ASTRONOMY
The Far, Far Future of Stars

DIGITAL
A “Shadow” Web to Protect the Internet

MEDICINE
Blocking HIV’s Attack on Cells

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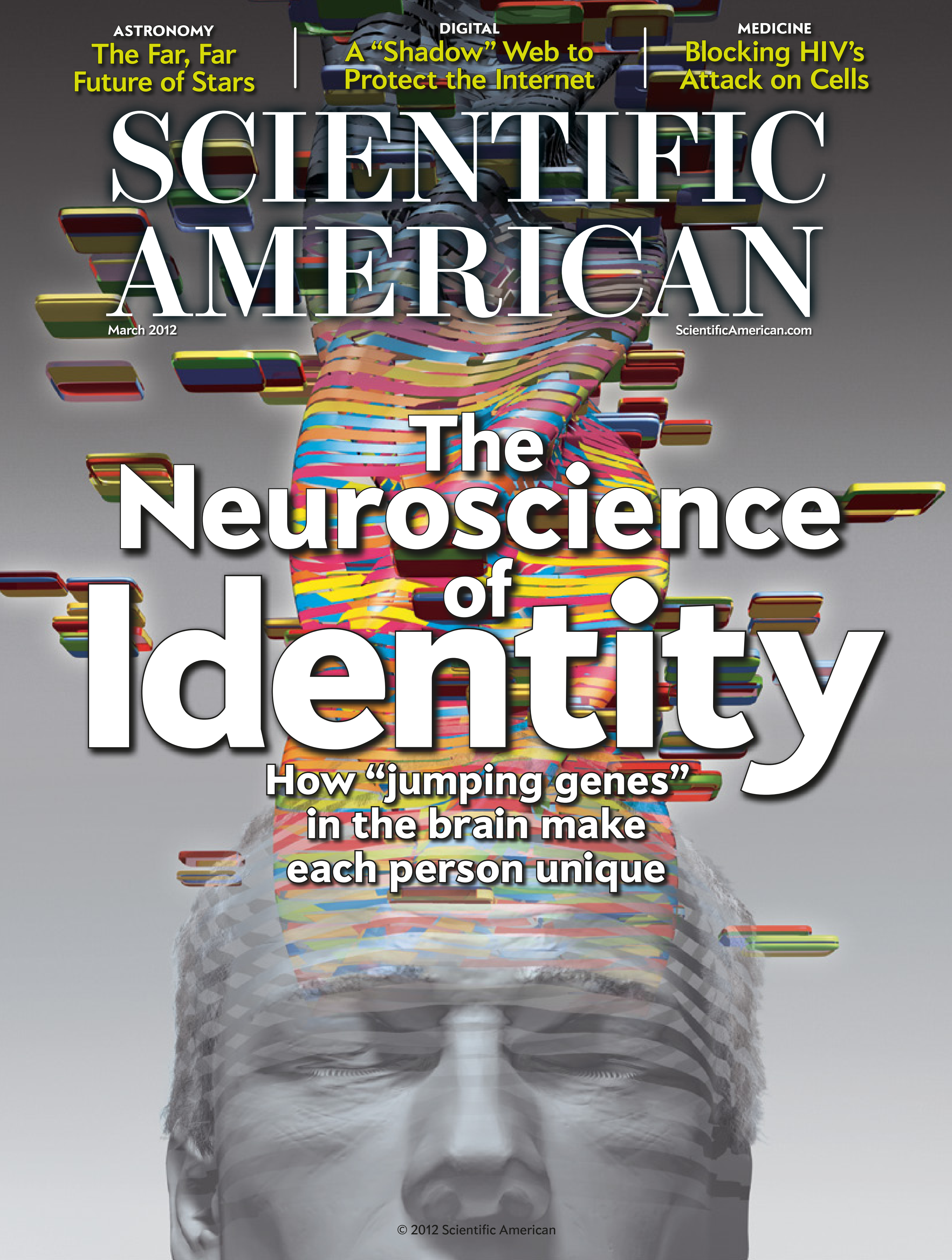
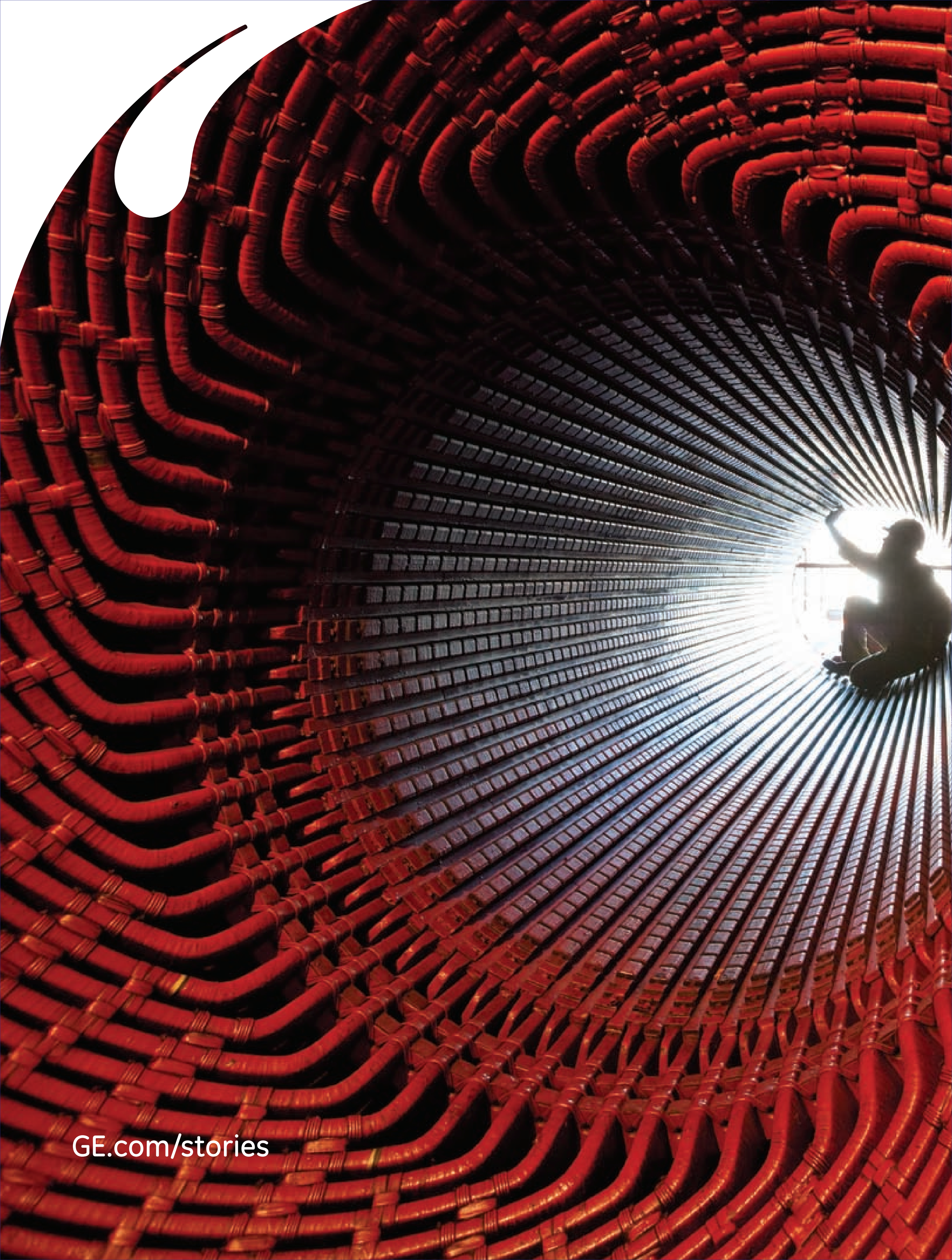


The Neuroscience of Identity

How “jumping genes” in the brain make each person unique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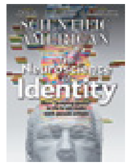
ON THE COVER



Each of our identities depends on a subtle interplay between genes and the environment. Neuroscience has begun to discover just how subtle the genetic contribution can be in the brain. Small fragments of DNA known as jumping genes can bounce around in neurons and alter the brain in ways that cause even identical twins to behave very differently. Image by Jean-Francois Podevin.

COURTESY OF MARK LOEWEN *Natural History Museum of Utah (Utahceratops skull)*

FEATURES

NEUROSCIENCE

26 What Makes Each Brain Unique
Jumping genes that move around in brain cells help to ensure that no two people are alike.
By Fred H. Gage and Alysson R. Muotri

ASTROPHYSICS

32 The Far, Far Future of Stars
The glory days may be long gone, but there's still some pizzazz left in the universe. New types of celestial phenomena will unfold over the coming billions and trillions of years. *By Donald Goldsmith*

PALEONTOLOGY

40 Dinosaurs of the Lost Continent
The American West once harbored multiple communities of dinosaurs simultaneously—a revelation that has scientists scrambling to understand how the land supported so many behemoths. *By Scott D. Sampson*

ENERGY

48 Gather the Wind
If renewable energy is going to take off, we need good ways of storing it for the times when the sun isn't shining and the wind isn't blowing. *By Davide Castelvecchi*

MEDICINE

54 Blocking HIV's Attack
Scientists are beginning human trials of a treatment that holds promise for eliminating the virus from the body.
By Carl June and Bruce Levine

INFORMATION TECHNOLOGY

60 The Shadow Web
Governments and corporations have more control over the Internet than ever. Now digital activists want to build an alternative network that can never be blocked, filtered or shut down. *By Julian Dibbell*

BIOTECHNOLOGY

66 Lifting the Black Cloud
Current antidepressants can take weeks to ease symptoms substantially, and for many people they don't work at all. Researchers are considering better options.
By Robin Marantz Henig

CLIMATE

72 Hit Them with the Hockey Stick
After years of playing defense, Michael E. Mann takes on his critics and speaks out about climate change.
Interview by David Biello

DEPARTMENTS

4 **From the Editor**

6 **Letters**

8 **Science Agenda**
Skimping on mental health care is shortsighted.
By the Editors

10 **Forum**
Supercomputers could revive small manufacturing.
By Donald Q. Lamb

11 **Advances**
Tsunami wreckage heads for the U.S. The pitfalls of cramming. Zombie bees. Space tycoons. Invisibility cloak. Death in the lab. Lizard-inspired vehicles.

23 **TechnoFiles**
Time to kill off Captchas.
By David Pogue

24 **The Science of Health**
Hospital gardens have medical benefits.
By Deborah Franklin

76 **Recommended**
The art and science of the unconscious.
The information revolution. Creative processes at work.
By Anna Kuchment

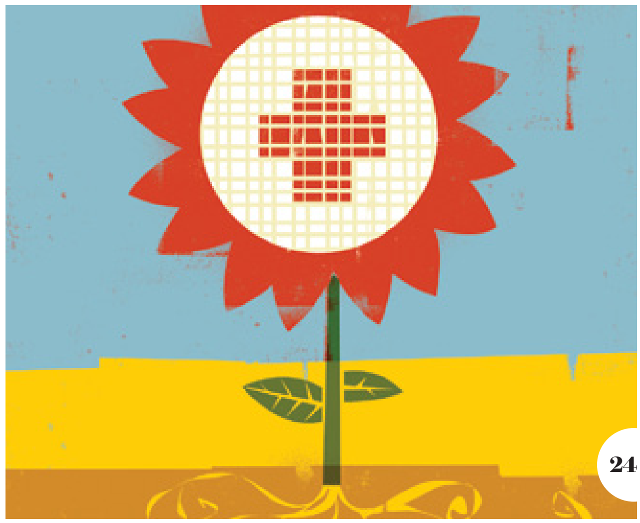
78 **Skeptic**
Opting out of overoptimism.
By Michael Shermer

80 **Anti Gravity**
Perils of paper cuts.
By Steve Mirsky

82 **50, 100 & 150 Years Ago**

88 **Graphic Science**
The reshaping of marine ecosystems.
By John Matson

11



24

78

ON THE WEB

Seeking Modern Solutions for Global Problems
Can global, cross-disciplinary science collaborations ensure food, water and energy for all? That was the question facing scientists and policy makers at the annual meeting of the American Association for the Advancement of Science.
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Mariette DiChristina is editor in chief of *Scientific American.* Find her on Twitter @mdichristina

The Moving Mind

IS THERE ANYTHING MORE EVERYDAY AND FAMILIAR (GIVEN THAT WE ALL possess one) and yet still so mysterious and puzzling as our own human brain? In about three pounds of tissue with the consistency of Jell-O, it packs 100 billion neurons, tens of trillions of neural connections and the low-watt processing power that has enabled our species to dominate this planet.

