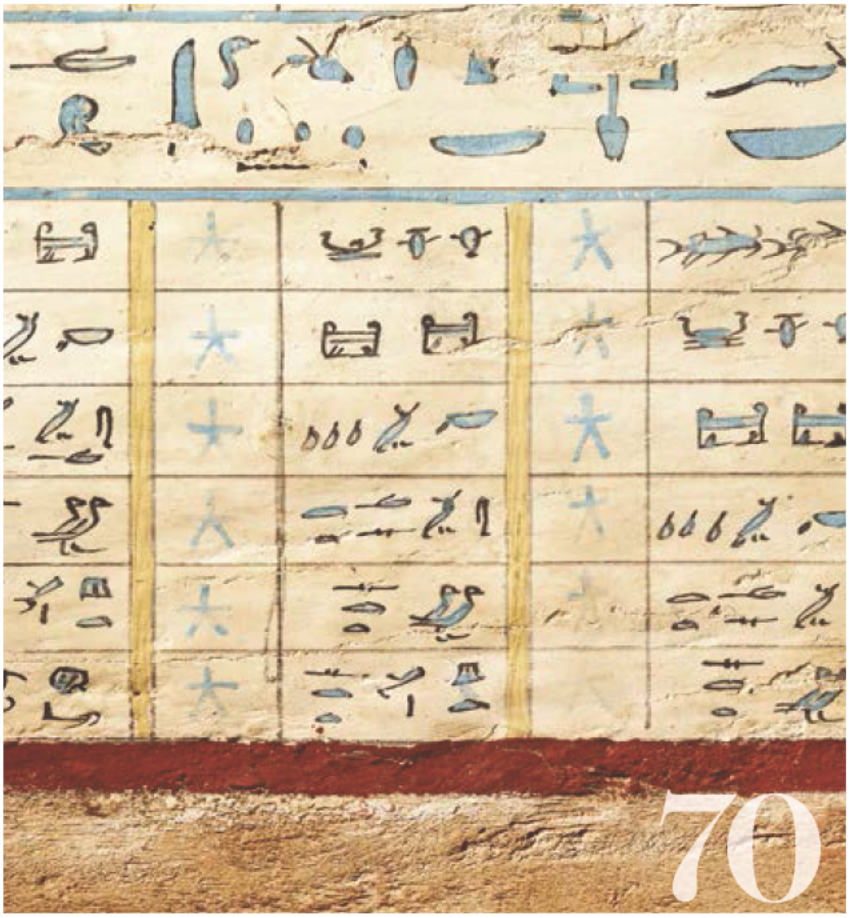

SPECIAL REPORT
STATE OF THE WORLD'S SCIENCE 2015

34 Big Science, Big Challenges
Dispatches from the intersection of science and society.

36 Trouble in Mind
A $1-billion-plus effort to simulate the human brain is in disarray. Is Big Science to blame?
By Stefan Theil

40 How Big Is Science?
Who spends the most on research? How does the Large Hadron Collider compare with the film *Avatar*—and other matters of scale.

43 More Evidence, Less Poverty
Money and good intentions are not sufficient. We need to know what works and what doesn't.
By Dean Karlan

46 An Antidote to Murder
How a Harvard-trained Ph.D. in public health cured a Colombian city of rampant violent crime.
By Rodrigo Guerrero Velasco

51 World Leaders
Ranking the nations and institutions that put out the most research.

NEUROSCIENCE

52 Sleep on It!
A good night's rest affects the mind and health more than anyone suspected.
By Robert Stickgold

ASTROPHYSICS

58 Neutrinos at the Ends of the Earth
A detector buried beneath South Pole ice has captured high-energy particles from halfway across the universe. They hold the key to long-standing cosmic mysteries.
By Francis Halzen

HEALTH

64 The Fat Gene
The pandemic of obesity and diabetes could trace back to a genetic mutation in prehistoric apes. *By Richard J. Johnson and Peter Andrews*

ARCHAEOASTRONOMY

70 Stars of the Dead
What were tables of intricate astronomical data doing in 4,000-year-old coffins?
By Sarah Symons and Elizabeth Tasker

LIFE SCIENCE

76 The Secret Lives of Horses
Long-term observations of wild equines reveal unexpected behaviors. *By Wendy Williams*

ON THE COVER

Sleep does not serve any single or simple function but rather enhances several aspects of our mental and physical health, the latest research shows. Different stages of sleep reinforce different types of thought processes, whereas the lack of sleep increases your chances of gaining weight, developing infections and becoming depressed. **Photography by Plamen Petkov.**

COVER: STYLING BY ANDI BURNETT; HAIR AND MAKEUP BY CINDY ADAMS FOR HALLEY RESOURCES; MODEL: JORDAN MICHELLE FOR RAMONA'S MODEL & TALENT

Photograph by Ferit Kuyas

SCIENTIFIC AMERICAN

12

26

80

4 From the Editor

6 Letters

10 Science Agenda
To reduce teen pregnancies, improve access to long-lasting contraceptives. *By the Editors*

12 Forum
Speeding up urbanization may protect the remaining wilderness. *By Linus Blomqvist, Ted Nordhaus and Michael Shellenberger*

14 Advances
Earth's orbit is primed for war. Ancient dental plaque tells of old diets. Graphene's rival. Pentaquarks discovered.

29 The Science of Health
Software tools and gene analyses could reduce fatal drug interactions. *By Jessica Wapner*

32 TechnoFiles
Will intelligent machines rule the world? *By David Pogue*

80 Recommended
Motion pictures at Earth's poles. Neuroscience of the self. Gender bias in science. India's environment in crisis. *By Clara Moskowitz*

82 Skeptic
Science versus pseudoscience. *By Michael Shermer*

84 Anti Gravity
TV science advisers help keep (some of) it real. *By Steve Mirsky*

86 50, 100 & 150 Years Ago

88 Graphic Science
Some small nations emit surprising amounts of carbon per capita. *By Mark Fischetti*

ON THE WEB

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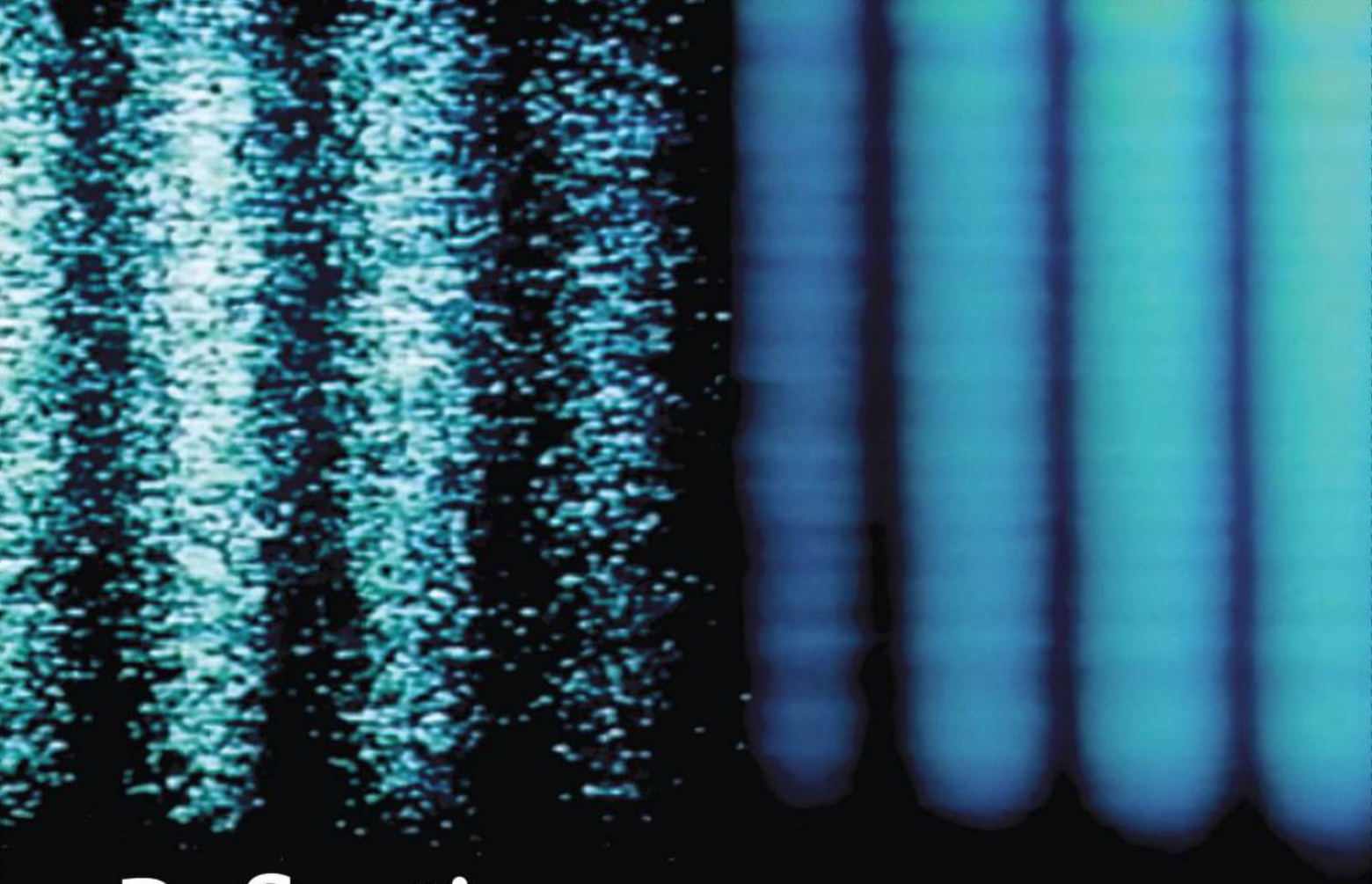

Reflecting on the Possibilities of Light

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

Sleep Science

Shakespeare wrote in his tragic play *Macbeth* that slumber is a "Balm of hurt minds" and "Chief nourisher in life's feast." In this issue's cover story, sleep researcher Robert Stickgold explains the many ways those statements are far more than pretty turns of phrase. In fact, it is physiologically vital that we spend about a third of our lives unconscious.

Dozing, Stickgold writes, is involved in a "multitude of biological processes—from the inner workings of the immune system to proper hormonal balance, to emotional and psychiatric health, to learning and memory, to the clearance of toxins from the brain." Losing a few hours of shut-eye depresses various functions, reducing our cognitive and memory powers, souring our mood, even reducing our body's ability to defend against infections. If we did not snooze at all, eventually we would die. Turn to page 52 to learn more about our remarkably restorative nightly visits to the land of Nod.

It has taken decades to develop even a rough understanding of the multiple benefits of catching 40 winks, but the weight of ongoing studies eventually has made the picture clearer. The clarifying effect of the gradual accumulation of data is a steady theme in the evolution of modern research in general and forms the underpinning of this year's "State of the World's Science" special report, organized by Fred Guterl, with editing support from Seth Fletcher and Mark Fischetti and graphic design by Jen Christiansen. It begins on page 34.

Data are the fuel for the engine known as Big Science—those bold projects that aim to tackle challenging large questions and to help make progress on some of humanity's toughest problems. In "Trouble in Mind," on page 36, for instance, journalist Stefan Theil looks at how researchers are trying to pry the operational secrets from the biological computing machines in our skulls. The uneven success to date of vast brain research projects in the European Union, the U.S. and elsewhere shows just how difficult managing large-scale efforts can be. Next, Dean Karlan asks in "More Evidence, Less Poverty," on page 43, do microloans really help the world's poorest? The answer will surprise you. In "An Antidote to Murder," on page 46, Rodrigo Guerrero Velasco describes his experiences as mayor of Cali, Colombia, where he used data to address an epidemic of violent homicides—with compelling results. And through the Nature Index, we showcase the top research institutions around the world; see "World Leaders," on page 51. (*Scientific American* is part of Springer Nature.)

The process of science can't solve all the world's problems, of course, but it is often deeply inspiring to me to realize how much it can help. SA

Illustration by Mirko Ilić (sleeper); Illustration by Nick Higgins (DiChristina)

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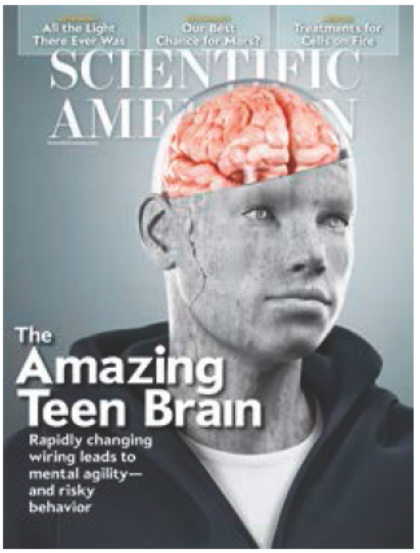

June 2015

> **"If monkeys are similar enough to humans to be useful experimental models, how can these trials be anything other than cruel and unethical?"**
>
> BILL TARVER *WOKINGHAM, ENGLAND*

ENDLESS LIGHT

In "All the Light There Ever Was," Alberto Domínguez, Joel R. Primack and Trudy E. Bell discuss measurement of the extragalactic background light, which is made up of all the accumulated light from galaxies throughout the universe's history.

How can that background radiation still be sloshing around? If light travels in a straight line, except for gravitational lensing, why didn't it become lost long ago?

DAVID MARANZ
via e-mail

In answering the question "Why is the night sky dark?" the authors did not discuss a simple model explaining the effect, based on special relativity, that I was taught as a graduate student.

In that model, the intensity of light from a moving light source decreases the faster that source moves away from an observer. In the quantum-mechanical version, the light intensity is proportional to the light frequency and the density of photons, and they, too, decrease the faster the light source moves away.

PHILIPP KORNREICH
Syracuse University

THE AUTHORS REPLY: In answer to Maranz's question: Galaxies shine for billions of years, and most of the light they have emitted has never been absorbed because space is so empty. Thus, the light continues to accumulate, and we continue to receive it from galaxies surrounding us at all different distances. The more distant the galaxy, the longer the light has been traveling toward us and the earlier it was emitted.

In response to Kornreich: As we mention in our article, the wavelength of light expands proportionally to the expansion of the universe, which does indeed cause the intensity of light from distant sources to decrease. The fact that the sources are moving away from us and that their clocks are moving slower also causes the intensity to decrease. These general relativistic effects are always included when we calculate the light we receive from distant galaxies.

ANIMAL TESTING

In "Ending a Cruel Legacy" [Forum], Barbara J. King exposes a paradox that experimenters must ignore if they wish to preserve the illusion of behaving ethically when studying infant monkeys: Researchers perform tests on primate infants to understand the behavior of humans raised under stressful conditions. For the results to have any value, they must therefore recognize that human and monkey brains and personalities share similar developmental pathways. But if monkeys are similar enough to be useful experimental models, how can these trials be anything other than cruel and unethical?

BILL TARVER
Wokingham, England

NARCISSISM'S CAUSE

"Kiddo Knows Best," by Andrea Alfano [Advances], reports that psychologists in the Netherlands led by Eddie Brummelman concluded that narcissism in children was associated with excessively praising parents. The article, however, did not rule out the possibility that children hardwired to be self-centered might have tended to seek praise from parents, who then responded accordingly. As a psychiatrist, I think it would be nearly impossible to determine the chronology of giving praise versus requesting it from a research study.

DOUGLAS M. BERGER
Tokyo

BRUMMELMAN REPLIES: As Berger points out, narcissistic children do crave admiration from others. But our work suggests that they don't lead their parents to adopt a grandiose view of them.

Our study consisted of four measurements, one every six months. In each, we assessed children's narcissism and how much parents saw their child as an extraordinary individual.

We consistently found that parents' overvaluation of their children predicted increased narcissism in those children six months later. Yet children's narcissistic traits didn't predict increased parental overvaluation in the same time period.

PLANETARY PRIORITIES

In "Birth of a Rocket," David H. Freedman reports that "the real justification for human spaceflight is to take steps toward expanding the human race's stomping grounds." Does he mean for a few elite astronauts or humanity generally? The former may be achievable—but why bother? The latter seems just shy of delusional. Either way, wouldn't it be more sensible to take the up to $1 trillion that a trip to Mars might cost and use it to prevent the collapse of livable conditions on Earth?

EVAN FALES
Iowa City, Iowa

INACCESSIBLE INFORMATION

David Pogue's "The Upgrade Game" [TechnoFiles] notes that we have little choice but to accept upgrades to software and devices because older versions will eventually no longer be "supported."

Many corporations, scientific groups and governmental entities have lost ready access to information that was stored just a couple of decades ago, using software and hardware that are no longer supported or

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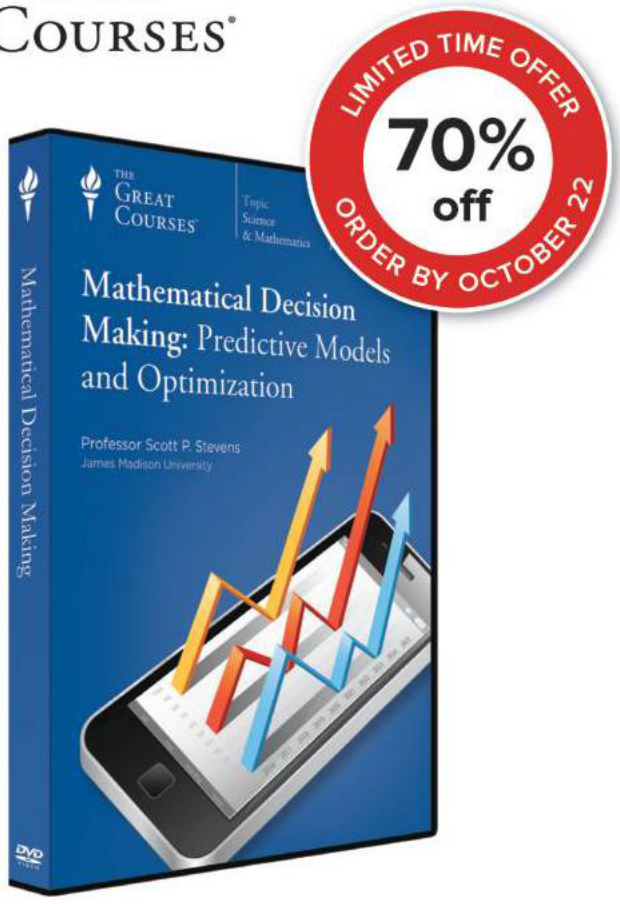

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available. Society has a legitimate interest in making certain that upgrades to operating systems and essential programs continue to support their predecessors in case we need to retrieve such information.

JOHN F. ROSSMANN
Tustin, Calif.

SLEEP APNEA

In "The Not So Silent Epidemic" [The Science of Health], David Noonan discusses remedies for sleep apnea, a disorder that causes snoring and can be life-threatening. He notes that the strap-on CPAP mask is effective, but many patients hate it.

The new Inspire Medical Systems device he reports on is exciting. But the way he dismisses "generic" oral appliances as targeting "the symptom, rather than ... the underlying problem" is appalling. There are professionally made oral appliances that are a first-line approach to treating mild to moderate sleep apnea and an alternative for moderate to severe sleep apnea for patients who do not tolerate CPAP. An 88-month study, published in 2013 in *Respirology,* showed that they were equal to CPAP. Their lower efficacy is balanced by greater utilization.

IRA L. SHAPIRA
Chair, Alliance of TMD Organizations
Diplomate, American Board of Dental Sleep Medicine

INFLAMMATION'S VALUE

"Cells on Fire," by Wajahat Z. Mehal, nicely elucidates how inflammation is now known to be triggered by structures within cells. But we must draw a distinction between exaggerated inflammatory response and subclinical inflammation. The latter is an absolute necessity: it allows fresh cells to replace degenerating older ones and helps to flush tissues out of accumulating debris that can potentially alter those tissues' functions.

ROMESH KHARDORI
Eastern Virginia Medical School

ERRATUM

"Birth of a Rocket," by David H. Freedman, incorrectly refers to a prototype of a Virgin Galactic suborbital rocket exploding last October. At that time, a nonprototype suborbital craft had crashed during a test flight but had not exploded.

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/oct2015

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How to Stop Teen Pregnancies

Contraceptives such as IUDs work best, but insurers often block access

By the Editors

When teenage girls have babies, they are in danger. They more likely will suffer serious health problems than mothers in other age groups and more often will drop out of school and become stuck at low-income levels for life. Children of these teens also navigate a tough road. They are prone to health and behavior trouble, tend not to do well in school and frequently become teen parents themselves.

Unfortunately, the U.S. has a lot of teen parents—273,000 births in 2013, which works out to a greater rate for the nation's population than for other developed countries, such as the U.K. and Canada. Abortion rates are also high. Longer-lasting birth-control methods can change this situation, and research now points to cost-effective ways to do so.

Whereas condoms are best for preventing sexually transmitted diseases, they are often not used, resulting in unwanted pregnancies. Girls need other choices. The evidence favoring long-acting implants such as intrauterine devices (IUDs) is so powerful that in September 2014 the American Academy of Pediatrics endorsed IUDs as the best contraception option for teens, and the American College of Obstetricians and Gynecologists has done the same. Here are some of the reasons: a study of more than 1,400 young women in the St. Louis area published last year in the *New England Journal of Medicine* found that providing teen girls with IUDs and other hormonal implants reduced pregnancy and abortion rates by more than 75 percent over three years. A 2012 study concluded that women using IUDs were 17 times less likely to get pregnant unintentionally than were women using pills, patches or vaginal rings.

But insurance companies often do not pay for IUDs or other long-duration devices, and an implant without insurance is 50 to 100 times the price of a condom package. Because of these costs and other access barriers, only 5 percent of American adolescents use effective, long-acting methods. When obstacles are removed, the numbers change dramatically. Seventy-two percent of the teens in the *New England Journal of Medicine* study chose IUDs or other implants when given that option.

Implants are not for everyone, but teens who use contraception and their parents, who are guiding these important life decisions, should be able to make the healthiest choices. That is, in fact, the law of the land. The federal Affordable Care Act requires that employer-provided insurance cover, without copayments, all forms of birth control approved by the U.S. Food and Drug Administration. There are, however, current court cases challenging the act's contraception provision, and many insurers flout the rule.

One state, Colorado, offers a good model for how to give the most effective birth control to at-risk teens, avoid the legal murk and save taxpayer money at the same time. It has had stunning success with a pilot program to distribute more than 30,000 contraceptive devices to low-income women through 68 family-planning clinics. By using clinics that did not charge for devices, Colorado sidestepped insurance coverage costs and made Affordable Care Act challenges irrelevant. The program also made a big difference to teens. It started in 2009. During the next four years, the teen birth rate plunged by 40 percent; between 2009 and 2012 the teen abortion rate fell by 35 percent. The initiative saved taxpayer money, too, according to the state. The multiyear program cost $27.3 million overall, but in just one year it saved Colorado $42.5 million in health care expenses.

Programs such as Colorado's should be expanded—yet even that one is threatened. The initiative was funded by a private donor, but money is running out, and the state's general assembly has voted against additional funding. The federal government can step in to fill the gap, there and in other states. It should finance the distribution of long-acting contraceptives at clinics that can reach teens directly. As in Colorado, these programs will ultimately save taxpayer dollars. Most important, such efforts will reduce rates of teen pregnancy, birth and abortion, along with their unhappy consequences for us all. SA

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Linus Blomqvist, Ted Nordhaus and **Michael Shellenberger** work at the Breakthrough Institute in Oakland, Calif. They wrote the institute's recent report *Nature Unbound: Decoupling for Conservation.*

Living off the Land

Intensifying agriculture and urbanization is the best way to save what wild places remain

By Linus Blomqvist, Ted Nordhaus and Michael Shellenberger

For the villager, who asks to be identified only as Bernadette, life is a running battle. On tiny plots of corn, millet and sweet potatoes next to Virunga National Park in the Democratic Republic of the Congo, she and her neighbors scrape a bare subsistence for themselves and their children. Her sweet potatoes, she told us last year, are under constant attack from baboons and elephants that stray from the park in search of food. Deep agrarian poverty of this kind is hard on nature, too. Virunga is home to half of the world's fewer than 900 remaining mountain gorillas, as well as endangered elephants and antelope. The park's forests are under pressure from the charcoal trade, and in 2007 the local charcoal mafia assassinated seven of the park's gorillas in retaliation for a crackdown on illegal logging. Poachers have killed 250 of Virunga's 300 elephants in recent years, probably with the acquiescence of residents fed up with crop raiding by the animals.

Rising affluence over the past several centuries has, overall, been hard on the environment. But on the front lines of conservation, where people live intimately with primary forests, biodiversity hotspots and endangered species, it is often grinding poverty that drives the destruction.

Improvements in productivity, as exemplified by Shigeharu Shimamura's farm in Japan, could hold the key for conservation in the 21st century. Shimamura oversees a 25,000-square-foot farm at the site of a former Sony microchip factory. Everything grows safely indoors. With a combination of water, plant food and 17,500 LEDs, he harvests as much as 10,000 heads of lettuce a day—100 times more per square foot than an ordinary farm—using 90 percent less water and producing 80 percent less waste. Humans use about half the world's ice-free surface, mostly for food production. Yet with continuing technological improvements, population and its impact on the environment could peak and then decline within the next few decades.

This phenomenon, called decoupling, means that people can increase their standard of living while doing less damage to the environment. Protecting remaining wilderness in the face of escalating demand for food, resources and energy will require accelerating decoupling—in other words, speeding up urbanization and intensifying modern agriculture. The idea may seem counterintuitive, but especially in the developed world, much of the harm that people inflict on the land has begun to flatten and even decline. Today, for example, humans require just half of the farmland per capita that they did 50 years ago. As a result, across much of the U.S. and Europe, marginal farmlands are reverting to forest.

Social changes will amplify these trends. More than half of humanity now lives in cities, and that figure could reach 70 percent by midcentury. When rural populations move to cities, birth rates tend to fall dramatically. That is why many demographers expect human population to peak and then decline before 2100. The rural exodus drives other, mutually reinforcing efficiencies as well, increasing both economic and resource productivity.

The implications for 21st-century conservation efforts are clear. Parks and protected lands remain part of the solution. But without tackling the demand side of the equation, real habitat protection will be difficult if not impossible. Success will require substituting human technology for natural resources. It will also require modern energy. Nearly three billion people still rely on solid fuels such as wood and dung. Moving all of humanity to energy technologies that are cheap, clean and abundant will improve their well-being without harming the environment.

Tools for shrinking our environmental footprint are in plain sight. Seizing those opportunities will require conservationists to focus on infrastructure and technology policies that traditionally fall outside their purview. Without accelerated decoupling, protected areas can't resist growing human demand for food and energy, and the elephants and gorillas of Virunga may face doom. SA

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Illustration by Sam Ward

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*And Get FREE 1 Year Supply Of Batteries**

The All New HCX!

- ✓ Digital sound processing chip provides **crystal clear sound and makes speech easier to understand** without feedback
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- ✓ Nearly invisible thin tube design
- ✓ Helpful **low battery warning** so you are never caught unprepared
- ✓ **Long lasting size 13 batteries**
- ✓ 10 bands of layered noise reduction helps to **emphasize voices while balancing out background noise**
- ✓ **100% Money Back Guarantee**


The HCX™

★ Customer Reviews ★

"I will definitely recommend your company to my patients."
- Dr. Arun P.

"I just want to let you know how happy my husband and myself are with his new hearing aids!..."
- Monique S.

Studies Show: Hearing Aids MAY HELP PREVENT DEMENTIA.

A study by Dr. Frank Lin at the John Hopkins University, found that patients with even a mild hearing loss were two times more likely to develop dementia. Fortunately, hearing aids help address hearing loss and may help prevent cognitive health due to hearing loss.
www.AdvancedHearing.com/Dementia

Digital Hearing Aid Technology... For Only $299!

All hearing aids work the same way. The **microphone** picks up the sound and sends an electrical signal to the digital signal processor. The **digital signal processor** is the "brains" of the hearing aid. It takes the sound it receives and adjusts the sound to amplify important speech sounds as well as filtering out unwanted noise. (To ensure the best in quality, our digital processor is designed and manufactured right here in the **United States.**) Once the processor has amplified the sound, it is passed to the **receiver** (also known as the speaker) which emits a corrected and amplified sound through the **sound tube** into your ear.

Most importantly, your new HCX hearing aids work at a **fraction of the cost** of name-brand hearing aids. In addition to the technical components of the hearing aid, you also have a **volume control** that can be modified with a light touch of the finger. Your new hearing aids come with **3 different audio programs** that help you listen in different sound environments. You will love the Open-fit design, that is so light you probably won't even feel that you are wearing your hearing aids – you'll just be hearing clearly!

You can spend thousands for a high-end hearing aid or you can spend **just $299** for a hearing aid that just plain works **(only $274 each when you buy a pair)**. We are so sure you will love our product, that we offer a **100% Money Back Guarantee - Risk Free** if you are not satisfied for any reason. It's time to get great digital technology at an affordable price!

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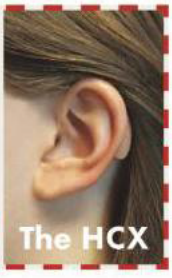
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ADVANCES

Antisatellite weaponry, such as the missiles shown in this artist's rendition, could spark a new arms race in outer space.

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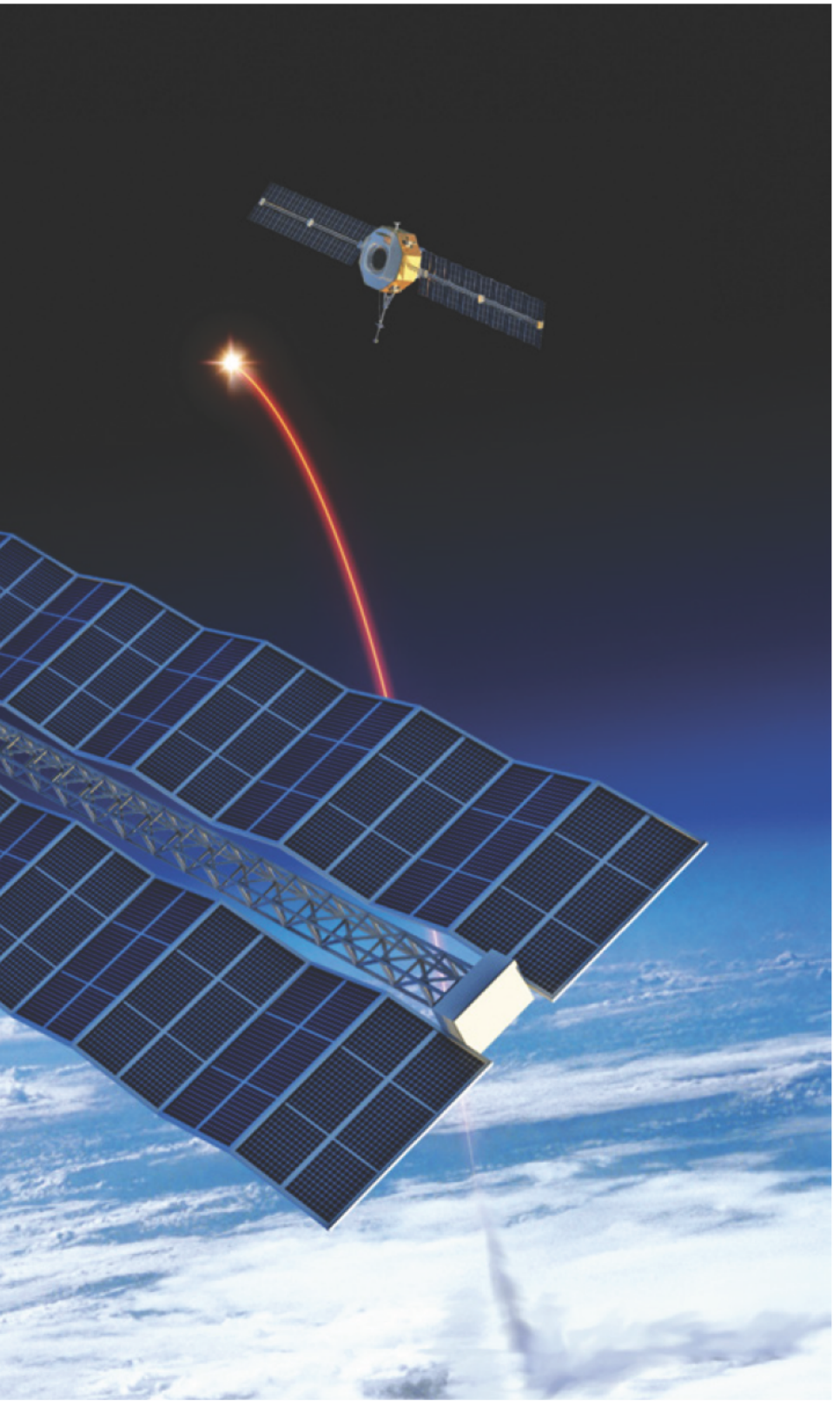
INSIDE

- Coral evolution gets fast-tracked.
- Ancient plaque could tell us what Stone Age farmers ate and drank.
- A toy company has nailed down how to bring lab robotics to store shelves.
- Pentaquarks make their debut.



DEFENSE TECHNOLOGY

Are We on the Cusp of War—in Space?

China, Russia and the U.S. are developing and testing controversial new capabilities to wage war in Earth's orbit

The world's most worrisome military flash point is arguably not in the Taiwan Strait, the Korean peninsula, Iran, Israel, Kashmir or Ukraine. In fact, it cannot be located on any globe. The contested territory? The no-man's-land of Earth's orbit, where a conflict is unfolding that is an arms race in all but name.