Yet even the often enigmatic workings of our mind are not immune to the probing of modern science. In recent decades imaging technologies have revealed what areas of the brain are active when we are performing various mental tasks, for instance. Now researchers can also explain "What Makes Each Brain Unique"—even those of genetically identical twins. That is the subject of our cover story on the neuroscience of identity, authored by Fred H. Gage of the Salk Institute for Biological Studies in La Jolla, Calif., and Alysson R. Muotri of the University of California, San Diego. Genes and environment have long been known to influence human behavior. But as Gage and Muotri explain, the significance of "jumping genes" is now becoming clear. These genes, which are especially active in the brain, copy and paste themselves into new places in the genome, resulting in new traits. Turn to page 26 for more.

When you are done, you might wrap your wetware around the mental sustenance offered in other features in the issue, such as "The Far, Far Future of Stars," by astronomer Donald Goldsmith, starting on page 32. He offers a reassuring view of our middle-aged cosmos, which is past its stellar-engine glory but still has trillions of years of vibrant activity to come. As Goldsmith eloquently puts it: "Our unfettered minds remain free to roam as far into the future as we choose." SA

SCIENCE IN ACTION

Entries Due

April 1 is the deadline for entries to the Google Science Fair—and all entries will automatically be considered for SCIENTIFIC AMERICAN's $50,000 Science in Action award. The online competition is open to students around the globe in three age categories, ranging from 13 to 18.

Science in Action is a new addition to the Google Science Fair this year and will honor a project that tackles a social, environmental or health issue to make a practical difference in the lives of a group or community and that possibly can be scaled. SCIENTIFIC AMERICAN is also finding mentors to provide advice and thus further foster the development of the Science in Action winner's work for a year.

The Science in Action winner will be announced in June and will join other Google Science Fair finalists at the company's Mountain View, Calif., campus for a special awards event on Monday, July 23. I'll be there and am looking forward to meeting these young scientists.

—M.D.

Illustration by Nick Higgins

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ENTOMOLOGICAL ETHICS

My emotional response to "The Wipeout Gene," in which Bijal P. Trivedi describes the use of genetic modification to destroy the mosquito species *Aedes aegypti,* was trepidation. We see *A. aegypti* as the vector of human diseases, but the global ecological significance of the species is unknown.

Also disturbing is the implication that assent obtained during a town hall or village meeting of lay individuals was meaningful when substantive understanding of arthropod gene manipulation and its ecological impact is limited among scientists.

It is arrogant, reckless and hazardous to make value judgments on the significance of a species.

Charles F. Lovell, Jr.
Past member,
National Vaccine Advisory Committee

STARVATION SOLUTIONS?

In addressing future food supplies and environmental degradation, Jonathan A. Foley's "Can We Feed the World *and* Sustain the Planet?" doesn't mention the elephant in the room: agricultural output has dramatically increased but so has population.

Until the countries that can help provide the means, at affordable prices, to enable people to control their family sizes as many want to do but can't, humanity is chasing its tail.

Les G. Thompson
Victoria, Australia

"It is arrogant, reckless and hazardous to make value judgments on the significance of a species."

Charles F. Lovell, Jr. *Past member, National Vaccine Advisory Committee*

Foley could have missed a viable answer to world hunger that would also help mitigate climate change: insects as human and other animal food. Most insects produce very little methane for high-quality protein.

The United Nations Food and Agriculture Organization is mounting an effort to address insects as human food and is planning a world conference for 2013. Academics who refuse to think out of the box and address entomophagy as a valid partial answer to world hunger ignore a useful, productive and highly nutritious solution.

Robert Eller Diggs
Bozeman, Mont.

Foley's article overlooked food from the sea. Properly designed fish farms can provide a healthy and plentiful supply of food by using our natural resources more efficiently.

Albert Rettig
Tel Aviv, Israel

MARTIAN MEASUREMENTS

In "Digging Mars," Peter H. Smith's overview of the science of exploring the Red Planet, the evidence seems to indicate significant variation in the Martian climate. Earth also has wide swings in climate that are thought to be caused by variations in its orbit. Serbian geophysicist Milutin Milanković identified three of these: orbit eccentricity, axial precession and tilt. Has Smith considered whether or not Mars also has these so-called Milankovitch cycles?

Jerry L. Lundry
Bellevue, Wash.

In discussing the Phoenix mission, Smith indicates the spacecraft traveled 600 million kilometers to Mars and estimates "the light travel time to Earth" as "about 15 minutes." But at 186,00 miles per second (about 18 million kilometers per minute), light would need about 33 minutes to make the trip from Mars to Earth.

Roger Rubens
Boynton Beach, Fla.

SMITH REPLIES: Regarding Lundry's question, Milankovitch cycles influence the climate on Mars even more than on Earth. Not only does the axis precess (every 51,000 years), but the proximity of Jupiter offers a strong gravitational forcing function that modifies the eccentricity of its orbit and the obliquity (tilt) of the spin axis. As the obliquity wanders with large, chaotic variations (cycles can be several million years), the climate is strongly affected to the point where, during large tilts, the polar ice caps can migrate toward the equator, forming large glaciers on the tall volcanoes.

To clarify Phoenix's light travel time: the spacecraft did not cruise straight to Mars but took a longer path following an elliptical orbit around the sun, with Mars at the aphelion. Because the distance from Mars to Earth was about 250 million kilometers during the mission, the one-way light travel time was a little less than 15 minutes.

MORAL MUSINGS

"Thought Experiments," by Joshua Knobe, describes the question of free will versus determinism. I think it's impossible to determine (pun intended) whether we live in a deterministic or free-will world.

I believe I have free will. But suppose I'm wrong. Then it's determined that I will believe that I have free will. We can conduct the experiments that Knobe talks about, but doing so assumes free will. Otherwise, the outcomes are determined.

Ted Grinthal
Berkeley Heights, N.J.

There is another way of thinking about morality than the one put forward by Knobe. Instead of it being essentially altruistic, noble and somehow emanating from inside us, we can think of it as focused largely on how we want others to behave toward us.

If others behave morally, they create an environment that is generally beneficial to us. Our own "moral" behavior, however, is dependent on whether there are effective social sanctions that make it advantageous to behave in a particular way. From this perspective, it is easy to understand the relatively constrained behavior of people who are part of a religious or other mainstream group and the more fluid "morality" of those who are "open to experience."

PETER ROWBOTHAM
West Vancouver, B.C.

CUMULUS CAUSALITY

In "A Formula for Economic Calamity," by David H. Freedman, David Colander of Middlebury College asserts that climate models often have no terms to account for the effects of clouds. This is not true. In my class on climate change problem solving, I use a 2005 paper by M. H. Zhang et al. that compares modeled clouds with observed ones from 10 climate models. There are many earlier and later references that document over three decades of ever more sophisticated inclusion of clouds in weather and climate models.

The statement that clouds are not included is misinformation that has been propagated in political arguments used to discredit such models. There is an important difference between physical climate models and economic ones: namely, physics. The physics of climate change are simple classical physics in a stunningly complex, multiscale system, so it is possible to design experiments based on cause and effect. The uncertainty associated with future climate projections linked to economic possibilities of what people will do is far larger than the uncertainty associated with physical climate models.

RICHARD B. ROOD
Department of Atmospheric, Oceanic and Space Sciences
University of Michigan

FREEDMAN REPLIES: Rood is right to point out that climate models are often designed to try to account for clouds. The statement in the article, which was attributed to an economist and not a climate scientist, was a vague oversimplification that suggested climate models frequently fail to account for clouds. In fact, the climate science literature is replete with papers that call out the challenges of accurately accounting for clouds in models. Surely if we have to err in gauging uncertainty in science, it's better to err on the side of overestimating it. If only economists working in financial risk models had done just that.

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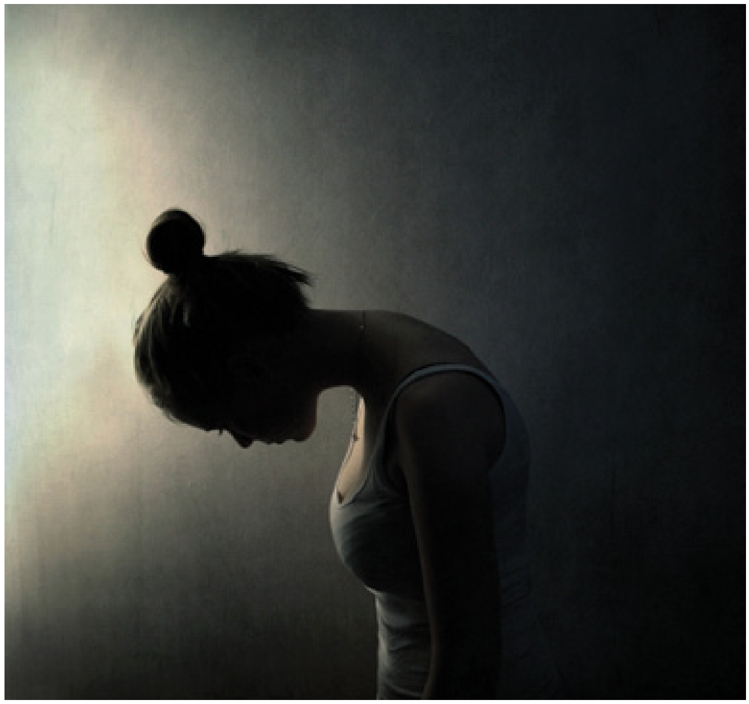
A Neglect of Mental Illness



By letting mental afflictions go untreated, we consign millions of Americans to misery and put a drag on our economy

Mental health care is one of the biggest unmet needs of our time. Nearly one in two people in the U.S. will suffer from depression, anxiety disorders or another mental health ailment at some point in their life, and about one in 17 Americans currently has a serious mental illness. Young people are especially prone to these troubles. Yet millions of people living with these conditions do not receive the care they require. In recent years the health system and state and federal governments have taken steps to right that wrong. Progress has been slow, and budget cuts and legal wrangling have now put many of these measures at risk. Doctors, insurers and politicians need to pick up the pace.

Mental illness strikes without regard for economic class, but the strain is acute for people with low incomes. About one in six adults living at just above the poverty line or lower has severe mental health problems. Without access to affordable treatment, many have a hard time holding down a job yet do not qualify as formally disabled, thus leaving them locked out from insurance coverage. A recent large study in California found that only 32 percent of uninsured residents with mental illnesses received any treatment at all and that less than 12 percent got adequate help.

The human and economic toll is enormous yet often hidden. Untreated mental illnesses in the U.S. cost more than $100 billion a year in lost productivity, according to the National Alliance on Mental Illness (NAMI). Local hospitals and clinics must cope with associated chronic physical diseases. Schools have to open more special education classes. Courts and jails handle a large number of individuals who suffer from untreated mental illnesses. Suicide ranks among the top 15 most common killers in the U.S. (in the top three among young people), and 90 percent of cases can be attributed to mental illness.

The severity of the problem has prodded politicians into action. By 2002, 29 states had mandated that health insurance packages cover mental illness on the same terms as physical illness, and in those states the suicide rate fell by an average of 5 percent. But equalizing coverage means little to those who lack insurance altogether, and states are increasingly failing to make provision for them. In the past three years states have cut up to 39 percent of their mental health budgets, according to NAMI.

The Patient Protection and Affordable Care Act, which President Barack Obama signed into law in 2010, should help fill these holes. It requires that insurance plans offer "behavioral health" coverage, including mental health and addiction and substance abuse help, as an "essential health benefit." At least 3.7 million Americans who are currently living with severe mental illness will get new benefits for their conditions by 2014, either through extended Medicaid coverage or insurance exchanges.

Yet these measures are in legal jeopardy. The U.S. Supreme Court will hear arguments for and against the constitutionality of the act late in March. If the court rules that states do not have to expand their Medicaid programs, as the act currently requires, it could shut out 16 million Americans who would otherwise receive Medicaid coverage for mental health. A ruling that closes the state insurance exchanges would deprive another 16 million. Scuttling the law would also do away with plans to build national centers for the treatment of depression and to improve the way behavioral health services are integrated into standard care.

If the law falls, Congress must reinstitute its most crucial provisions, and even if it stands we all have more to do. Insurance alone does not guarantee that people get the care they need; doctors and social workers must work to ensure that. Drug companies must refill the research pipeline for new drugs, which has been sorely neglected [see "Lifting the Black Cloud," by Robin Marantz Henig, on page 66], and develop other treatments. And all of us should get over the stigma we still tend to attach to these conditions. The rewards will be that millions of our friends, neighbors and children will have a chance to become healthier, happier and more productive members of society. SA

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JENNI HOLMA *Getty Images*

Commentary on science in the news from the experts

Donald Q. Lamb is Robert A. Millikan Distinguished Service Professor in the astrophysics and astronomy department at the University of Chicago and director of the Flash Center for Computational Science there.