About 1,300 active satellites now reside in the region of outer space immediately surrounding our planet, where they provide worldwide communications, GPS navigation, weather forecasting, and more. For nations that rely on a select number of those satellites for modern warfare, space has become the ultimate high ground, with the U.S. as the undisputed king of the hill. Now, as China and Russia aggressively seek to challenge our superiority in space with ambitious defense and exploration programs of their own, this power struggle risks sparking a conflict that could cripple the entire planet's space-based infrastruc-

Continued on page 18

Illustration by Kenn Brown, Mondolithic Studios

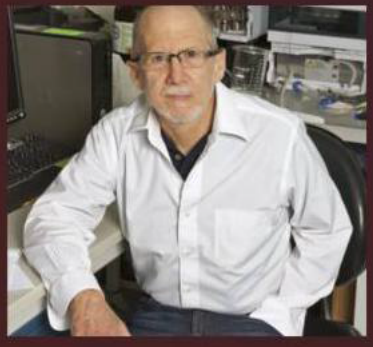
THE DR. PAUL JANSSEN AWARD

FOR BIOMEDICAL RESEARCH

Johnson & Johnson is proud to celebrate today's outstanding scientists and honor the legacy of Dr. Paul Janssen with the Dr. Paul Janssen Award for Biomedical Research.

Congratulations to Dr. Bert Vogelstein, winner of the 2015 Award, and all past Award winners, for making a significant positive impact on human health.

2015 WINNER



Dr. Bert Vogelstein, M.D.

Clayton Professor of Oncology and Pathology, Johns Hopkins University, Director, Ludwig Center for Cancer Genetics & Therapeutics, Johns Hopkins Kimmel Cancer Center, Investigator Howard Hughes Medical Institute

For his breakthroughs in oncology research, which have spanned more than two decades and have formed the basis of modern cancer research.

Johnson & Johnson

PREVIOUS AWARD WINNERS

'14


Jennifer Doudna, Ph.D. & Emmanuelle Charpentier, Ph.D.
For their co-discovery of the basis for adaptive immunity in bacteria, and the development of this system for facile genome editing.

'13


David Julius, Ph.D.
For his work elucidating the molecular mechanism for heat and pain perception.

'12


Victor R. Ambros, Ph.D. & Gary Ruvkun, Ph.D.
For their co-discovery of microRNAs as central regulators of gene expression and development.

'11


Napoleone Ferrara, M.D.
For his research on angiogenesis, the process of new blood vessel formation that plays a key role in cancer proliferation and a number of other diseases.

'10


Erik De Clercq, M.D., Ph.D. & Anthony S. Fauci, M.D.
For their pioneering work in understanding and combating viral diseases, particularly HIV/AIDS.

'09


Axel Ullrich, Ph.D.
For his pioneering work in applying molecular biology and molecular cloning to the discovery of protein therapeutics for the treatment of a wide range of diseases, including diabetes and cancer.

'08


Professor Marc Feldmann, FMedSci, FAA, FRS & Emeritus Professor Sir Ravinder Maini, FMedSci, FRCP, FRS
For their role in the discovery of tumor necrosis factor-alpha as an effective therapeutic target for rheumatoid arthritis and other chronic inflammatory conditions.

'06


Craig C. Mello, Ph.D., Nobel Laureate
For his role in the discovery of RNA interference and the elucidation of its biological functions.

ADVANCES

Continued from page 15

ture. And though it may begin up high, such a conflict could easily ignite full-blown war on the surface of Earth.

Testifying before Congress earlier this year, director of national intelligence James Clapper echoed the concerns held by many senior government officials about the growing threat, saying that China and Russia are both developing capabilities to sabotage crucial U.S. military satellites. China in particular, Clapper said, has demonstrated "the need to interfere with, damage and destroy" U.S. satellites, referring to a series of Chinese antisatellite-missile tests that began in 2007.

The latest Chinese test took place on July 23 of last year and involved, like all its predecessors, the launch of a missile that could be used as a "kinetic weapon" to hit and destroy satellites. Chinese officials insist the tests are peaceful in their purposes and only meant for missile defense and scientific experimentation, but outside experts are skeptical. One test in May 2013 especially sent shock waves through the U.S. intelligence community. That maneuver sent a threatening missile soaring as high as 30,000 kilometers above Earth, approaching the lofty realm of geosynchronous orbit, where satellites move at the same speed as the turning Earth below and thus stay perched over one position on the globe. Those orbits are home to strategic U.S. satellites, including ones that watch for the launch of nuclear missiles, as well as many commercial communications satellites.

The U.S., too, has been active. Shortly after China's 2013 test, the U.S. declassified details of its covert Geosynchronous Space Situational Awareness Program (GSSAP), a planned set of four satellites capable of monitoring Earth's high orbits and even rendezvousing with other satellites to inspect them up close. The first two GSSAP spacecraft were launched into orbit in July 2014. "This used to be a black program—something that didn't even officially exist," says Brian Weeden, a security analyst and former U.S. Air Force officer who studied and helped to publicize the Chinese test. "It was declassified to basically send a message saying, 'Hey, if you're doing something funky in and around the geosynchronous belt, we're going to see.'"

Meanwhile the Obama administration has budgeted at least $5 billion to be spent over the next five years to enhance both the defensive and the offensive capabilities of the U.S. military space program. An enemy could provocatively blow up our satellites with missiles, but officials and technology also must prepare for more subtle and devious disabling tactics that appear innocuous at first glance. A spacecraft could simply approach a satellite and spray paint over its optics, manually snap off its communications antennas or destabilize its orbit.

Lasers, too, could be used to temporarily cripple or permanently damage a satellite's components, particularly its delicate sensors. And radio or microwaves could jam or hijack transmissions to or from ground controllers. U.S. defense leaders want to be ready for anything.

Aside from its militaristic initiatives, the U.S. also aims to deescalate the problem through diplomacy, although efforts so far have floundered; in late July at the United Nations, long-awaited discussions stalled entirely on a European Union–drafted code of conduct for spacefaring nations because of opposition from Russia, China and several other countries, including Brazil, India, South Africa and Iran. The failure placed diplomatic solutions for the growing threat in limbo, quite likely leading to years of further debate within the U.N.'s General Assembly.

In the end, debris from a downed satellite—not an initial attack—could be the largest threat to Earth's delicate orbital infrastructure. Satellites race through space at speeds of thousands of kilometers per hour, so even the impact of an object as small as a marble could disable or entirely destroy a billion-dollar spacecraft. And such a destructive collision would itself generate even more threatening shrapnel, potentially creating a cascade of debris that could transform Earth orbit into a demolition derby for centuries.

Without rigorous international accountability and oversight, the risk of accidental collisions and debris strikes will continue to grow as more nations launch and operate more satellites. And as the chance of accidents increases, so, too, does the possibility of their misinterpretation as deliberate, hostile actions in the high-tension, cloak-and-dagger military struggle in space.

—Lee Billings

COMMENT AT ScientificAmerican.com/oct2015

ANIMAL BEHAVIOR

Mother, May I… Eat You?

The biology behind one spider's baby food

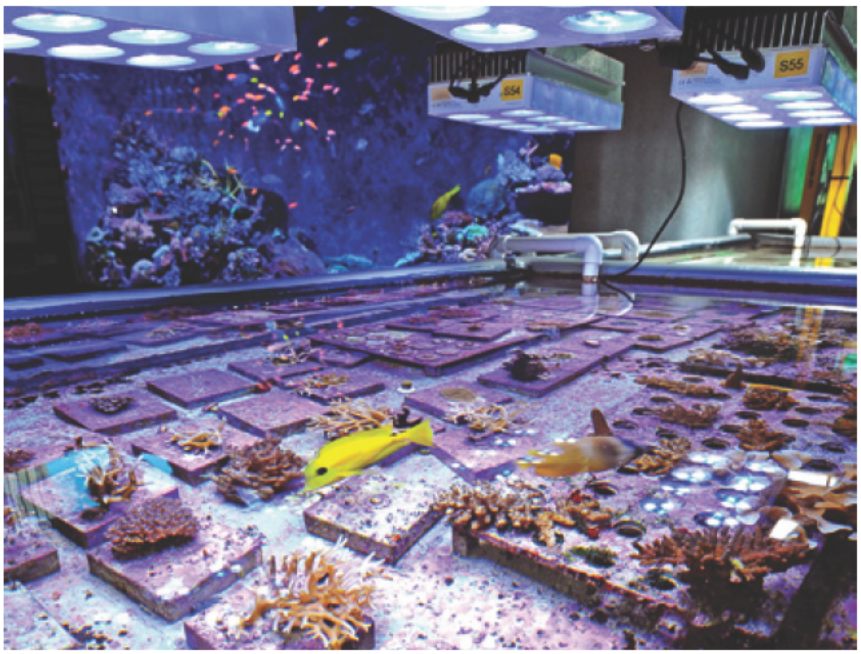
Motherhood typically entails sacrifice, but for most species, the altruism is temporary. Eggs are laid, the young leave the nest, life goes on. Not so for *Stegodyphus lineatus*, a velvet spider that inhabits Israel's Negev Desert. *S. lineatus* practices the most extreme—and permanent—form of maternal devotion: matriphagy, in which offspring consume their mother.

Entomologists have wondered about the gory details of this caregiving strategy for years. Is the mother simply eaten as is, or does she prep her innards to make them go down easy? The latter turns out to be the case. Her tissues begin degrading before her young have even hatched, according to research published in the *Journal of Arachnology*. "Everything is really reprogrammed, as if she's planning ahead," says Mor Salomon, an entomologist then at the Hebrew University of Jerusalem.

Salomon and her colleagues examined microscopic cross sections of female velvet spiders at each stage of the reproductive process. The tissues began showing light signs of degradation immediately after the egg sac was laid. Then, when the babies emerged 30 days later, the degeneration intensified. "Where the boundary of an organ was very clear, in the next picture you see it becomes blurry, and in the next one, it's gone," Salomon says. That breakdown allows the spider to regurgitate portions of her liquefied gut to feed her growing young.

As early as nine days after hatching, the mother stops regurgitating, and the juveniles descend on their still living mother for a final family meal. They suck dry all remaining fluids and then vacate the nest, leaving behind the husk of her exoskeleton. Within a year the matured females will pay that maternal largesse forward—offering up their own bodies to the next generation. —*Rachel Nuwer*

Illustrations by Thomas Fuchs



CONSERVATION

Test-Tube Corals

Manipulation of the Great Barrier Reef's corals could save them

At 135,000 square miles, the Great Barrier Reef reigns as the world's largest living structure. Located off the northeastern coast of Australia, it houses more than 600 species of coral and thousands of other types of marine animals, too. Yet the reef's future looks bleak. In the 27 years from 1985 to 2012, half of its coral cover vanished. A significant proportion of the loss is attributable to climate change, which has strengthened destructive tropical cyclones and made surrounding waters warmer and more acidic. Conservation efforts alone, including protected zones and water-quality improvements, will not do the job. To further combat coral loss, marine biologists at a new research facility in Australia, called the National Sea Simulator (*above*), have devised a more radical approach: they are manually breeding supercorals capable of living in the increasingly inhospitable sea.

Over the next five years geneticist Madeleine van Oppen and her team will breed global warming–ready corals in a handful of the National Sea Simulator's 33 tanks. Van Oppen can precisely control each tank's salinity, temperature, water quality and pH, which allows her to select for individuals that can withstand stressful environments. A few tanks, for example, replicate the oceanic conditions that models predict for later this century. The specimens most tolerant to heat and low pH will be crossed to breed offspring with these traits and so on down the generations—a process called assisted evolution. The process might happen naturally if corals could adapt quickly enough to their changing habitat, but with little time to spare, humans have stepped in to speed up the clock. "The predictions are very grim for coral reefs," van Oppen says. "So we feel we have to explore whether assisted evolution is a possible approach that could help us restore the reef."

Assisted evolution is a novel approach to marine conservation and not without controversy. Some experts are concerned that these supercorals will outcompete the native ones, for example. If van Oppen's work shows success, the Australian government, which funds the National Sea Simulator, could then consider transplanting the laboratory corals onto the Great Barrier Reef. The race against the reef's extinction is on.

—*Annie Sneed*

COURTESY OF AUSTRALIAN INSTITUTE OF MARINE SCIENCE

COMMENT AT ScientificAmerican.com/oct2015

DEVELOPMENTAL BIOLOGY

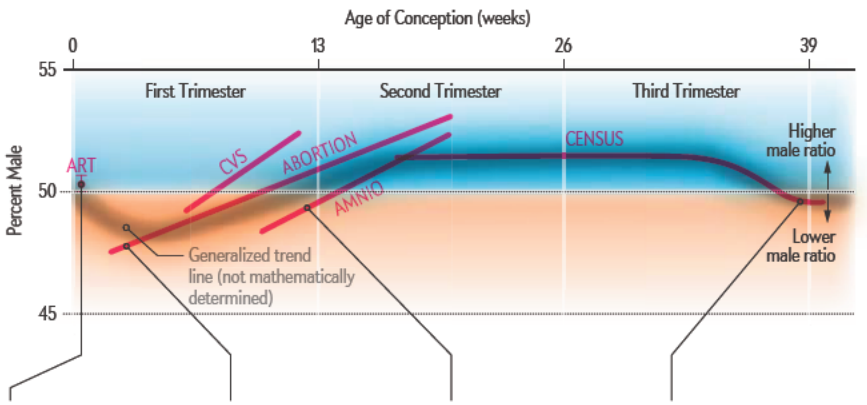
The Vicissitudes of Sex

Prebirth demographics reveal that the probability of finding one sex over another changes with time

In the delivery room, the (slight) odds are that a newborn is a baby boy, not a girl. Males make up 51.3 percent of live births in the U.S., a rate that has remained about constant for the past seven decades. Experts assumed that this male-skewed sex ratio began at conception, but a new analysis of fetal records shows that the chances overall of finding a boy or a girl start out at 50–50 and change over the course of pregnancy—leaning female, then male, then female again as nine months pass.

In the most comprehensive study of its kind to date, biologist Steven Hecht Orzack of the Fresh Pond Research Institute in Massachusetts and his collaborators analyzed roughly 36 million fertility treatment records, prenatal tests, induced abortions and U.S. Census data points. They discovered several nodes at which the sex ratio wavered from 50–50. Those vacillations most likely arise because of genetic and chromosomal abnormalities that cause natural abortions at various stages of gestation, write the study's authors in the *Proceedings of the National Academy of Sciences USA*.

"This is basic knowledge about human pregnancy that we didn't have before," Orzack says. "Demographers, developmental biologists, and many more can all get something out of this study." —*Kat Long*



At conception, the chances of finding a male or female embryo are equal—a conclusion drawn from an analysis of records of three- to six-day-old embryos derived from assisted reproductive technology (ART), which includes in vitro fertilization, fertility medication and surrogacy.

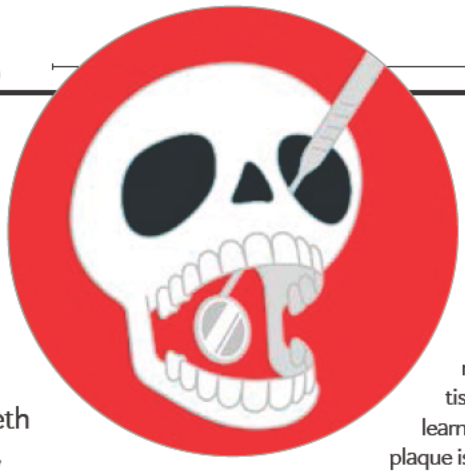
One to two weeks after conception, embryos that bear abnormalities on the sex chromosomes or the 15th and 17th chromosomes are aborted naturally. Data from medically induced abortions and a prenatal test called chorionic villus sampling (CVS) indicated that more males had these chromosomal problems than females, resulting in a female-biased ratio at this point in pregnancy.

More females than males die during the first trimester and at the beginning of the second, the researchers found after looking at records from the prenatal diagnostic test amniocentesis. They attribute the deaths to developmental abnormalities with one of the two X chromosomes, but the underlying cause is unclear.

At about the 38th week of pregnancy, boys reach their critical fetal weight, which triggers birth. Thus, the sex ratio of unborn fetuses for the 39th and 40th weeks of pregnancy skews slightly female. For all live births, Census records show that males account for a little more than half, demonstrating that more females than males die overall for the duration of gestation.

GETTY IMAGES (babies); SOURCE: "THE HUMAN SEX RATIO FROM CONCEPTION TO BIRTH," BY STEVEN HECHT ORZACK ET AL., IN *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA*, VOL. 112, NO. 16; APRIL 21, 2015 (conception graph)

Graphic by Daisy Chung



ARCHAEOLOGY

Dentist to the Dead

Cemented to the teeth of people long gone, plaque offers new clues about ancient health

The best teeth that Christina Warinner sees in her office are the ones with chunks of plaque as big as lima beans fixed to their enamel. Warinner is not a dentist, although she uses some of the same tools. She is an anthropologist at the University of Oklahoma, and she performs centuries-delayed dental cleanings on the likes of Vikings and Stone Age farmers to scrape up details about how humans once lived.

Fresh, sticky plaque picks up everything in the mouth, and when it hardens, it can entomb bits of plants, pollen, bacteria, starch, meat, charcoal, textile fibers, and more. As scientists have recently learned, fossilized plaque is the richest source of DNA in the archaeological record. "One of the biggest challenges with ancient DNA is not having enough material to work with," Warinner says. Plaque eliminates that problem: it carries between 100 and 1,000 times more nucleic acids per milligram than any other known source.

A top priority in Warinner's laboratory is to compile a DNA inventory built from the plaque found on corpses in museum collections and archaeological sites from around the world. The hunt now commences for increasingly ancient and diverse patients to find out how human health and eating habits have changed throughout history. —*Megan Gannon*

THREE PLAQUE PROJECTS

MILK TEETH

Without regular brushing and flossing, plaque fossilizes on teeth and serves as a time capsule for otherwise ephemeral bits of a person's diet. Long after a milk carton finds its way into the trash bin, for example, an extremely long-lasting and abundant milk protein called beta-lactoglobulin may remain on the drinker's teeth. Warinner's lab looks for this protein in plaque on ancient bodies to understand why many groups of humans can consume fresh milk without getting sick, even though all other mammals lack the ability to digest it after infancy. A tolerance for dairy shows up in several different cultures, but scientists debate when it first evolved in our species. Plaque analysis can reveal exactly who was drinking milk at an archaeological site and from which animal—be it a cow, or a sheep, or a camel—the liquid originated. This approach eliminates some of the ambiguity of other archaeological methods, such as searching for milk fats on ancient pottery. Last year Warinner's team found the first direct evidence for milk drinking by sequencing beta-lactoglobulin proteins in plaque dating as far back as the Bronze Age in parts of Europe and southwestern Asia. Now the researchers are examining plaque samples from the Neolithic period, when humans first domesticated animals.

PALATE CLEANSER

Regardless of one's commitment to dental hygiene, every person harbors hundreds of species of bacteria on the surface of his or her teeth. Last year Warinner and her colleagues found that skeletons from a medieval cemetery in Germany had remarkably modern oral microbiomes despite changes in hygiene and diet over the past 1,000 years. The medieval plaque had bacteria associated with periodontitis, a common gum disease that causes teeth to fall out and occurs in nearly 50 percent of American adults today. To better understand when humans became susceptible to such dental diseases—and how they might be linked to factors such as diet, environment and culture—Warinner's lab is now scraping plaque from chompers dating all the way to the Stone Age and from humanity's closest living relatives, chimpanzees.

FILLING THE HOLES

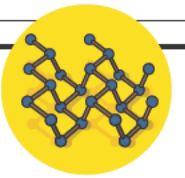
Bones buried in frozen ground can yield extremely well preserved genetic material. The oldest full genome sequenced so far (700,000 years old) came from a horse leg bone uncovered in permafrost in northwestern Canada. The oldest human genome (45,000 years old) to be sequenced was extracted from a femur found in Siberia. But not all biological samples are found in natural freezers. Densely mineralized plaque may be an ideal source for intact DNA both in and out of frozen areas because it is hardier than porous bones. To date, Warinner's team has reliably extracted DNA and proteins from plaque samples up to 10,000 years old. Now the scientists are working to collect genetic material from even further back in time. The oldest example of preserved plaque that Warinner knows of is more than eight million years old and was taken from a fossil of an orangutan ancestor.

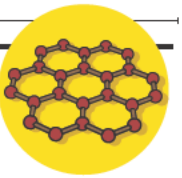
COMMENT AT ScientificAmerican.com/oct2015

MATERIALS SCIENCE

Graphene's Top Competitor

Phosphorene could make a better transistor





PROPERTY	PHOSPHORENE	GRAPHENE
Structure	Puckered hexagon	Flat hexagon
Conductivity	Currents are easily turned on and off	Current leaks from switches
Flexibility	Very flexible; compressible because of puckered structure	Very flexible across *x*-*y* axes
Purity	Difficult to separate into single-atom layers, but lower quality will likely improve	Easy to separate into single-atom layers, with few impurities to thwart electric current
Sensitivity	Reacts with light, water, air—would need a protective coating in everyday electronics	Stable under normal conditions; no extra coating necessary
Other Applications	Lasers, pH sensors, flexible electronics	Batteries, screens, solar panels, bionic implants

Graphene currently sits atop engineering's list of wonder materials. The single layer of carbon atoms exhibits incredible physical strength and flexibility, as well as unique electrical properties. These characteristics have enabled researchers to use it in everything from phone chargers to water filters. But along one dimension, it disappoints: graphene is not a natural semiconductor. Although engineers are forging ahead to find ways to manipulate it so that it works in transistors—devices that modify electric currents to power gadgets—they are also now turning to a promising alternative with a similar structure: a single layer of black phosphorus atoms, called phosphorene.

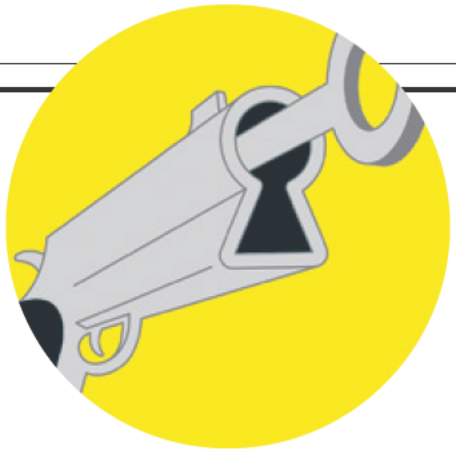
Under high pressure, phosphorus becomes black phosphorus, a material with superconductive properties discovered about a century ago. Recently, in 2014, a team of researchers at Purdue University isolated just one layer of black phosphorus atoms. Since then, others in the field have started investigating phosphorene. More than 400 papers with the two-dimensional material's name have been published this year alone.

The excitement has mounted over phosphorene's potential to replace less efficient materials in electronics, says Thomas Szkopek, who specializes in 2-D materials at McGill University. Black phosphorus is a "bona fide semiconductor," he says, meaning its conductivity can be switched on and off. Because of this property, engineers can modify how much energy flows through phosphorene across many orders of magnitude. Such control minimizes the amount of current that leaks out, which could bring transistors a step closer to perfect efficiency. Conventional transistors, typically made of silicon, are less efficient than the thermodynamic limit by about a magnitude of a million.

Although materials scientists have high hopes for phosphorene, it does have other qualities that compromise its future use in transistors [*see table above*]. If researchers cannot work around them, the material may have other uses. Because it is less brittle than silicon, it could appear in flexible electronics. And because phosphorus emits light, phosphorene is also a candidate for lasers or LEDs. Or its best application could be in a device no one has invented yet. "There is an explosion of interest around the globe in new 2-D materials like phosphorene that give us access to unique blends of properties," Szkopek says. Similar structures await their turn in the spotlight—germanene, silicene and stanene all stand on deck.

—Alexandra Ossola

Illustration by Daisy Chung



TECHNOLOGY

Unlocking Safer Guns

Three firearm technologies aim to prevent deaths and crime

For the first time in decades the annual number of gun-related deaths in the U.S. is expected to surpass the annual count of automobile fatalities. In 2013, the most recent year for which data are available, the two were on par: motor vehicles killed 33,804 people, and firearms killed 33,636, according to the U.S. Centers for Disease Control and Prevention. Firearm deaths and injuries have grown to pose a major public health problem, says Stephen Teret, co-director of the Johns Hopkins Center for Law and the Public's Health. Teret studies how to make safer guns for consumers. And he is not the only person doing so. The first symposium on smart guns—weapons that only specific users can fire—was held earlier this year. Several gun technologies to prevent unauthorized or accidental discharge and to stem crime have moved beyond proof of concept and into production—albeit at a limited scale. —*Erik Schechter*

RADIO-FREQUENCY IDENTIFICATION (RFID)

The most mature smart guns on the market are RFID systems equipped with a locking mechanism that releases only when a gun draws close to a device broadcasting a particular radio band. German firm Armatix introduced an RFID gun to the U.S. in 2013 that activates when a person enters a PIN on a nearby paired watch. Similarly, the company TriggerSmart Technologies sells a gun that automatically unlocks when the owner's ring, which contains an authorization tag, comes within two inches of a reader in the weapon's handle. These guns could cut down on teen suicides and accidental shootings, Teret says.

BIOMETRICS

Biometric smart guns require proof of identity—via human body characteristics—to operate. In theory, anything from a voiceprint to a retinal scan could serve as a key, but most versions available analyze hand-related features, such as fingerprints. The company Intelligun, for example, sells a fingerprint-locking system for $399 that can be mounted on the grip of a model 1911 pistol. As soon as the owner relaxes his or her hold, the gun relocks. But gloves, dirt and blood can interfere with these readers. So engineers at the New Jersey Institute of Technology have worked with the U.S. Army Armament Research, Development and Engineering Center on a dynamic recognition technology that reads the pressure profile of the owner's clutch. Tests with a prototype of the technology on the SIG Sauer P228 (a handgun used by police departments in New Jersey and elsewhere) are ongoing.

MICROSTAMPING

A technique called microstamping imprints tiny identifying marks from a gun onto a cartridge as it fires. The resulting indentations could help law enforcement quickly link an individual weapon, and therefore a suspect, to a shooting. During manufacturing and assembly, lasers etch microscopic markings on internal parts of the gun, such as the firing pin. When the gun is fired, those imprinted parts strike the softer metal of the cartridge, transferring the markings. In 2013 experts tested the system on different types of firearms and ammunition and found that the success of transfer varied widely. The technology, however, continues to make inroads. In February a district court judge upheld the constitutionality of a 2007 California law that bans the sale of new handguns without microstamping capability. New York State is now considering a similar law.

COMMENT AT ScientificAmerican.com/oct2015

IN THE NEWS

Quick Hits

U.K.

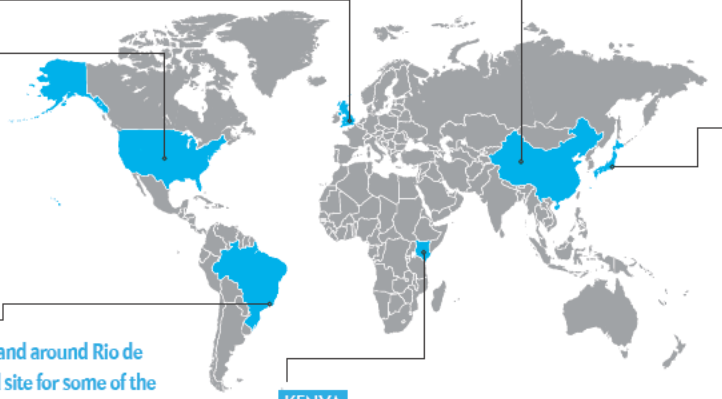
European regulators based in London green-lit for the first time a vaccine for malaria—a disease that kills more than 500,000 people a year, most of them children in sub-Saharan Africa. The World Heath Organization will further review the vaccine's effectiveness this month before distribution begins as early as 2017.

CHINA

The nation's space program began assembling a reflector for the Five-hundred-meter Aperture Spherical radio Telescope (FAST)—set to become the world's largest single-dish radio telescope when completed sometime next year.

U.S.

The Food and Drug Administration approved the world's first 3-D-printed drug, for an epilepsy treatment called Spritam. The number of extruded layers determines the dosage per pill.



JAPAN

Engineers successfully drove a car over a mobile, expandable bridge inspired by origami. The 57-foot-long prototype is made from steel and aluminum alloy and could temporarily replace structures destroyed by floods or earthquakes.

BRAZIL

Analysis of 37 water samples from in and around Rio de Janeiro's Guanabara Bay, the planned site for some of the 2016 Summer Olympic events, revealed abnormally high levels of harmful bacteria, including human adenovirus, which causes intestinal and respiratory diseases.

KENYA

On a tour of his father's homeland, President Barack Obama announced new rules that will ban almost all ivory sales within the U.S., the second-largest ivory market after China. Illegal poaching accounts for the deaths of at least 50,000 African elephants every year.

For more details, visit
www.ScientificAmerican.com/oct2015/advances

ENGINEERING

Bots on a Budget

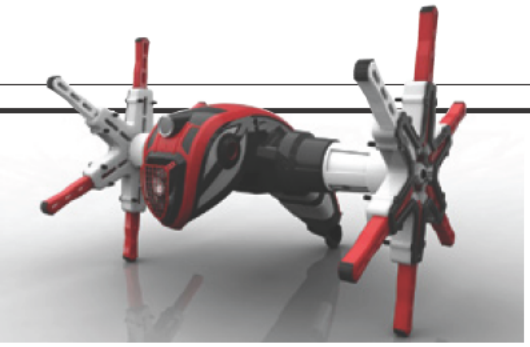
More consumer-friendly droids and drones might come from an unexpected place

The robotic butlers and sentries of sci-fi fantasies already roam our planet, but you can't have them—not yet. The fate of most would-be home robots breaks in one of two ways: Bots such as Honda's Asimo, a bipedal assistant, exist only as demonstrations from multimillion-dollar research and development laboratories. Robots that consumers could purchase, such as the $1,600 Pepper companion robot, are unaffordable for most. Toy company WowWee aims to change all that when it delivers the first sub-$600 multifunction home-service robot. The freestanding, self-navigating Switchbot—part concierge, part security guard—will roll out in 2016.

Hong Kong–based WowWee's success stems from bringing university research projects to life that might otherwise languish in the prototype stage. A licensing agreement with the Flow Control and Coordinated Robotics Labs at the University of California, San Diego, for example, provides WowWee with access to patents and the labs with a healthy cash infusion. The collaboration has already netted a series of toy robots that balance like Segways. More recently, the avionics lab at Concordia University in Montreal began working with the company to perfect flight algorithms for a four-rotor drone. Next, chief technology officer Davin Sufer says he has his eye on the Georgia Institute of Technology and its work with swarming behaviors, which would allow a group of robots to function in tandem.

In the case of Switchbot, WowWee adapted a locomotion system developed in part by former U.C. San Diego student Nick Morozovsky. The robot moves on tank-tread legs either horizontally to navigate uneven terrain or on end to stand and scoot fully upright. Morozovsky built his prototype with off-the-shelf parts, including a set of $50 motors. The motors were a compromise; each one had the size and torque he wanted but not the speed. Over the past few years he has worked with WowWee to customize a motor with the exact parameters needed and to cut the final cost of the part down to single digits.

That back and forth yields low-cost, mass-producible parts, which means university-level robotics could become available to everyday



OutRunner

people. "One of the reasons I went into mechanical engineering was so I could create real things that have a direct impact," Morozovsky says. "I didn't expect that to necessarily happen in the process of grad school."

Academic research that translates directly to consumer electronics is rare, especially given how quickly WowWee can turn products around, says Fred Reinhart, president of the Association of University Technology Managers, which promotes transfer of intellectual property from universities to companies. But WowWee *has* to innovate quickly because toy companies need new stuff every year. Unlike a lab, "there isn't the luxury of being able to develop the technology just to see where it will take us," Sufer says. "That pressure makes cool things happen." —*Corinne Iozzio*

COURTESY OF WOWWEE

Tech Transfer

WowWee has a long track record of bringing lab-borne robots to reality

MiP *(mobile inverted pendulum)* The first product to come out of WowWee's collaboration with U.C.S.D, MiP's self-balancing system—including sensors, wireless radios, motors and processors—had to be reimagined to cut the cost of raw materials significantly.

OutRunner The spiky-wheeled land cruiser, based on an unfunded Kickstarter project by former Florida Institute for Human and Machine Cognition scientists, can hit speeds of up to 20 miles per hour. WowWee is working with the team to bring the prototype system's sticker price down from $500 to sub-$200, primarily by sourcing smaller, more efficient motors.

Switchbot The U.C.S.D. research project that led to Switchbot was about twice the size of the two-foot final product and cost nearly $1,800 in parts to build. To trim the price substantially, WowWee is working directly with suppliers and researchers to perfect new motors and balancing sensors.

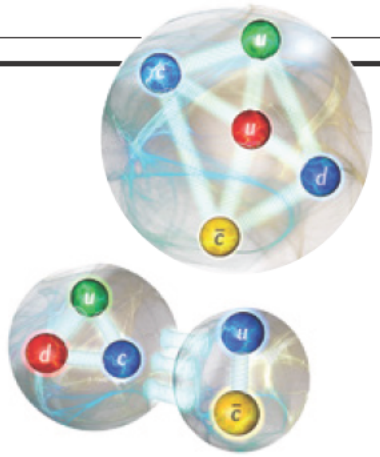
Intellicopter WowWee has been paying attention to the shortfalls of many remote-controlled quadcopters—particularly that the learning curve for flying them is steep. That's why it is working with Concordia University researchers to create flight-control algorithms to help better train new pilots.

Switchbot

PHYSICS

Particular Joy

An exotic quark cluster shows off a new way particles can bind together to form matter



A veritable zoo of never-before-seen particles, including the famed Higgs boson, was generated in recent years inside the Large Hadron Collider (LHC) at CERN near Geneva. Hiding amid the data, another new particle has recently made itself known: the pentaquark, a composite of five quarks, the fundamental bits that make up protons and neutrons. The long-awaited discovery—pentaquarks were first predicted more than 50 years ago—provides insight into how matter's building blocks stick together to organize the universe as we know it.

Before the pentaquark observation, the hundreds of quark-constructed particles splintering out of subatomic collisions were known to exist only as trios of quarks called baryons (including protons and neutrons) or quark-antiquark pairs known as mesons. The limited number of arrangements perplexed physicists because the mathematical model that described quark behavior did not forbid them from combining in other ways. Some research groups reported other permutations—including $Z_c(3900)$, a particle composed of two quarks and two antiquarks—but such cases remain contentious, says Eric Swanson, a physicist at the University of Pittsburgh. And claims of spotting pentaquarks about a decade ago amounted to false positive results.

The new signatures, however, seem to be the real deal. "I've been in this game for 30 years now, and I've seen data come and go," says Swanson, who was not involved in the recent finding. "In this case, the data are clear, and I don't see a compelling alternative explanation." The LHC researchers describe their work in a paper published in August in *Physical Review Letters*.

The data fail to reveal whether all five quarks are bound tightly together or whether a baryon is loosely bound to a meson, like some kind of subatomic molecule (*left*). Future experiments at the LHC, which rebooted at higher energy levels in April, could tease apart the relation or probe the existence of other pentaquark configurations, says Sheldon Stone, a physicist on the collider's quark project. The mere confirmation of pentaquarks, however, shows that the garden variety of particles previously seen in ordinary matter and even high-powered collisions hardly paints a complete picture of the universe's matter. The finding has reignited curiosity about additional exotic particles yet to be uncovered. —*Maria Temming*

Illustration by Moonrunner Design

Jessica Wapner is a science writer and author of *The Philadelphia Chromosome: A Genetic Mystery, a Lethal Cancer, and the Improbable Invention of a Lifesaving Treatment* (The Experiment, paperbound, 2014).

Deadly Drug Combinations

New software and gene analyses may predict which medicines can become harmful when taken together

By Jessica Wapner

Tucking a spreadsheet in among the toiletries in the bathroom cabinet might seem a bit odd, but for 76-year-old Barbara Pines, it is the easiest way to keep track of all the prescription medications, over-the-counter pills and supplements that she and her husband take. The document lists 20 drugs—along with the strength, number of times taken and purpose. "I print this schedule and take it to any new doctor we go to," she says.

Pines is among the 40 percent of Americans who are 65 years of age or older and take more than five prescription drugs. Although older individuals account for the majority of prescription drug users, they are hardly alone. More than four billion prescriptions were filled at U.S. pharmacies in 2014—an average of nearly 13 per citizen at that time.

The need to take multiple drugs poses a special risk that too often goes unrecognized by doctors and patients: certain combinations of medicines (prescription or otherwise) cause side effects that do not arise when the individual substances are taken alone. Studies published over the past two decades suggest that such "drug interactions" cause more than 30 percent of side effects from medications. Unfortunately, pharmaceutical manufacturers cannot always predict when a new agent will mix badly with other medicines—not to mention supplements or foods—and so unexpected deaths are sometimes the first sign of danger.

Not all side effects are lethal, but the widespread danger from drug interactions is prompting new efforts to prevent people from taking risky combinations. Much of this work depends on finding informative patterns in huge masses of disparate data.

PILLS AND PATHWAYS

DRUG INTERACTIONS typically occur when the body breaks down, or metabolizes, medicines. Common trouble spots are the intestine, where ingested drugs are released into the bloodstream, and the liver, where most drugs get degraded.

In the liver, breaking down drugs is primarily the task of a family of enzymes called cytochrome P450. In fact, just six of the approximately 50 enzymes in this family digest 90 percent of all known medications. Problems can arise when two drugs require processing by the same cytochrome. If one of the drugs blocks this enzyme's activity, then too little of the second drug will be degraded and too much will remain in the bloodstream. If, on the other hand, the cytochrome gets a boost from the first drug, then the second drug will have a diminished effect because the enzyme will remove it from the body too quickly. Drugs can also bind to one another in the intestinal tract before ever reaching the liver, preventing the needed chemicals from being absorbed.

Prescription drugs are not the only culprits here. Grapefruit juice, for example, inhibits cytochrome P450 3A4, the same enzyme that metabolizes estrogen and many statins prescribed to lower cholesterol, whereas the herbal supplement Saint-John's-wort boosts the activity of this enzyme. The result, in either case: unpredictable variations in the potency of the medications.

Studies show that once more than four drugs are introduced to the body, the potential for adverse reactions increases exponentially. The trick to avoiding unwanted consequences from drug interactions, says Douglas S. Paauw, who teaches internal medicine at the University of Washington, is "knowing when you're stepping into dangerous territory."

BANKING ON DATA

AND THEREIN LIES THE RUB. The U.S. Food and Drug Administration does maintain a record of reported drug side effects and possible interactions through its Adverse Event Reporting System. But the agency does not know of all, or even most, of the complications—or, indeed, whether or not the reported problems are merely

Illustration by Thomas Fuchs

chance events. Clinical trials of new drugs usually do not reveal any issues before a drug is approved, because they are relatively short, focus on a single medication and enroll a small number of participants. As a result, to learn of a possible new interaction, the FDA has to rely on prescribing physicians to take the time to announce problems to the Adverse Event Reporting System.

Nigam H. Shah, who teaches biomedical informatics at the Stanford University School of Medicine, hopes to improve the odds of discovery by collecting information about specific online searches performed by consumers on the Internet and by physicians on a pharmaceutical Web site called UpToDate. Using more than 16 million pieces of data—electronic records of diagnoses, prescriptions, clinical notes, and the like—on nearly three million people, Shah and his colleagues recently published a previously unsuspected association between heart attacks and a group of popular heartburn medications sold under such brand names as Prilosec and Prevacid; Shah's computer program calculated a 16 percent increase in heart attacks with these types of drugs, which are prescribed more than 21 million times every year in the U.S. By definition, such a correlation does not prove causation, however, and the drug's label information has not been changed.

GENES AND A BOTTLE

IMPROVED ABILITIES for tapping the wealth of information available in human DNA may one day dramatically enhance the power to predict who will suffer most from drug interactions. "Everybody metabolizes drugs a little differently," Paauw says. And now advances in computational biology are beginning to link variations in our genes to differences in how our body absorbs, distributes, metabolizes and eliminates specific medications.

At Duke University's Center for Personalized and Precision Medicine, geneticist Susanne Haga is investigating how to use this quickly accruing genetic knowledge to improve safety, starting at the drugstore. In a recent unpublished survey, Haga found that 17 percent of responding pharmacists had offered or used results from genetic tests (which do not need to be prescribed by a physician) within the previous 12 months. For example, many pharmacists now offer such a test to patients filling prescriptions for clopidogrel, a blood thinner, to confirm the absence of gene variants that could interfere with the drug's action.

Haga is not trying to find previously unknown side effects. Instead she wants to make sure that known genetic complications are widely understood and identified as needed. To facilitate genetic testing and analysis by local pharmacists, Haga recently started the Community Pharmacist Pharmacogenetic Network. Still under development, the network's Web site—rxpgx.com—helps pharmacists access and interpret genetic tests. Although no national databank for collecting such information exists as of yet, Haga hopes that the Precision Medicine Initiative, a project led by the National Institutes of Health, will help lay the foundation for such an effort.

Because prescriptions often come in batches and multiple genes can affect a single drug, Haga envisions a future in which we get tested in advance for key genetic variants that affect our body's ability to process different drugs. But these kinds of tests—which would allow individuals and their physicians to obtain the information whenever needed—are costly, which means that for now, one-off tests suited to elicit information about a single, specific prescription are the more viable option.

INTERIM STEPS

MEANWHILE THE FDA is trying other approaches for identifying potentially dangerous drug interactions before they occur. At the Center for Drug Evaluation and Research, deputy director Shiew-Mei Huang and others are creating computer models that use clinical research data to calculate how one drug will alter the concentration of another when both drugs are metabolized by the same enzyme. Armed with the concentration and the time it takes for the drugs to move through the body, mathematicians can predict how they will interact.

The approach is bearing fruit. The information sheet for the anticancer drug ibrutinib warns that its concentration could increase drastically if taken with erythromycin, a CYP3A inhibitor, and decrease with efavirenz, an HIV drug. These alerts were generated through computer calculations, not by clinical studies of the effects of both drugs taken simultaneously.

The trouble is that many companies and academics are likely to resist Huang's invitation to share the necessary data for a drug in development—such as its metabolic pathway or its most effective dose—to create useful computer models. Such information could include proprietary data, and sharing it might give competitors an edge.

The FDA is also trying new ways to make the drug information packaged with prescription medicines, termed drug "labels," more useful to prescribers and the public. The aim is to give patients clearer warnings about possible drug interactions and easy-to-understand recommendations about how, for example, a dose should be altered (based on computer modeling) when a second drug is introduced. According to Huang, some of the new labeling changes are already being used for some recently approved drugs.

Even with improved labels, physicians may still be hard-pressed to prevent and diagnose such problems, given the ever expanding roster of medications and supplements. One interim solution may be for doctors and pharmacists to pay particular attention to the risk of interactions when patients take commonly used drugs. Among the estimated 100,000 annual hospitalizations for adverse events among older adults in the U.S., about a third are tied to the anti-blood-clotting agent warfarin. Other anticlotting agents, as well as insulin and other drugs meant to lower blood glucose, also have trouble playing nicely with various medications. If doctors were more vigilant about the potential harm associated with the 10 most commonly prescribed drugs in their practice, many problematic interactions could be avoided, Paauw says.

Consumers can do their part by making sure to tell each physician they see about all the medications, supplements and recreational drugs (such as alcohol or marijuana) they take. When it comes to preventing unwanted interactions between drugs, forewarned is definitely forearmed. SA

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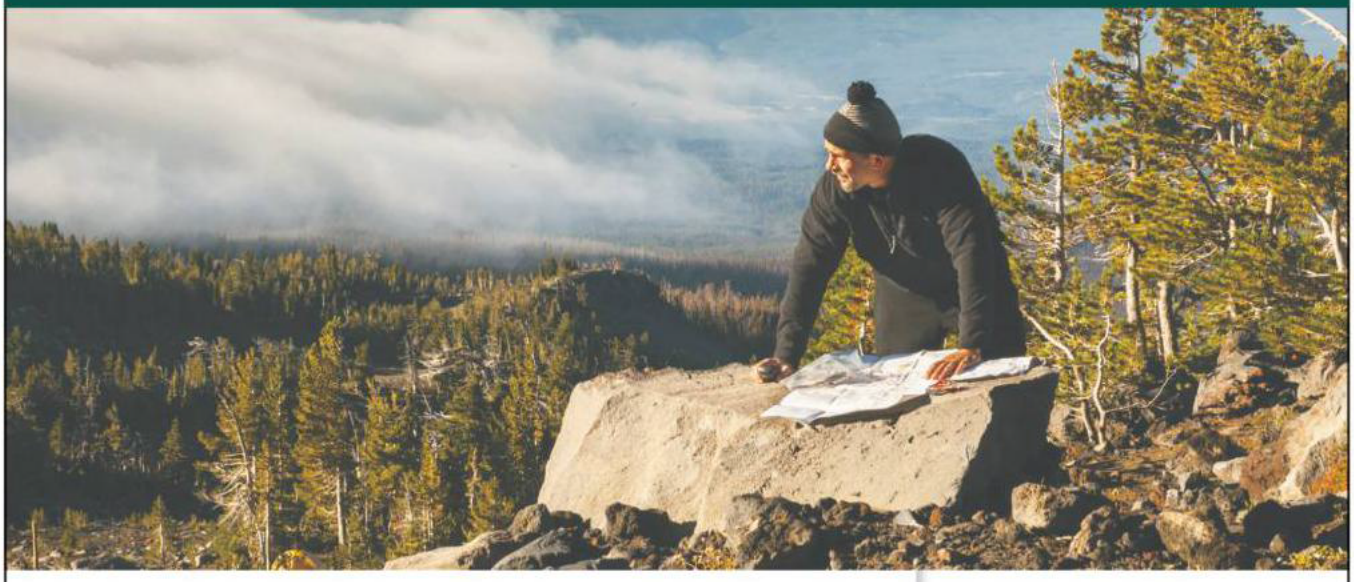
5 Ways to Avoid Running Out of Money During Retirement



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- **Where do you want to go?** Determine your short- and long-term goals such as maximizing terminal value, maintaining value, depleting assets or targeting an ending value. (p. 4)
- **What do you need for the journey?** Calculate your spending projections and cash flow needs. (p. 5-7)
- **Prepare for forks in the road.** Anticipate likely life events and learn how they might affect your investment strategies and cash flow needs. (p. 8-9)
- **How do you get there?** Manage your wealth and achieve your objectives so you don't run out of money in retirement. (p. 10-11)

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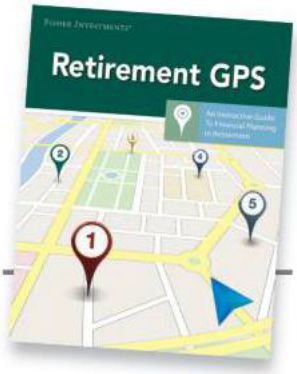

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David Pogue is the anchor columnist for Yahoo Tech and host of several *NOVA* miniseries on PBS.

Robots Rising

Are we ready for intelligent machines to rule the world?

By David Pogue

For most of my life, I've been disappointed in robots. Movies always depicted them as walking, talking, humanoid, smart—and cool. But for decades, real robots have been little more than assembly-line arms at car factories.

In the past three years, though, something has shifted. Self-driving cars have logged nearly two million miles on public roads. Drones have gotten smart enough to avoid hitting things. And two-legged, walking robots are suddenly real.

Now luminaries—including Bill Gates, Stephen Hawking and Elon Musk—are speaking out about the dangers of our increasingly smart machines. "Full artificial intelligence could spell the end of the human race," Hawking has told the BBC.

It's one thing for an easily spooked public to mistrust artificial intelligence. But Gates, Hawking *and* Musk?

As it turns out, all three were responding to an initiative by Massachusetts Institute of Technology professor Max Tegmark. In 2014 he co-founded the Future of Life Institute, whose purpose is to consider the dark side of artificial intelligence.

"When we invented less powerful technology, like fire," Tegmark told me, "we screwed up a bunch of times; then we invented the fire extinguisher. Done. But with more powerful technologies like human-level artificial intelligence, we want to get things right the first time."

The worry is that once AI gets smart enough, it will be able to improve its own software, over and over again, every hour or minute. It will quickly become so much smarter than humans that—well, we don't actually know. "It could be wonderful, or it could be pretty bad," Tegmark says.

In many of Isaac Asimov's futuristic tales, humans programmed robots with the Three Laws of Robotics. For example: "A robot may not injure a human being or, through inaction, allow a human being to come to harm." Wouldn't that kind of software safeguard work?

"The funny thing about Asimov's novels," Tegmark says, "is almost all of the Three Laws stories are about how something goes wrong with them."

Programming machines to obey us precisely can backfire in unexpected ways. "If you tell your super-AI car to get to the airport as fast as possible, it'll get you there—but you'll arrive chased by helicopters and covered in vomit." Not exactly as intended.

But there are bigger dangers. In July, Tegmark's group released an open letter expressing alarm over the rising threat of autonomous weapons—a terrorist's dream. (Hawking, Musk and Apple co-founder Steve Wozniak were among the letter's 2,500 co-signers.) The United Nations is discussing a ban on AI weapons.

On a more day-to-day scale, robots will likely take even more of our jobs. The first to go, of course, will be the ones that are the most repetitive or the most easily automated, such as store clerks, tax preparers and paralegals. (Some Japanese banks already employ robots to assist customers.) "If you teach kindergarten or you're a massage therapist, you'll get to keep your job a lot longer," Tegmark says. He imagines that, finances aside, the loss of jobs will also mean a loss of human fulfillment. "Today so much of our sense of purpose comes from our jobs. We should think hard about the sort of jobs that we would like to keep doing and getting our identity from. Education? The arts, culture, service jobs? Or what, exactly?"

Such alarm bells prompted Musk (co-founder of Tesla Motors and founder of SpaceX) to donate $10 million to the Future of Life Institute (and serve, with Hawking and others, as a scientific adviser for the cause). The group has so far received hundreds of research-grant proposals, funded dozens of them and held major meetings on the topic.

The message, in the end, is not that AI will lead us inevitably to doomsday or a life of ennui but that our contemplation of its effects should keep pace with rapid developments in AI itself. "AI also has enormous upsides—potential to cure all diseases, eliminate poverty, help life spread into the cosmos—if we get it right. Let's not just drift into this like a sailboat without its sail up properly. Let's chart our course, carefully planned," Tegmark says. SA

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STATE OF THE WORLD'S SCIENCE 2015

BIG SCIENCE BIG CHALLENGES

WHAT HAPPENS WHEN YOU PUT THE LIFE OF the mind and the problems of a global civilization in a jar and shake it? The powerful and sometimes uneasy alliance between science and the society it serves is the theme of this year's special report on the "State of the World's Science."

We start with the phenomenon of Big Science, which occurs when society deems an area of research important enough to throw money and resources at it. But the goals and methods of research scientists and politicians can be difficult to sync up. In "Trouble in Mind," starting on the next page, journalist Stefan Theil looks at the travails of the Human Brain Project, a vast research program that the European Commission established in 2013 to advance the field of neuroscience and boost European research. Theil shows what can go wrong when a top-down funding bureaucracy tries to orchestrate the unpredictable progress of scientific discovery.

Science is increasingly called on to develop social programs that evaluate evidence with some rigor. Years ago Dean Karlan asked a naive question about microlending initiatives, which showed promise as a tool for lifting people out of poverty: How do we know they really work? He never got a satisfying answer, and it bugged him. Since then, Karlan, now at Yale University, has endeavored to bring the methods of science to bear on assessing the effectiveness of poverty-fighting programs. In "More Evidence, Less Poverty," beginning on page 33, he describes his search for a science of ending poverty and discusses what has been proved successful so far.

Rodrigo Guerrero Velasco conducted his social science research from an unusual vantage point: city hall. Twice mayor of Cali, a city of now more than two million people in Colombia, Guerrero Velasco was in a position to bring a measure of scientific method to governance. In particular, he sought to tackle an epidemic of violent homicides using methods based on evidence. Drawing on his graduate education in epidemiology at Harvard University, he crafted a program that entailed posing hypotheses about the causes of crime, implementing policies to address them and testing to see if they worked. The results were so dramatic that Guerrero Velasco's approach became a model for Colombia's capital city Bogotá and elsewhere. Turn to page 36.

We round out the section with a graphical snapshot (*page 41*) of the top research nations and institutions around the world, powered by the Nature Index of the scientific literature. (*Scientific American* is part of Springer Nature.) The results, we hope, will surprise and delight you.

BY THE EDITORS

Illustrations by Mario Wagner

TROUBLE IN MIND

Two years in, a $1-billion-plus effort to simulate the human brain is in disarray. Was it poor management, or is something fundamentally wrong with Big Science?

BY STEFAN THEIL

FOR DECADES HENRY MARKRAM HAS DREAMED OF REVERSE ENGINEERING THE HUMAN brain. In 1994, as a postdoctoral researcher then at the Max Planck Institute for Medical Research in Heidelberg, Germany, he became the first scientist to "patch" two living neurons simultaneously—to apply microscopic pipettes to freshly harvested rat neurons to measure the electrical signals fired between them. The work demonstrated the process by which synapses are strengthened and weakened, making it possible to study and model how the brain learns. His work landed him a position as senior scientist at the prestigious Weizmann Institute of Science in Rehovot, Israel, and by the time he was promoted to professor in 1998, he was one of the most esteemed researchers in the field.

Then he began to get frustrated. Although researchers worldwide were publishing tens of thousands of neuroscience studies every year, neither our understanding of basic brain functions nor our ability to treat brain disorders seemed to be progressing much. Markram's consternation was also deeply personal. While he was still in Germany, his son Kai had been diagnosed with autism. As he told *The Guardian* in 2013, he wanted "to be able to step inside a simulation of my son's brain and see the world as he sees it." The only way to do that, he reasoned, was to go beyond individual experiments with behaviors, diseases and brain anatomy and instead model the circuitry of the entire human brain.

In a 2009 TED talk, he first presented to the general public his vision of mathematically simulating the brain's 86 billion neurons and 100 trillion synapses on a supercomputer. "We can do it within 10 years," he promised the audience, suggesting that such a mathematical model might even be capable of consciousness. After those 10 years, Markram told the audience, "we will send … a hologram to talk to you." In various talks, interviews and articles, he suggested that a mathematical brain model would deliver such fundamental breakthroughs as simulation-driven drug discovery, the replacement of certain kinds of animal experiments and a better understanding of disorders such as Alzheimer's. As if that were not enough, the simulated brain would also spin off technology for building new and faster computers and create robots with cognitive skills and possibly

STEFAN THEIL is a journalist and editor based in Berlin and a recent Joan Shorenstein Fellow at Harvard University.

intelligence. Plenty of neuroscientists were skeptical, but Markram had many supporters. His vision seemed vindicated in January 2013, when the European Union awarded him $1.3 billion, spread over 10 years, to build his simulated brain.

Less than two years later the Human Brain Project (HBP) is in disarray, facing controversy and even derision. Takedowns in the science press have used phrases such as "brain fog" and "brain wreck." A spoof of the project on YouTube features a Spanish talk-show guest suffering uncontrollable spasms of laughter as fake subtitles make it appear that he is describing Markram's plans (the guest was actually talking about cooking paella). Several scientists who know Markram personally now describe him as a kind of genius gone off track. He lost his position in the executive leadership of the project, and his own management has ordered him not to talk to the press, including to *Scientific American*. (Markram is co-founder of Frontiers. Frontiers and *Scientific American* are both owned in part by Holtzbrinck Publishing Group. Markram also wrote about his research for this magazine in June 2012.) The project's new executive director, Christoph Ebell, says Markram recently stopped attending internal HBP meetings; instead he has sent a representative to interact with the management team.

The Human Brain Project created a deep, public schism among Europe's neuroscientists. A July 2014 open letter attacking the HBP's science and organization quickly gathered more than 800 signatures from scientists. This past March, with the signatories threatening a boycott of what was supposed to be a Europe-wide collaboration, Markram initiated a mediation process to address the critics' claims. A committee of 27 scientists reviewed both sides' arguments, and, with the exception of two dissenters, the group agreed, almost point by point, with the critics.

In their 53-page report, the mediators called for a massive overhaul of the HBP, including a new management structure and change in scientific focus. The HBP is now undergoing a major reorganization, and the project's future shape and direction are in flux. Few of the E.U. member states, whose research ministries and other institutions were expected to contribute $570 million to the overall budget, have yet made any commitments, which could affect the project's ambitious scope and timeline.

Most accounts of this high-profile project gone awry have focused on Markram and his management style, but that is only part of the story. By all accounts, Markram is earnestly trying to do good science. And as much dysfunction as there has been around the HBP's Swiss headquarters, the ultimate source of the problem is located some 300 miles to the north, in Brussels. There, at the seat of the European Commission, the executive arm of the European Union, a system of Big Science funding that marries politics with scientific objectives, allows little transparency and exercises insufficient control has enabled the mess that the HBP has become. "The real problem is not the HBP but the decision-making process at the E.U.," says Andreas Herz, a professor of computational neuroscience at the Ludwig Maximilian University of Munich and a member of the mediation committee.

BIG SCIENCE, BIG QUESTIONS

SINCE BIG SCIENCE first emerged in the aftermath of World War II and the Manhattan Project, researchers and policy experts have been debating its worth. Writing in *Science* in 1961, the late Alvin M. Weinberg, director of Oak Ridge National Laboratory, pondered whether big-ticket projects such as particle colliders and manned-spaceflight initiatives were "ruining science" or "ruining us financially." He argued that Big Science was responsible for "the injection of a journalistic flavor" into research, "which is fundamentally in conflict with the scientific method"—a situation in which "the spectacular rather than the perceptive becomes the scientific standard." He further worried that with huge sums of money available to researchers, "one sees evidence of scientists' spending money instead of thought."

These concerns are still with us, and no recent endeavor has brought them to the fore like the Human Brain Project. Today Big Science consists of large-scale, collaborative, often interdisciplinary R&D projects, which governments around the world are increasingly funding in an attempt to jump-start innovation. Neuroscience is only the latest branch of research where multibillion-dollar budgets, once reserved for defense and aerospace technology, have spread and multiplied.

There are important reasons why Big Science is proliferating. Many areas of research have grown so complex and expensive that large-scale collaboration is the best tool for moving forward. Big Science has long been the norm in physics, where probing nature's frontiers requires massive particle accelerators such as the Large Hadron Collider at CERN near Geneva. In biology, Big Science had its debut in 1990 with the Human Genome Project, a 13-year, roughly $3-billion (in 1991 dollars) effort co-founded by the National Institutes of Health and the Department of Energy to sequence human DNA. In the early 2010s it was neuroscience that seemed ripe for a big push forward. Almost concurrently with Europe's Human Brain Project, the U.S. unveiled the potentially multibillion-dollar BRAIN (Brain Research through Advancing Innovative Neurotechnologies) Initiative. Israel, Canada, Australia, New Zealand, Japan and China have all announced major new brain research initiatives as well. Thomas R. Insel, director of the National Institute of Mental Health, one of several agencies orga-

IN BRIEF

In 2013 the European Commission awarded neuroscientist Henry Markram $1.3 billion to pursue an audacious goal: building a simulation of the human brain.

Markram's initiative, the Human Brain Project (HBP), is now in disarray. Critics blame HBP management and the project's unreasonably ambitious goals.

Yet plenty of blame for the HBP's woes rests with the project's funders in Brussels, who put politics ahead of science and exercised poor oversight.

The American BRAIN Initiative has shown that big neuroscience projects can succeed. The HBP is now being reorganized to help it do just that.

nizing the BRAIN Initiative (others include the National Science Foundation and the Defense Advanced Research Projects Agency), says it was worry about the spread and cost of mental disorders, combined with excitement about new brain-manipulation technologies such as optogenetics, that galvanized policy makers and scientists to push for a new wave of brain research. "You see a whole generation fired up to do this kind of research now, not just in the United States but around the world," Insel says.

Yet by showing how easily such a project can get off track, the HBP demonstrates the limits of throwing money at hard problems. Though successful when applied to well-defined technological goals such as building rockets or decoding the genome, are big-budget initiatives run by a small group of scientists and administrators the best way to develop something as basic as a new understanding of the human brain?

RISE AND FALL OF THE HBP

AMONG HIS GENERATION of neuroscientists, few stand out like Markram, now aged 53, both for his accomplishments as an experimental researcher and for the scale of his ambition. In 2005 he founded the Blue Brain Project, to which IBM contributed a Blue Gene supercomputer, at the Swiss Federal Institute of Technology in Lausanne. The project uses data and software to simulate a small subset of a rat's brain, focusing on a collection of neurons known as a cortical column. But while the venture is generating knowledge about how to mathematically model some parts of the brain's circuitry, critics say the simulation can do very little that is useful or helps us understand how the brain actually works. To this day, Markram has not published a comprehensive paper of Blue Brain's findings in a peer-reviewed journal. Yet he quickly drafted plans to scale up the effort into an even more ambitious endeavor: building a supercomputer simulation of the entire human brain.

In addition to his scientific credentials, Markram had a powerful talent for advocacy. Charismatic and photogenic, he won a reputation and following as neuroscience's great visionary. He was also quick to dismiss his critics as unwilling to embrace the "paradigm shift" he has said the HBP represents. Many of those critics disputed the basic science behind Markram's project. Even if it were possible, mainstream neuroscientists say, reengineering the brain at the level of detail envisioned by Markram would tell us nothing about cognition, memory or emotion—just as copying the hardware in a computer, atom by atom, would tell us little about the complex software running on it. Others accused Markram of exaggerating the HBP's potential breakthroughs. "We all know Henry, and he's always been a megalomaniac," says Eilon Vaadia, director of the Edmond and Lily Safra Center for Brain Sciences at the Hebrew University of Jerusalem. "None of us believe that what he's promised can be done."

Despite skepticism in the neuroscience community, Markram won over the people who really mattered: funders at the European Commission, who seem to have looked less closely at the proposal's scientific feasibility than at its potential economic and political payoff. "The project's genesis was that politicians wanted to do something for European industry to catch up," Ebell says. In 2009, driven by fear of falling further behind the U.S. in computers, digital services and other technologies, what is now the European Commission's Directorate General for Communications Networks, Content and Technology began creating a competition for "flagship" projects funded with at least €1 billion each. As much industrial policy as science, these initiatives were to "enable Europe to take the lead" in future and emerging technologies, according to a 2009 European Commission paper. Markram's brain on a supercomputer—and his promises of what it would achieve for neuroscience, medicine, robotics and computer technology—was a good fit for a bureaucracy that believed a 10-year, top-down plan for "disruptive" innovation was possible. "It was exactly the kind of thing someone like Henry would find exciting, and he told them exactly what they wanted to hear," Ebell says.

> **"Is there any politician who wouldn't love to stand up and say, 'We Europeans are building a brain?'"**
>
> —*CHRISTOPH EBELL, HBP'S EXECUTIVE DIRECTOR*

"Is there any politician who wouldn't love to stand up and say, 'We Europeans are building a brain'? That's thrilling—that's like a moon shot."

Because the flagship program was envisioned as a showcase project outside the usual science-funding process—and because of the big budget that needed to be justified—politicians, bureaucrats and even scientists had strong incentives to exaggerate its promises. "You sit in a meeting, and someone says that you have to write that up in a more exciting way," Ebell says. "Then you start promising more, and everyone starts repeating it, even the scientists. It's a feedback loop. And with so much money at stake, the feedback loop is very effective."

A secret jury of 25 experts from all corners of Europe—at least one neuroscientist was included, but the rest were from other fields—chose the HBP, plus one other project, from among six finalists to receive about €1 billion (then $1.3 billion) each, to be paid out in €100-million increments. Contrary to common practice in the U.S., the European Commission did not divulge the jury members' names even after they made their decision. In a statement sent to *Scientific American*, the commission defended this practice as necessary to prevent "repercussions on the personal and professional life of the experts concerned as well as on the quality and efficiency of the procedures."

The other winner was Graphene Flagship, a 23-country consortium of academic and corporate researchers who will develop this promising nanomaterial with many applications in electronics, energy and other industries. The graphene project is also designed to help European industry, which risks falling behind Asian nations such as South Korea, where Samsung is developing the futuristic material. But unlike the HBP, Graphene Flagship has avoided controversy, and industrial research partners are rapidly signing on across Europe. One crucial difference is that Graphene Flagship is not based on a single person's vision; it is set up

Continued on page 42

HOW BIG IS SCIENCE?

MAMMOTH INSTRUMENTS OF SCIENCE SUCH AS CERN'S Large Hadron Collider are often held up as symbols of the human commitment to decoding the world. But how highly does humanity as a whole actually regard science? How big *is* science—all of it? This is not an easy question to answer, but by gathering what credible data exist, we can approximate an answer. —*The Editors*

Manhattan Project
$23,000 million–$27,000 million ($2,200 million in 1945)
Total cost
1942–1945

THE BOMB

The Manhattan Project, which developed the first atomic bombs, cost more than $23 billion and employed 130,000 people. For better or worse, it became a model of what "Big Science" could achieve.

U.S.
$453,544 million*
2012

**All country R&D values expressed in purchasing parity dollars, a currency conversion designed to reflect the varying cost of living in different countries.*

BRAIN Initiative
$300 million+
Federal investment through 2015
Launched in 2013

Human Brain Project
$1,630 million
Estimated total project costs
2012–2023

BRAIN STUDIES

One of the greatest remaining scientific mysteries is how the three-pound lumps of meat in our heads produce consciousness. Several large, well-funded initiatives, including the Human Brain Project in Europe and the BRAIN Initiative in the U.S., aim to develop basic tools to help scientists solve this puzzle and cure brain diseases.

Human Genome Project
$4,730 million†
Total project costs
1990–2003

100,000 Genomes Project
$471 million
Current investments
2012–2017

THE GENOME

The $4.7-billion, 13-year Human Genome Project, which in April 2003 finished sequencing the entire human genetic code, was arguably the first true Big Science project in the realm of biology and medicine. New efforts include the 100,000 Genomes Project, which aims to sequence the full genomes of 100,000 U.K. National Health Service patients to search for genetic links to disease.

GLOBAL SCIENCE SPENDING

No single data set captures every dollar spent on scientific research worldwide, but by looking at R&D spending by the world's biggest economies, we can get a sense of the scale of global research.

† All project values converted to 2015 U.S. dollars.