Big Computers for Little Engineers

The key to reviving manufacturing in the U.S. may lie in the nation's supercomputers

The U.S. used to be a powerhouse in manufacturing. In the past quarter of a century we have relinquished this leadership position, in large part because we made a decision—consciously or unconsciously—that the service and financial sectors are sufficient to sustain our economy. But they are not. Service jobs pay little. The financial industry makes nothing of value and therefore cannot maintain, let alone raise, the nation's standard of living.

The fate of manufacturing is in some ways linked to our prowess in the physical sciences. In the 1960s and 1970s high-performance computing (HPC) developed at the national labs made its way to the manufacturing sector, where it now powers much of the innovation behind our most successful commercial firms. Yet we are ceding leadership in the physical sciences, too. Canceling the Superconducting Super Collider in the 1990s ended U.S. dominance in particle physics. NASA's decision to delay, and possibly eventually abandon, the Wide-Field Infrared Survey Telescope could do the same for cosmology.

Fortunately, the nation's lead in high-performance computing still stands. HPC is the advanced computing physicists use to model the dynamics of black holes, meteorologists use to model weather and engineers use to simulate combustion. This expertise may also be our best chance to rescue U.S. manufacturing. If we can successfully deliver it to engineers at small firms, it might give the sector enough of a boost to compete with lower labor costs overseas.

We already know how useful HPC is for big firms. When Boeing made the 767 in the 1980s, it tested 77 wing prototypes in the wind tunnel. When it made the 787 in 2005, it tested only 11. In the future, Boeing plans to bring that number down to three. Instead of physical wind tunnels, it uses virtual ones—simulations run on supercomputers—saving much time and money and quickening the pace of new products development. HPC modeling and simulation has become an equally powerful tool in designing assembly lines and manufacturing processes in a broad range of fields—big manufacturers such as Caterpillar, General Electric, Goodyear and Procter & Gamble use it routinely. Small manufacturers could get similar benefits from these tools, if only they had access to them.

I first came to appreciate the potential of HPC to help small manufacturers in 2009 as part of the Obama transition team. Working with the Council on Competitiveness, we identified lack of software, cost of entry and shortages of expertise as the main obstacles to the use of HPC by small manufacturers and proposed a partnership among government, manufacturers and universities to help. The result is the National Digital Engineering and Manufacturing Consortium, or NDEMC, a pilot program created by the council and the federal government.

Recently NDEMC made HPC resources available to a handful of firms, including Jeco Plastic Products. This 25-employee firm in Plainfield, Ind., makes plastic pallets for packaging of auto parts. The plastic pallets are a less expensive alternative to steel pallets, which are heavier and prone to rusting. When Jeco makes a new product, its engineers build a prototype, test it in the lab to see how it bears up under the stress it is likely to encounter in the field and repeat the process until they arrive at the best design. Last December, however, Jeco engineers got a chance to tap expertise at Purdue University to develop simulations of a pallet designed for a German automotive company and ran them on hardware at the Ohio Supercomputing Center in Columbus. As a result, Jeco bypassed that trial-and-error process completely, arriving at a design in only a few hours of computer time.

Many other small firms could reap similar benefits. NDEMC's goal is to find the best business models for getting HPC to these firms and eventually take the effort nationwide. Small manufacturers today are in some ways like farmers at the beginning of the 20th century, most of whom did not know what contour farming, crop rotation and fertilizers could do for productivity. When the U.S. agricultural extension service, in conjunction with land-grant universities, made the requisite expertise available, it triggered a revolution in agricultural productivity. A similar revolution could be in the cards for small manufacturers if we can get supercomputing technology into the hands of their engineers. SA

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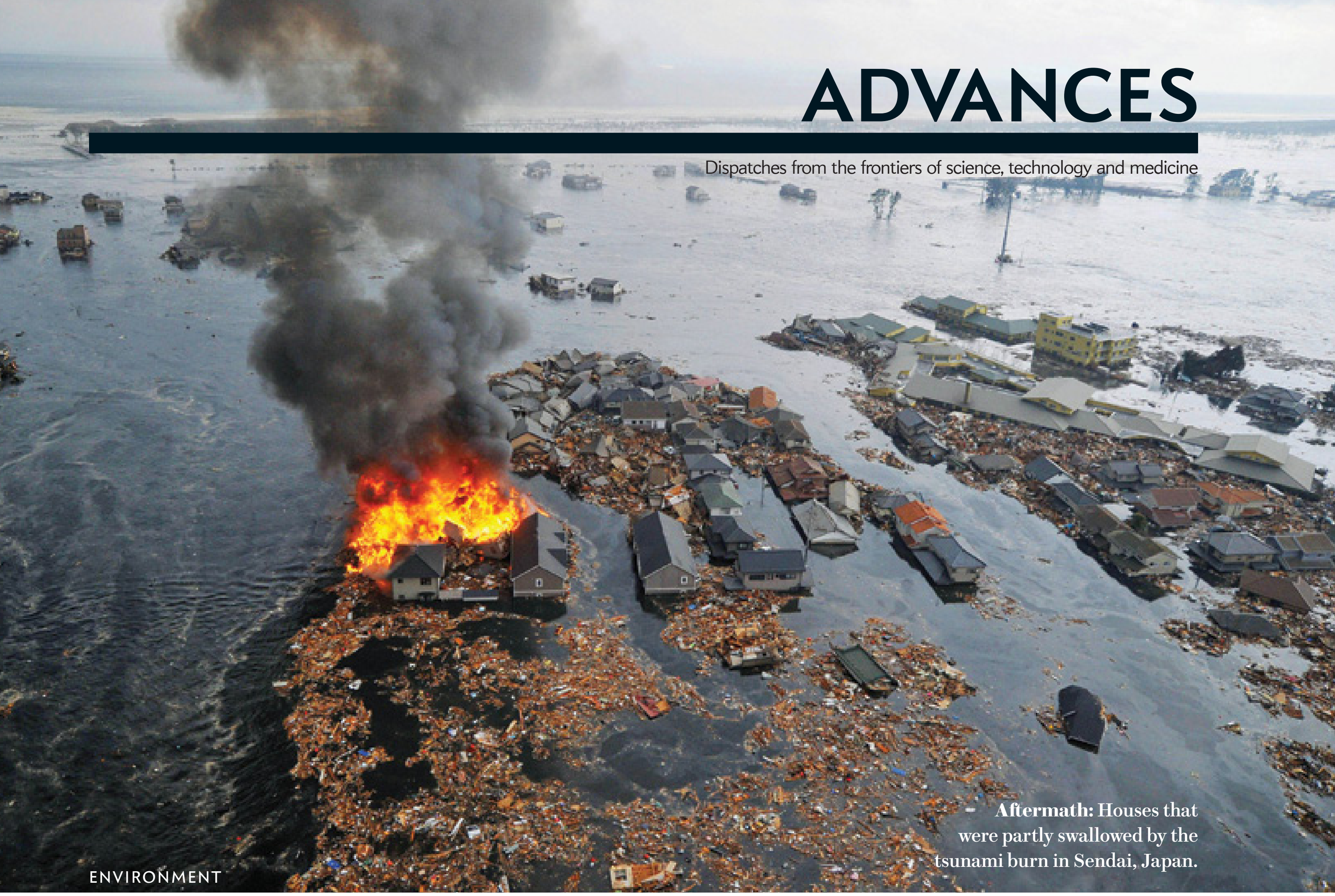
Illustration by Richard Mia



Aftermath: Houses that were partly swallowed by the tsunami burn in Sendai, Japan.

ENVIRONMENT

Remains of the Day

One year after Japan's tsunami scientists fear marine debris from the disaster may hit Hawaii's coral reefs

The earthquake and tsunami that struck Japan last March created an estimated 25 million tons of debris, large amounts of which washed into the ocean. Soon after the disaster, satellites photographed and tracked large mats of wreckage—building parts, boats and household objects—floating off the Japanese coast. Now, according to computer models developed by Nikolai Maximenko and his colleagues at the University of Hawaii and at the U.S. National Oceanic and Atmospheric Administration, the detritus is on course to reach the northwestern Hawaiian Islands early this year.

Given what is known about the hazards of floating refuse, scientists are taking the potential threat seriously. Already as much as 40 percent of the world's ocean surfaces harbor garbage that ranges in size from shipping containers to derelict fishing gear to small bits of plastic that can entangle or poison marine mammals. Researchers want to find out not only if the influx will threaten Hawaii but how it might interact with what is now out there.

Water and wind currents have broken up the tsunami wreckage so that it is no longer visible using NOAA's satellites, so the agency has been working to gain access to higher-resolution satellites to locate it. Later this year scientists affiliated with 5Gyres, a nonprofit that specializes in tracking and analyzing marine debris, will set sail across the North Pacific to investigate what is left of Japan's devastation.

Some scientists have already encountered tsunami rubble at sea. In September a Russian ship found a Japanese fishing vessel, a refrigerator, a television set and other household appliances bobbing west of Midway Atoll. In December large Japanese fishing floats washed up in Neah Bay in Washington State and near Vancouver, B.C.

If these types of objects collide with the fragile coral reefs surrounding Hawaii's northwestern islands, the results could be catastrophic. Risks include physical damage to the reefs as well as the fouling of beaches that provide important habitats for albatross, Hawaiian monk seals, green sea turtles, and other threatened and endemic species. Hazardous materials are also a concern, although recent studies show the offshore impacts from debris contaminated with radiation have been minimal.

Nancy Wallace, director of NOAA's Marine Debris Program, says the agency is preparing for "best- and worst-case scenarios." NOAA and other organizations have plans to cope with the debris, including any that may be contaminated. Whether or not tsunami wreckage makes landfall in significant volumes, however, it is somewhere at sea, adding to a serious and growing problem. *—Elizabeth Grossman*

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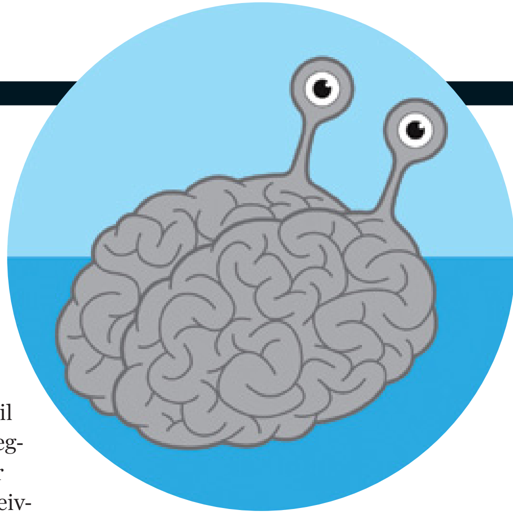


NEUROSCIENCE

Forget Cramming

Short, irregular training intervals may work best for learning

High school and college teachers always entreat their charges to forgo the cramming. Studying bit by bit over the course of a semester is the way to go. A study published online in *Nature Neuroscience* last December appears to demonstrate the biological underpinnings of this pedagogical truism. It also goes one step further by suggesting a way to optimize training intervals, an insight that could, in theory, translate into strategies for committing to memory the molecular structure of maitotoxin or a Chinese ideogram. (*Scientific American* is part of Nature Publishing Group.)

The study, lead by neurobiologist John H. Byrne of the University of Texas Medical School at Houston, has brought a new twist to a learning method developed in the Columbia University laboratory of Nobel laureate Eric R. Kandel. The technique consisted of shocking the tail of the sea slug *Aplysia californica* at regular intervals and then seeing whether the animal overreacted later when receiving a lesser zap, a sign that it remembered the prior experience all too well.

The quest Byrne and his team took up was to determine whether the chemical reactions that underlie this response could be tweaked in a way that enhanced the learning process. Instead of using a whole slug, they put a few of the animal's nerve cells (sensory and motor neurons) in a dish. They applied five pulses of the neurotransmitter serotonin (the equivalent of shocks), each pulse 20 minutes apart. The serotonin prompted enzymes in the neurons to initiate a biochemical cascade that ultimately strengthens the firing of neurons, signals that are the equivalent of "I remember this. It hurts."

The two enzymes involved work in tandem. Using this standard set of evenly spaced pulses, the enzymes do not reach peak activation inside a cell at the same time, a hint that the usual way of doing things might not be the best way.