Proposed Collider in China
$3,020 million
Estimated construction costs
Approvals pending

Large Hadron Collider
$5,370 million
Personnel, materials, R&D, tests and preoperation costs
Operational in 2008

European Spallation Source
$2,260 million
Projected construction costs
Broke ground in 2014

PARTICLE COLLIDERS

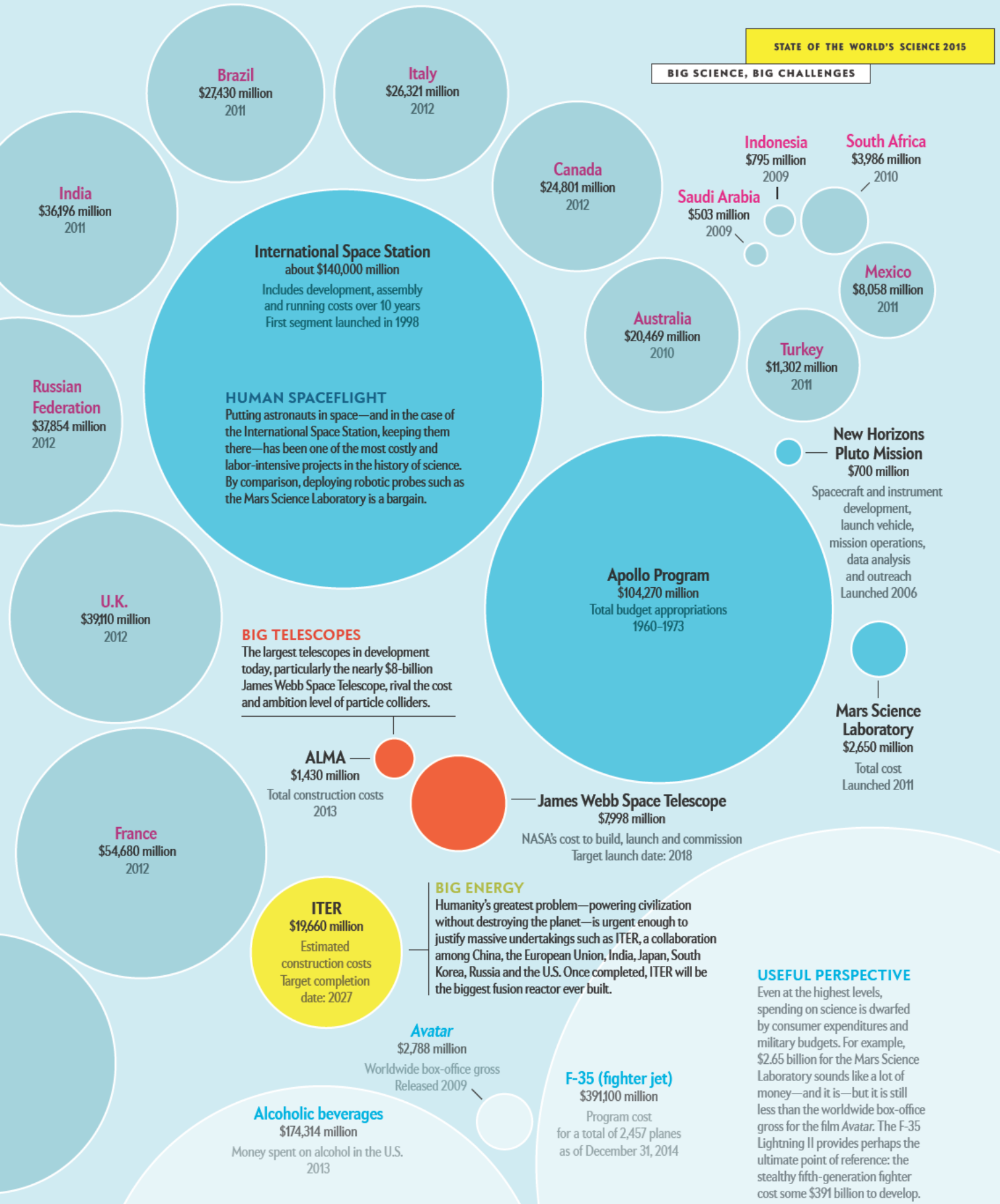
They are expensive, enormous and, for physicists, essential: there is no way to test certain theories without replicating the conditions immediately following the big bang. The 27-kilometer Large Hadron Collider near Geneva is the world's largest, but China has proposed a collider that, if built, will be almost twice the size.

China
$243,293 million
2012

South Korea
$58,380 million
2011

Japan
$148,389 million
2011

Germany
$100,248 million
2012



Graphic by Jen Christiansen

SOURCES: UNESCO INSTITUTE FOR STATISTICS (*expenditure on research and development, by country*); *THE MANHATTAN PROJECT, THE APOLLO PROGRAM, AND FEDERAL ENERGY TECHNOLOGY R&D PROGRAMS: A COMPARATIVE ANALYSIS*, BY DEBORAH D. STINE, CONGRESSIONAL RESEARCH SERVICE REPORT FOR CONGRESS, JUNE 30, 2009 (*Manhattan Project*); *APOLLO BY THE NUMBERS: A STATISTICAL REPORT*, REVISED, BY RICHARD W. ORLOFF, NASA, SEPTEMBER 2004 (*Apollo project*); EUROPEAN SPACE AGENCY (*International Space Station*); NATIONAL HUMAN GENOME RESEARCH INSTITUTE (*Human Genome Project*); "HUMAN GENOME: UK TO BECOME WORLD NUMBER 1 IN DNA TESTING," BY U.K. PRIME MINISTER'S OFFICE ET AL., AUGUST 1, 2014 (*100,000 Genomes Project*); *THE HUMAN BRAIN PROJECT: A REPORT TO THE EUROPEAN COMMISSION*, BY HBP-PS CONSORTIUM, APRIL 2012 (*Human Brain Project*); WHITE HOUSE BRAIN INITIATIVE *www.whitehouse.gov/brain* (*BRAIN Initiative*); *LHC: THE GUIDE*, BY CERN, FEBRUARY 2009 (*Large Hadron Collider*); FAQ FUNDING AND COSTS *http://europeanspallationsource.se/faq-funding-and-costs* (*European Spallation Source*); "CHINA PLANS SUPER COLLIDER," BY ELIZABETH GIBNEY, IN *NATURE*, VOL. 511; JULY 24, 2014 (*proposed collider in China*); "ALMA INAUGURATION HERALDS NEW ERA OF DISCOVERY," BY EUROPEAN SOUTHERN OBSERVATORY ORGANIZATION, MARCH 13, 2013 (*ALMA*); ITER WEB SITE *www.iter.org* (*ITER*); NASA (*James Webb Space Telescope, Mars Science Laboratory, New Horizons*); "DEPARTMENT OF DEFENSE SELECTED ACQUISITION REPORTS (SARS) (AS OF DECEMBER 31, 2014)," BY U.S. DEPARTMENT OF DEFENSE, MARCH 19, 2015 (*F-35*); BOX OFFICE MOJO (*Avatar*); FOOD EXPENDITURES, USDA ECONOMIC RESEARCH SERVICE (*alcoho*)

Continued from page 39

to be inclusive, collaborative and decentralized. For example, whereas Markram and a few others controlled the HBP's structure and funding, the graphene project is an open network only loosely coordinated by its leaders at Sweden's Chalmers University of Technology. Perhaps more important, Graphene Flagship has a strict engineering mission: to develop technology capable of commercializing a known material. Unlike brain modeling, this goal does not require bridging vast gaps in basic knowledge.

Inexplicably, the European Commission failed to insist on the usual checks and balances in the management of the HBP as it was being set up in 2013. According to the mediation report, the project's governance has been riddled with conflicts of interest. The report says that not only did Markram and two other scientists control the board of directors and thus the distribution of funds among the consortium of 112 institutions but that Markram's and several other board members' projects were the beneficiaries of their own funding decisions. "Furthermore," the report states that Markram is "a member of all the advisory boards and reports to them at the same time." "It's a shocking reflection on the level of decision making at the E.U.," says Peter Dayan, director of computational neuroscience at University College London and a member of the mediation committee. Dayan says he cannot remember a project of this size that was so atrociously run: "Governance of large science projects is not rocket science."

It was not until after the neuroscientists' open letter that the European Commission began to mention governance problems at the HBP. Just days before the mediators released their critical, detailed report, the commission issued its own review (by a secret panel known only to the commission and the HBP) that remained much less explicit than the mediators on governance problems but nonetheless mandated changes at the HBP. The commission also said it welcomed the mediation process. Yet had the European Commission exercised early, effective oversight, the HBP may never have run aground. Without the neuroscience community's revolt, it is not clear that the organizational changes at the HBP would be happening now.

LEFT BRAIN, RIGHT BRAIN

SO FAR THE U.S.'S BRAIN INITIATIVE has fared much better than the HBP. Unveiled by President Barack Obama in April 2013 as "the next great American project," the initiative was met by a similar wave of skepticism at the start. Just as in Europe, many U.S. neuroscientists worried that the BRAIN Initiative was poorly conceived and would siphon funding away from other neuroscience research to strive for nebulous, possibly unattainable goals.

But instead of proceeding with closed-door panels and confidential reviews, the NIMH reacted to the criticism by putting the initiative on hold and engaging the neuroscience community. The agency named a panel of 15 leading brain experts and, in a series of public workshops, let the scientists define the project. A year of deliberations produced an ambitious, interdisciplinary program to develop new technological tools that will enable researchers to better monitor, measure and stimulate the brain. The endeavor brings together neuroscientists with nanotechnology specialists and materials engineers to solve issues such as applying electrical stimulus to very small groups of neurons, which may make it possible to treat brain conditions with vastly improved precision.

The key difference between Europe's HBP and the U.S.'s BRAIN Initiative is that the latter does not depend on a single scientific vision. Instead many teams will compete for grants and lead innovation into different, unplanned directions. Competition is happening via the NIMH's traditional peer-review process, which prevents the conflicts of interest that plagued decision making at the HBP. Peer review is not perfect—it tends to favor known scientific paradigms—and American science funding has plenty of problems of its own. But the BRAIN Initiative's more competitive and transparent decision making is far removed from the political black box in Brussels that produced the HBP.

The BRAIN Initiative has a good chance of succeeding because despite its packaging as a moon shot–style megaproject, it is not so much Big Science as a model of distributed innovation under a central funding umbrella, with rules that encourage collaboration. The initiative's megaproject label is, perhaps, just clever PR to raise funds and galvanize support. "When I talk to members of Congress, they always want to know what the new idea is," Insel says. "They don't want to spend money on more of the same." Media coverage also flocks to big new ideas. The result is that a Big Science project—or one packaged as such—is often an easier sell to politicians, their constituents and journalists. "There is a zeitgeist now of Big Science being more effective," says Zachary Mainen, head of systems neuroscience at the Lisbon-based Champalimaud Foundation and co-organizer of the open letter against the HBP. "But that doesn't mean you have to eliminate competition."

UNCERTAIN LEGACY

SINCE ACCEPTING the mediation report's criticism, the HBP is undergoing a radical overhaul—and that may yet turn it into a success. Ebell says the project is building a new management structure that will no longer concentrate so much power with Markram and his closest associates. There will be new bodies for independent oversight. A key subproject in cognitive neuroscience, whose removal from the core research program accelerated the attacks against the HBP last year, has been reinstated. A more open, competitive process for collaborative projects to access HBP funding is also in the works. From now on, Ebell says, every group involved in the consortium, including Markram's, will have to reapply for funding every two years.

The project is also focusing more tightly on data tools and software that are not exclusively aimed at simulating the brain. Although the mediators criticized the HBP for raising "unrealistic expectations" with regard to understanding the brain and treating its diseases, resulting in a "loss of scientific credibility," even critics such as Dayan and Mainen fully support the project's parallel goals of delivering computational tools, data integration and mathematical models for neurological research.

Concentrating on Big Data, a core part of Markram's vision from the start, might even make Europe's HBP a perfect complement to the U.S.'s BRAIN Initiative, whose new technologies are expected to generate huge volumes of neurological data. If the HBP scales down to its technological core—developing useful computational tools and models for neurological research, as mundane as that may sound—then Henry Markram may well leave a great and lasting legacy to neuroscience. SA

MORE EVIDENCE, LESS POVERTY

Money and good intentions are not enough to fight poverty effectively. We also need data about what works and what doesn't

BY DEAN KARLAN

YOU CAN'T MAKE MONEY WITHOUT MONEY. THAT WAS THE EXCITING AND INTUITIVELY OBVIOUS IDEA BEHIND microloans, which took off in the 1990s as a way of helping poor people out of poverty. Banks wouldn't give them traditional loans, but small amounts would carry less risk and allow entrepreneurs to jump-start small businesses. Economist Muhammad Yunus and Bangladesh's Grameen Bank figured out how to scale this innovation and won the 2006 Nobel Peace Prize for their work.

DEAN KARLAN is a professor of economics at Yale University and president and founder of Innovations for Poverty Action, a nonprofit research group.

The trouble is that although microloans do have some benefits, recent evidence suggests that on average they increase neither income nor household and food expenditures—key indicators of financial well-being.

That a program could be celebrated for more than 20 years and lavished with money and still fail to help people out of poverty underscores the paucity of evidence in antipoverty programs. Individual Americans, for instance, spend $335 billion a year on charity, yet most people give on impulse or a friend's recommendation—not because they have evidence that their giving will do any good. Philanthropies also often give money to projects without really knowing if they are successful.

Fortunately, we are living in the age of big data: decisions that used to be made on instinct can now be based on solid evidence. In recent years social scientists have begun to marshal the tools of big data to ask the hard questions about what works and what doesn't. The goal is to turn philanthropy into a science, where money gets directed to programs for which there is strong evidence of their effectiveness.

I learned about microloans in 1992, on what was supposed to be a short detour from a career in hedge funds. As a 22-year-old intern in El Salvador for one of the largest microlenders, I was struck by how little the organization knew about their effect on clients—usually women—and the local economy.

They knew that many customers were coming back for more loans and saw "client retention" as proof of their success. Why else would customers keep borrowing if it was not helping? But the microlenders did not have any serious evidence that the loans were helping women get their families out of poverty. When I asked about evidence on impacts, I was directed to a perfunctory questionnaire. I wondered: maybe repeat borrowing is not good if the client's business does not continue to grow. Perhaps true success would be to provide *one* loan to help someone in need and then down the road to discover the borrower to be stable enough not to need another.

Here was a huge nongovernmental organization pulling in large grants to help the poor, with no real measurement of whether their efforts were working. For-profit businesses have benchmarks to know how they are performing, but most donors are not accustomed to asking charities about their results. Sometimes they ask what proportion of money goes to overhead, but that number is mostly meaningless. The question that needs to be asked—and that needs to be asked every time someone writes a check to a charity or a government commits to a multimillion-dollar aid project—is, Will this actually work to alleviate poverty? In other words, how will people's lives change, compared with how their lives would have changed without the program?

This question knocked me off my Wall Street track and into graduate school for economics. One of my professors, Michael Kremer, had just started conducting randomized controlled trials to learn what programs work to help kids stay in school and improve the education they receive. He was borrowing this method from health and other sciences—randomly assigning schools to either receive a particular resource (the treatment group) or remain as they would have been otherwise (the control group) and then comparing school performance across these two groups.

His approach gave me an idea about how to return to the microlending questions that had brought me to academia in the first place. When I presented my questions and described a simple experiment that could address them, I thought that I was proposing a side project, not a dissertation. I had just finished reading complicated papers for two years, papers that often tackled empirical questions with fancy econometrics, and I assumed a dissertation must do the same. But I still remember Kremer's response: ask an important question and do not worry about whether your method is complicated and demonstrates "smarts." Just worry about answering the question well.

So off I went in my fourth year of graduate school to South Africa to set up my first experiment on the question of whether microlending is effective. I trained a team that would seek individuals who wanted a loan from a microlender. Of the ones who qualified, I randomly assigned them into treatment and control groups and provided the lender with the list of those assigned to treatment. The lender would approach them and offer them loans. It seemed fairly straightforward.

Instead the research project failed miserably. Each time I passed names to the lender, it would take months for them to find the potential client, and sometimes they never would. And then the lender poached my best team member, killing my best shot at gathering more people for the project.

It turns out to be difficult for academics at universities to carry out studies far away with the level of detail that good scientific trials require. You need reliable staff on the ground who understand the science but who also have the social skills to work with partners and manage field operations.

By 2002, as I was starting out as a professor, I founded a nonprofit called Innovations for Poverty Action (IPA) to help fill these knowledge gaps in finance, health, education, food, and peace and postconflict recovery. IPA connects my curious number-crunching academic colleagues at the Massachusetts

IN BRIEF

Philanthropies often give away their money to projects without really knowing if they are successful.
Microloans, for instance, are not effective at increasing income on average for the poorest people on the planet.
Social scientists have begun to marshal the tools of big data to find out what works and what doesn't. The goal is to turn philanthropy into a science, where money gets directed to programs for which there is strong evidence of their social effectiveness.
Evidence-based programs are no panacea for poverty, but they are an important step forward.

Institute of Technology, Yale University, and the like, with a trained staff of more than 500 people working in 18 countries on randomized controlled trials. We have now conducted upward of 500 trials. A chief insight has been that simple interventions that take human behavior into account can have outsized effects. Putting chlorine dispensers right next to water sources, to make it easy to remember and publicly observable, increases use of clean water sixfold. Adding a simple bag of lentils to a convenient monthly immunization camp for families in India roughly sextuples rates of full immunization for kids (while making the entire process cheaper because more families show up). And cheap and simple text message reminders can be effective in helping people accomplish their goals, from saving money to completing their medication regimens. Naturally not everything works. We must figure out what works and what doesn't.

We have also learned that information is only part of the solution. Having strong relationships with local governments, nonprofits, businesses and banks keeps the academic experts working on questions that matter and gets answers into hands of the people who can use them.

Over the years microloans kept nagging at my colleagues and me. Fifteen years after my first study attempt in South Africa, we now have seven randomized trials completed on traditional microloans and one on consumer lending back in South Africa. The seven projects are spread out around the world and have been conducted by different researchers with similar research designs: in Bosnia and Herzegovina, Ethiopia, India, Mexico, Mongolia, Morocco and the Philippines. These studies found some benefits of microloans, such as helping families weather hard times, pay off goods over time and even make small investments in businesses. But there was no average impact on the main financial well-being indicators—income and household and food expenditures. To the chagrin of microloan critics, there also were no big negative effects.

So what *does* work to increase income for the world's poorest?

We just recently studied another program that addresses some of the shortcomings of microloans. One sad failure of many programs (including microloans) has been in reaching the poorest of the poor—known in the field as the ultrapoor. They live on less than what $1.25 would buy in the U.S. a day, and they account for more than a billion people, or one seventh of the world's population. The things keeping them poor are usually complicated enough that no one individual fix is going to help, but one program being run in Bangladesh by BRAC, the world's largest nonprofit organization, and a few other places stands out. It saw extreme poverty as a complex problem deserving of a complex solution. Its "graduation" approach, designed to move the extreme poor out of their current conditions, offers a package of six items:

1. A "productive asset," that is, a way to make a living (livestock, beehives to make honey or supplies to start a simple store).
2. Technical training on how to use the asset.
3. A small, short-term regular stipend, to meet immediate needs for daily living so the individual does not have to sell the asset while learning how to use it.
4. Access to health support, to stay healthy enough to work.
5. A way to save money for the future.
6. Regular (usually weekly) visits from a coach, to reinforce skills, build confidence and help participants handle any challenges they encounter.

The Ford Foundation and Consultative Group to Assist the Poor in Washington, D.C., came to me with an ambitious idea: test an identical program, implemented by different organizations in multiple places. We ended up conducting similar studies in six places: Ethiopia, Ghana, Honduras, India, Pakistan and Peru. What we found was unprecedented—everywhere the program worked, it worked well. When we came back a year after the program had ended, we found the impact had lasted: people had more money to spend and food to eat. When we calculated the costs (labor, asset costs, transportation and overhead) as compared with the benefits, the overall returns were positive in five out of six countries—ranging from 133 percent in Ghana to 433 percent in India. In other words, every dollar invested in India yielded $4.33 more food and spending for ultrapoor households.

Simple interventions that take human behavior into account can have outsized effects. Putting chlorine dispensers right next to water sources, to make it easy to remember and publicly observable, increases use of clean water sixfold.

The one exception was Honduras, where the productive asset most used by the local organization—chickens—was an outside breed that was not resistant to local disease and so became sick and died. This was a humanitarian failure, but it demonstrated that the asset is an essential component of the program. Remove that component, and the other five components did not generate positive impacts on their own. As the programs are expanding in Ethiopia, India and Pakistan, we hope to learn more about how to make this program work better, either by reducing costs or by improving the services.

There is no panacea in the fight against poverty. Even a graduation program for the ultrapoor, which is ready to scale and yields an excellent return for a charitable buck, is not going to transform the ultrapoor into car-buying middle-class households. The vision statement for Innovations for Poverty Action is appropriately modest: more evidence, less poverty. We are not going to end poverty, but with proper evidence we can make important strides. SA

AN ANTIDOTE TO MURDER

City leaders across the Americas are exploiting science to reduce homicide

BY RODRIGO GUERRERO VELASCO

VIOLENCE IS A BIG PROBLEM IN MODERN SOCIETY AND IN CITIES IN PARTICULAR. HOMICIDES WERE RAMPANT in my hometown of Cali, Colombia, when I became mayor in 1992. Few people saw murder as a pressing health problem, but I did—probably because I had earned a Ph.D. in epidemiology at the Harvard School of Public Health. I decided to apply the statistical methods used by public health experts to identify the sources of homicide and to reveal social and policy changes that might make a difference.

At the beginning of my first term, the people of Cali and all of Colombia generally believed, mistakenly, that little could be done because we Colombians were "genetically violent." Other skeptics maintained that violent crime would not diminish unless profound changes were made on socioeconomic issues such as unemployment and educational levels. My administration and I proved all these people wrong.

We developed an epidemiological database about the many societal factors that significantly raised the risk that a homicide would happen. These included sometimes subtle aspects of human behavior, such as the desire to carry guns in certain places or the tendency to drink alcohol on certain days. This exhaustive and fine-grained information led to new laws and policies built on data, not politics.

The method worked. In 1994 annual homicides in my city, then home to nearly 1.8 million, dropped from 124 per 100,000 residents to 86 in just three years after the leading causes were found and policies were applied. An even larger decline took place over nine years in Bogotá, after our capital city adopted the same methods. And when I was elected mayor of Cali for a second time, in late 2011, after being out of office for almost 18 years, the same approach reduced homicide rates again. Let me tell you the story of how big data and scientific analysis can help solve entrenched social problems.

PINPOINT THE ROOT CAUSES

WHEN I BEGAN my first term, I did what epidemiologists generally do: plot cases on a map. I hung a big printout of Cali on my office

wall and stuck color-coded pins in it at each location of a death, intentional injury, traffic accident, home burglary or other violent event. When a journalist saw the map, his local newspaper ran a headline that read: "Mayor Guerrero Intends to Curb Violence with Acupuncture."

Even to smart journalists, evidently, it was strange to look at homicide in a statistical way. But to me, it made perfect sense: if epidemiological methods could find the causes of medical diseases, they could find the causes of a societal disease.

Using statistics was crucial because Colombia had a long record of violence that left many misimpressions. Beginning in the late 1940s, *La Violencia,* a fierce struggle for power between the two main political parties, sparked over 200,000 killings across more than 10 years. Guerrilla warfare followed for decades. The cultural tolerance for violent responses to conflict was so high when I took office that quarrels between neighbors or drivers in traffic accidents frequently ended in homicide. In 1991 Medellín, the second-largest city in Colombia, had an annual homicide rate of 380 per 100,000. Around that time, Chile's rate was 2.9.

My epidemiological approach began with a definition of violence scripted by the World Health Organization: the use of force with the intention to cause harm or death. This definition does not include accidents or psychological or political violence.

Despite the media's preoccupation with domestic warfare, only 36 percent of the deaths in Colombia in 1991 were caused by guerrillas, mostly in rural areas. I thought drug dealers would arise as the culprits in the other 64 percent. As we investigated the who, where and when of each death in Cali, however, we found that homicide victims and aggressors were predominantly young, unemployed males who had low levels of education, came from the poorer sectors of the city and were frequently involved in gang fights. We also found that close to 80 percent of homicides were carried out with firearms. When we discovered that two thirds of homicides took place on weekends, we decided to chart blood alcohol levels in victims; more than half of them had been intoxicated. These facts pointed to social disintegration more than drug-related violence.

Drug traffic still had an effect, but it was not the direct cause of most homicides. As we analyzed the numbers, we realized that drug traffic was to society as HIV is to the human body: the virus attacks defense mechanisms, making the body vulnerable to other diseases. Likewise, drug dealers attack the police and the judiciary and political systems—the defense mechanisms of society. These weakened institutions arose as risk factors for violence. For example, the police identified a suspect in only 6 percent of homicides, and the judiciary system brought even fewer to trial.

Also, children were often exposed to violence and maltreatment, and violent content was prevalent in the media. In a culture of violence, economic inequality and ineffective public security, people killed and got killed, often under the influence of alcohol, over conflicts as simple as noisy neighbors or settling debts.

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has been mayor of Cali, Colombia, since 2012. He was also mayor from 1992 to 1994. After his first term, he worked for the Pan American Health Organization and helped to start ValleNPaz to create economic programs in guerrilla-infested and illicit drug-producing rural Colombia.

CHANGE THE CULTURE

OUR GOAL WAS TO REVEAL risk factors we could control directly. Because firearms were used in a large proportion of homicides and alcohol was often associated with the deaths, in November 1993 I began to change gun and alcohol laws.

In my country, guns are manufactured and sold by the Colombian National Army, so military authorities opposed my idea of a permanent ban on weapon-carrying permits. But they agreed to our suspending the permits in public places on select dates identified by the data as posing a high risk, which was generally associated with high alcohol consumption. These dates included New Year's Eve and (strangely) Mother's Day, as well as days when payments to employees, made on the 15th and 30th of each month in Colombia, coincided with a Friday.

I also restricted alcohol sales in public places after 2 A.M.—a measure my administration called the semidry law. Nightclub owners objected adamantly, so I proposed a deal: I would apply the law for three months, and if violent deaths and injuries did not diminish, I would drop it. After only two weeks, hospitals reported such a drastic reduction in violence-related emergencies that abandoning the measure was not an option. I enforced the semidry law until the end of my term.

An epidemiological strategy also calls for evaluating interventions. After several months, we found that when both alcohol sales and firearms permits were restricted, there was a 35 percent reduction in homicides versus days when neither were in force. The reduction was 14 percent when firearms alone were restricted.

Other interventions included adding more prosecutors, as well as putting more police on the streets and improving their equipment, such as surveillance cameras, cars and radios. To support these people in their challenging careers, we launched a privately funded program to help police officers become homeowners and gave computers and training to members of the judiciary. Crime prevention rose, and more suspects were brought to trial.

We also created two Houses of Justice—premises within violent neighborhoods on the outskirts of Cali in which all law-enforcement institutions operated 24 hours a day. Previously these services were available only downtown and during business hours. This change was particularly helpful in reducing domestic violence because investigations would begin immediately after fo-

IN BRIEF

An epidemiological approach of data analysis can reveal the root causes of violence and the best steps to curtail it. **In Cali, Colombia,** the method reduced homicides from 124 per 100,000 inhabitants to 86 in just three years. In Bogotá, the rate dropped from 80 to 20 over nine years.

Changes in gun and alcohol laws were crucial. So were increasing police presence and giving youth social activities and jobs.

Today numerous cities across the Americas hold regular meetings of all crime agencies to analyze data, plan interventions and evaluate them.

rensic medical personnel certified a victim's injuries, which lessened the chance that women would withdraw their complaints under pressure from their husbands. In an effort to offer young males in poor districts greater opportunities for education, recreation, income and social connections, I launched DESEPAZ—a program to restore public safety by improving the cohesiveness of a neighborhood. As part of the program, we opened "youth houses" in several communities where people could socialize and gather around cultural and sports activities. City workers also trained youth who were involved with gangs to run small businesses. The city even hired one such business dedicated to manufacturing cobblestones to pave streets.

IMPROVE THE DATA

WE REALIZED EARLY ON that the data we were working with were not always cohesive. For example, in my first security council meeting in July 1992, it became clear that the police and judiciary used different definitions of homicide, which complicated our efforts to pin down causes of deaths. To fix the issue, I established weekly security meetings that involved officials from the police, judiciary and forensic authorities, members of the Institute for Research and Development in Violence Prevention and Promotion of Social Coexistence (CISALVA) at the University of Valle, cabinet members responsible for public safety, and the municipal statistics agency. Information was reported weekly to me and to police commanders. We held a security council meeting every week of my term. Slowly the data coalesced. The meetings evolved into "observatories of crime," sometimes called "social observatories." CISALVA, which is dedicated to studying violence prevention, has kept the observatory's weekly data running for 22 years—to my knowledge, the longest reliable set of information on violence in any Colombian city.

Based on the improved analysis of risk factors, we began interventions at the end of 1993 and widened them before my two-and-a-half-year period as mayor ended in December 1994. My successor continued them. The homicide rate in Cali dropped from 124 per 100,000 in 1994 to 112 in 1995, 100 in 1996, and 86 in 1997. It is difficult to say how much of the decline was a direct result of the interventions because the national government was also changing how police fought drug cartels. But evaluations in Cali and Bogotá confirm that the epidemiological approach played an important role. I believe that is true in part because the mayors who followed my successor did not keep in place unpopular measures such as the restriction of alcohol consumption, and the homicide rate climbed back up.

Experience in Bogotá, the country's largest city, backs up the data-intensive method. When Antanas Mockus became mayor there in January 1995, he applied and improved our strategy. His most important tactical interventions were increasing the police budget 10-fold, improving police education about violent crime, developing temporary detention centers for minor offenders and creating a government position of subsecretary of violence prevention. The social interventions included rebuilding dilapidated public spaces and tripling investment in health and education.

Mockus also implemented a semidry law and restrictions on firearms, which quickly reduced homicide rates as much as they had in Cali. In Bogotá, strict use of the epidemiological method spanned three administrations over nine years, from 1995 through 2003. Across that time, homicide rates dropped from 59 per 100,000 to 25. As in Cali, some of that improvement may have been helped by changes at the national level.

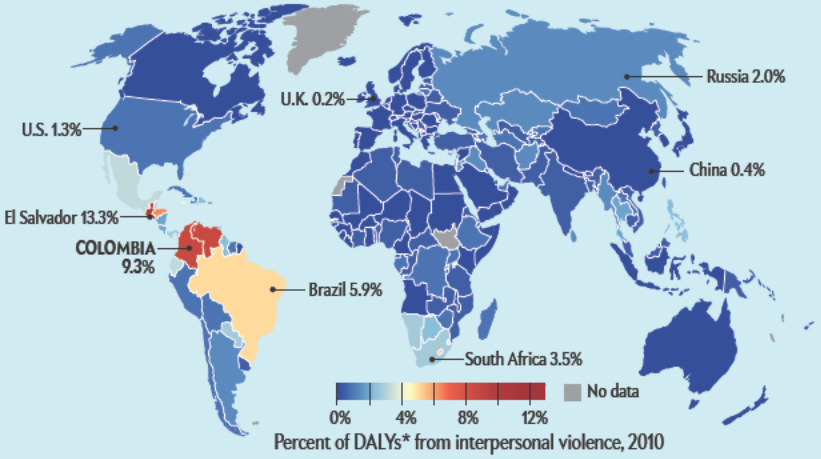
NEW TACTICS, 20 YEARS LATER

IN COLOMBIA, mayors cannot be reelected consecutively (and I had other plans anyway). After I left office, I dedicated myself to spreading the word that urban violence could be controlled and to doing further research about that goal. I went to work at the Pan American Health Organization in Washington, D.C., was instrumental in actions that created the Inter-American Coalition for the Prevention of Violence and helped to garner approval of a loan from the Inter-American Development Bank to Cali, Medellín and Bogotá for deterring violence. After three years, I returned to Cali and helped to launch VallenPaz, an organization devoted to creating economic programs in rural southwestern Colombia as an alternative to the lure of money from guerrillas and illicit drug crops.

Years later, however, I found that there is no lifelong immunity to politics. I ran again for mayor of Cali.

When I took office on January 1, 2012, I found a different city. Cali had grown from 1.8 million inhabitants in 1994 to 2.4 mil-

MOST VIOLENT NATIONS: Central and South America top the charts in premature death and disability caused by violence between individuals, such as shooting or stabbing. In most countries worldwide, less than 3 percent of the population (*dark and medium blue*) suffers this fate, but in parts of the Americas, the figure rises higher, as in Colombia (9.3 percent) and El Salvador (13.3 percent). Data-driven steps to reduce violence in Colombian cities are succeeding and starting to be used elsewhere.



*Disability-adjusted life years: years of life lost to premature death or spent in ill health or disability.

SOURCE: GLOBAL HEALTH DATA EXCHANGE, INSTITUTE FOR HEALTH METRICS AND EVALUATION, UNIVERSITY OF WASHINGTON

Map by Terra Carta

lion. Most of the additional people were migrants, primarily from Colombia's Pacific coast and neighboring rural areas. After years of incompetent administrations and one mayor ousted from office, collective self-esteem was low, and unemployment was up from 6.9 percent in 1994 to 13 percent in 2013. Although the large Colombian drug cartels were dismantled in the 1990s, they had fragmented into smaller cartels that worked rather independently in the nation's cities, particularly in Medellín and Cali. Drug dealing was still present, and new forms of crime had emerged, such as small "vaccine" payments required by gangs to protect local businesses and war over the territorial control of drug distribution and selling within cities.

The good news was that the Colombian police had become professional and trustworthy. The national homicide rate had dropped from 79 in 1991 to 36 in 2011. Yet Cali's homicide rate was around 80, compared with 22 in Bogotá and 70 in Medellín.

I immediately reinstated the weekly security council meetings. Soon our data analyses showed that the proportion of homicides resulting from interpersonal conflict such as quarrels and alcohol-related brawls had diminished compared with the period of 1992 to 1994. But killings that we classified as organized crime—those that were premeditated and involved sophisticated weapons such as machine guns—accounted for 67 percent of violent deaths in 2012. Data suggested that organized crime was playing a bigger role. The data also showed that social inequalities had gotten worse since my earlier term.

We presented our data to the national government and suggested it create specialized groups of criminal investigators, police and prosecutors to dismantle criminal bands. My administration also began a massive social investment plan in 11 districts that were home to a total of 800,000 people, 26 percent of them living in poverty and another 6.5 percent in extreme poverty.

The plan that resulted, called Territories of Inclusion and Opportunities, is still in effect today. It applies a geographical approach to fighting poverty, focusing interventions in impoverished areas and encouraging local residents to play big roles. Local and national officials work on raising incomes, extending school schedules, promoting cultural activities and sports, and improving housing, health facilities and public education. We also teach parenting skills and peaceful conflict resolution.

Together with the effort from the national government to fight organized crime, our interventions again reduced violence. Cali's homicide rate of 83 in 2012 dropped to 62 in 2014. This pattern has continued; the number of homicides in the first trimester of 2015 is less than in the same period in any of the past 12 years.