Byrne's team used a computer to model 10,000 distinct intervals between pulses. Each series of intervals was assessed to determine which ones occurred when both enzymes were fully activated. The best learning protocol, it turned out, was not the usual, even-spaced one but a series of three serotonin pulses emitted 10 minutes apart, then one five minutes later, with a final spritz 30 minutes afterward. With this regimen, interaction between the two enzymes rose by 50 percent—an indication that the learning process was operating more efficiently.

So should you be studying Riemann sums every other day for two weeks and then take a month off before going back to them? Too early to say. The timing protocol Byrne found may be the slug's adaptation to fleeing a predator, allowing the animal to escape lobster claws crunching its tail. Studying integral calculus might be a bit different.

Yet the implication of Byrne's work is that the best way to learn may not occur in simple time chunks—and that leaves a meaty set of new research questions for neuroscientists to pursue.

For their part, Byrne and company will now use these same techniques to try to optimize other aspects of the memory formation process in sea slugs. If that proves successful, they may eventually move on to humans. Motor skills would probably be the first target—throwing a baseball, doing the high jump or helping a stroke victim to walk again—because researchers know more about the brain circuits in the cerebellum, involved with movement, than in the hippocampus, a locus for initiating the type of factual memories needed for organic chemistry. For now science homework will just have to wait. *—Gary Stix*

STAT

17

The minimum number of clues required for a Sudoku puzzle to have a unique solution. The finding, announced in January, is considered a major breakthrough in mathematics.

77: Maximum number of clues a Sudoku puzzle can have without having a unique solution.

6.67 sextillion: The number of all possible Sudoku puzzles.

SOURCES: "There Is No 16-Clue Sudoku: Solving the Sudoku Minimum Number of Clues Problem," by Gary McGuire et al.; January 1, 2012; Preprint online at arxiv.org/abs/1201.0749; "Taking Sudoku Seriously: The Math Behind the World's Most Popular Pencil Puzzle," by J. Rosenhouse and L. Taalman, Oxford University Press, 2012

Illustrations by Thomas Fuchs

TECHNOLOGY

It Watches Your Wallet

A new Web site uses credit-card data to rate stores and restaurants

Amazon, Yelp and similar Web sites rely on customer reviews to help users with their purchases. A nagging concern of shoppers, however, is how reliable these critiques are. Bundle, a New York City–based start-up, has turned to a source it deems more objective: credit-card data.

Bundle receives data on credit-card transactions from Citi, one of its investors. The data are stripped of personal details, but every cardholder is tagged with a unique identifier so spending can be tracked. The data also retain demographic information such as salary, marital status and household size. Bundle then compares each transaction against a commercially available list of 15 million merchants that accept credit cards, which includes the merchants' locations. The idea is "to see people putting money where their mouth is," says Bundle CEO Jaidev Shergill. The company tracks such information as how many repeat customers a business has, the amounts customers usually spend, what types of people go there, and what other places customers of an establishment frequent.

The site went national with its data and its iPhone app in January, allowing users to find places they might like to check out, either in their hometown or someplace they are visiting, or to see what spending levels are like in cities to which they are thinking of moving. The site hasn't completely done away with the Yelp model of subjective feedback, however. It partners with companies that provide traditional qualitative reviews for a human touch, as well as to fill in gaps, such as businesses that only accept cash or American Express, which Citi does not track.

—Charles Q. Choi

COURTESY OF CHRISTOPHER QUOCK

ENTOMOLOGY

Body-Snatching Flies

Scientists have uncovered a surprising clue to the causes of colony collapse disorder

The heap of dead bees was supposed to become food for a newly captured praying mantis. John Hafernik, a biology professor at San Francisco State University, had collected the belly-up bees (*Apis mellifera*) from the ground underneath lights around the university campus. "But being an absent-minded professor," he noted in a prepared statement, "I left them in a vial on my desk and forgot about them." He soon got a shock. "The next time I looked at the vial, there were all these fly pupae surrounding the bees," he said. A fly (*Apocephalus borealis*) had inserted its eggs into the bees, using their bodies as a home for its developing larvae. The pile of dead bees ended up revealing a previously unrecognized suspect in colony collapse disorder—a mysterious condition that for several years has been causing declines in U.S. honeybee populations, which are needed to pollinate many important crops. It turns out that the parasitic flies that had attacked Hafernik's bees have been taking over the bodies of honeybees in other parts of the country. A detailed description of the newly documented relationship was published online in January in *PLoS ONE*.

Hafernik believes that the fly, which also parasitizes bumblebees and paper wasps, may have only recently begun attacking honeybees. "Honeybees are among the best-studied insects in the world," Hafernik said. "We would expect that if this has been a long-term parasite of honeybees we would have noticed."

The fly lays eggs in a bee's abdomen. Several days later the parasitized bee bumbles out of the hive—often at night—on a solo mission to nowhere. Such bees often fly toward light and wind up unable to control their own body. After the bee dies, as many as 13 fly larvae crawl out from the bee's neck.

The team members found evidence of the fly in 77 percent of hives they sampled in the San Francisco Bay Area, as well as in some hives in California's agricultural Central Valley and in South Dakota. Earlier research had found signs that mites, a virus or a fungus, or a combination of these factors, might be responsible for the widespread colony collapse. In the case of the affected hives that Hafernik's group studied, the bees—and the parasitizing flies and their larvae—contained genetic traces of a parasite and a virus that were previously implicated in colony collapse disorder. This double infection suggests that the flies might be spreading additional hive-weakening traits.

—*Katherine Harmon*

TECHNOLOGY

Know Your Space Tycoons

How their plans stack up

You've probably used their technologies or shopped in their stores. But would you trust them to fly you into space? Microsoft billionaire Paul Allen is the latest to join the commercial space race with his new venture, Stratolaunch Systems. Stratolaunch plans to build the world's biggest airplane to launch rockets from the sky. The appeal of this kind of air launch is that the aircraft flies a rocket to the most favorable launch latitude for a specific mission. Here's how the entrepreneurs' aspirations (and fortunes, as estimated by *Forbes*) compare. —*John Matson*

NAME	SOURCE OF FORTUNE	NET WORTH	SPACE VENTURE	KEY HARDWARE	FIRST FLIGHT	POTENTIAL PASSENGERS
Paul Allen 	Microsoft	$13.2 billion	Stratolaunch Systems	Launch aircraft for SpaceX rockets	2016 (planned unmanned test)	NASA astronauts
Jeff Bezos 	Amazon.com	$19.1 billion	Blue Origin	Reusable rocket for suborbital flights	Undisclosed	Space tourists
Richard Branson 	Virgin (media, airlines, retail)	$4.2 billion	Virgin Galactic	Suborbital space plane	2013 (planned)	Space tourists
Elon Musk 	PayPal	$680 million	SpaceX	Rocket and orbital crew capsule	December 2010 (unmanned test)	NASA astronauts

MICHAEL LOCCISANO *Getty Images (Allen)*; LEE CELANO *Getty Images (Bezos)*; GETTY IMAGES *(Branson and Musk)*

COMMENT AT ScientificAmerican.com/mar2012

EVOLUTION

Backseat Drivers

The bacteria that live quietly in our bodies may have a hand in shaping evolution

We are one: Biologists say common gut microbes such as *Bacteroides fragilis* may be as important as our genes.

PHOTO RESEARCHERS, INC.

The human body harbors at least 10 times more bacterial cells than human cells. Collectively known as the microbiome, this community may play a role in regulating one's risk of obesity, asthma and allergies. Now some researchers are wondering if the microbiome may have a part in an even more crucial process: mate selection and, ultimately, evolution.

The best evidence that the microbiome may play this critical role comes from studies of insects. A 2010 experiment led by Eugene Rosenberg of Tel Aviv University found that raising *Drosophila pseudoobscura* fruit flies on different diets altered their mate selection: the flies would mate only with other flies on the same diet. A dose of antibiotics abolished these preferences—the flies went back to mating without regard to diet—suggesting that it was changes in gut microbes brought about by diet, and not diet alone, that drove the change.

To determine whether gut microbes could affect an organism's longevity and its ability to reproduce, Vanderbilt University geneticist Seth Bordenstein and his colleagues dosed the termites *Zootermopsis angusticollis* and *Reticulitermes flavipes* with the antibiotic rifampicin. The study, published in July 2011 in *Applied and Environmental Microbiology,* found that antibiotic-treated termites showed a reduced diversity in their gut bacteria after treatment and also produced significantly fewer eggs. Bordenstein argues that the reduction of certain beneficial microbes, some of which aid in digestion and in the absorption of nutrients, left the termites malnourished and less able to produce eggs.

These studies are part of a growing consensus among evolutionary biologists that one can no longer separate an organism's genes from those of its symbiotic bacteria. They are all part of a single "hologenome."

"There's been a long history of separating microbiology from botany and zoology, but all animals and plants have millions or billions of microorganisms associated with them," Rosenberg says. "You have to look at the hologenome to understand an animal or plant." In other words, the forces of natural selection place pressure on a plant or animal and its full array of microbes. Lending support to that idea, Bordenstein showed the closer the evolutionary distance among certain species of wasps, the greater the similarities in their microflora.

Researchers believe that the microbiome is essential to human evolution as well. "Given the importance of the microbiome in human adaptations such as digestion, smell and the immune system, it would appear very likely that the human microbiome has had an effect on speciation," Bordenstein says. "Arguably, the microbiota are as important as genes."

—Carrie Arnold

PHYSICS

A New Wrinkle in Time

Scientists develop a "time cloak" that can obscure an object at a given moment

For years physicists have been refining invisibility cloaks—physical setups that cleverly reroute light around a region in space, effectively concealing any object that might be inside. Now researchers at Cornell University have built the first temporal cloak, a device that obscures an object or event at a specific moment in time.

In a preliminary demonstration Cornell postdoctoral researcher Moti Fridman and his colleagues shone a laser beam through an experimental apparatus and into a detector. A physical object or even another beam of light in the laser beam's path would typically create a change in the laser light that the detector would register. With some clever optics, however, Fridman and his co-workers were able to open up a brief time gap in the beam and then close it back up as if the beam had gone undisturbed and in such a way that the detector did not register the interruption. The gap allows anything that would have otherwise affected the beam, such as an object, to instead slip right through, leaving no trace for the detector to pick up.

The researchers used the cloak to obscure an optical pulse that ordinarily interacts with the laser beam to produce a telltale spike at a certain wavelength. Yet when the event was cloaked, the telltale spike was nearly undetectable.

The cloak, described in the January 5 issue of *Nature,* relies on the fact that light of different colors moves at different speeds through certain media. Using a device that they call a time lens, the researchers split a single-color laser beam into a spread of wavelengths, then slowed half those wavelengths while speeding up the others. That created a very brief time gap that could be closed again before the beam reached the detector by reversing the lensing process, restoring the beam to a single, seemingly undisturbed wavelength.

The gap achieved by Fridman and his colleagues was extremely small—just 50 picoseconds, or 50 trillionths of a second, in duration. The investigators note that it is possible to extend the gap somewhat but that scattering and dispersion effects limit the scope of the temporal cloak to a few nanoseconds. *—John Matson*

COMMENT AT ScientificAmerican.com/mar2012

WHAT IS IT?

Pressure-sensitive: The experience of indulging in your favorite foods involves not only tasting flavors but also feeling the textures sweep across your tongue. Most of the bumps on the tongue's surface are filiform papillae, which enable tactical sensation. In this scanning electron microscope image of the human tongue, magnified 1,500 times, the papillae appear as cone-shaped buds. "They sense being deflected by something that touches them, including pressure from a heavy liquid," says Robert F. Margolskee, associate director of the Monell Chemical Senses Center in Philadelphia. He adds that the papillae appear to be scaly because they are constantly in a state of shedding old cells and growing new ones. *—Ann Chin*

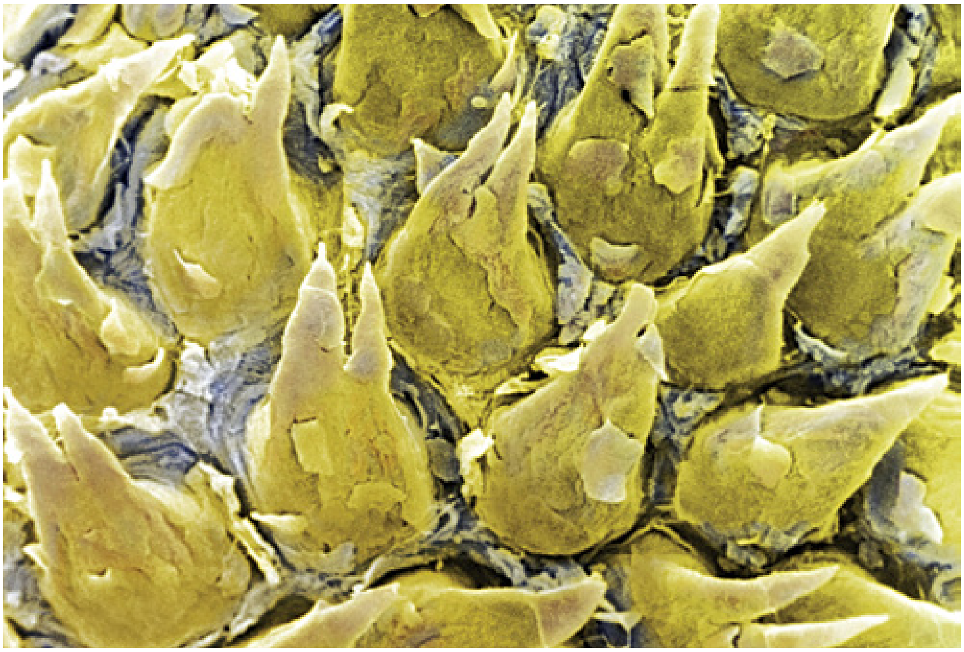


PHOTO RESEARCHERS, INC.

SCIENTIST IN THE FIELD

Probing the Depths

A marine biologist describes her upcoming mission to some of the deepest hydrothermal vents in the ocean

Where will you be sailing?
We'll sail onboard the research vessel *Atlantis* to the Mid-Cayman Spreading Center, which harbors the world's deepest chain of volcanoes. It's south of the Cayman Islands and west of Jamaica and Cuba. We first visited the site two years ago with a submarine called Nereus, and we found evidence of three new hydrothermal vents. On this cruise, we want to send our remotely operated underwater vehicle [ROV] Jason down to do a sampling mission at one of those vents and at another one discovered in 2010 by a team led by the U.K.'s National Oceanography Center, Southampton.

Tell me more about the area you'll be exploring.
The Mid-Cayman Spreading Center is a really exciting place to work, partly because of the diversity of the environment there. It's an ultraslow-spreading ridge, which means it has a low level of volcanic activity and a lot of tectonic activity. There are many different types of rocks, from volcanic basalt to peridotite, a rock that's more like the mantle and gets pulled up from deeper within the earth. The rock composition around a vent is a big driver of that vent's chemistry, and what I hope to understand is the chemistry of these two systems and how the pressure and rocks can cause the chemistry to change.

How do you find a hydrothermal vent?
We use a sensor that looks for the reducing potential of the water—how much oxygen is present. A deep-sea hydrothermal vent emits water that contains very low levels of oxygen. That low-oxygen water comes up from the vent, and as it drifts along we can detect the plume.

Once you find a vent, what do you need to do to sample it?
We're sending Jason on the sampling mission with four titanium bottles that will hold water samples; other people are sending bioboxes and things to put sulfide structures in. Jason is a workhorse. It's a really powerful submarine. It can stay down for more than 24 hours and has strong manipulator arms.


Nereus

PROFILE

NAME
Jill McDermott

TITLE
Ph.D. candidate, Woods Hole Oceanographic Institution

LOCATION
Woods Hole, Mass.

What else are you hoping to find?
Our studies seek to extend the known limits of life on earth. One of our goals is to understand whether or not organic molecules can be synthesized abiotically [without living organisms] in deep-sea hydrothermal vents, which carries implications for the origin and sustenance of life on the early earth and will inform future missions searching for life on other planetary bodies. *—Rose Eveleth*

COURTESY OF ADVANCED IMAGING AND VISUALIZATION LABORATORY, WOODS HOLE OCEANOGRAPHIC INSTITUTION

COMMENT AT ScientificAmerican.com/mar2012

RESEARCH

Are University Labs Criminally Dangerous?

MARTIN SHIELDS *Photo Researchers, Inc.*

Felony charges against U.C.L.A. raise the issue of science safety on campus

On a late afternoon in December 2008, the experiment Sheharbano "Sheri" Sangji was working on went up in flames. The 23-year-old laboratory assistant at the University of California, Los Angeles, suffered second and third degree burns over 43 percent of her body and died almost three weeks later in a hospital burn unit.

Now the Los Angeles County district attorney's office has brought felony charges against U.C.L.A. chemistry professor Patrick Harran, the head of Sangji's lab, and the Regents of the University of California for violations of safety regulations resulting in her death. If convicted on all three counts, Harran faces up to four and a half years in prison, and U.C.L.A. faces $4.5 million in fines. The university terms the charges "outrageous" and Sangji's death a "tragic accident." It is planning a vigorous defense.

The charges, apparently the first to be brought in an academic safety incident, raise the widely neglected issue of safety standards at university labs. A scathing report issued last October by the U.S. Chemical Safety Board (CSB) brought additional attention to the problem. The investigation, launched after a January 2010 explosion at Texas Tech University maimed a graduate student, mentions 120 mishaps, including the one involving Sangji. The report outlines systemic problems common on many campuses, such as failure to report accidents, and a lack of proper safety training for students and staff. Many university labs operate as quasi-independent "fiefdoms," according to the report; lab chiefs have great authority to observe or ignore safety standards and often see outside safety checks as "infringing upon their academic freedom."

The California criminal charges arise from citations and fines that the state's Division of Occupational Safety and Health leveled against U.C.L.A. in May 2009 for "serious" violations, among them failing to make timely corrections of unsafe conditions or to provide required training and personal protective gear. (Not only was Sangji not wearing a lab coat, but her synthetic sweatshirt may have "caught fire," according to the citation.)

The rate of serious mishaps in industrial labs is lower than that in academic labs, in part because industrial labs are more tightly regulated, according to experts, including James Kaufman, president of the Laboratory Safety Institute in Natick, Mass. Some experts believe that attaching criminal responsibility to preventable mishaps may encourage greater accountability.

—*Beryl Lieff Benderly*

ENGINEERING

It's All in the Tail

Leaping lizards are helping scientists build more stable vehicles

Science fiction often envisions worlds populated by humanoid robots. In reality, insects, reptiles and nonhuman animals often serve as a more practical template for automatons. The more legs a robot has, the more easily it can navigate tough terrain. Likewise, claws are less challenging to emulate than primate-esque hands, and, as a team of researchers reported recently, tails are an incredibly versatile stabilizing mechanism.

The back end of snakes, ants or even grasshoppers has served as such an inspiration to some roboticists. Now Robert J. Full, a biologist at the University of California, Berkeley, and his colleagues have turned to the red-headed African *Agama* lizard. The researchers' work, published in the January 12 issue of *Nature,* describes how a careful study of the *Agama*'s approach to leaping on slippery surfaces led to improvements in robotic design.

High-speed videography and motion capture revealed how the *Agama* raises its tail to counteract a lack of footing on slippery surfaces when vaulting from a flat, rectangular block to a vertical surface. When the block was covered with sandpaper, the lizard required less stabilization and its tail remained in a down position during a leap.

Full and his team applied the lizard's tail-raising schemes to a small, robotic four-wheeled vehicle dubbed Tailbot. After attaching a stabilizing tail to the rear of the vehicle and sending it off a ramp, the researchers noted that Tailbot sank nose down with its tail in the down position. When the tail was raised like the *Agama*'s, based on the Tailbot's attitude coming off the ramp, the robot was able to land on its wheels in a more balanced position. Full and his students are now investigating the role of the tail in controlling roll—and pitch and yaw—while running.

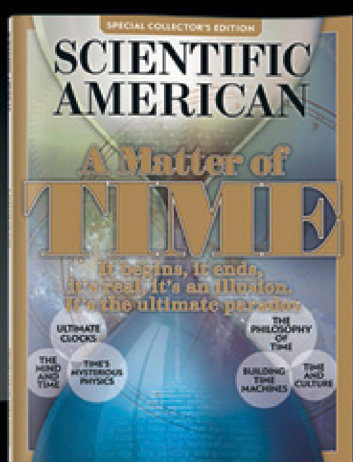
These are just the latest developments in Full's full-on flirtations with lizard-inspired robots. Stickybot, a mechanical collaboration with Stanford University in 2006 that could walk up smooth surfaces such as windows using an adhesive, was modeled after microscopic hairs found on the feet of geckos.

Other examples of so-called biomimetic machines include Boston Dynamics's Legged Squad Support System (LS3), which resembles a headless pack mule, and a wormlike robot under development at Harvard University.

By focusing on these nonhuman robot models, investigators can improve robotic design piece by piece, examining specific problems and learning from the ways in which animals solve them.

—Larry Greenemeier

MINDEN PICTURES



COMMENT AT ScientificAmerican.com/mar2012

CLIMATE

Soot Soldiers

Curbing methane and soot may be a fast, if incomplete, way to slow global warming

Humanity has done little to address climate change. Global emissions of carbon dioxide reached (another) all-time peak in 2010. The most recent international talks to craft a global treaty to address the problem pushed off major action until 2020. Fortunately, there's an alternative—curbing the other greenhouse gases. An economic and scientific analysis published in January in the journal *Science* found that taking steps to curb methane and black carbon (otherwise known as soot) could improve air quality, human health and agricultural yields. Even better, the team found that implementing just 14 soot and methane emissions-control measures globally would deliver nearly 90 percent of the potential benefits. An extra bonus: the 14 steps also curb global warming by roughly 0.5 degree Celsius by 2050, according to computer modeling.

Both methane and black carbon remain in the atmosphere for a short time compared with CO_2. By some accounts, we could see an effect within weeks or months, rather than decades, as with CO_2 emissions. The methods that would immediately slow global warming include eliminating methane releases from coal mines by capturing the gas and burning it; eliminating the venting or accidental release of methane co-produced by oil and gas drilling; capturing the gas from landfills in the U.S. and China; and promoting the recycling and composting of biodegradable trash.

This doesn't mean we wouldn't have to deal with CO_2 emissions. By continuing to emit at present rates, we'd still be storing up future trouble. But starting with soot and methane would buy time and, perhaps even more important, significantly reduce the chances of catastrophic climate change.

—*David Biello*

Lights out: A white dwarf emerges from a gas cloud.

Best of the Blogs

ASTRONOMY

Stars That Go Out with a Bang

A new supernova yields clues to how white dwarfs flame out

When a star becomes a white dwarf—an old, extremely dense star that would have once had a mass similar to our own sun's—the eventful part of its life is over. It releases what heat and light it has left over billions of years, slowly cooling until it no longer shines. Some white dwarfs, however, are not content with this ending.

If a white dwarf exists in a two-star system with a companion, it can avert its fate and go out with a bang, not a whimper. It does so by causing a particular type of stellar explosion called a type Ia supernova. A type Ia supernova starts when the white dwarf drags material from its companion onto itself. It grows and grows until it cannot get any bigger. At this point, it implodes, then rebounds and explodes in a supernova bright enough to outshine whole galaxies.

The companion star from which the white dwarf steals matter is instrumental in this dramatic event. Its identity, however, has long been a mystery. Theoretical models say the companion star can be anything from a red giant to a main sequence star like the sun to another white dwarf.

Astronomers have been able to narrow the range of possible companions for a type Ia supernova spotted late last year. A telescope belonging to the Palomar Transient Factory (PTF) survey in Pasadena, Calif., spotted a bright spot at one minute before 9 P.M. on August 24. The new supernova, known as supernova 2011fe, won Palomar astronomers the record for the earliest ever detection of a type Ia supernova: just 11 hours after its initial explosion.

Last December researchers published two papers in *Nature* analyzing observations of supernova 2011fe. One paper, with lead author Peter Nugent of Lawrence Berkeley National Laboratory and PTF, found that the companion star was probably a main sequence star. The other work, spearheaded by Weidong Li of the University of California, Berkeley, rules out a red giant.

Li used observations from the Keck II telescope in Hawaii to pinpoint the location of the supernova, then analyzed Hubble Space Telescope images from before the supernova explosion to look for clues about the pair of stars from which it was born.

Supernova 2011fe is the nearest type Ia supernova to be discovered in many years and, because instrumentation has moved on considerably in that time, will be the most studied supernova in history. These two papers are just the beginning. *—Kelly Oakes*

Adapted from Oakes's Basic Space blog at blogs.ScientificAmerican.com/basic-space

ANATOMY

Your Appendix Could Save Your Life

The humble organ may help us recover from serious infections

You may have heard that the appendix is a relic of our past, like the hind leg bones of a whale. Bill Parker, a professor of surgery at the Duke University School of Medicine, heard that, too; he just disagrees. Parker thinks the appendix serves as a "nature reserve" for beneficial bacteria in our gut. When we get a severe gut infection such as cholera (which happened often during much of our history and is common in many regions even today), the beneficial bacteria in our gut are depleted. The appendix allows them to be restored. In essence, Parker sees the appendix as a sanctuary for our tiny mutualist friends, a place where there is always room at the inn.