All these coordinated police and social actions help the crime interventions. A good example of the strategy is Comuna 6, a political district of Cali where 212,000 residents, most of whom are middle-income, live. We energetically implemented the coordinated police and social interventions, and homicides went down 44 percent within a year's time, from 160 in 2013 to 89 in 2014.

The epidemiological approach to reducing violence is passing the test in other cities in Colombia and across the Americas. Crime observatories—the evolution of our regular security council meetings—are essential to the approach. The Inter-American Development Bank, the U.S. Agency for International Development and the World Bank, among others, now recommend that cities or states create the observatories when seeking financial support for violence-prevention programs. Today four national and numerous municipal-level observatories are meeting systematically in 26 countries and cities in the Americas.

A study published in the *International Journal of Injury Control and Safety Promotion* found that homicides were significantly reduced in 22 Colombian cities in the three-year period after the observatories were implemented. Studies directly comparing cities in different countries are difficult, however, because countries have diverse definitions of crimes and varying criteria for collecting information. To improve the situation, the Inter-American Development Bank is supporting a project to standardize violence indicators across the Americas.

POLITICAL WILL IS THE TOP PRIORITY

USING AN EPIDEMIOLOGICAL STRATEGY to help solve a social issue may seem straightforward, but it is not. The first lesson I can espouse is that such a move takes strong political will because the strategy frequently requires public officers to do things they would rather not do, such as making necessary but unpopular decisions to close bars or ban firearms. Making crime data public can also be uncomfortable, but it is essential, just as economists releasing unemployment and gross domestic product numbers is essential to formulating economic strategy. Data on social issues such as violence and education are now published periodically for various Colombian cities by nonprofit groups called Bogotá How Are We Doing, Cali How Are We Doing, and so on. The information makes public officials and mayors accountable in their communities.

The second lesson is that there is no one-size-fits-all approach in applying epidemiological methods to social issues because cities and countries have different risk factors. Data-driven observation is needed in each context to guide public officials.

The process also requires perseverance and patience. Certain risk factors can be controlled rapidly—for example, by banning firearms or restricting bar hours—but other measures, such as improving the reach of police and judiciary services, take longer. Steps such as correcting social inequalities or establishing healthy child-rearing practices need not only time and patience but also considerable resources.

Urban violence is socially regressive because it mostly affects the poor, and fighting crime devours a portion of the public budget, which could instead be invested to eradicate poverty. Violence prevention must therefore be a priority for humanity. SA

MORE TO EXPLORE

The Evaluation of a Surveillance System for Violent and Non-Intentional Injury Mortality in Colombian Cities. Maria Isabel Gutierrez-Martinez et al. in *International Journal of Injury Control and Safety Promotion*, Vol. 14, No. 2, pages 77–84; 2007.

More Than Good Intentions: How a New Economics Is Helping to Solve Global Poverty. Dean Karlan and Jacob Appel. Dutton, 2011.

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FROM OUR ARCHIVES

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WORLD LEADERS

THE NATURE INDEX, A DATABASE OF AUTHOR-AFFILIATION information from 68 high-quality science journals, ranks the relative scientific output of nations and institutions by analyzing some 57,000 research articles. (*Scientific American* is part of Springer Nature.) The results show us who leads the world in scientific output. —*The Editors*

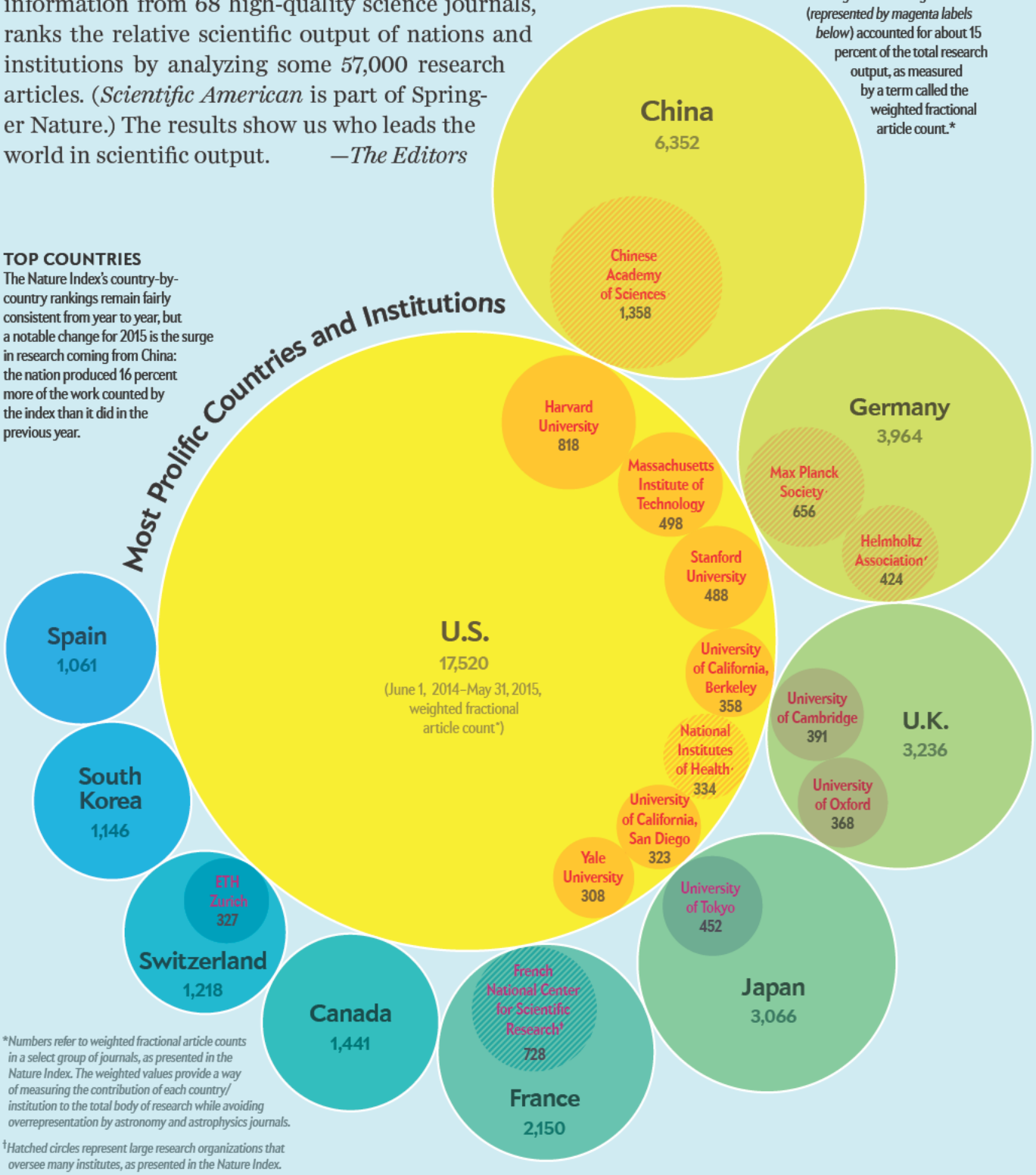
TOP INSTITUTIONS

Out of a total of 8,208 institutions, the top 10 universities and five large research organizations (*represented by magenta labels below*) accounted for about 15 percent of the total research output, as measured by a term called the weighted fractional article count.*

TOP COUNTRIES

The Nature Index's country-by-country rankings remain fairly consistent from year to year, but a notable change for 2015 is the surge in research coming from China: the nation produced 16 percent more of the work counted by the index than it did in the previous year.

Most Prolific Countries and Institutions



*Numbers refer to weighted fractional article counts in a select group of journals, as presented in the Nature Index. The weighted values provide a way of measuring the contribution of each country/institution to the total body of research while avoiding overrepresentation by astronomy and astrophysics journals.

†Hatched circles represent large research organizations that oversee many institutes, as presented in the Nature Index.

SOURCE: NATURE INDEX (accessed August 10, 2015)

Graphic by Jen Christiansen

NEUROSCIENCE

SLEEP ON IT!

Your nightly rest turns out to affect your mind and health more than anyone suspected

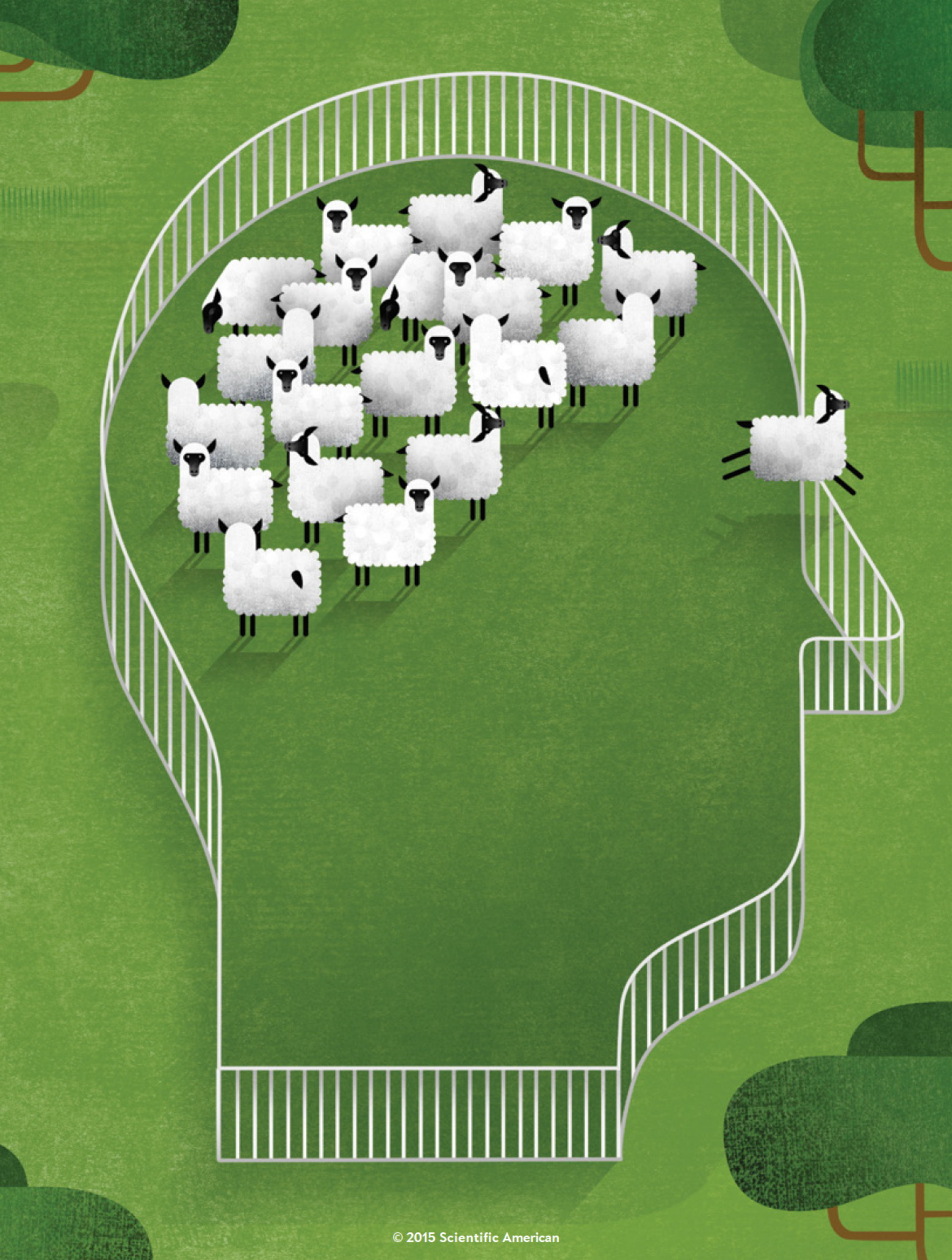
By Robert Stickgold

"Do I really need to sleep?" As I travel around the world talking about sleep, I am asked this question over and over. The answer has always been clear—yes, everyone needs to do it. Just like hunger, thirst and sexual desire, the urge to sleep is a physiological drive. Exactly what spending a third of our lives unconscious gets us, however, has long mystified scientists.

In acknowledging our lack of an answer, Allan Rechtschaffen, one of the world's foremost sleep researchers, said in 1978, "If sleep does not serve an absolutely vital function, then it is the *biggest mistake* the evolutionary process has ever made" (emphasis mine). In the 1990s J. Allan Hobson, another leading sleep researcher, quipped that the only known function of sleep was to cure sleepiness.

Research over the past 20 years has finally begun to provide at least a partial explanation for why we must sleep. The clearest finding is that sleep does not serve just a single purpose. Instead it appears to be needed for the optimal functioning of a multitude of biological processes—from the inner workings of the immune system to proper hormonal balance, to emotional and psychiatric health, to learning and memory, to the clearance of toxins from the brain. At the same time, none of these functions fails completely in the absence of sleep. In general, sleep seems to *enhance* the performance of these systems instead of being absolutely necessary. And yet anyone who lives for months without sleep will die.

Illustration by Maria Corte Maidagan



Even this imperfect understanding has taken decades to develop. By the end of the 20th century researchers had replaced ancient notions about sleep—that it was caused by blood retreating from the surface of the skin or by the buildup of warm vapors from the stomach—with detailed measurements of brain-wave activity, breathing patterns, and daily oscillations in the amount of hormones and other molecules in the blood. More recently, investigators have begun identifying the exact aspects of sleep that are important for each of its benefits. Ironically, though, the more researchers uncover about the unconditional necessity of a good night's sleep for the proper functioning of mind and body, the less time 21st-century citizens spend in the soothing arms of Morpheus, the Greek god of dreams.

Robert Stickgold is director of the Center for Sleep and Cognition at Beth Israel Deaconess Medical Center and an associate professor at Harvard Medical School.

FATAL INSOMNIA

THE CLEAREST EVIDENCE of our absolute need for sleep comes from a study published in 1989 by Carol Everson when she was working in Rechtschaffen's laboratory. Everson, now at the Medical College of Wisconsin, found that rats totally deprived of sleep all died within a month. In actuality, all she had to do to achieve this fatal result was to prevent the animals from entering the stage of sleep characterized by rapid eye movement (REM). But a quarter of a century later researchers still cannot explain *why* the rats died. A series of experiments in the intervening years has only served to eliminate possible causes; it is not caused by, for example, increased stress, excessive energy consumption, or failure of the body's internal heat regulators or the immune system.

Death by sleep deprivation is not unique to rats. Fatal familial insomnia, first described about 30 years ago, is, as the name suggests, a heritable human disorder that leads first to unremitting insomnia and thence to death. A team of Italian researchers, then at the University of Bologna's medical school, reported it in 1986. The group, led by Elio Lugaresi and Rossella Medori, told the story of a 53-year-old man who died within months of developing intractable insomnia—as had many of his relatives over two generations. Postmortem analysis of his brain showed massive loss of nerve cells in two regions of the thalamus, a structure about the size of a walnut that is found in the midbrain and generally acts as a way station for incoming sensory input. The two particular regions in question, however, are known more for their role in regulating emotional memory and producing so-called sleep spindles, a key pattern of waves found in electroencephalograms of the sleeping brain.

How this deterioration in the thalamus might lead either to insomnia or to death is unclear. But the immediate cause of the damage itself is now known. In the early 1990s Medori, by then at Case Western Reserve University, and her colleagues determined that a malformed protein, called a prion, was responsible for the destruction. Prions are also known to cause scrapie in sheep and bovine spongiform encephalopathy ("mad cow disease") in humans—though in the case of fatal familial insomnia, the prion is inherited from one generation to the next rather than being ingested from the environment, as in the other two ailments.

Fortunately, there are no other reported instances of human death caused by sleep deprivation (aside from accidental deaths when, for example, a sleepless driver falls asleep at the wheel). But there are also no other reports of people going several months without sleep. We are thus left with two examples of prolonged and total sleep deprivation leading to death—experimentally induced sleep deprivation in rats and a heritable prion disease in humans—and with no understanding of the exact cause of death in either case.

ANTIBODIES AND HORMONES

MEANWHILE WE DO KNOW that as little as one night of complete or even partial sleep loss can interfere with various bodily functions, such as hormonal activity and protection against infections. Two studies looking at the body's response to immunization with hepatitis vaccines show how dramatic the effects of sleep deprivation can be on the immune system. In the first experiment, from 2003, a small group of college students received a standard hepatitis A vaccination consisting of inactivated virus in the morning, after which investigators permitted half of them to sleep normally; the other half were kept awake all night.

The sleep-deprived subjects were not allowed any sleep until the following night. Four weeks later researchers took blood samples from the students and measured the amount of protective antibodies that their immune system had produced in response to the virus in the vaccine. Higher levels of antibodies would indicate a better response to the vaccine and thus likely greater protection against future infection with disease-causing versions of the virus. After the four weeks, the group that had enjoyed a normal night's sleep had 97 percent higher antibody levels than the one that had been sleep-deprived.

Negative effects are measurable with less than a full night's sleep as well. In the second study, adults received the standard three doses of hepatitis B vaccine over the course of six months. (Repeat vaccination is required to build up full immune protection.) Researchers gave each participant a motion detector similar to a watch, which monitored their sleep at home. By com-

IN BRIEF

Many studies—not to mention common experience—support the link between a good night's sleep and improved mood, memory and learning.

A growing number of experiments carried out over the past two decades have also found that the mechanism of sleep directly affects other workings of the body, from hormonal balance to immune protection.

Despite these findings, researchers still do not understand exactly why we need our daily visit to the land of Nod, but they are learning a great deal about what precisely happens when we sleep.

paring the subjects' average amount of sleep during the week of their first shot to the level of antibody protection they displayed after the second shot, investigators determined that antibody levels increased 56 percent for every additional hour of sleep. Six months after the final vaccination, those who had averaged less than six hours of sleep a night during the week around the first vaccination were seven times more likely to have such low amounts of antibodies in their blood that they were considered unprotected against future infection with the hepatitis B virus.

Impressive evidence for impaired hormonal function came from a series of studies performed by Karine Spiegel, who was at that time working with Eve Van Cauter of the University of Chicago. In one of these experiments, researchers allowed 11 healthy young men to get just four hours of sleep a night. After five nights of restricted sleep, the men's ability to clear glucose from the blood—a process that the hormone insulin manages—was reduced by 40 percent. In a separate study, Spiegel and her colleagues similarly limited the amount of sleep of 12 men for two nights. The scientists measured the amount of ghrelin, an appetite-stimulating hormone, found in the volunteers' blood and found it had jumped by 28 percent. At the same time, amounts of a different hormone, known as leptin, decreased by 18 percent; leptin inhibits hunger by signaling the brain that there is no need to eat. Not surprisingly, the sleep-deprived men reported an average 23 percent increase in their hunger levels.

Taken as a whole, these studies of human physiology suggest that reduced sleep could lead to increased weight gain—a hypothesis that is now supported by at least 50 other studies. In several of the investigations, children from six to nine years of age who got fewer than 10 hours of sleep were one and a half to two and a half times more likely to be obese, and studies in adults suggest a 50 percent increase in obesity among participants with fewer than six hours of sleep. Research also shows an association between sleep restriction and the development of type 2 diabetes.

NEGATIVITY BOMB

DESPITE THE REMARKABLE EFFECTS of restricted sleep on immune and hormonal function, its greatest impact probably occurs in the brain. In a 2006 study I conducted with Matthew P. Walker, now at the University of California, Berkeley, we looked at how a single night of sleep deprivation affected the emotional memories that people laid down. Twenty-six subjects—half of whom had been sleep-deprived the night before—were shown positive, negative and neutral words (for example, "calm," "grief" or "willow") and asked to rate their emotionality. Then, after two nights of recovery sleep, they were given a surprise memory test.

Compared with the subjects who had slept normally, those who were sleep-deprived before seeing the words for the first time showed a 40 percent deterioration in their ability to recognize them. But more striking was the relative impact of sleep deprivation on the three categories of words. When subjects were sleep-deprived, their recognition of positive and neutral words both deteriorated by 50 percent. Their ability to recognize words with negative connotations, however, deteriorated only 20 percent. In contrast, the memory formed after normal sleep for positive and negative words differed little, with neutral words being less memorable than either positive or negative words. In other words, the memory of negative words appeared to be at least twice as strong as positive or neutral words after study volunteers were forced to cut back on their sleep.

FINDINGS

Don't Skimp on Sleep

Research has uncovered many ways that sleep deprivation impairs mental and physical health. Some of the best-studied and most significant impacts are highlighted below.

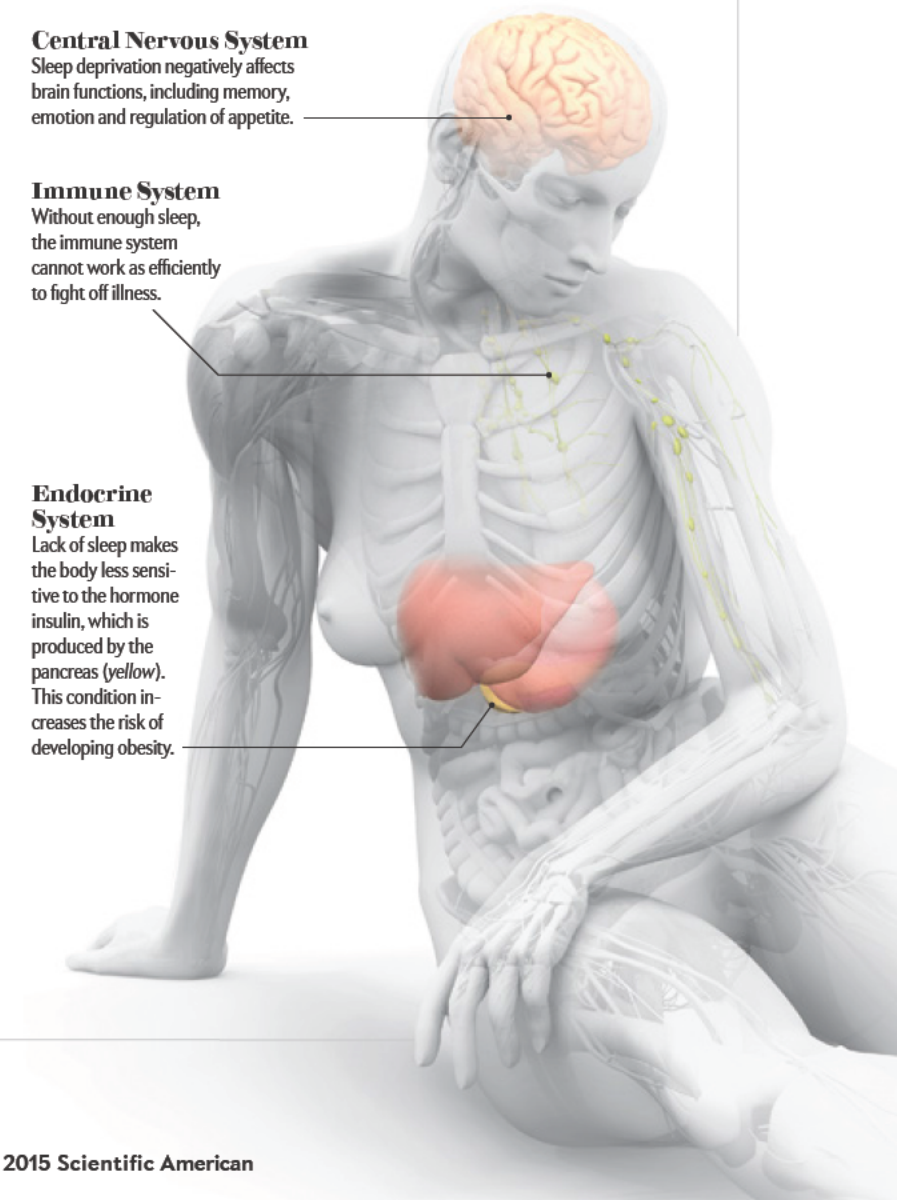


Illustration by Bryan Christie

This result suggests the rather horrifying possibility that when you are sleep-deprived, you effectively form twice as many memories of negative events in your life as of positive events, producing a biased—and potentially depressing—memory of your day. Indeed, several studies over the past 25 years have now concluded that poor sleep can, under certain circumstances, lead to depression severe enough to be diagnosed as major depression and may contribute to other psychiatric disorders as well.

The evidence of a causal link with depression in particular has grown significantly in recent years and comes to a large extent from studies of sleep apnea, a disorder in which the flow of air into the lungs becomes interrupted during sleep. It may lead to snoring, gasping and other disruptions of respiration. Each time individuals with sleep apnea briefly stop breathing, they awaken momentarily to start breathing again. As a result, sufferers of severe apnea might wake up every minute or two throughout the night. A 2012 study by the U.S. Centers for Disease Control and Prevention found that men and women with a diagnosis of sleep apnea are, respectively, 2.4 and 5.2 times more likely to have major depression compared with their better-rested counterparts.

Of course, finding a correlation between these two conditions is not the same thing as proving that one causes the other. But a recent analysis of 19 studies found that treating sleep apnea with so-called CPAP devices (for *c*ontinuous *p*ositive *a*irway *p*ressure), which restore normal breathing and sleep, significantly reduces symptoms of depression. Indeed, one of the studies, which coincidentally had included a greater percentage of depressed patients at the outset than the others, found a 26 percent reduction in depression symptoms in CPAP users.

These results still do not prove conclusively that fitful sleep can bring on depression, nor was the effect of the CPAP treatment compared with that of antidepressant medication. Nevertheless, these suggestive findings deserve further investigation. Similarly, a 2007 study found that treatment of apnea in children who also had attention-deficit/hyperactivity disorder led to a 36 percent decrease in hyperactivity symptom ratings—a significantly larger reduction than the 24 percent achieved with typical ADHD medications.

Several studies over the past 25 years have now concluded that poor sleep can, under certain circumstances, lead to depression severe enough to be diagnosed as major depression.

FUTURE MEMORIES

ALTHOUGH RESEARCHERS still do not know the physiological mechanism by which sleep and its lack affect mental health, they suspect that the role sleep plays in helping the brain transform people's daily experiences into memories has a lot to do with it. The past two decades have seen an explosion of discoveries showing that sleep participates in memory processing in everyone—no matter what their emotional state. Among the findings: sleep after learning leads to the selective stabilization, strengthening, integration and analysis of new memories. In doing so, it controls what we remember and how we remember it.

In the late 19th and early 20th century scientists considered memories to be fragile until they went through a process of so-called consolidation, which transformed them into a stable form that could then last a lifetime. More recent research has shown that memories retain the ability to change even after the brain records and consolidates them. Indeed, reactivation of a memory can return it to an unstable state long after it was first formed, requiring reconsolidation; while in this labile form, it can be changed or lost altogether. This finding is both a curse and a blessing—a curse because originally accurate information can be corrupted and a blessing because inaccurate information can be corrected. Researchers have thus begun to talk about memory *evolution* instead of memory consolidation, especially when discussing sleep-dependent memory processing.

The modern era of research into sleep and memory began just over 20 years ago, when Avi Karni and his colleagues in Israel demonstrated that subjects trained on a visual discrimination task actually improved over a night of sleep but only if they were allowed to enter REM sleep. (As an aside, most dreams take place during REM sleep.) Their experiment showed that sleep does more than just stabilize memories, keeping them from deteriorating over time; it actually improves them.

In 2000 Walker came into my office waving a journal article and predicting, "This one is sleep-dependent, too!" The paper described a task in which subjects learned to tap out a particular sequence of finger movements, which became easier for them to do over time, even without additional practice. Still, the authors had not looked at how sleep might contribute to this improvement. Within two weeks Walker had the answer. He found that sleep had indeed improved their performance, and he later determined that the benefit depended on experiencing a light stage of non-REM sleep rather than on REM sleep, as in the Karni vision experiments. The inescapable conclusion: the brain strengthens different types of memories during different stages of sleep.

Further research showed that not all memories undergo this sleep-dependent stabilization. In 2008 Jessica Payne, now at the University of Notre Dame, conducted a study in which she showed volunteers various scenes with aversive objects—such as a dead cat in the middle of a road. She found that after a night of sleep the subjects could accurately recognize the image of the dead cat, but they had forgotten the background street scene. What was most impressive was that this selective forgetting of the background details did not happen when she trained

SCIENTIFIC AMERICAN ONLINE Watch as Stickgold talks about sleep, memory and dreams at ScientificAmerican.com/oct2015/sleep

subjects in the morning and then tested them in the evening after a day spent awake. And it did not happen if the central image was nonaversive—for example, if it was just a cat crossing the road. Thus, sleep, but not wakefulness, caused the brains of the study participants to retain the highly emotional central images in preference to either the neutral images (cat crossing the road) or their background scenes.

But it is not just emotional memories that are preferentially enhanced during sleep. It appears that anything you think is important will be selectively retained while you are asleep. Two groups in Europe have shown that telling subjects who have been trained on a particular task that they will or will not be tested on that information after they sleep affects what happens during that sleep. As you might expect, only the information that subjects are told they will be retested on shows improvement the next day. In contrast, when subjects are trained in the morning, informing them that they will or will not be tested that evening does not seem to make any difference. Sleep, then, and not wakefulness, selectively strengthens memories that our brain deems valuable.

These findings provide elegant support for the arguments of Daniel Schacter of Harvard University that memory is about the future, not about the past. He has argued that we have evolved memory systems not so we can reminisce about the past but so we can use prior experience to enhance our future performance. In this context, it is not surprising that sleep seems to care most about information that is likely to be of future relevance. When we talk about sleeping on a problem, we are not merely asking the sleeping brain to remember something. We want our brain to take the information that is already stored there and do some kind of calculation, to juxtapose different possibilities, to find the best solution to a problem. Lucky for us, it can!

An example of this analytic ability is highlighted in a weather-prediction experiment developed by Barbara J. Knowlton and her colleagues at the University of California, Los Angeles. Knowlton showed subjects one or more cards from a set of four—each of which displayed a particular geometric design (circles, diamonds, squares or triangles). Before the subjects began the task, the researchers assigned each card to a particular imaginary weather outcome—rainy or sunny—without sharing the information with the participants. Then, based on the cards shown, investigators asked those participants to predict whether the cards indicated the weather would be rainy or sunny. Over time subjects got a sense of how the cards related to the weather. For example, the first trial might show the diamonds card, and the weather, the subjects are told, turns out to be sunny. Then, on the second trial, the circles and triangles cards are both displayed, and the weather turns out to be rainy. Even after just these two trials, subjects inevitably would begin to construct hypotheses about the relations, such as that diamonds mean sunshine. But then, on the third trial, the diamonds card might appear again, only to be followed by rain.

The trick here is that the cards are only *probabilistically* related to the weather. Thus, the diamonds card predicts sun 80 percent of the time, but for the other 20 percent, it is followed by rain. Other cards end up predicting sun just 20 to 60 percent of the time. In Knowlton's study, even after 200 trials, subjects still had not mastered the task, guessing the most likely outcome only about 75 percent of the time.

Use of such tasks has allowed researchers to discriminate between different memory systems within the brain—those involved in remembering facts (the "what" system) and those involved in learning skills (the "how" system). As subjects train on the weather-prediction task, they slowly shift from using the *what* system to the *how* system. When Ina Djonlagic in my lab asked what happens to this information with sleep, she obtained an amazing result. When volunteers who had trained in the morning were retested the same evening, they also performed at around 75 percent, apparently fully retaining the information they had learned that morning. But when other subjects were trained in the evening and tested after a night of sleep, they were 10 percent better at predicting the outcome than they had been the evening before. Somehow the sleeping brain was actually able to improve participants' understanding of the relation between the cards and the subsequent weather. They had gained a better model of how the world worked.

The more researchers explore what happens while we sleep, the more they discover new benefits to a good night's sleep. The most recent possible addition to the list is the clearance of waste products from the brain. In 2013 Lulu Xie and her colleagues at the University of Rochester Medical Center reported that the space between cells in the brain increases during sleep, allowing for better flow of cerebrospinal fluid between the brain and the spine. When the investigators injected beta-amyloid (the precursor of the amyloid plaques found between neurons in Alzheimer's disease) into mice, they found that it was cleared from the brain during sleep at twice the rate seen in awake animals. Presumably the increased flow of cerebrospinal fluid helped to move the potentially toxic molecule out of the brain, away from the areas where it could cause the most damage. Now researchers would like to find out whether the increased flow normally seen during sleep is impaired in people who have Alzheimer's.