Parker's hypothesis, which he and collaborators first published in 2007 in the *Journal of Theoretical Biology,* is a fundamentally new idea about how an organ in our body works. A paper published last December provides new data to back up the theory.

James Grendell, chief of the division of gastroenterology, hepatology and nutrition at Winthrop University-Hospital on Long Island, and his team studied 254 patients with a history of gut infections caused by the bacterium *Clostridium difficile. C. difficile,* known as *C. diff* among the medical in-crowd, is a deadly pathogen often encountered in hospitals, particularly when patients must be treated by prolonged courses of antibiotics. *C. diff* does not appear to compete well with the native biota of patients' guts, but when the native biota are depleted (as is the case after several courses of antibiotics), *C. diff* can grow quickly and take over. If Parker's idea is right, individuals without an appendix should be more likely to have a recurrence of *C. diff* than those with one.

And that is precisely what Grendell's group found: patients without an appendix were more than twice as likely to have a recurrence of *C. difficile.* Recurrence in individuals with their appendix intact occurred in 18 percent of cases. Recurrence in those without their appendix occurred in 45 percent of cases.

Where does this leave us? In your body is an organ that appears to be helping out the bacteria in your life so they can, in turn, help keep you alive. More tests, even true experiments, need to be done before we can be sure. Until then, doctors will keep cutting out infected appendixes. When they do, when they hold them up, they hold up a symbol—a somewhat gross, pinky finger-size symbol—both of our complex relationship with other species and of how little we know. *—Rob Dunn*

Adapted from the Guest blog at blogs.ScientificAmerican.com/guest-blog

COURTESY OF NASA, R. CIARDULLO *Pennsylvania State University* AND H. BOND *STScI*

COMMENT AT ScientificAmerican.com/mar2012

David Pogue is the personal-technology columnist for the *New York Times.* He is the host of "Hunting the Elements" on *NOVA,* which airs April 4 on PBS.

Time to Kill Off Captchas

How the bot-proofing of the Internet is bringing humans down

Whenever there's a problem in the modern world, we try to solve it by building barriers. Music piracy? Copy protection. Hacked Web sites? More complicated passwords.

Unfortunately, these barriers generally inconvenience the law-abiding citizen and do very little to impede the bad guys. Serious music pirates and Web hackers still find their way through.

Maybe all the hurdles are enough to thwart the *casual* bad guys. That seems to be the thinking behind the Web blockades known as Captchas. (It's a contrived acronym for Completely Automated Public Turing Test to Tell Computers and Humans Apart.) Surely you've seen them: visually distorted words—sometimes real English ones and sometimes nonsense words—represented as a graphic when you try to sign up for something online. You're supposed to type the words you see into a box.

Captchas were designed by their Carnegie Mellon University inventors to thwart bots (automated hacker programs) that might bring online services to their knees. For example, some bots sign up for Hotmail or Yahoo e-mail accounts by the thousands for the purpose of spewing spam. Some post bogus comments in hopes of raising a site's search-results ranking.

In theory, only an actual human being can figure out what word is in the Captcha graphic. The letters are just twisted enough and the background is just cluttered enough that a person can read them, but not a computer. Good guys in, bad guys out—the perfect barrier.

In practice, Captchas have just replaced one public nuisance with another. First of all, the images are often so distorted that even a human can't read them. That's a particular problem in nonsense words like "rl10Ozirl." Are those lowercase Ls or number ones? Zero or letter O? Second, there's the vision thing. If you're blind, you can't do a visual Captcha puzzle.

The best Captchas (if that's not an oxymoron) offer alternatives to fix these problems. There might be a button that offers you a second puzzle if the first is too hard to read or an audio Captcha option for blind people. Above all, though, increasing evidence shows that Captchas are losing the technology war. Researchers and spammers have both been able to get around them.

There have been efforts to replace visual Captchas with less user-hostile puzzles. Some ask you to take an easy math test, answer a simple question, identify a photograph or listen to garbled audio. All of them exclude one group or another, though—such as non-English speakers or deaf people.

Overall, the Carnegie Mellon team estimates that we spend a cumulative 150,000 hours at the gates of these irritating obstructions every single day. In a newer variant, called reCaptcha, at least that time is put to public use. You see a muddied-looking word that comes from a wonky scanned Google book; when you type what it really says, you're actually helping out with the process of cleaning up and recognizing an actual text.

Nevertheless, we the law abiders are still wasting 17 person-years every single day. That's a disgraceful waste of our lives. Surely there are better solutions worth exploring.

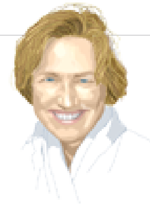
Maybe we should invent a voluntary Internet identity card so we're already known when we sign up for something. Maybe Web sites should enforce a short-term limit of one new account or posted comment per "person." Or the Web site should look at the speed or irregularity of our typing to determine if we're human.

Or fingerprints. Or retinal scans. *Something.*

Spammer bots are a problem, yes. But Captchas are a problem, too. They're a bother, they're not foolproof and they assume that everyone is guilty until proven innocent. What Captcha really stands for, in other words, is Computers Annoying People with Time-Wasting Challenges That Howl for Alternatives. SA

SCIENTIFIC AMERICAN ONLINE:
Eight alternatives to the Captcha: **ScientificAmerican.com/mar2012/pogue**

Illustration by Thomas Fuchs



Deborah Franklin is based in San Francisco and has reported on science and medicine for National Public Radio, the *New York Times*, *Fortune* and *Health Magazine*.

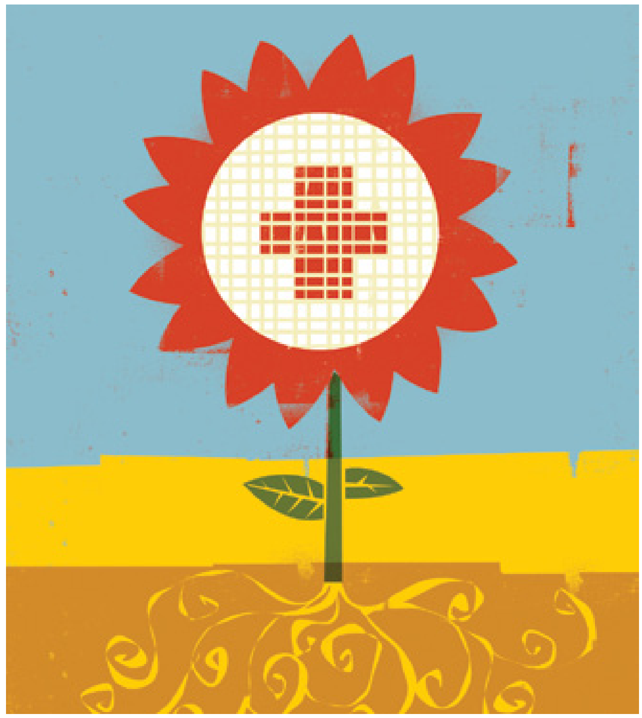
Nature That Nurtures

Hospital gardens turn out to have medical benefits

To get an inkling of what a well-designed hospital garden can mean to a seriously ill child, watch the home video posted on YouTube last August of Aidan Schwalbe, a three-year-old heart-transplant recipient. The toddler is shown exploring the meandering paths, sun-dappled lawn and gnarled roots of a branching shade tree in the Prouty Garden at Children's Hospital Boston. "He loves to be out in the garden feeding the birds and squirrels," wrote Aidan's grandmother in an August blog entry. "They will all weigh 30 lbs. each by the time we leave here!"

The garden that Aidan loves—with its vibrant greenery, shaded places to sit and walk, and small, half-hidden animal sculptures that fascinate visitors of all ages—is "one of the most successful hospital gardens in the country," says Clare Cooper Marcus, an emeritus professor in landscape architecture at the University of California, Berkeley.

Dismissed as peripheral to medical treatment for much of the 20th century, gardens are back in style, now featured in the design of most new hospitals, according to the American Society of Landscape Architects. In a recent survey of 100 directors and architects of assisted-living residences, 82 percent agreed that "the design of outdoor space should be one of the most important considerations in the design." But can gardens, in fact, promote healing? It turns out that they often can. Scientists around the world are now digging into the data to find out which features of gardens account for the effect.



COMMON SENSE PUT TO THE TEST

The notion that the fresh breezes, dappled sunlight and fragrant greenery of a garden can be good for what ails us has its roots in ancient tradition and common sense. But a much cited study, published in 1984 in the journal *Science* by environmental psychologist Roger Ulrich, now at Texas A&M University, was the first to use the standards of modern medical research—strict experimental controls and quantified health outcomes—to demonstrate that gazing at a garden can sometimes speed healing from surgery, infections and other ailments.

Ulrich and his team reviewed the medical records of people recovering from gallbladder surgery at a suburban Pennsylvania hospital. All other things being equal, patients with bedside windows looking out on leafy trees healed, on average, a day faster, needed significantly less pain medication and had fewer postsurgical complications than patients who instead saw a brick wall.

Esther Sternberg, a physician and neuroimmunologist at the National Institute of Mental Health, calls Ulrich's work "groundbreaking." At the time, studies showing that loud sounds, disrupted sleep and other chronic stressors can have serious physical consequences were only just beginning. "In 1984 we all took it for granted that hospitals were noisy, smelly, disorienting mazes," says Sternberg, who details the history in her book *Healing Spaces: The Science of Place and Well-Being*. "But it hadn't occurred to us that stress could affect a patient's healing—or that we could do anything about that."

Fortunately, as the evidence implicating hospitals as major engines of stress builds, the stack of data suggesting that gardens and planted alcoves can encourage healing has grown, too. Just three to five minutes spent looking at views dominated by trees, flowers or water can begin to reduce anger, anxiety and pain and to induce relaxation, according to various studies of healthy people that measured physiological changes in blood pressure, muscle tension, or heart and brain electrical activity.

Indeed, the benefits of seeing and being in nature are so powerful that even pictures of landscapes can soothe. In 1993 Ulrich and his colleagues at Uppsala University Hospital in Sweden randomly assigned 160 heart surgery patients in the intensive care unit to one of six conditions: simulated "window views" of a large nature photograph (an open, tree-lined stream or a shadowy forest scene); one of two abstract paintings; a white panel; or a blank wall. Surveys afterward confirmed that patients assigned the water and tree scene were less anxious and needed

Illustration by Shaw Nielsen

fewer doses of strong pain medicine than those who looked at the darker forest photograph, abstract art or no pictures at all.

"Let's be clear," Cooper Marcus says. "Spending time interacting with nature in a well-designed garden won't cure your cancer or heal a badly burned leg. But there is good evidence it can reduce your levels of pain and stress—and, by doing that, boost your immune system in ways that allow your own body and other treatments to help you heal."

What Makes a Garden Healing?

The following checklist, based on research, shows what works:

✔ Keep it green
Lush, layered landscapes with shade trees, flowers and shrubs at various heights should take up roughly 70 percent of the space; concrete walkways and plazas about 30 percent.

✔ Keep it real
Abstract sculptures do not soothe people who are sick or worried.

✔ Keep it interesting
Mature trees that draw birds and chairs that can be moved to facilitate private conversation foster greater interaction.

✔ Engage multiple senses
Gardens that can be seen, touched, smelled and listened to soothe best. But avoid strongly fragrant flowers or other odors for patients undergoing chemotherapy.

✔ Mind the walkways
Wide, meandering paths that are tinted to reduce glare allow patients with low eyesight, wheelchairs or walkers to get close to nature. Paving seams must be narrower than one eighth of an inch to prevent trips by patients trailing wheeled IV poles.

✔ Water with care
Fountains that sound like dripping faucets, buzzing helicopters or urinals do not relax anyone, and neither does the strong smell of algae.

✔ Make entry easy
Gardens should not be far away or behind doors that are too heavy for a frail or elderly person to open.

GROWING INSIGHT

Still, research shows that not all gardens are equally effective. In 1995 Cooper Marcus and landscape architect Marni Barnes received a grant from the nonprofit Center for Health Design to analyze the physical layout and daily use of several hospital gardens in northern California. In 32 hours of observations, which included taking detailed notes and interviewing users (who collectively made 2,140 visits), the researchers noticed several patterns that have been borne out in subsequent studies of other sites.