Given all the latest research on the many functions of sleep and the likelihood that yet more will be discovered, skimping on sleep is looking like a worse and worse strategy for dealing with the demands of daily life. Taken together, the results of studies looking at the role of sleep in hormonal, immunological and memory functions suggest that if you do not get enough, you could—besides being very tired—wind up sick, overweight, forgetful and very blue. SA

MORE TO EXPLORE

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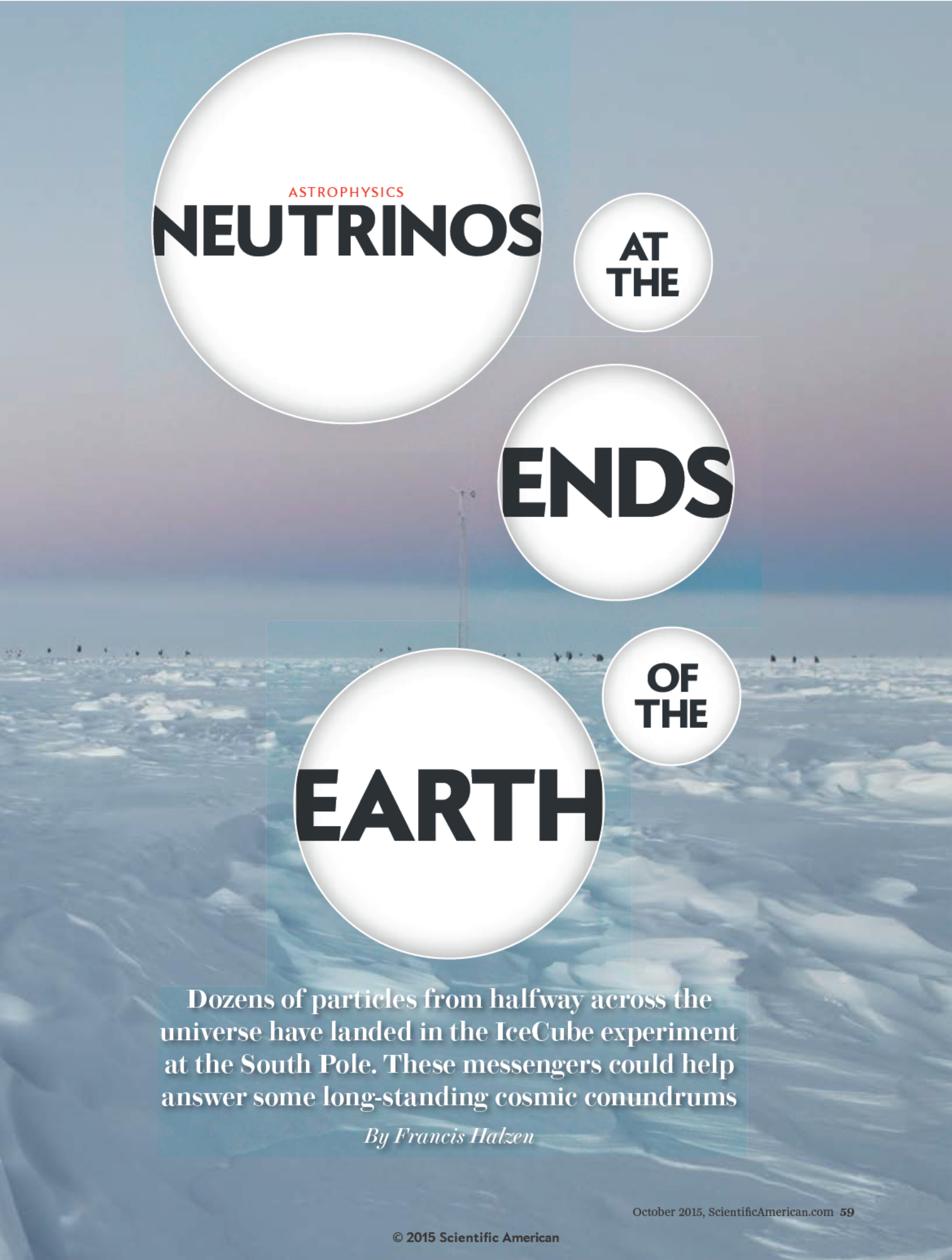


ASTROPHYSICS

NEUTRINOS AT THE ENDS OF THE EARTH

Dozens of particles from halfway across the universe have landed in the IceCube experiment at the South Pole. These messengers could help answer some long-standing cosmic conundrums

By Francis Halzen

Francis Halzen studies particle physics, astrophysics and cosmology at the University of Wisconsin–Madison. He is principal investigator of the IceCube experiment.

ONE OF THE MOST AMBITIOUS AND EXTREME experiments on Earth opened at the South Pole in 2010. IceCube, a giant particle detector buried in the polar ice, captures elusive, high-energy species of neutrinos—fundamental particles that fly straight through almost everything they touch. The project, for which I am the principal investigator, aims to use neutrinos to study distant cosmic phenomena—particularly the mysterious, violent processes thought to produce the charged particles known as cosmic rays that continually bombard Earth.

We expect IceCube to catch these very high energy neutrinos only rarely. The particles have almost no mass and no electrical charge (which is why they seldom react with other particles), and they travel at nearly the speed of light. Once they arrive on Earth from near or far away, most do not stop to linger; they keep traveling, zipping straight through our planet and continuing on their way. Because of these difficulties, we were not surprised that the experiment's first few years of data, taken while the detector was still under construction, turned up nothing extraordinary. But in 2012 that changed.

One day, during a routine conference call for team members, our screen lit up with patterns we had never seen before. The signals reflected two neutrinos carrying more than 1,000 times the energy of the most energetic neutrino ever produced by an accelerator on Earth and almost a billion times the energy of the neutrinos regularly spat out by the sun. Clearly, they came from some spectacularly energetic process occurring far from our planet. Exhilaration spread through the room as we realized we were looking at something game changing. Capturing the whimsy of the moment, one of our graduate students nicknamed the two particles "Bert" and "Ernie," after the *Sesame Street* characters (the names are not just fun; they are easier to keep straight than the long strings of numbers we usually assign to neutrino events).

It took us another year and a totally redesigned analysis of the same data to satisfy ourselves that these were indeed what they seemed: the first pixels of the first pictures of the distant neutrino universe. Since then, we have found 54 high-energy neutrinos in total—many of them given Muppet names, including one dubbed "Big Bird" with an energy twice that of Ernie or Bert.

We are now trying to identify where in the sky these high-energy neutrinos came from and how they originated. Their suspected sources are extreme cosmic events such as supernovae and other stellar explosions called gamma-ray bursts—two phenomena rumored to give rise to cosmic rays. If we can definitively trace the high-energy neutrinos to these likely sources of cosmic rays, we will open a new frontier in our understanding of the physics behind the extraordinarily dramatic events that are thought to produce them.

POWERFUL PARTICLES

COSMIC RAYS, which constantly bombard Earth from space, are made of extremely high energy protons and other charged particles. More than a century after their discovery, the processes that birth them are still unknown. When they arrive at Earth, we cannot deduce where in the universe they came from because their electrical charge allows galactic and intergalactic

IN BRIEF

IceCube is a neutrino-hunting particle detector buried in ice at the South Pole. Neutrinos usually fly straight through matter but occasionally smash into atoms in the ice to create signals IceCube can detect.

The project has discovered dozens of neutrinos with higher energies than any found before, many of which most likely originated in extreme cosmic events taking place in the far-off universe.

These cosmic neutrinos can be used as tracers to study the nature of the mysterious distant events and should help explain the strange sources of the cosmic rays that bombard Earth from deep space.

PRECEDING PAGES: COURTESY OF SVEN LIDSTROM IceCube/NSF

magnetic fields to alter their course as they cross space. Luckily, however, theory suggests that cosmic rays also interact at their birthplaces with photons to produce neutrinos.

Neutrinos, unlike cosmic rays, do point back to where they started. Because they shun other matter, almost nothing can divert them from their path. Therefore, although cosmic rays themselves cannot lead us to where they began, the highly energetic neutrinos they presumably produce can do so for them.

Of course, astronomers have some ideas about how cosmic rays are born, but we need data to help us confirm or discard those possibilities. One probable source of cosmic rays is the death throes of massive stars. At the end of a large star's life, when its nuclear core can no longer support its mass, it will collapse into a dense object called a neutron star or into an even denser black hole, from which nothing escapes. In addition to creating a bright blast of light—a supernova—the collapse converts large amounts of gravitational energy into thrust for the acceleration of particles, presumably through shock waves. Supernova remnants were proposed as a likely source of cosmic rays as early as 1934 by astronomers Walter Baade and Fritz Zwicky; after 80 years, the hypothesis is still debated. About three supernova explosions in the Milky Way every century, converting a reasonable fraction of a star's mass into fuel for particle acceleration, could account for the steady flow of cosmic rays seen in the galaxy.

Extragalactic cosmic rays, which originate from beyond our home galaxy, are generally even higher in energy than the cosmic rays coming from nearby, and they require a more energetic source to create them. One contender is gamma-ray bursts. Even brighter than regular supernovae, gamma-ray bursts are somewhat mysterious but probably occur during a special class of star collapse that involves very high mass stars under extreme conditions.

Another theoretical source of extragalactic cosmic rays is active galactic nuclei—a class of galaxies suspected to have a supermassive black hole at their center that is absorbing large quantities of matter. As matter falls into such a black hole, some particles could be deflected outward and accelerated to high speeds to become cosmic rays.

BURIED about 1.5 kilometers underneath the Antarctic ice cap, the IceCube detector consists of 86 strands of sensors strung through a cubic kilometer of ice. Each strand was installed by being lowered into a hole made by a hot-water drill.

TO CATCH A NEUTRINO

TO DETECT NEUTRINOS produced by the cosmic rays coming from such processes, IceCube has to be extraordinarily huge. The experiment uses a full cubic kilometer of 100,000-year-old Antarctic ice 1.5 kilometers below the surface of the South Pole for the job. Ice is a perfect natural neutrino detector because when a neutrino does occasionally interact with atoms in the ice, the material lights up by releasing a shower of charged particles that radiates blue light. This so-called Cherenkov radiation travels hundreds of meters through the pure, ultratransparent ice. IceCube is equipped with 5,160 optical sensors spaced throughout its volume to spot this light.

The sensors chart, in exquisite detail, the light pool produced by the nuclear debris created when a single neutrino hits. This pattern reveals the neutrino's type (or "flavor"), energy and arrival direction. The energies of Ernie and Bert and the others that we have seen so far are about a peta–electron volt (PeV), or 10^{15} eV; Ernie and Bert were 1.07 PeV and 1.24 PeV, respectively. For comparison, the particle beams at the Large Hadron Collider at CERN near Geneva, the world's most powerful particle accelerator, are in the tera–electron volt (TeV), or 10^{12} eV, range, about three orders of magnitude less. These energies made them the most energetic neutrinos ever found, by a wide margin. The light pool of roughly 100,000 photons created by Ernie and Bert extended over more than 500 meters, or about six city blocks.

Most important, the PeV energies of these two neutrinos tell us that they must be part of some cosmic signal—their energies are just too large to have been produced nearby. Local neutrinos are a dime a dozen. Every six minutes, IceCube detects a neutrino that is produced in the interactions of cosmic rays with hydrogen and oxygen nuclei in Earth's atmosphere. But these neutrinos, because they are made in our own backyard, are useless for telling us anything about the nature of cosmic rays or other astrophysical phenomena. We therefore have to screen out these distractions to detect cosmic neutrinos. From past experience, we know the light patterns produced by garden-variety neutrinos, so we ignore those.

Therefore, we can be quite sure the PeV-energy neutrinos that IceCube is seeing come from the distant cosmos. They very well could have reached us from the same sources as cosmic rays. But there are also other possible, more exotic explanations for these particles. One suggestion is that they may be

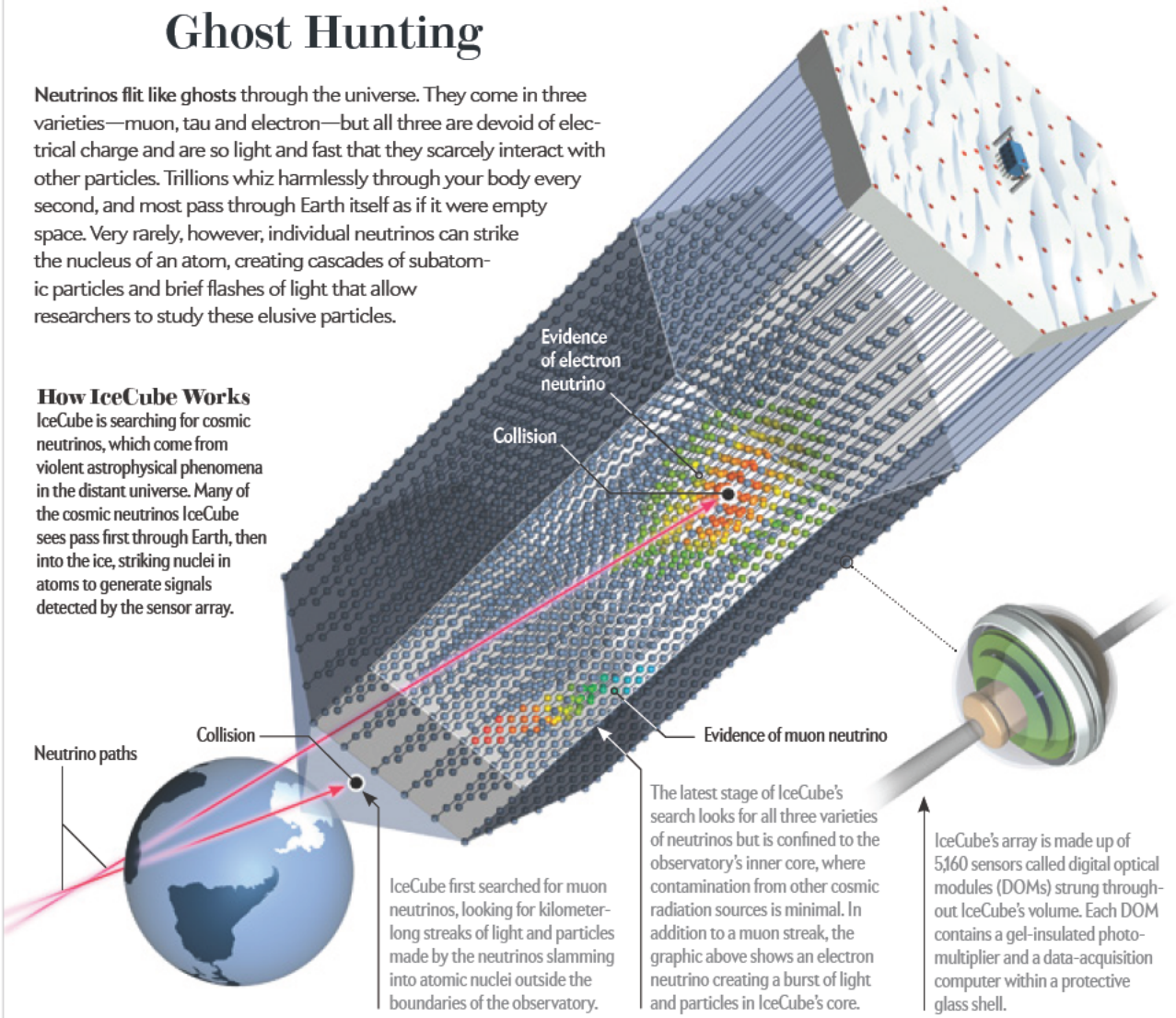
COURTESY OF JIM HAUGEN *IceCube/NSF*

Ghost Hunting

Neutrinos flit like ghosts through the universe. They come in three varieties—muon, tau and electron—but all three are devoid of electrical charge and are so light and fast that they scarcely interact with other particles. Trillions whiz harmlessly through your body every second, and most pass through Earth itself as if it were empty space. Very rarely, however, individual neutrinos can strike the nucleus of an atom, creating cascades of subatomic particles and brief flashes of light that allow researchers to study these elusive particles.

How IceCube Works

IceCube is searching for cosmic neutrinos, which come from violent astrophysical phenomena in the distant universe. Many of the cosmic neutrinos IceCube sees pass first through Earth, then into the ice, striking nuclei in atoms to generate signals detected by the sensor array.



IceCube first searched for muon neutrinos, looking for kilometer-long streaks of light and particles made by the neutrinos slamming into atomic nuclei outside the boundaries of the observatory.

The latest stage of IceCube's search looks for all three varieties of neutrinos but is confined to the observatory's inner core, where contamination from other cosmic radiation sources is minimal. In addition to a muon streak, the graphic above shows an electron neutrino creating a burst of light and particles in IceCube's core.

IceCube's array is made up of 5,160 sensors called digital optical modules (DOMs) strung throughout IceCube's volume. Each DOM contains a gel-insulated photomultiplier and a data-acquisition computer within a protective glass shell.

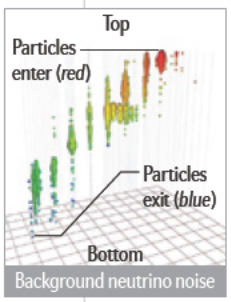
What We've Seen and What We're Still Looking For

Most neutrinos IceCube sees are just "background noise" from processes in Earth's atmosphere. They have low energies and create showers of secondary particles that streak down from the detector's top (*left panel*) at a detection rate of 3,000 per second.

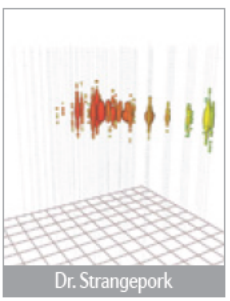
Cosmic neutrinos can come from any direction—even up through Earth. Muon neutrinos ("Dr. Strangepork," *below*) make long streaks, whereas electron or tau neutrinos appear as bursts of light and particles ("Ernie," "Bert" and "Big Bird," *below*).

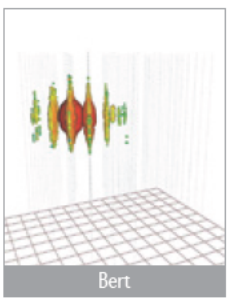
IceCube is still searching for the streaks or bursts from "GZK" neutrinos made by interactions with the big bang's afterglow. A GZK could be distinguished by its high energy, which can be more than 1,000 times greater than that of other cosmic neutrinos.

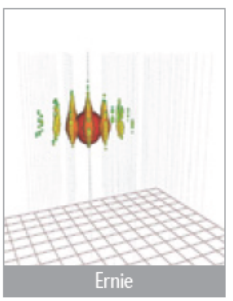
Low Energy ⟵ ⟶ High Energy

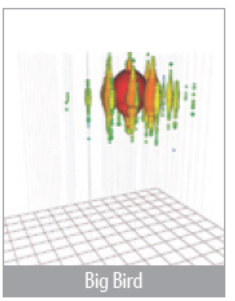


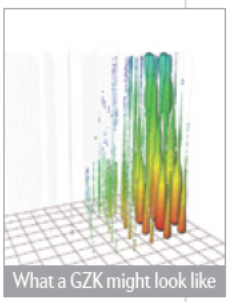
Background neutrino noise


Dr. Strangepork


Bert


Ernie


Big Bird


What a GZK might look like

SOURCE: COURTESY OF ICECUBE COLLABORATION (*bottom six panels*)

SCIENTIFIC AMERICAN ONLINE Watch a video of Halzen discussing IceCube at ScientificAmerican.com/oct2015/ice-cube

Illustration by George Retseck

signatures of dark matter—the invisible material that seems to make up more than 80 percent of all matter in the universe. That notion would be plausible if dark matter were made of very heavy particles with an average lifetime longer than the current age of the universe. In such a scenario, dark matter particles could occasionally decay to produce the PeV-energy neutrinos that we observe.

COUNTING NEUTRINOS

BEFORE THE DISCOVERY of PeV neutrinos, IceCube's search for cosmic neutrinos had almost exclusively focused on one of the three flavors of neutrinos: muon neutrinos (the others are electron and tau neutrinos). Scientists expect cosmic neutrinos to come in roughly equal numbers of the three categories when they reach Earth, but some are easier to look for because of the signal they produce in our detector. We had originally optimized IceCube to search for muon neutrinos that slammed into atoms primarily outside the detector's boundaries, producing kilometer-long light trails that would extend through the detector volume. This technique allows us to essentially expand our neutrino "collecting" area so that it is larger than the volume of the actual detector, but it also opens the door wider for contamination from particles other than cosmic neutrinos, so we must take extra measures to screen out this background.

We also ran another analysis, focused on searching for a particular class of extremely high energy neutrinos called Greisen-Zatsepin-Kuzmin (GZK) neutrinos, which arise from interactions between cosmic rays and photons from the cosmic microwave background, left over from the big bang. Such neutrinos would have energies in the range of exa–electron volts (EeV)—roughly 10^{18} eV.

This second search homed in on a more limited region of IceCube—the inner half of the detector, leaving less room for contamination to get in. The great advantage of confining the search in this way is that the detector can measure the full energy each neutrino deposits in the ice with about 10 to 15 percent accuracy—a big improvement on measurements we can make of neutrinos interacting outside the detector. We have yet to find GZK neutrinos, but this search has turned up plenty of cosmic neutrinos in all three flavors.

Since the discovery of Ernie and Bert, we have found more cosmic neutrinos through both this search method and our original plan of looking for muon neutrinos. Our first year's worth of data revealed 26 neutrinos with energies between 30 and 1,200 TeV, bringing our total to 28 when we include Ernie and Bert. This number is more than four standard deviations above what we would expect purely from the atmospheric background, meaning that the probability is greater than 99.9999 percent that these events truly come from deep space. When we later added an additional year of data, we brought the tally to 54 cosmic neutrinos and raised the significance of the signal to well over five standard deviations, the statistical threshold for a "discovery."

Exactly where in the universe do all these neutrinos point back to? The events we have collected so far are not a large enough sample to provide a conclusive answer. They do not seem to be restricted to our galaxy—the sky map indicating their arrival directions shows only marginal evidence for an overlap with the plane of our galaxy; most come from directions far off the plane and are almost certainly of extragalactic origin. There does, however, appear to be a somewhat higher than average number of neutrinos coming from the center of the Milky Way. Bert, still one of the highest-energy neutrinos observed, is part of that cluster and points to within one degree of the galactic center. We cannot say for sure why this area is spewing out such numbers of neutrinos, but we know the galactic center is packed with supernova remnants, as well as a giant black hole, and thus holds many likely candidates for the neutrinos' source.

IceCube is just beginning to scratch the surface of what it can discover. It is built to operate for 20 years—maybe more.

We hope to gain a better idea of where cosmic neutrinos originate as we steadily collect more muon-flavored neutrinos reaching us through Earth. Because these particles produce kilometer-length light trails, their directions can be reconstructed with better than 0.5-degree resolution, yielding a map of the sky that will be more revealing. This map will show where in the sky cosmic rays are coming from; if their directions happen to overlap with known objects in the sky, such as bright galaxies that host active galactic nuclei or gamma-ray bursts, we may be able to finally pinpoint some of the sources of cosmic rays.

IceCube is just beginning to scratch the surface of what it can discover. The experiment is built to operate for 20 years—maybe more. In the meantime, we are already looking toward its sequel. Our team is proposing to eventually build an expanded detector using roughly 10 cubic kilometers of ice—about 10 times the volume of IceCube. With that increased size, we may collect thousands more cosmic neutrinos to finally determine where they and their cosmic-ray cousins come from. SA

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scientificamerican.com/magazine/sa

THE FAT GENE

A genetic mutation in prehistoric apes may underlie today's pandemic of obesity and diabetes

By Richard J. Johnson and Peter Andrews

IN 1962 A HUMAN GENETICIST NAMED JAMES NEEL PROPOSED A HYPOTHESIS TO SOLVE A VEXING EVOLUTIONARY puzzle. What is now called type 2 diabetes—which he thought was caused by a single variant of some unidentified gene—can cause debilitating symptoms, including blindness, heart disease and kidney failure. It can also affect people in their reproductive years. In ancient humans, when no treatments were available, those features could have kept afflicted individuals from finding a mate, having children and passing the disease-causing gene down to future generations. In other words, natural selection should have eliminated the gene and, thus, the disease.

Yet the disorder was common and growing more so. How could people with such a debilitating gene have survived, Neel wondered, and why was diabetes, which is defined by the presence of abnormally high levels of the sugar glucose in the blood, becoming more prevalent?

Neel spent much of his time studying indigenous populations such as the Yanomami in the Amazon, who presumably had the same diabetes-related gene variant in their gene pool as other modern humans yet were almost never diabetic or fat. (Obesity increases risk for type 2 diabetes.) The contrast between native people and those in developed societies gave him an idea. In the distant past, he argued, there were most likely times when food was in short supply, causing hunger or even widespread famine. People with a gene variant that made their body particularly

Illustration by Tim Bower

"efficient in the intake and/or utilization of food," Neel wrote, would have socked away more of the scarce calories as fat. That extra fat would have given individuals with this so-called thrifty gene a survival edge in times of famine. In times of plenty, though, such as today, the same trait would lead to excessive weight gain and diabetes.

The thrifty gene hypothesis has drawn criticism, but it has endured in one form or another for half a century. The idea that our body can be genetically programmed to store fat and that our rich modern diet and sedentary ways can send this program into overdrive has prompted a good deal of research into possible thrifty genes at the root of diabetes and other obesity-linked diseases: hypertension (high blood pressure), nonalcoholic fatty liver disease and heart disease. But critics of the hypothesis have argued that starvation in ancient humans happened too rarely and was over too quickly to select for genes that favor fat storage and that no definitive thrifty genes have been found.

Recently, though, the two of us have looked deeper into our evolutionary past and found solid evidence confirming the essence of Neel's hypothesis—that a mutation in a single gene made modern humans thrifty with calories. This mutation arose in ancient apes millions of years ago and in so doing, we think, enabled them to survive long periods of hunger. If we are correct, our hypothesis could also help reveal how those apes evolved into the earliest human ancestors, and it may pinpoint a gene that is behind many of the major diseases of modernity.

Richard J. Johnson is a professor of medicine at the University of Colorado Anschutz Medical Campus in Aurora, Colo. His research focuses on the underlying causes of obesity, diabetes, hypertension and kidney disease. He is author of more than 500 research articles and two lay books, *The Sugar Fix* (Rodale, 2008) and *The Fat Switch* (Mercola.com, 2012).

Peter Andrews is an emeritus research scientist at the Natural History Museum in London and a professor in the department of anthropology at University College London. He has described many new genera and species of fossil apes and was among the first to propose that the ancestors of today's great apes and humans evolved outside of Africa.

BACK TO AFRICA

AT FIRST NEEL AND OTHER SCIENTISTS assumed that a thrifty gene appeared when ancestral humans were roaming the plains of East Africa. But our story starts much earlier, when apes were relatively new to the planet. It's a tale of global climate change, famine and a struggle for survival.

The earliest apes evolved from a common ancestor with monkeys, probably in East Africa around 26 million years ago. Those apes, the best known of which is *Proconsul,* walked on all fours and lived in trees like monkeys but had a big body, no tail, and a larger skull and brain. At the time, Africa was a tropical Eden, full of deciduous woodlands and rain forests, where the apes feasted primarily on fruit. The apes living there thrived and diversified, with as many as 14 ape species identified from the fossil record.

The world, though, was gradually cooling. The polar ice caps expanded, and sea levels fell. By 21 million years ago Africa, which had been an island continent like Australia and Antarctica today, became connected to Eurasia by the first of a series of land bridges. Giraffes, elephants, antelope and even aardvarks migrated from Africa to Eurasia, according to fossil digs by one of us (Andrews) and others in Turkey, Germany and Spain. Apes were among the emigrants. By 16.5 million years ago apes such as *Griphopithecus* and *Kenyapithecus* were living at a site near the modern-day Turkish village of Paşalar.

In Europe the newly arrived apes flourished at first in subtropical evergreen forests and moist, broadleaf woodlands, in part because fruit was plentiful. They diversified into at least eight species in five genera, including *Dryopithecus* and *Ankarapithecus.* Andrews and his colleagues concluded from 16.5-million-year-old deposits near Paşalar that seasonal climate resembled that of northern India now, with summer monsoon rains followed by long, dry periods and cool, frost-free winters.

As global cooling continued and the climate got drier, forest gave way to savanna, and fruit became scarce in the winter months. Through fossil digs conducted in the 1980s and 1990s, Andrews found evidence that the fossil apes were living on the ground rather than in trees, which would have helped them range farther and forage more effectively. Studies of the wear on fossil teeth and thickening of their enamel suggested to him that the hungry apes had turned to fallback foods such as tubers and roots.

Eventually the European apes began starving during the winter. In Paşalar, Andrews and Jay Kelley, now at Arizona State University, found young adult *Kenyapithecus kizili* fossils whose incisors displayed telltale striations that reveal intermittent dietary stress or starvation. Other paleontologists discovered that *Dryopithecus* apes, which lived 12 million to nine million years ago in the Vallès-Penedès basin in Spain, also had striations on their teeth. All the time, it kept getting cooler, and by about seven million years ago the European apes had disappeared.

Or so it seemed. Fossil evidence now suggests that some European apes journeyed to Asia and became the ancestors of gibbons and orangutans, whereas others returned to Africa and evolved into African apes and humans. One likely candidate for the move from Eurasia to Africa is *K. kizili,* which had similar teeth and jaws to those of *Kenyapithecus wickeri,* an ape that lived in East Africa two million years later.

Genetic evidence confirms the fossil evidence of hard times in Europe, and together the two lines of evidence led us to revive the

IN BRIEF

Fossil evidence shows that apes thrived beginning around 16 million years ago in then subtropical Europe. Global cooling subsequently changed the forest, making the fruit they ate scarce.

A mutation in a gene called uricase helps to convert fruit sugar (fructose) into fat, which enabled the European apes to survive famines.

Persistence of the same mutation in all modern great apes and all modern humans, along with the fossil evidence, implies that the now extinct European apes evolved into today's great apes and the earliest hominids.

The uricase mutation predisposes humans to obesity and diabetes today. The results suggest a need to eat and drink much less fructose to fight obesity and prevent its dangerous complications.

thrifty gene hypothesis in its new form. Our hypothesis centers on a gene that in many animals gives rise to an enzyme called uricase. In all modern great apes (gorillas, orangutans, chimpanzees and bonobos) and all modern humans, however, the gene is mutated, blocking uricase production. In addition, both groups possess the same mutant form of the gene, which is a sign that humans inherited the gene from a common ancestor we share with the great apes. By analyzing changes that occurred in the uricase gene over evolutionary time employing a method known as the molecular clock, Naoyuki Takahata of the Graduate University for Advanced Studies in Hayama, Japan, and his colleagues and, independently, Eric Gaucher of the Georgia Institute of Technology determined that the common ancestor of great apes and humans lived between 17 million and 13 million years ago—the same tumultuous time period when European apes were struggling to survive seasonal famines.

A different mutation separately silenced the uricase gene in the ancestors of lesser apes (gibbons), which probably lived in Europe at about the same time. Together these finds suggested to us that disabling uricase helped ancient European apes to survive famine. The question was, How exactly did it help?

GOOD TIMES, BAD TIMES

A CLUE TO HOW THE URICASE MUTATION might prevent starvation in times of famine ultimately came from a separate line of research into the roots of high blood pressure and heart disease. In most animals, uricase breaks down a substance called uric acid, which is a waste product produced when some foods are metabolized—that is, converted to fuel and raw materials needed by cells. The ancient mutation in the apes would have crippled the enzyme and thus would have caused uric acid to build up in the blood.

At first blush, this buildup would seem harmful rather than helpful because excess uric acid can precipitate as crystals in the joints to cause gout or in the kidneys to produce stones. Under normal conditions, however, humans and apes can excrete uric acid in urine quickly enough that the mutation would have elevated uric acid levels only moderately. Indeed, modern African apes do in fact have slightly higher uric acid levels than other animals, as do indigenous humans who have retained their ancient way of life, such as the Yanomami.

In societies with Western diets and sedentary habits, however, average uric acid levels are soaring. Physicians also know that obese people and patients with heart disease have higher uric acid levels in their blood than lean, fit people, just as they often have elevated cholesterol and triglycerides.

The authors of the influential Framingham Heart Study had monitored patients for decades and used statistics to identify which of these substances truly caused heart disease. In 1999 they reported that elevated uric acid did not by itself cause the disease. Instead, they argued, high blood pressure elevated the risk of heart disease, and it also happened to raise uric acid levels.

This conclusion, however, bothered the other of us (Johnson) because the authors had violated a basic tenet in biological science: they had drawn their conclusion without testing their hypothesis on laboratory animals. Marilda Mazzali, a doctor working with Johnson, proceeded to do such a study. Johnson's team had reported a few years before that subtle kidney injuries in rats could cause high blood pressure. Mazzali checked whether raising uric acid levels with a drug that blocked uricase would elevate blood pressure or harm kidney function. In earlier experiments we had found that raising uric acid did not cause any obvious kidney damage, so we predicted that the rise was unlikely to affect either blood pressure or the kidneys. But Mazzali shocked us all when she reported that the rats developed high blood pressure.

Johnson and his colleagues then conducted a series of studies showing that elevated uric acid levels in rats cause high blood pressure via two mechanisms. At first uric acid acts quickly, causing a series of biochemical reactions collectively called oxidative stress that constrict blood vessels, which forces the heart to pump harder to circulate blood and elevates blood pressure. Lowering uric acid reverses this effect. An ongoing excess of uric acid, however, causes lasting low-grade injury and inflammation in the kidneys, which make them less able to excrete salt. This, in turn, causes high blood pressure that can be reversed with a low-salt diet but not by lowering uric acid.

To see if humans respond the same way to elevated uric acid, Johnson and Dan Feig, a pediatric nephrologist then at the Baylor College of Medicine, measured uric acid in obese adolescents with newly diagnosed hypertension, finding to their amazement that it was elevated in 90 percent of them. Then, in a clinical trial, they treated 30 of these patients with a uric acid–lowering drug called allopurinol. The drug restored blood pressure to normal in 85 percent of the patients whose uric acid levels went down significantly. Other pilot studies have replicated the results, which Johnson and Feig reported in 2008 in the *Journal of the American Medical Association*. We will need a large clinical trial, however, before we can trust that lowering uric acid with a drug can ease newly diagnosed high blood pressure.

THE ENDLESS FEAST

BECAUSE HIGH BLOOD PRESSURE tends to follow from obesity and inactivity, Johnson wondered if uric acid was triggering not only high blood pressure but obesity itself. In thinking through this problem, Johnson took the long view. He considered how our evolutionary predecessors, from rodents to apes, adjusted their metabolism as they careened from feast to famine.

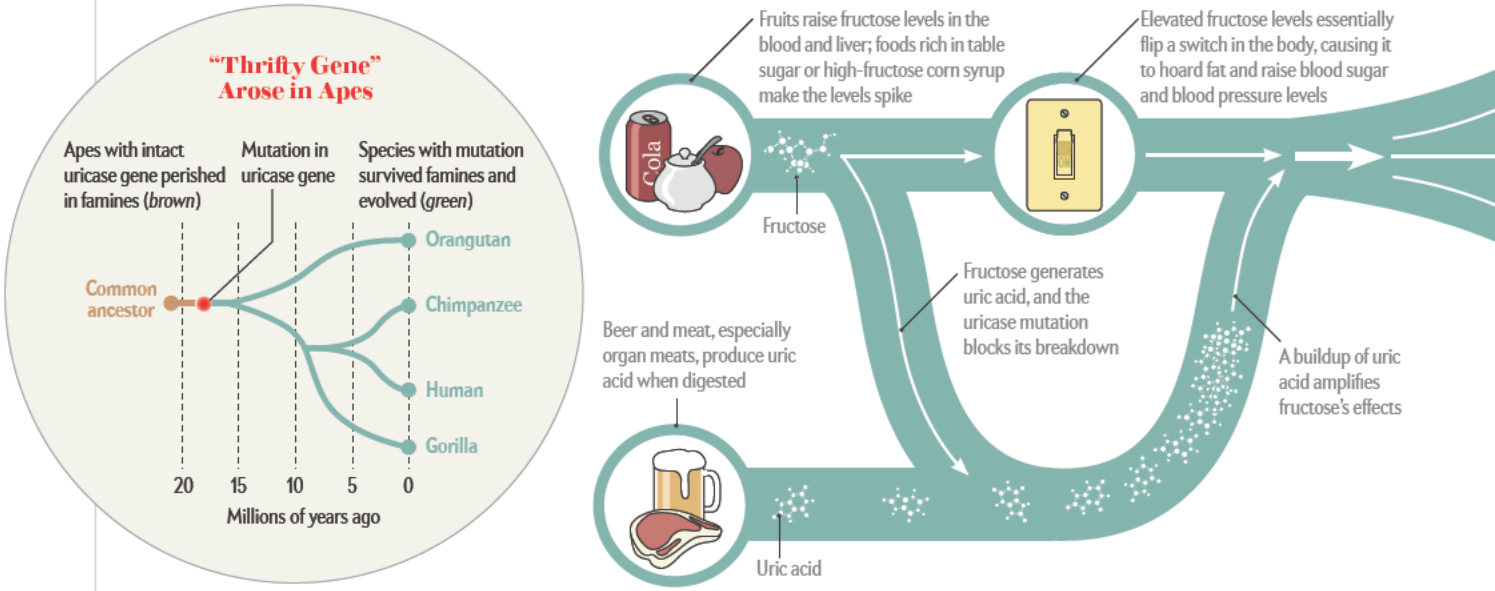
During prolonged food shortages in nature, the rule of thumb is survival of the fattest. Mammals increase their fat reserves to increase their odds of surviving hibernation, birds fatten up to survive a long migration and the Emperor penguin puts on pounds to nest during a tough winter. And when these animals sense hard times approaching, they are driven to forage, gorge and fatten themselves.

Birds and mammals also switch naturally at these times into a prediabetic state. Normally when the body digests carbohydrates, it produces glucose, which accumulates in the bloodstream. The pancreas responds by releasing insulin, which signals the liver and muscles to convert glucose into a starchlike energy-storage molecule called glycogen. When food is scarce, though, animals must persist in their foraging to survive, and their brain requires a steady supply of glucose to do so. For this reason, hungry animals from squirrels to warblers undergo a metabolic change that makes the body's cells start ignoring insulin's prompts. This "insulin resistance" keeps scarce glucose in their blood to supply their brain.

Johnson and others realized that there must be a kind of switch that alerted the animal's body to both get fat and become prediabetic, and he took to calling it "the fat switch." Because

A Jekyll-and-Hyde Mutation

The authors propose that a gene mutation in an ape species millions of years ago helped the animals to survive food shortages that felled other apes. The survivors then passed the mutation to later species that diverged from them, ultimately including humans (*lineage below*). The mutation, in a gene that encodes the enzyme uricase, favored survival during food shortages because, among other effects, it made the body "thrifty" with food—causing it to store calories as fat rather than burning them for energy on the spot. Today, though, when food is plentiful, the mutation may well contribute to obesity and disease (*diagram*).



birds, bears and orangutans gorge on fruit to store fat for lean times, he suspected that fruit sugar (fructose) might flip that switch. Experiments on mice by Takuji Ishimoto and Miguel Lanaspa, both then in Johnson's lab, showed that it did. Mice on a high-fructose diet eat more and move less than mice with a healthier diet, and they tend to accumulate fat. This buildup happens in part because fructose blunts the effect of the hormone leptin, which tells the brain it is time to stop eating.

Fructose, unlike other sugars, produces uric acid when it is broken down inside cells, and Johnson wondered whether the uric acid might mediate some of fructose's effects. To find out, Takahiko Nakagawa, then in Johnson's group, fed rats a high-fructose diet and gave half of them allopurinol to lower uric acid. The drug lowered the rats' blood pressure, confirming earlier results from the group. At the same time, it blocked many of the features of metabolic syndrome, a cluster of conditions that include low blood levels of HDL (the "good" cholesterol), high blood glucose, elevated triglycerides, excess belly fat and high blood pressure. And in a separate study on lab-grown human liver cells, the researchers found that lowering uric acid could prevent cells from turning fructose into fat.

A clear picture was emerging. A diet high in fructose flips the fat switch, and the lack of a working uricase in great apes and humans leads to elevated uric acid levels, which amplifies fructose's effects. This combination helps to steer people down the path toward metabolic syndrome, which raises the risk of heart disease, stroke and diabetes.

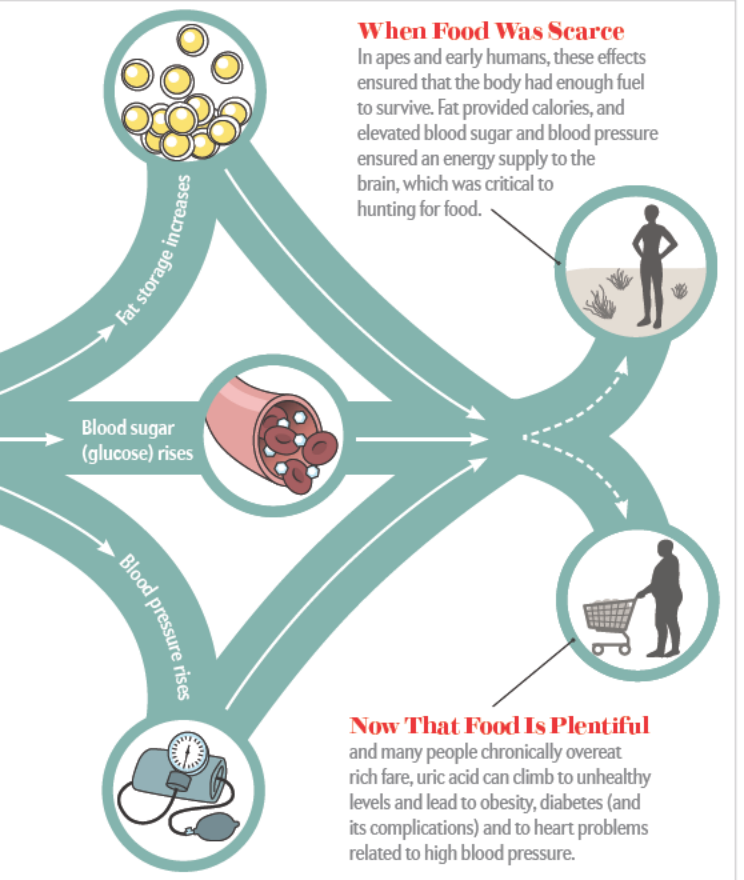
A LASTING CHANGE

IN JUNE 2008, AS THAT PICTURE was emerging, Johnson visited Andrews at the Natural History Museum in London, where Andrews was leading research efforts on ape and human evolution. For hours, we imagined ways that a mutated uricase gene, leading to an absence of uricase, could have helped now extinct apes to survive as global climate cooled. Johnson suggested that this lack of a working uricase and the resulting elevated uric acid levels would have helped apes turn fruit into fat and given them a survival advantage as winters became cool and dry beginning 15 million years ago, in the mid-Miocene. Andrews then provided an important insight. Although Africa was cooling, it was still hot enough to support tropical fig trees that were widespread and produced fruit throughout the year. African apes would thus have been able to eat fruit, especially figs, year-round, as chimps, gorillas and orangutans do now. But as Europe cooled from subtropical to temperate, fig trees grew scarce and stopped fruiting in winter. As a result, European apes regularly went hungry.

We hypothesized that a mutation that disabled uricase would have enabled the European apes to convert fructose into fat for lean times. The descendants of those apes would have carried that mutation to Africa a few million years later, better equipped to survive famine than whatever African apes remained. If those ancient European apes then outcompeted African apes of the era, they are the most likely ancestors of today's African apes—and of humans. And the mutated gene that produces uricase is James Neel's long-sought thrifty gene.

SOURCE: "EVOLUTIONARY HISTORY AND METABOLIC INSIGHTS OF ANCIENT MAMMALIAN URICASES," BY JAMES T. KRATZER ET AL., IN *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA*, VOL. 111, NO. 10; MARCH 11, 2014 (*timeline*)

SCIENTIFIC AMERICAN ONLINE Hear an interview with Johnson at ScientificAmerican.com/oct2015/obesity



OPEN QUESTIONS

DESPITE THE EXTENSIVE EVIDENCE we and others have gathered, our hypothesis that the silenced uricase gene is a thrifty gene is not yet proved. Some researchers have searched extensively for thrifty genes by seeking human genetic polymorphisms (variants of genes) that explain the epidemic of obesity and diabetes. They have found some that predispose people to these conditions but none that can explain the epidemic. A hunt for polymorphisms, though, would miss the silenced uricase gene because it does not vary; all humans have it. Skeptics have also argued that a thrifty gene would have evolved only if being fat offered ancient humans an advantage. But the silenced uricase evolved millions of years ago to help prevent the ape ancestors of humans from starving, not to make them fat.

Still others say that if we all had a thrifty gene, then obesity would be much more common in humans today. On its own, though, a silenced uricase only mildly increases blood uric acid levels, according to Johnson's studies on great apes and the Yanomami on their native diets. Instead, we propose, the gene enables uric acid levels to spike in response to two types of foods in the Western diet: those, like beer, that produce uric acid, and those that contain or produce a lot of fructose. The latter include honey and processed foods that are high in table sugar or high-fructose corn syrup (which each contain glucose and fructose). And when uric acid levels spike, we become far more susceptible to obesity and diabetes.

In 2014 Gaucher, James T. Kratzer, then on Gaucher's team, and Lanaspa on Johnson's team reported some of the strongest lab evidence yet fingering the mutant uricase as a thrifty gene. After deducing the DNA sequence of uricase genes from long-gone primates, mammals such as pigs, rats and dogs, and their common ancestors, they engineered human liver cells to produce the corresponding enzymes. The ancient uricases became less and less active as ancestral apes evolved until they were crippled entirely in the common ancestor of humans and great apes, they reported in 2014 in the *Proceedings of the National Academy of Sciences USA*. This loss would have made apes and humans better at storing fat and at releasing glucose to supply the brain, and it would have given them a survival edge when food was scarce.

The ultimate test of our hypothesis, however, will come from trials that lower uric acid levels in humans. Pilot trials so far have shown that reducing uric acid with an antigout drug can lower blood pressure, reduce insulin resistance, slow kidney disease and prevent weight gain. But larger trials are still needed to prove that the mutant uricase is in fact a thrifty gene.

SLASHING SUGAR

IF CRIPPLED URICASE IS THE THRIFTY GENE, then preventing obesity, diabetes and heart disease might require treating elevated uric acid as well as treating high cholesterol or elevated triglycerides. Down the line, it might even be possible to use new gene-editing methods to reclaim human uricase so we can break down uric acid more effectively rather than simply excreting it.

Until then, however, we can keep weight off and prevent diseases by exercising and adopting a healthier diet. Honey and table sugar both supply fructose, and for thousands of years, wherever wealthy people ate them, they became fat and often developed gout. In recent decades, as we have added more and more table sugar and high-fructose corn syrup to packaged foods, obesity and diabetes have skyrocketed and average uric acid levels in our blood have increased. By cutting way back on our fructose intake—and getting most of it from fresh fruit, which has substances such as vitamin C and antioxidants that can neutralize the effects of fructose and uric acid, we should be able to protect ourselves from multiple diseases. For such reasons, the American Heart Association, after weighing the science, has recommended slashing sugar intake to six teaspoons a day in women and nine teaspoons a day in men. Even less would be healthier.

Five decades after Neel's pioneering work, we may now know the identity of at least one of his thrifty genes, and it could well have had a large hand in today's twin epidemics of obesity and diabetes. Thrift is indeed a virtue, but when it comes to metabolism, there can be too much of a good thing. SA

MORE TO EXPLORE

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FROM OUR ARCHIVES

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Illustration by Amanda Montañez

ARCHAEOASTRONOMY

STARS OF THE DEAD

Mysterious tables of astronomical information have been found in 4,000-year-old coffins. What in the world was their purpose?

By Sarah Symons and Elizabeth Tasker

The Egyptian town of Mallawi is not on the main tourist beat, given its location 260 miles and a seven-hour train ride north of the temple complexes at Luxor. But one of us (Symons) traveled there in May 2013 with Robert Cockcroft, a postdoctoral researcher in her laboratory, hoping to see one of the oldest astronomical records in the world. The record, which had been described only vaguely, was indeed there, but to their astonishment, it was not the only one.

"I can see writing!" Cockcroft exclaimed. At that moment, he was crouched beside a display case that enclosed a coffin in the central room of the Mallawi Monuments Museum, craning his neck to peer at the underside of the propped-up wood lid. Symons flicked the beam of her flashlight to illuminate a thin batten—a cross piece—that held the flat panels of wood together. The batten's surface was painted with graceful hieroglyphics representing star names, and Symons and Cockcroft immediately realized that the cross piece was part of yet another ancient astronomical record. Until that moment, no one had recognized the batten's significance; it had been attached to this particular coffin by mistake.

Archaeologists first began discovering these intriguing coffin records in the 1890s while exploring tombs in the nearby burial complex at Asyût. After opening up certain rectangular caskets that held the mummified remains of local nobility, the explorers found very specific designs on the inside lids instead of the plain wood or the extracts from religious texts seen in most ancient Egyptian coffins. These special drawings depict an organized table of star names, recording the movements of selected stars, such as Sirius, throughout the year.

As a historian of science, Symons has spent the past 20 years cataloguing and analyzing these astronomical tables. Depending on how one counts certain fragments, only 27 have come to

IN BRIEF

Ancient Egyptians paid close attention to the movement of certain stars in the nighttime sky.
Records of their observations have been found in astronomical tables inside several 4,000-year-old coffins.
Long thought to serve as a kind of clock for the proper timing of religious rituals at night, these star tables may, recent research suggests, actually have acted more as a map for directing the dead to new realms of existence in the afterlife among the stars.

Photographs by Ferit Kuyas

DETAIL of a 4,000-year-old astronomical table found on the underside of a coffin lid in Egypt shows deities of the skies (*large images*) and offerings to gods (*horizontal strip*) in the center. The flanking columns each list stars that astronomers monitored during a given week of the year.

light, of which just one is not from a coffin: it adorns the ceiling of a temple. Most of the tables date from about 2100 B.C. By examining these and other ancient hieroglyphics and taking advantage of sophisticated planetarium software, she hopes to reconstruct how and why the Egyptians developed the tables and discern the observational methods used to construct them. Her work so far casts doubt on the prevailing view of why Egyptians of the Middle Kingdom period constructed the charts and may ultimately help clarify what these Egyptian astronomers did and did not know about the stars that filled their skies.

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Elizabeth Tasker is an assistant professor at Hokkaido University in Japan. Her work concentrates on science communication and exploring the formation of galaxies, stars and planets in a computer-simulated universe.

STAR CLOCKS?

THE EXCAVATORS who found the charts knew that they depicted stars, but not until the 1960s did anyone put forward a comprehensive hypothesis to explain what the tables may have represented and what their function was. In a three-volume work entitled *Egyptian Astronomical Texts,* science historian Otto Neugebauer and Egyptologist Richard A. Parker described the 13 tables that had been recovered by that time and proposed that they traced the order in which selected stars (or small clusters of stars) first rose over the eastern horizon during the nights of each week throughout the year. They speculated this information was recorded to tell the time during the night. Someone noting which star was on the horizon at any given moment would have a sense of how much time had passed since sunset, and so Neugebauer and Parker referred to them as star clocks.

Such clocks, if they were also available somewhere other than the hidden surface of coffin lids, could have been important to priests of the time. According to Egyptian mythology, the sun undergoes a dangerous journey during the night, when it must overcome multiple obstacles. By performing specific rituals at key moments during the dark hours, priests could mirror the sun's journey and provide assistance.

Neugebauer and Parker's description of the star tables was certainly consistent with such a use. A complete table is divided into quarters by a horizontal and a vertical strip. The horizontal strip contains a line from a religious text making an offering to a number of Egyptian gods, and the vertical strip pictures four images of the gods themselves. What drew Neugebauer and Parker to the idea of a clock is that running along the top of the table is the ancient Egyptian civil calendar [*see box on pages 74 and 75*].

Each month in the ancient Egyptian civil calendar contained three 10-day weeks; 12 months followed by five days make up the 365-day year. A complete star table, read from right to left, consists of 40 columns, where the first 36 columns each denote one "week." The next three columns show a complete list of all the names of stars described in the chart (represented by the numbers 1 through 36), and the final, 40th column represents the remaining half week in the civil year. Because a different star heads the top of the column corresponding to each 10-day week, the stars are today called decans, from the Greek word *deca,* meaning "ten."

Every column of decans consists of 12 rows, where the vertical placement, Neugebauer and Parker argued, reflects the order in which the decans appeared over the horizon in the night sky. (Thus, each row represents a different "hour" of the night.) The topmost cell contains the name of the decan that rises in the east shortly after the sun sets. (In the sky, the star then moves west across the sky as the night progresses.) The next

STAR TABLE shown on the preceding page is displayed at the University of Tübingen Museum, where it is mounted on the wall above the coffin it adorned.

11 decans then rise behind it in the order they are listed down the column. Ten days later, week two of the civil calendar begins, and the sky has changed; now a different decan—decan 2—rises with sunset, so it appears at the top of that week's column. The result is a diagonal pattern of decans, where the same decan moves in a diagonal line from bottom right to top left as it rises steadily earlier over the year.

If the year were exactly 360 days, the pattern in the star charts would form a seamless cycle of 36 decans. After the 36th decan had risen in the night sky, the first decan would reappear behind it the following week. The half week of the remaining five days in the year prevents this procession, however. To cope, Neugebauer and Parker concluded, the ancient Egyptians recorded the motions of an entirely new decan set. As these new decans marched diagonally up the table, they collectively formed a triangular shape at the left-hand side of the table.

In schematic representations of the tables, researchers label

the triangle decans differently from the others—with letters, rather than numbers. But the drawings on the coffins themselves give no indication that the Egyptians considered the triangle decans to be of more or less importance than the other 36 decans. Other astronomical depictions on temple and tomb ceilings (of a design that is probably contemporary with the coffin tables), however, made the distinction, which has led to debates among Egyptologists about which came first—the idea of 36 "perfect" decans processing regularly across the sky from east to west or the actual observations of various real stars in their more complex annual journeys.

In any event, the presence of the triangle confirms that the tables are the result of real astronomical observations. The extra level of complication introduced by the additional decans argues against the tables being simply an idealized model of the cosmos.

COMPLICATIONS

DESPITE THE ELEGANCE of Neugebauer and Parker's explanation of what the charts showed, their scheme left a number of big questions. One problem, recognized in the 1960s by Neugebauer and Parker themselves, was raised by the realization that the star tables they knew about were not all alike.

To the untrained eye, the format of all tables looks identical, with a layout of ordered columns populated by many of the same decan names. A closer comparison, however, reveals that they fall into two major groups in which the decans are shifted by several columns. Neugebauer and Parker suggested that the variance stemmed from the absence of a leap-year system in the civil calendar. If ancient table makers, ignoring the extra quarter day a year, made two tables 40 years apart, 40 quarter days of slippage would mean the later table had star positions shifted by exactly one 10-day week, or a movement of one cell per decan. Neugebauer and Parker assumed that if more star tables or related documents were uncovered, examples of layouts in between the then known groups would appear.

But work by Symons raises doubt about this thesis. She has studied directly or examined photographs of all the known star tables, including ones discovered after the 1960s. Every one falls into one of the two groups now accepted by Egyptologists, with none showing an alternative pattern of decans. Moreover, the separation between matching pairs of decans varies; a leap-year progression would move all decans together and preserve their spacing.

Neugebauer and Parker also could not be certain that the charts actually tracked the rising of stars on the horizon, as their scheme suggested. Symons's analyses have revealed some alternative possibilities that seem equally feasible. Her clues come from inconsistencies between the two table types that go beyond decans shifting their columns. The order of appearance of some decans, for instance, differs as well, and she has some tools at her disposal that Neugebauer and Parker did not.

Symons has access to powerful planetarium software that can roll back the millennia to display the night sky above ancient Egypt. When we look at the night sky today, Earth's axis of rotation points approximately at the star Polaris. But the axis actually wobbles very slowly in a circle about every 25,800 years. Therefore, although the overall behavior of the sky has not changed (the sun still rises in the east and sets in the west) and the relative positions of the stars to one another has not changed, the wobble means that everything in the sky is in a different place as compared with where it was 4,000 years ago.

Having an accurate, moving view of the ancient sky can help offer explanations that are otherwise hard to visualize. Researchers can describe the old positions of the stars mathematically, but the equations are long and complex. A computer model performs the calculation automatically, at the click of a button.

As the planetarium software helps to make clear, the inconsistencies between the two groups of tables can most easily be explained if the stars were observed using two different methods. The computer simulation shows that all stars that rise at the same time along the eastern horizon—as viewed from anywhere in Egypt—will set at different times on the western horizon because of Earth's tilt relative to the celestial sphere. This feature of stellar movement would serve to distort or even jumble the order of decans somewhat if a table tracked the setting of decans; the movement seen in the two different types of star tables is consistent with one set representing the rising and the other the setting of stars.

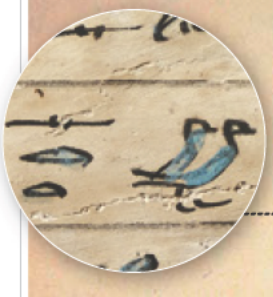
Planetarium software can also be used to check other possibilities and eliminate ones that do not work. An alternative explanation for the differences between the two groups of tables could be that the stars were being observed from two different locations within Egypt. Comparing planetarium simulations at different latitudes with the real tables strongly suggests that this was not what happened. Observations would have to have been made at the far northern coast of Egypt and deep into the extreme south for the latitude of these observations to make enough of a difference to match the surviving tables.

Simulation has its limits, however. The rising-and-setting scenario works, but so do variants, such as imagining that the "horizon" used was not the natural horizon but the edge of a wall or a point above a particular tree. The models, for all their computing power, can only mesh with the available data and are therefore best suited at present to excluding possibilities rather than attempting to "prove" what actually happened.

The same limitations apply when trying to use planetarium software to identify which stars in our own sky the ancient decan names represent. So far computer simulations have confirmed that one of the decans was the star Sirius (transliterated from the hieroglyphs as *spdt* and pronounced and written as *Sopdet*), the brightest star in the sky then as now and an important celestial object in Egyptian astronomy. A few people have come up with plausible identifications of other stars that were monitored, but the level of confidence varies from decan to decan.

Most researchers think that the decan *Khau* denotes the Pleiades, a supposition that is supported by the software as well. *Tjemes en Khentet* is probably a red star because *tjemes* means "red"; that phrase and the location of the decan in relation to Sirius/Sopdet, the computer program shows, are therefore consistent with Antares. Beyond those fairly obvious deductions, however, any historian of ancient Egypt could argue for this star or that and not agree with the opinions of others, because each researcher would have different ideas about what the Egyptians would have used as their criteria for selecting a star to be a decan. Where precisely in the sky should we look to see the rising of a star? Due east? Within five degrees of east? Within 10 degrees? Would a star that was bright and familiar but not in exactly the right position have been chosen over one that was

Navigating the Stars



More than 4,000 years ago ancient Egyptians observed the night sky and made complex tables listing the order in which certain stars appeared or disappeared over the horizon. Some researchers believe these charts were used to keep track of time after sunset. Sarah Symons, on the other hand, suspects the tables—most of which have been found inside coffins—were meant to help the newly deceased find their way to a new home in the sky. The idealized depiction below shows how a table that focused on rising stars would have worked.

ORIGINAL HIEROGLYPHS, such as this one, are replaced with numbers and letters.

THREE SEASONS (Akhet, Peret and Shemu) are divided into four months of three weeks each.

List columns				IV She						III Shemu						II Shemu						I Shemu				IV Peret						III Peret			
A	25	13	(1)	36	35	34	33	32	31	30	29	28	27	26	25	24	23	22	21	20	19														
B	26	14	2	A	36	35	34	33	32	31	30	29	28	27	26	25	24	23	22	21	20														
C	27	15	3	B	A	36	35	34	33	32	31	30	29	28	27	26	25	24	23	22	21														
(D)	28	16	4	C	B	A	36	35	34	33	32	31	30	29	28	27	26	25	24	23	22														
E	29	17	5	D	C	B	A	36	35	34	33	32	31	30	29	28	27	26	25	24	23														
F	30	18	6	E	D	C	B	A	36	35	34	33	32	31	30	29	28	27	26	25	24														
Strip of text with religious offerings to gods																																			
G	31	19	7	F	E	D	C	B	A	36	35	34	33	32	31	30	29	28	27	26	25														
H	32	20	8	G	F	E	D	C	B	A	36	35	34	33	32	31	30	29	28	27	26														
I	33	21	9	H	G	F	E	D	C	B	A	36	35	34	33	32	31	30	29	28	27														
J	34	22	10	I	H	G	F	E	D	C	B	A	36	35	34	33	32	31	30	29	28														
K	35	23	11	J	I	H	G	F	E	D	C	B	A	36	35	34	33	32	31	30	29														
L	36	24	12	K	J	I	H	G	F	E	D	C	B	A	36	35	34	33	32	31	30														

EXTRA DAYS: The 360-day table needs five additional days to complete a year. The stars for these days are shown in the final column, which, combined with the three preceding columns, forms a list of all decan names in the star table.

Images of deities associated with the sky

TRIANGLE DECANS, named after the recognizable shape they make.

ORDINARY DECANS

more obscure but rose or set in exactly the right spot for table-making purposes?

Ultimately, if we knew more precisely which stars were used, we could deduce the observational procedure. If we knew the observational procedure, we could guess the stars. The fact that we know neither leaves us having to make assumptions.

Perhaps even more fundamental than the issues raised by having two types of tables is the question of their purpose. As mentioned, Neugebauer and Parker viewed the tables as clocks. The term implies a system akin to modern timekeeping: the tables are an instrument, with a focus on accuracy and a precise delineation of time. This view is inconsistent, however, with the Egyptian treatment of the passage of time generally. Although people in the 21st century consider time as the abstract passing of regular hours, minutes and seconds, the ancient Egyptians did not. Instead, events such as the celestial motions of the sun or stars determined the time of day or night. Midnight or dawn, for instance, would be periods when certain stars were visible or the sun was in a particular region of the sky rather than a single, well-defined instant.

This aspect of the culture runs counter to the view that the charts were developed as a way to keep time accurately, and so the more general term "star tables," rather than "star clocks," now seems more apt. In addition, planetarium software shows that the ancient sky did not always have a bright star exactly where and when you would need one. Furthermore, the stars cannot be seen at all until the sky is dark enough. Overall, the "hours" told by a star clock would be shorter than 60 minutes and would probably be quite irregular. Symons's current view is that the tables are more like almanacs or charts, recording the state of the sky over time, than they are like practical clocks.

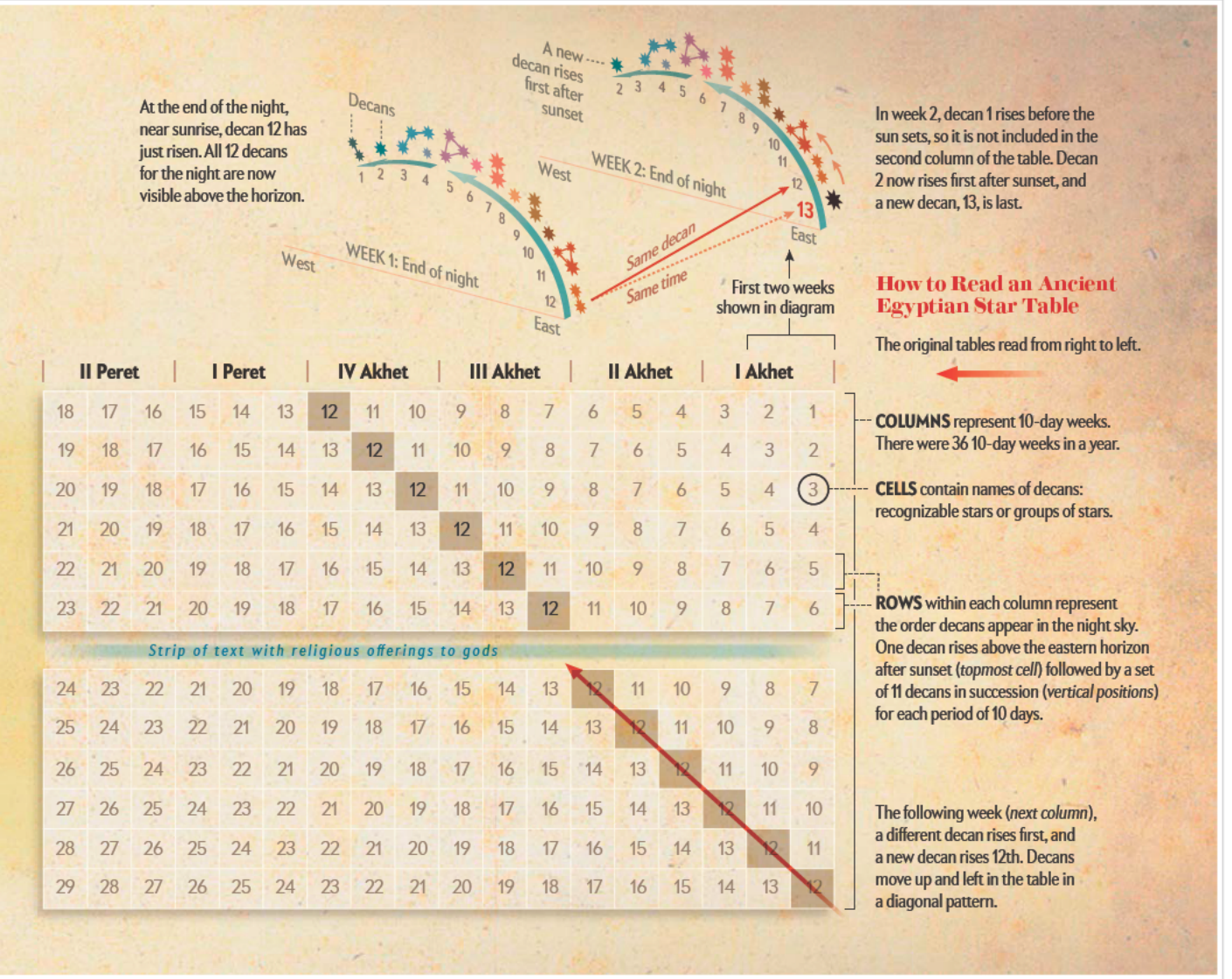
Of course, the obvious remaining question is, Why are the star tables found primarily inside coffins? And why did dead people need to tell the time? Did they need to know how the sky moved?

The probable answer has a lot to do with ancient Egyptian beliefs about the afterlife. Temples, tombs and even coffins were model worlds in which the ceiling or inside lid represented the sky. Furthermore, even some of the earliest religious writings, the Pyramid Texts, contain the notion that souls can be reborn as stars. After death, a pharaoh was thought to become part of the circumpolar stars whose proximity to the northern celestial pole means that they never rise or set; they

FERIT KUYAS (*Hieroglyph at top left*)

SCIENTIFIC AMERICAN ONLINE See a slide show with more photographs of a star table at ScientificAmerican.com/oct2015/star-tables

Graphic by 5W Infographics



are immortal stars. Later thinking could have extended this vision to allow other notable individuals—such as the local gentry around Asyût—to rise as lesser stars whose paths dipped below the horizon at different times of the year. In such a case, the deceased might need the star table to guide them as they rose to join the decans.

DIGITIZING THE PAST

TO FACILITATE FURTHER RESEARCH into the function of star tables, Symons has developed an online database that now contains the information found in all the known examples. This compilation provides researchers with a common base of knowledge for further study and negates the need to maneuver, and thus potentially damage, the fragile coffins.

There is some hope for finding additional tables. New specimens occasionally turn up in archaeological digs in Egypt. Unfortunately, the existing relics are not necessarily secure. Several weeks after Symons and Cockcroft's visit and the discovery of the new fragment, for instance, the museum in Mallawi was looted as part of the civil strife in 2013. Although a number of objects have since been recovered, the current status of the star tables is unknown. Returning to Egypt this year, Symons and Cockcroft were, however, able to complete their survey of the star tables in other Egyptian museums and will continue to document and analyze the astronomical heritage of ancient Egypt. Each new fragment brings additional insight and the possibility of a breakthrough in our understanding of the ancient astronomers' work. All the more reason to carefully preserve what we have and to continue searching for more. SA

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LIFE SCIENCE

The Secret Lives of HORSES

Long-term observations of wild equines reveal a host of unexpected behaviors

By Wendy Williams

WILD AT HEART: Untamed horses roam free in the Pryor Mountains of Montana.

Wendy Williams is a journalist and equestrian based in Mashpee, Mass. She has written for the *New York Times*, the *Wall Street Journal* and *Audubon*, among other publications. *The Horse* is her sixth book.