Among their findings: users mostly visited gardens seeking relaxation and restoration from mental and emotional fatigue. Tree-bordered vistas of fountains or other water features, along with lush, multilayered greenery of mature trees and flowering plants, appealed most. Those results are consistent with Ulrich's findings of the healing power of a "window view" and also correspond with the theories of evolutionary biologists that people prefer views that are reminiscent of the savannas where humans evolved. Throughout human history, trees and water have signaled an oasis, and flowering plants have been a sign of possible food. Open views deter surprises by predators, and shaded alcoves offer a safe retreat.

The more greenery versus hard surfaces, the better. "We found that a ratio of at least 7:3 seems to work best," Cooper Marcus says. Less greenery signals a "plaza or shopping mall courtyard" and is not as relaxing.

What you can do in the garden is as important as what you see. The results of "behavioral maps" tracking visitors' actions while in a garden suggested a need for private conversation areas; smooth, tree-lined paths that invite strolls but that will not trip wheelchairs or intravenous poles; lightweight furniture that can be tugged into the shade or sun; and naturalistic landscaping that lures birds, squirrels and other wildlife.

One finding, in particular, surprised Cooper Marcus and Barnes. Stressed hospital employees accounted for as many visits to hospital gardens as stressed patients, and interviews confirmed that staffers depend on the greenery. "I feel like one of the Mole People," an employee who works in the basement radiology department of a Berkeley, Calif., hospital told the researchers. She said she comes to sit amid the trees of the rooftop garden daily to relax and meditate. "It's a big mental, emotional lift."

Different generations seem to value the same things in gardens, but research has turned up differences, too. In 2005 clinical psychologist Sandra A. Sherman and her colleagues conducted a study of three gardens at a children's cancer center in San Diego to try to figure out what worked and what did not. Some of the findings made intuitive sense. A mosaic turtle sculpture that small children could climb, for example, was more alluring than a crane sculpture the kids could only look at. Other results were less obvious. A riverlike water feature where kids and parents could splash and float boats together was twice as popular with the kids as a child-size playhouse that adults could not enter.

Focusing on the other end of the age spectrum, Susan Rodiek of Texas A&M has looked at long-term care institutions. In her studies, published in 2009, of a random sampling of 68 assisted-living facilities, Rodiek talked to 1,100 residents and 430 employees. "Older people," she found, "need and benefit from outdoor space and greenery just as much as the young."

But the adults desire some different features. Middle-aged adults, for example, tend to look for peace and quiet in the garden, and older adults are more likely to seek stimulation. At one new senior residence Rodiek studied, the facility's architect had created a lovely, secluded lawn and pond at the back of the apartment building. But every afternoon, the researchers noticed, at around the same time, the elderly residents dragged their lightweight aluminum chairs to the front of the building to be part of the community of commuters passing by. "You can only watch a pond for so long," Rodiek says. "And a grass lawn doesn't change much."

THE SEARCH FOR STANDARDS

To help ensure that outdoor areas promote as much healing as possible, Rodiek has recently created a checklist, drawing on the evidence described above, that administrators of long-term care facilities and others can use to evaluate their garden design. And she is working on one geared specifically to hospitals so that hospital-accrediting agencies can set standards.

Codified standards are needed because therapeutic gardens are becoming so popular. "New hospitals are now competing on the basis of whether they have a 'healing garden' or not," Cooper Marcus says. "But when you go to look, some are not much more than a rooftop with a chaise lounge and a few potted plants." Designing a good garden for health care settings "isn't rocket science," she adds. Yet basing the design on good science instead of whim will strengthen the healing nature of nature. SA

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Fred H. Gage is a professor specializing in how neurons are generated in the brain at the Laboratory of Genetics at the Salk Institute for Biological Studies in La Jolla, Calif.

Alysson R. Muotri is an assistant professor in the department of pediatrics and cellular and molecular medicine at the University of California, San Diego. He was a postdoctoral fellow in Gage's laboratory from 2002 to 2008.

NEUROSCIENCE

WHAT MAKES EACH BRAIN UNIQUE

How can identical twins grow up with different personalities? "Jumping genes" move around in neurons and alter the way they work

By Fred H. Gage and Alysson R. Muotri

IN BRIEF

Genes we inherit and environmental factors both influence human behaviors. Scientists have recently discovered other underlying processes at work.

So-called jumping genes, segments of DNA that can copy and paste themselves into new places in the genome, can alter the activity of full-length genes. Occasionally they will turn on neighboring genes in these locations. That activity occurs more in the brain than other areas, resulting in different traits and behaviors, even in closely related individuals.

These mobile genetic elements may also turn out to play a role in people's disposition to psychiatric disorders.

Researchers are now beginning to investigate whether jumping genes help us adapt to rapidly changing environmental conditions.

Illustration by Jean-Francois Podevin

YOUR BRAIN IS SPECIAL.

So is mine. Differences arise at every level of the organ's astonishingly intricate architecture; the human brain contains 100 billion neurons, which come in thousands of types and collectively form an estimate of more than 100 trillion interconnections. These differences, in turn, lead to variances in the ways we think, learn and behave and in our propensity for mental illness.

How does diversity in brain wiring and function arise? Variations in the genes we inherit from our parents can play a role. Yet even identical twins raised by the same parents can differ markedly in their mental functioning, behavioral traits, and risk of mental illness or neurodegenerative disease. In fact, mice bred to be genetically identical that are then handled in exactly the same way in the laboratory display differences in learning ability, fear avoidance and responses to stress even when age, gender and care are held constant. Something more has to be going on.

Certainly the experiences we have in life matter as well; they can, for instance, influence the strength of the connections between particular sets of neurons. But researchers are increasingly finding tantalizing indications that other factors are at work—for instance, processes that mutate genes or affect gene behavior early in an embryo's development or later in life. Such phenomena include alternative splicing, in which a single gene can give rise to two or more different proteins. Proteins carry out most of the operations in cells, and thus which proteins are made in cells will affect the functioning of the tissues those cells compose. Many researchers are also exploring the role of epigenetic changes—DNA modifications that alter gene activity (increasing or decreasing the synthesis of specific proteins) without changing the information in genes.

In the past few years the two of us and our colleagues have come on especially intriguing suspects that seem to operate more in the brain than in other tissues: jumping genes. Such genes, which have been found in virtually all species, including humans, can paste copies of themselves into other parts of the genome (the full set of DNA in the nucleus) and alter the functioning of the affected cell, making it behave differently from an otherwise identical cell right next to it. Many such insertions in many different cells would be expected to yield subtle or not so subtle differences in cognitive abilities, personality traits and susceptibility to neurological problems.

Our early findings of gene jumping in the brain have led us to another question: Given that the brain's proper functioning is essential to survival, why has evolution allowed a process that tinkers with its genetic programming to persist? Although we still do not have a definite answer, mounting evidence suggests that by inducing variability in brain cells, jumping genes may imbue organisms with the flexibility to adapt quickly to changing circumstances. Therefore, these jumping genes—or mobile elements, as they are called—may have been retained evolutionarily because, from the standpoint of promoting survival of the species, this adaptation benefit outweighs the risks.

ANCIENT INVADERS

THE IDEA THAT MOBILE ELEMENTS EXIST and move about in the genome is not new, but the recent evidence that they are so active in the brain came as a surprise. Gene jumping was first discovered in plants, even before James Watson and Francis Crick spelled out the double-helical structure of DNA in 1953. In the 1940s Barbara McClintock of Cold Spring Harbor Laboratory observed that "controlling elements" moved from one place to another in the genetic material of corn plants. She discovered that under stress, certain regions in the genome could migrate and turn genes on and off in their new location. The products of McClintock's experiments were the now famous ears of corn with seeds of varying colors—a demonstration of genetic mosaicism, in which genes in a particular cell may be switched on or off in a pattern that differs from that of neighboring cells that are otherwise identical.

McClintock's research, which at first encountered skepticism within the scientific community, eventually resulted in her receiving a Nobel Prize in 1983. In subsequent years it became clear that the phenomenon of genetic mosaicism is not restricted to plants but also occurs in many organisms, including humans.

McClintock did her work on transposons, which are mobile elements that use a cut-and-paste mechanism to move a stretch of DNA around the cell's genome. More recent research on mobile elements in the brain had focused on retrotransposons, which employ a copy-and-paste approach to insinuate themselves into new areas of the genome. They basically replicate themselves rather than popping out of the surrounding DNA, after which the copy takes up a new position elsewhere.

Retrotransposons make up as much as half of the nucleotides, or DNA building blocks, in the human genome. In contrast, the approximately 25,000 protein-coding genes we possess make up less than 2 percent of mammalian DNA. The jumping genes are descendants of the first primitive molecular replication systems that invaded the genomes of eukaryotes (organisms having cells that contain a nucleus) long ago. A group led by Haig H. Kazazian, Jr., at the University of Pennsylvania showed in 1988 that retrotransposons, which were once thought of as nonfunctional junk DNA, were active in human tissues.

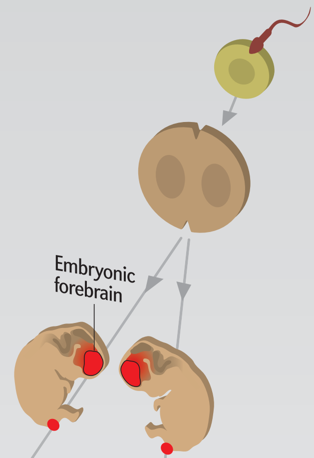
In particular, one type of retrotransposon, known as a long in-

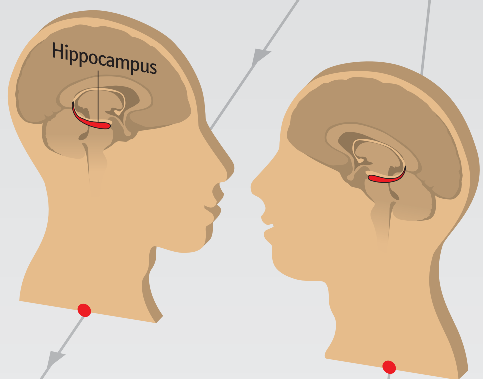
Copy-and-Paste Genetics

Sequences of DNA known as jumping genes, which are active in the brain, particularly during development, can make copies of themselves and then insert the same sequences elsewhere within the genome of a cell. In their new locations, jumping genes, also called retrotransposons, sometimes have no effect at all on nearby genes that serve as blueprints for proteins. In some cases, though, they may activate those genes and thereby influence the functioning of individual cells. The cellular changes may ultimately result in differences in brain function among people, even between identical twins.

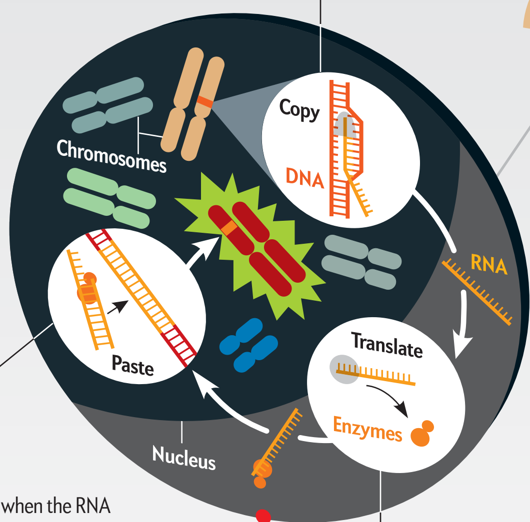
How Genes Jump

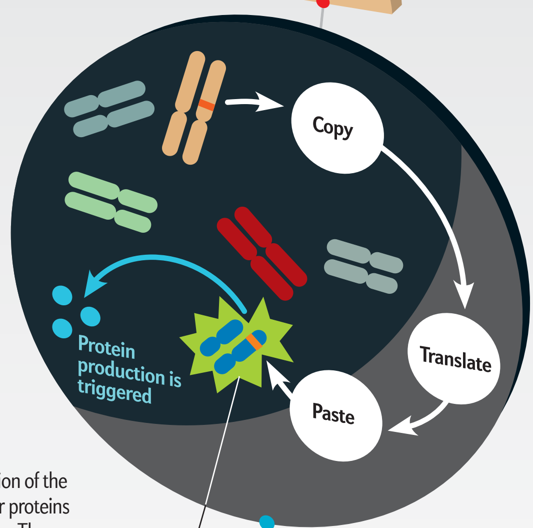
Nonheritable changes in genetic code can occur when a retrotransposon—a "junk" segment of the genome—copies itself into the RNA, then back to the DNA and reinserts itself, ending up in a different position. These mobile elements can move around in both the embryonic and adult brains—actions that are depicted here in a set of identical twins.