SOME TIME AROUND 35,000 YEARS AGO, WHEN MUCH OF EUROPE WAS LOCKED UP IN SHEETS of ice, an artist acquired a bit of mammoth ivory and began carving. A masterpiece emerged in the form of a two-inch-long horse. Its magnificently arched stallion's neck combines muscular potency and natural grace. Its head, slightly cocked, gives the animal an air of deep contemplation. One can almost hear him snort and see him toss his head, warning rivals to take care. No one knows who created this miniature marvel, dubbed the "Vogelherd horse" after the cave in Germany in which it was found, but it is clear that this ivory carver spent a lot of time watching wild horses, studying their social interactions and learning their body language.

Sadly, in the modern world, this pastime became something of a lost art. Equine scientists have studied the best way to train show horses, the best way to feed racehorses, the best way to heal the delicate bones in a lame horse's feet. But in contrast to the behaviors of wild chimpanzees, whales and elephants, among other species, the natural ways of horses have rarely garnered scientific interest. And of the few studies that were done, very few were long-term projects.

Recent efforts have begun to fill that gap—with surprising results. Scientists have documented behaviors among free-ranging horses that upend many long-held ideas about how these animals bond and interact with one another.

MARES VS. STALLIONS

HORSES ARE UNUSUAL among hoofed mammals. Many members of this group typically roam in large herds, seeking safety in numbers. Wild horses, in contrast, live year-round in small groups, or bands, of three to 10 individuals. Closely allied mares and their young offspring form the core of the band.

Members of a horse band are not simply group animals with ganglike mentalities. Researchers have found that, as with humans, individual bonds within bands may be more important than group identity. These bonds are sometimes based on family ties, but often they are just based on individual preference. These preferences can and do change: friendships come and go, foals grow up and depart to live elsewhere, male-female relationships sometimes work out and sometimes don't. As a result, the social lives of horses are nothing if not tumultuous. Indeed, long-term observation of these animals in the wild is like following a soap opera. There is a constant undercurrent of arguing, of jockeying for position and power, of battling over personal space, of loyalty and betrayal.

The latest ethological investigations—which is to say, objective studies of behavior under natural conditions—show that these power dynamics are more complicated than previously thought. The conventional view, as described in a recent National Academy of Sciences report, is that "a harem, also known as a band, consists of a dominant stallion, subordinate adult males and females, and offspring." At first glance, this assessment would seem to be true: what people notice when watching wild horses is the uproar created by the stallions. But research by Jason Ransom of Colorado State University and others has shown that this male-centric view is wrong. Far from being subordinate, mares frequently initiate the band's activities. The stallions are quite often little more than hangers-on.

Ransom was once watching a band of mares that stopped grazing and began heading for water. The stallion didn't notice. When he looked up and saw his female companions leaving, he panicked. "He started running after them," Ransom told me. "He was like a little boy calling out, 'Hey, where's everybody going?'" The mares ignored him. Whether the stallion caught up or not didn't appear to concern them.

Mares also sometimes have stallion preferences. They resist males they don't like with surprising persistence, even when that male has established himself as the band's stallion. Joel Berger of the University of Montana studied the behavior of two nonrelated mares that had spent several years together. The pair joined a band that was then taken over by a new stallion that asserted himself by attempting to copulate with them forcibly on numerous occasions. The mares refused his attentions and repeatedly aided one another by kicking and biting the stallion as he tried to mate, Berger observed in *Wild Horses of the Great Basin*. It's long been known that female elephants cooperate, but before

IN BRIEF

Scientists have long studied the best ways to train and treat domesticated horses, but they largely ignored the behavior of free-ranging horses. Recent research has begun to fill that gap. **Observations from** long-term studies of wild horses show that the conventional, male-centric view of their power dynamics is wrong. **In fact, females often** call the shots, employing tactics such as cooperation and persistence to get their way.

PRECEDING PAGES: LISA DEARING

SCIENTIFIC AMERICAN ONLINE See photographs of wild horses at ScientificAmerican.com/oct2015/horses

ethologists began systematically studying free-roaming horses, few people suspected that cooperating mares were capable not only of waging such a fight—but of winning it. Given the truth about mares, "harem" seems like such an old-fashioned word.

Fending off unwanted suitors is not the only means by which mares rebel. For years Laura Lagos and Felipe Bárcena, both at the University of Santiago de Compostela in Spain, have been studying the behavior of Garranos, an unusual type of free-roaming horse. Garranos live rough, tough lives in the rugged hills of northwestern Spain and northern Portugal, where they are under constant threat from wolves. In the course of their work, Lagos and Bárcena catalogued the behavior of a pair of mares in one band that were strongly bonded with each other and that often stood just a bit apart from the rest of the band.

At breeding time, the mares went together to visit the stallion of another band. Lagos watched one of the mares consort with this stallion rather than with the stallion from her own band. Then the mares returned to their original group. When the second mare was ready to breed, the duo again deserted their original band and its stallion to consort with the other stallion. Then, again, they returned to their original group. This was not an anomaly. The mares did the same thing the following year. "They prefer their own territory, but the stallion of the other band," she told me.

PERSISTENCE PREVAILS

UNTIL SCIENTISTS applied ethological research techniques to horses, few observers believed mares to be capable of such subtle deceit. They just weren't looking closely enough. It turns out that, unlike stallions, mares do not need to have huge fights to get what they want. Instead they use the technique of persistence. By way of example, Ransom tells the story of High Tail, a plain-Jane mare with a sagging back and poor coat. High Tail, so named because the dock of her tail sat a bit too high on her croup, is part of a population of wild horses that roam the Pryor Mountains in the American West. If you didn't know her life story, you could easily mistake her for a child's riding pony or a retired plow horse. With her glory days clearly over, you probably wouldn't give her a second glance. Yet Ransom's data showed that this mare had had a rich and varied life that involved a number of long-term male associates of her choosing.

Ransom first caught up with High Tail in 2003. The mare was passing her days in the company of Sam, a stallion born in 1991. Ransom thinks the two probably encountered each other during the wanderings of their youth. They stayed together for years. Eventually other mares joined them, forming a band. Research shows that roughly half the time mares and stallions bond in this peaceful fashion. There's no need for a stallion to "conquer" the mare; she is often a more than willing partner.

Shortly after Ransom began following High Tail and Sam's band, he noticed a second young stallion hanging around a short distance away. Sam did not welcome this new stallion, dubbed "Sitting Bull." The more Sitting Bull tried to become part of the group, the more Sam fought him off. Sam spent a good deal of energy trying to drive away the younger stallion but to no avail.

Whenever Ransom saw High Tail's band during this period, Sitting Bull was usually there, hanging around on the outskirts, stalking the mares and dogging Sam, waiting for his chance to take over. The scientific literature contains accounts of satellite stallions learning how to cooperate with the lead stallion and thus gradually gaining the ability, on a limited basis, to mate with some mares, but this was not the case with Sam and Sitting Bull. The two fought continuously. Still, Sitting Bull stayed near, biding his time.

His chance came in 2004. Horses that live at the base of the Pryor Mountains constantly face the challenge of finding freshwater. High Tail's band often descended the steep walls of the Bighorn Canyon gorge, where they could drink their fill. One day they went down as a group. Sam did not allow Sitting Bull to come along. While the young stallion waited above, the rest of the horses stood on a small ledge and drank. Off in the distance heavy rains broke out. A flash flood inundated the gorge, cutting off the animals' escape route. For about two weeks High Tail and her band, along with Sam, remained trapped without food.

Realizing that the situation was dire, people intervened and helped them escape. The severely emaciated animals managed to climb up out of the gorge. Sam in particular had lost his muscular physique. Almost dead from starvation, he was easy pickings for Sitting Bull, who had hung around above the gorge. When the horses came up, Sitting Bull "just swooped right in and drove Sam off," Ransom says. Sam tried repeatedly to repel his younger competitor, but he was no longer strong enough.

Most of the band accepted the young stallion. Not High Tail. At every opportunity she left her band and headed off in search of her longtime mate, Sam. Each time she left, Sitting Bull chased her back, snaking his head and baring his teeth to threaten her with injury. To avoid being bitten, she complied and returned to the band, but the next time Sitting Bull failed to pay attention, High Tail took off again. This went on for many weeks until the younger stallion gave up chasing her. "From then on it was just Sam and High Tail," Ransom says. "They got their weight back, and at first Sam tried to drive Sitting Bull off and get back with the other mares, but each time he tried, he failed."

High Tail stayed with Sam until he died in 2010. (Because of the stress of constant fighting with other males, stallions often live much shorter lives than mares.) After Sam's death, researchers saw High Tail with a stallion they called Admiral. Eventually Admiral fell out of favor with her. Ransom doesn't know why.

We saw High Tail one afternoon that July. She was with two other horses. One was a mare from her original band, an animal she had known for years. The other was Sitting Bull. Rejected by High Tail in her younger years, he was now one of her boon companions. Primate field researchers long ago discovered the ebb and flow of alliances within primate troops, but until recently no one has watched horses in the wild closely enough to understand that they, too, behave this way. I asked Ransom if he thought there were any hard and fast rules about horse behavior in the wild. "They rarely choose to be alone," he replied. SA

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scientificamerican.com/magazine/sa

RECOMMENDED

By Clara Moskowitz

MORE TO EXPLORE
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Polar: A Photicular Book

by Dan Kainen and Carol Kaufmann. Workman, 2015 ($25.95)

The ground at the earth's polar regions may be frozen, but the stillness stops there. Open *Polar,* and the icy expanses of the top and bottom of the world melt into motion: penguins waddle in packs, snowy owls swoop down on prey and auroras swirl in the nighttime sky (*left*). The reader actually sees the mirage of motion. To craft this illusion, artist Kainen sliced a series of images into thin, vertical strips and arrayed them like a picket fence behind a plane of lenses to create hologramlike, moving collages. Alongside the pictures, writer Kaufmann's lively essays dive into the vital details of each creature and phenomenon depicted. With sly poignancy, the book reminds the reader of the beauty that dwells at the ever shrinking ends of the planet. *—Sabrina Imbler*

The Man Who Wasn't There:

Investigations into the Strange New Science of the Self

by Anil Ananthaswamy. Dutton, 2015 ($26.95)

"From the Buddha to the modern neuroscientist and philosopher, humans have pondered the nature of the self," writes science journalist Ananthaswamy, but the "self" remains largely shrouded in mystery. Here he probes selfhood by exploring neurological conditions that rob people of something we often consider integral to human identity—from body integrity identity disorder (which makes people feel that a part of their body is not their own) to Alzheimer's disease. In each chapter, Ananthaswamy details the neuroscience of the disorder and uses personal stories to illustrate the ailment's often heartrending effects. By framing each condition as a perturbation in a person's sense of self, Ananthaswamy demonstrates how intimately brain functions are linked to identity. *—Maria Temming*

The Only Woman in the Room:

Why Science Is Still a Boys' Club

by Eileen Pollack. Beacon, 2015 ($26.95)

Author Pollack long wanted to become a theoretical physicist, but discrimination, she says, drove her to abandon that dream after college. One of the first two women to earn a bachelor's of science in physics from Yale University, Pollack graduated summa cum laude. But years of ostracism from her male peers and professors, she asserts, hammered in the message: you are not welcome here. Pollack candidly traces the disadvantages she faced as a woman in a world of men. She recounts lonely nights spent struggling through problem sets while male students worked together, and she describes her fights with bulimia, depression and physical tics she says were brought on by her stress at school.

Pollack's book gives painful scrutiny to the relentless opposition that still confronts female scientists and leads many to walk away from the field. *—S.I.*

A River Runs Again:

India's Natural World in Crisis, from the Barren Cliffs of Rajasthan to the Farmlands of Karnataka

by Meera Subramanian. PublicAffairs, 2015 ($26.99)

India is a land of contradictions—it houses both a rapidly rising middle class and a third of the population that lives without electricity. Much of the development that is improving people's lives is also threatening their future by harming India's natural environment. If the nation's progress is to continue, people must find a way to live sustainably, journalist Subramanian says. To illustrate India's challenges and opportunities, she tells five true stories themed around the five elements in Hinduism: earth (organic farming), water (rejuvenating a dried-up river), fire (the quest for smokeless cooking stoves), air (restoring the vulture population) and the abstract ether permeating the space we live in (teaching sexual health to limit population growth).

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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

The Electric Universe Acid Test

Discerning science from pseudoscience

By Michael Shermer

Newton was wrong. Einstein was wrong. Black holes do not exist. The big bang never happened. Dark energy and dark matter are unsubstantiated conjectures. Stars are electrically charged plasma masses. Venus was once a comet. The massive Valles Marineris canyon on Mars was carved out in a few minutes by a giant electric arc sweeping across the Red Planet. The "thunderbolt" icons found in ancient art and petroglyphs are not the iconography of imagined gods but realistic representations of spectacular electrical activity in space.

These are just a few of the things I learned at the Electric Universe conference (EU2015) in June in Phoenix. The Electric Universe community is a loose confederation of people who, according to the host organization's Web site (thunderbolts.info), believe that "a new way of seeing the physical universe is emerging. The new vantage point emphasizes the role of electricity in space and shows the negligible contribution of gravity in cosmic events." This includes everything from comets, moons and planets to stars, galaxies and galactic clusters.

I was invited to speak on the difference between science and pseudoscience. The most common theme I gleaned from the conference is that one should be skeptical of all things mainstream: cosmology, physics, history, psychology and even government (I was told that World Trade Center Building 7 was brought down by controlled demolition on 9/11 and that "chemtrails"—the contrails in the sky trailing jets—are evidence of a government climate-engineering experiment).

The acid test of a scientific claim, I explained, is prediction and falsification. My friends at the NASA Jet Propulsion Laboratory, for example, tell me they use both Newtonian mechanics and Einstein's relativity theory in computing highly accurate spacecraft trajectories to the planets. If Newton and Einstein are wrong, I inquired of EU proponent Wallace Thornhill, can you generate spacecraft flight paths that are more accurate than those based on gravitational theory? No, he replied. GPS satellites in orbit around Earth are also dependent on relativity theory, so I asked the conference host David Talbott if EU theory offers anything like the practical applications that theoretical physics has given us. No. Then what does EU theory add? A deeper understanding of nature, I was told. Oh.

Conventional psychology was challenged by Gary Schwartz of the University of Arizona, who, in keeping with the electrical themes of the day, explained that the brain is like a television set and consciousness is like the signals coming into the brain. You need a brain to be conscious, but consciousness exists elsewhere. But TV studios generate and broadcast signals. Where, I inquired, is the consciousness equivalent to such production facilities? No answer.

A self-taught mathematician named Stephen Crothers riffled through dozens of PowerPoint slides chockablock full of equations related to Einstein's general theory of relativity, which he characterized as "numerology." Einstein's errors, Crothers proclaimed, led to the mistaken belief in black holes and the big bang. I understood none of what he was saying, but I am confident he's wrong by the fact that for a century thousands of physicists have challenged Einstein, and still he stands as *Time*'s Person of the Century. It's not impossible that they are all wrong and that this part-time amateur scientist sleuth is right, but it is about as likely as the number of digits after the decimal place in Einstein's equations accurately describing the relativistic effects on those GPS satellite orbits.

The EU folks I met were unfailingly polite, unquestionably smart and steadfastly unwavering in their belief that they have made one of the most important discoveries in the history of science. Have they? Probably not. The problem was articulated in a comment Thornhill made when I asked for their peer-reviewed papers: "In an interdisciplinary science like the Electric Universe, you could say we have no peers, so peer review is not available." Without peer review or the requisite training in each discipline, how are we to know the difference between mainstream and alternative theories, of which there are many?

In his book *The Electric Kool-Aid Acid Test,* Tom Wolfe quotes Merry Prankster Ken Kesey: "You're either on the bus or off the bus." It's not that EUers are wrong; they're not even on the bus. SA

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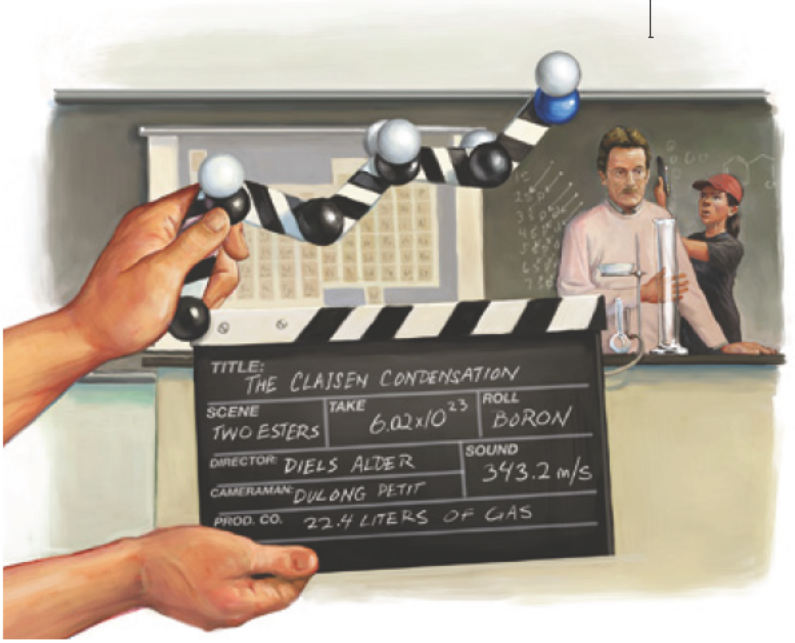
Steve Mirsky has been writing the Anti Gravity column since a typical tectonic plate was about 34 inches from its current location. He also hosts the *Scientific American* podcast Science Talk.



Breaking Bad TV Science

Tech advisers tell STEM-winders

By Steve Mirsky

Donna Nelson, a University of Oklahoma chemistry professor, used to help a notorious drug dealer. Fortunately, the criminal in question was the mythical meth maker Walter White of AMC's *Breaking Bad* fame. "I actually had a lot of concerns," said Nelson at STEM Summit 3.0 on August 4 in New York City, an event sponsored by *Scientific American* and Macmillan Education to foster ideas about teaching STEM: science, technology, engineering and math—including the public communication of science, for example, on television shows. "I was thinking, 'This is going to ruin my reputation. Professionally, I'll be dead.'" (Spoiler alert: Nelson is professionally just fine—she's been elected the next president of the 160,000-member American Chemical Society.)

Nelson was joined at the STEM summit by another TV veteran, John Sotos. If you recognize the catchphrase "It's never lupus," then you'll know that Sotos, who trained as a transplant cardiologist, was the medical consultant for the Fox show *House M.D.* (Hugh Laurie's Gregory House scoffed at the diagnosis because lupus shares symptoms with many other conditions.)

When *Breaking Bad* began in 2008, Nelson saw an article in *Chemical & Engineering News* in which series creator Vince Gilligan appealed to the chemical community for technical help. She was the only expert who responded. Despite the negative subject matter, Nelson decided to volunteer—no fake-drug money exchanged hands. "I considered it a service to the community," she said. "To the science community, not Hollywood. I helped get the science correct, but they already had in mind how they were going to depict the scientist." Not to worry. Bryan Cranston's Walter White may paradoxically be the favorite TV scientist since the Professor on *Gilligan's Island*. No relation to Vince.

Besides, Nelson was primarily signed on to help keep the chemical reactions and structures correct on the blackboards in the high school flashbacks—although she was also consulted about White's signature meth. "Vince asked me what I thought about making the meth blue," Nelson recalled. "And I said I wouldn't do it. And he said, well, wouldn't really pure meth be blue? And I said no, really pure meth would be white. But Walt had to have a trademark. It's fiction—it's not a science documentary."

Nelson also mentioned that the technical consultants for White's Winnebago and the other meth labs were DEA agents. "That wasn't my doing," she made clear. "I do not make meth in my garage. Never have, never will."

While still in medical school, Sotos wrote *Zebra Cards: An Aid to Obscure Diagnosis* (American College of Physicians, 1989). The book's title refers to the diagnostician's adage that when you hear hoofbeats, think horses, not zebras. That is, a runny nose is most likely a run-of-the-mill cold (that's a horse), unless you've been running around a mill, in which case you might have be having an allergic reaction to some unfamiliar dust. There's your zebra.

In 2004, "when *House* came on the air," Sotos said, "I sent them a copy of my book. And they said, 'Why don't you come down and visit the show?'" And so an adviser was born.

Sotos talked about his tasks: "The writer would call and say, 'The patient faints in scene two, and then in scene three we have to find a reason the patient is going to be in the MRI machine.'" At times Sotos came up with theoretically possible scenarios, "never reported in the medical literature but with enough of a justification for us." Also, because of the requirements of each hour's dramatic arc, Greg House, the world's greatest diagnostician, had to be wrong the first four times each episode.

When I asked Sotos, "It's never *ever* lupus?" he revealed that in one episode, which I'd apparently missed, they *did* give the patient that autoimmune condition. Sotos then told the producers, "Hey, we should now have lupus two weeks in a row!" But as any TV doc from Ben Casey to *ER*'s Kerry Weaver knows, it's never lupus on consecutive episodes.

SCIENTIFIC AMERICAN ONLINE
COMMENT ON THIS ARTICLE AT
SCIENTIFICAMERICAN.COM/OCT2015

Illustration by Matt Collins

Chicago Doctor Invents *Affordable* Hearing Aid
Outperforms Many Higher Priced Hearing Aids

Reported by J. Page

CHICAGO: A local board-certified Ear, Nose, and Throat (ENT) physician, Dr. S. Cherukuri, has just shaken up the hearing aid industry with the invention of a medical-grade, affordable hearing aid. **This revolutionary hearing aid is designed to help millions of people with hearing loss who cannot afford—or do not wish to pay—the much higher cost of traditional hearing aids.**

"Perhaps the best quality-to-price ratio in the hearing aid industry" — Dr. Babu, M.D.
Board-Certified ENT Physician

Dr. Cherukuri knew that untreated hearing loss could lead to depression, social isolation, anxiety, and symptoms consistent with Alzheimer's dementia. **He could not understand why the cost for hearing aids was so high when the prices on so many consumer electronics like TVs, DVD players, cell phones, and digital cameras had fallen.**

Since Medicare and most private insurance do not cover the costs of hearing aids, which traditionally run between $2,000-$6,000 for a pair, many of the doctor's patients could not afford the expense. Dr. Cherukuri's goal was to find a reasonable solution that would help with the most common types of hearing loss at an affordable price, not unlike the **"one-size-fits-most" reading glasses** available at drug stores.

He evaluated numerous hearing devices and sound amplifiers, including those seen on television. Without fail, almost all of these were found to amplify bass/low frequencies (below 1000 Hz) and not useful in amplifying the frequencies related to the human voice.

Inspiration From a Surprising Source

The doctor's inspiration to defeat the powers-that-be that kept inexpensive hearing aids out of the hands of the public actually came from a new cell phone he had just purchased. **"I felt that if someone could devise an affordable device like an iPhone® for about $200 that could do all sorts of things, I could create a hearing aid at a similar price."**

- **Designed by a Board-Certified Ear, Nose, and Throat (ENT) Doctor**
- **Doctor-Recommended, Audiologist-Tested**
- **★★★★★Top rated hearing aid online—thousands of satisfied customers**
- **Batteries Included! Comes Ready To Use**
- **FDA-Registered**
- **Save Up To 90%**
- **Free Shipping Available**
- **100% Money-Back Guarantee**

Affordable Hearing Aid With Superb Performance

The high cost of hearing aids is a result of layers of middlemen and expensive unnecessary features. Dr. Cherukuri concluded that it would be possible to develop a medical-grade hearing aid without sacrificing the quality of components. The result is the **MD**HearingAid ***PRO***, well under $200 each when buying a pair. **It has been declared to be the best low-cost hearing aid that amplifies the range of sounds associated with the human voice without overly amplifying background noise.**

Tested By Leading Doctors and Audiologists

The **MD**HearingAid ***PRO*** has been rigorously tested by leading ENT physicians and audiologists who have unanimously agreed that the **sound quality and output in many cases exceeds more expensive hearing aids.**

MDHearingAid® PRO

Proudly Assembled in the USA
from Domestic & Imported Components.

100% Money-Back Guarantee **45-DAY RISK-FREE TRIAL**

BBB A+ RATING ACCREDITED BUSINESS

Doctors and patients agree:
"BEST QUALITY SOUND"
"LOWEST AFFORDABLE PRICE"

"I have been wearing hearing aids for over 25 years and these are the best behind-the-ear aids I have tried. ***Their sound quality rivals that of my $3,000 custom pair of Phonak Xtra digital ITE."***
—Gerald Levy

"I have a $2,000 Resound Live hearing aid in my left ear and the **MD**HearingAid ***PRO*** *in the right ear.* ***I am not able to notice a significant difference in sound quality between the two hearing aids."***
—Dr. May, ENT Physician

"They work so great, my mother says she hasn't heard this well in years, even with her $2,000 digital! ***It was so great to see the joy on her face.*** *She is 90 years young again."*
—Al Peterson

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Use Offer Code CE58 to get FREE Batteries for a Full Year!

FREE Shipping Available

October 1965

Protein from Oil

"In a pilot plant at Lavera in France, substantial amounts of high-grade protein are being produced by microorganisms growing on a diet consisting mainly of petroleum hydrocarbons. This unusual concept, tested by a research team of the Société Française des Petroles BP, has proved so successful that there is good reason to believe petroleum will become an important food resource for the earth's growing population. Why turn to petroleum to solve the food problem? After all, the store of petroleum in the earth is limited. We have calculated that with an outlay of some 40 million tons of petroleum (a small fraction of the 1.25 billion tons of crude oil produced in 1962) 20 million tons of pure protein could be produced per year. For comparison, consider sea fishing. At present it brings in some 40 million tons of fish a year, representing about six million tons of pure protein."

October 1915

Arctic Explorer

"Vilhjalmur Stefánsson has come out of the ice floes of the north with a tale of new found land, and hardly waiting to send word to the world that thought him dead, he has again set face to the north, where nameless mountains and an unguessed shore line await him. This statement means more than the words alone would indicate; it means that victory has been wrung from defeat and overwhelming misfortune, and that when the last story is written, the names of the lost will be joined to a successful undertaking. It is safe to say that no Arctic expedition has triumphed over as great an initial handicap as that sustained by Stefánsson's party in the tragic destruction of the 'Karluk,' with the subsequent loss of eleven lives."

Cretaceous Park

"The American Museum of Natural History in New York City now exhibits a skeleton of the largest flesh-eating animal that has ever lived. This is *Tyrannosaurus,* the tyrant lizard, a dinosaur that lived during the close of the Cretaceous period. An idea of its immense size can be formed from measurements of the skeleton, 47 feet in length and 18 ½ feet in height. This skeleton is part of a group of three posed to represent a scene of daily occurrence in the dim distant past [*see illustration*]. It is early morning along the shore of a lake three million years ago. A herbivorous dinosaur, *Trachodon,* venturing from the water for a breakfast of succulent vegetation has been caught and partly devoured by a giant flesh-eating *Tyrannosaurus.* As this monster crouches over the carcass, busily dismembering it, another *Tyrannosaurus* is attracted to the scene."

More images from the science of natural history in 1915 are at www.ScientificAmerican.com/oct2015/natural-history

NATURE, RED IN TOOTH AND CLAW: A view of *Tyrannosaurus rex,* 1915

October 1865

Rinderpest Plague

"The disease which has been prevailing among horned cattle in Europe was, at last accounts, unchecked, and so great were its ravages that in some quarters of Germany not an animal is to be seen. The disease spreads rapidly when an infected animal appears in any district, and is liable to be spread by persons carrying the infection in their clothes. It has not yet appeared in this country, and it is to be hoped will not. As it is by no means impossible that this malady may be introduced into this country by accident, carelessness, or design, the Agricultural Report (official) suggests that the greatest care be exercised with regard to imported cattle, and that a quarantine for such beasts be established."

Steel: Backbone of Modernity

"Mr. Henry Bessemer reports, 'there are at present erected and in course of erection in England no less than sixty Bessemer converting vessels, each capable of producing from three to ten tuns at a single charge. When in regular operation these vessels are capable of producing fully 6,000 tuns of steel weekly, equal to fifteen times the entire production of cast steel in Great Britain before the introduction of the Bessemer process. The average selling price of this steel is at least £20 per tun below the average price at which cast steel was sold.'"

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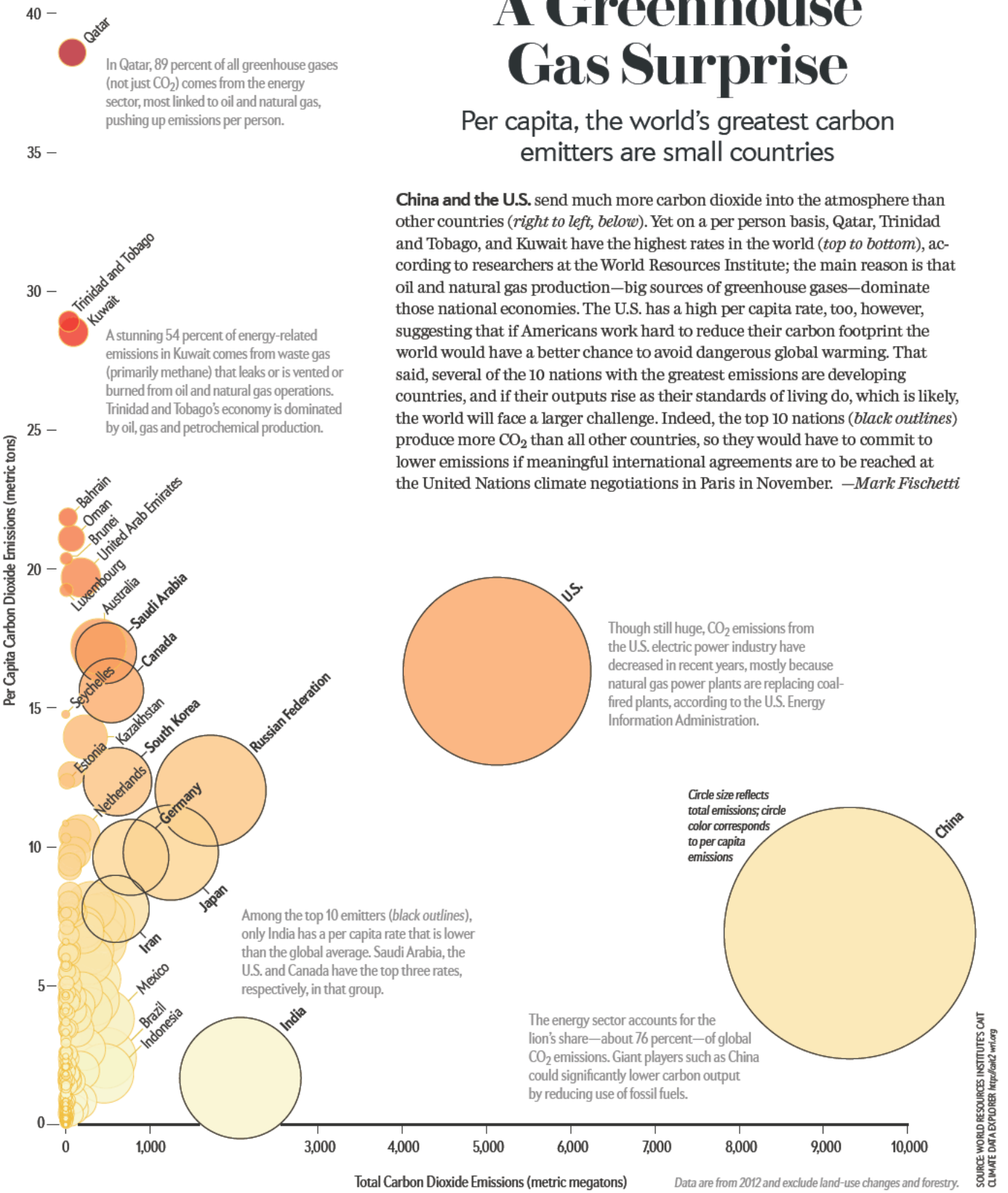
SCIENTIFIC AMERICAN ONLINE
TO SEE WHICH COUNTRIES HAVE LOWERED PER CAPITA EMISSIONS, GO TO SCIENTIFICAMERICAN.COM/OCT2015/GRAPHIC-SCIENCE

A Greenhouse Gas Surprise

Per capita, the world's greatest carbon emitters are small countries

China and the U.S. send much more carbon dioxide into the atmosphere than other countries (*right to left, below*). Yet on a per person basis, Qatar, Trinidad and Tobago, and Kuwait have the highest rates in the world (*top to bottom*), according to researchers at the World Resources Institute; the main reason is that oil and natural gas production—big sources of greenhouse gases—dominate those national economies. The U.S. has a high per capita rate, too, however, suggesting that if Americans work hard to reduce their carbon footprint the world would have a better chance to avoid dangerous global warming. That said, several of the 10 nations with the greatest emissions are developing countries, and if their outputs rise as their standards of living do, which is likely, the world will face a larger challenge. Indeed, the top 10 nations (*black outlines*) produce more CO_2 than all other countries, so they would have to commit to lower emissions if meaningful international agreements are to be reached at the United Nations climate negotiations in Paris in November. —*Mark Fischetti*



Graphic by Jan Willem Tulp

JOHN KNEW IF LUNG CANCER DIDN'T TAKE HIS LIFE, IT WOULD SURELY TAKE HIS LUNG.

WE HELPED HIM KEEP BOTH.

When John Morale came to Memorial Sloan Kettering with a lung tumor, he had already gone to four different hospitals, each telling him lung-removal surgery was his only option. Needless to say, by the time John met with Dr. Bernard Park at MSK, he was scared. Dr. Park gave him the option of a surgery that would remove only a small part of his lung and ultimately cure his cancer. After talking it over with his wife, Tina, John decided to have the surgery that ended up saving his life, and kept him whole.

See John's story at MSKCC.ORG/MORESCIENCE

MORE SCIENCE. LESS FEAR.

1884

Memorial Sloan Kettering Cancer Center

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