1 **Copying occurs** during cell division, when a sequence of DNA "transcribes" itself into a single strand of RNA, which then moves from the nucleus to the cell cytoplasm.

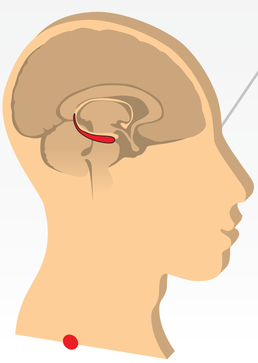




3 **Pasting begins** when the RNA makes a copy of the original DNA, which then gets inserted at a new place in the genome after a protein nicks open a chromosome.

2 **"Translation"** of a portion of the RNA strand into helper proteins occurs in the cytoplasm. The original RNA strand and the newly formed proteins join and then reenter the cell nucleus.

4 **Activation** of a neighboring gene may occur after the jumping process occurs. In the embryo, this process happens in the forebrain and all other areas. In the adult, jumping takes place only in the hippocampus and the few other areas that contain neural progenitor cells.



Result: Nonidentical Twins

Even when twins originate from the same egg, jumping genes may leave the two of them with different gene activation patterns and thus quite different brains.

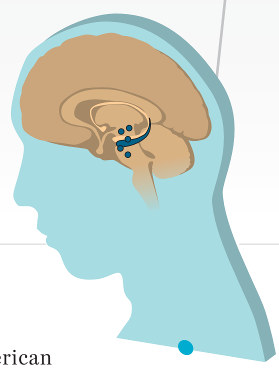


Illustration by Jen Christiansen

terspersed element 1 (L1), appears to be a key player in the human genome. It is able to hop around frequently probably because it, unlike other mobile elements in humans, encodes its own machinery for spreading copies of itself far and wide in the cellular genome. Analysis of its behavior in cells reveals that when something prompts an L1 in the nuclear genome to begin the "jumping" process, it first transcribes itself into single-stranded RNA, which then travels from the nucleus to the cytoplasm, where it serves as a template for constructing proteins specified by some parts of the L1 DNA. The proteins then form a molecular complex with the still intact RNA, and the whole complex heads back to the nucleus. There one of the proteins, an enzyme called an endonuclease, makes a nick in specific sites in the DNA. It also uses the RNA as a template for producing a double-stranded DNA copy of the original L1 retrotransposon and inserts this duplicate into the genome where the cut was made. Such reverse transcription, from RNA to DNA, is familiar to many people today as part of the way that the HIV virus gets a DNA copy of its RNA genome to take up a permanent home in the genome of the cells it infects.

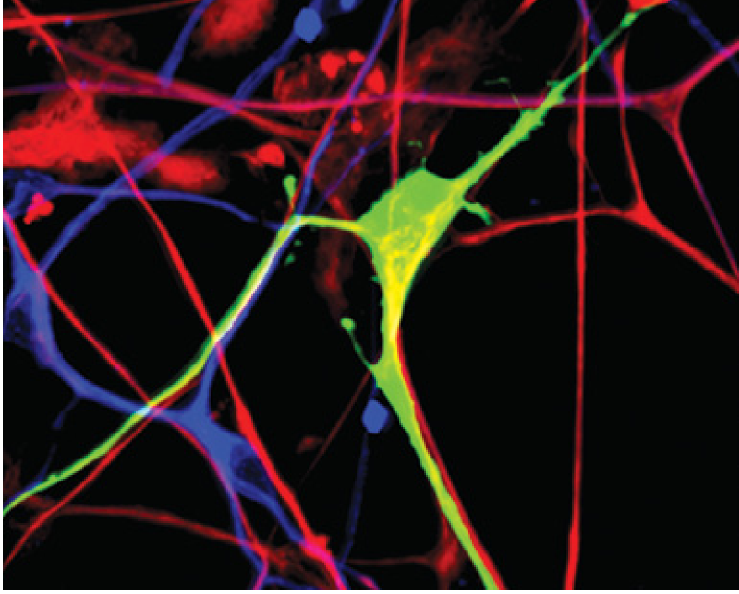
Retrotransposition often fails to run its course, which produces truncated, nonfunctional copies of the original L1 DNA. Sometimes these snippets (or the whole L1 copy) have no effect on a protein-coding gene. Other times, though, they can have any of several consequences, both good and bad, for a cell's fate. They may, for instance, drop into and thus alter the protein-coding region of a gene. This maneuver can lead to creation of a new variant of the protein that helps or harms an organism. Or this positioning may stop a given protein from being made. In other instances, the newly pasted DNA may fall outside of a coding region but act as a promoter (a switch that can turn on nearby genes) and alter the level of gene expression—the amount of protein made from the gene—with, once again, good or bad results for the cell and the organism. When LI retrotransposons end up in many places in neurons or in many cells of the brain, or both, the brain will be very different from the one that would have formed without their influence. It stands to reason that such genetic mosaicism could affect behavior, cognition and disease risk and could also help explain why one identical twin may remain disease-free when a sibling is diagnosed with schizophrenia, for example.

WHERE DOES JUMPING OCCUR?

UNTIL RECENTLY, most investigators aware of L1 retrotransposition assumed that it mostly took place in germ cells (ovaries or testes). Although a few clues suggested that L1 genes stay active in somatic tissues (nonsex cells) during early development or later, these clues were generally dismissed. If genes exist merely to propagate themselves, as one evolutionary theory holds, jumping genes would have little cause to remain active in somatic cells because such cells would not pass the DNA to an organism's next generation: after all, the affected cells die when their owner does.

Better detection tools have now revealed that retrotransposons can move around somatic tissues during early development and even later in life. These events happen more often in the brain than in other tissues—a direct challenge to the longstanding dogma that the genetic codes of brain cells in adults are identical to one another and remain stable for the cells' life.

In our lab at the Salk Institute for Biological Studies in La Jolla, Calif., for instance, we monitored gene jumping in a mouse whose



Jumped gene: Nomadic DNA in a neuron gives rise to a protein that glows green after moving to a new spot in the cell nucleus.

cells were genetically engineered to undergo retrotransposition and fluoresce green when an L1 element inserted itself in genomes of a cell anywhere in its body. We observed glowing green cells only in germ cells and in certain brain areas, including the hippocampus (a region important to memory and attention)—which suggests that L1s may move around more in the brain than in other somatic tissues. Interestingly, the jumping was occurring in progenitor cells that give rise to hippocampal neurons.

In various organs of fully formed organisms, a small population of progenitor cells stands by, ready to divide and give rise to specialized cell types needed to replace cells that die. The hippocampus is one of two regions of the brain where neurogenesis, generation of new nerve cells, occurs. Thus, L1s appear to be active during early development when neurons are being born, but they can also move around in the adult brain in the areas where new neurons continue to be born into adulthood.

Even with the mouse experiments, more evidence was needed that retrotransposition was actually occurring in the brain. We undertook an analysis of human postmortem material that compared the number of L1 elements in brain, heart and liver tissues. We found that the brain tissue contained significantly more L1 elements in each cell nucleus than the heart or liver tissues did.

Much of the jumping had to have occurred during the brain's development because retrotransposition requires cell division—a process that does not take place in the brain, except in two circumscribed areas—to happen after early childhood. An analysis suggested that each neural cell in humans undergoes an average of 80 L1 integration events, a rate that could well lead to a great deal of variation among cells and in the overall brain activity of different individuals.

A recent finding from researchers at the Roslin Institute near Edinburgh and their colleagues supplies further confirmation of L1 activity in the human brain. The researchers reported in 2011 in *Nature* that a total of 7,743 insertions of L1s in the hippocampus and caudate nucleus (which is also involved in memory) in three deceased individuals contained integrated L1 elements. (*Scientific American* is part of Nature Publishing Group.) That study also implied that the emerging portrait of genetic diversity in the brain will only get more complicated as this research moves forward. The Roslin team was surprised to come on about

FROM "L1 RETROTRANSPOSITION IN HUMAN NEURAL PROGENITOR CELLS," BY NICOLE G. COUFAL ET AL., IN NATURE, VOL. 460; AUGUST 27, 2009

15,000 members of a class of retrotransposons known as short interspersed elements (SINEs). The preponderant SINE, part of a group known as Alu elements, had never been encountered before in the brain.

Our findings made us wonder what might trigger L1 activity. Knowing that the hippocampus is also a site where neurogenesis transpires and that exposure to novel situations and exercise trigger neurogenesis in mice, we decided to see if exercise might be one spur to gene jumping. We found that after our transgenic mice ran on a wheel, the number of green fluorescing cells increased about twofold in the rodents' hippocampus. Given that novelty and challenge also prompt neurogenesis, we are entertaining the possibility that a new or unfamiliar environment could be another instigator of retrotransposition.

If we are correct and L1 jumping does increase as the nervous system learns and adapts to the outside world, the finding would indicate that individual brains and the neuronal networks that make them up are constantly changing and alter with each new experience, even in genetically identical twins.

ORIGINS OF DISEASE

WE ARE CONTINUING TO EXPAND the evidence for the hypothesis that jumping genes contribute to human variation in brain processing by moving beyond just counting L1s in DNA. In our quest to link our data to real events that have either positive or detrimental effects on living people, it is sometimes easiest to pinpoint the bad outcomes that resulted from a gene that jumped, if only because the consequences are so obvious.

In November 2010 our team reported in *Nature* that a mutation in a gene called *MeCP2* affected L1 retrotransposition in the brain. Mutations in the *MeCP2* gene can induce Rett syndrome, a severe disorder of brain development that almost exclusively affects girls. The discovery that *MeCP2* was mutated in patients with Rett syndrome and other mental disorders raised multiple questions about the molecular and cellular mechanisms of this disease. Our research showed that the mutation in the brains of mice and humans with Rett syndrome resulted in a significant increase in numbers of L1 insertions in their neurons—a finding that suggests that the jumping genes might account for some of the effects of the *MeCP2* mutation.

L1 activity has also turned up in other disorders. An analysis of the frontal cortex regions of individuals with schizophrenia revealed increased production of mobile element sequences compared with those without the condition. Circumstantial evidence suggests that L1 elements are an important component of various brain disorders, including autism. Understanding the role of mobile elements in the development of psychiatric diseases might lead to new methods for diagnosis, treatment and prevention.

The continuing research into jumping genes in the brain could potentially challenge an entire academic discipline. Behavioral geneticists often follow groups of identical twins over long periods to control for the effects of genes and determine the environmental contributions to such disorders as schizophrenia. The new findings showing that jumping genes actively revise genomes after an embryo forms question the assumption that "identical" twins are genetically alike. Indeed, the new discoveries will make it ever harder to disentangle the relative effects of nature and nurture on our psyches.

The question remains: Why has evolution not destroyed these vestiges of ancient viruses from within our cells, given that jumping genes have a high chance of introducing potentially fatal genetic flaws? To answer the question, we should acknowledge that humans have always been under attack by viral parasites and other invaders that expand the size of our genomes with jumping DNA. The bodies of humans and our evolutionary forebears may not have been able to fully eliminate the interlopers, but they have adapted to at least coexist with the invaders by silencing them through a variety of clever mechanisms that mutate and disable them. It also appears that, in some cases, our genomes have commandeered the genetic machinery of L1 retroelements to enhance our own survival, which is one reason that cells may sometimes allow, or even encourage, L1s to jump around the genome under carefully controlled conditions.

One clue to why they persist may come from closer analysis of the finding that mice from a single genetic strain raised under highly controlled conditions vary greatly in their responses to stress. The observed behavioral differences are distributed typically in the population (picture a bell curve), a pattern that implies that the mechanisms producing this variability are random, as the sites of L1 retrotransposon insertions seem to be.

The putatively random nature of how L1s move from place to place in the genome implies that natural selection may, in effect, be rolling the dice in the hope that benefits from helpful insertions will outweigh any deleterious consequences of other insertions. And nature may be placing bets frequently on the neural progenitor cells of the hippocampus so as to maximize the possibility that at least some of the new positions will give rise to a population of adult neurons particularly well suited to the tasks the brain will confront. A somewhat similar process occurs when the DNA in immune cells rearranges itself to produce an array of antibodies, after which only the antibodies best equipped to fight off a pathogen are selected for full-scale production.

This scenario does not seem far-fetched. L1-mediated effects do not need to be large and do not have to occur in many cells to influence behavior. In rodents, a change in the firing pattern of a single neuron might be enough to make a difference.

More possible support for this idea is the discovery that the only lineage of L1 jumping elements currently active in the human genome evolved about 2.7 million years ago, after the evolutionary split from chimpanzees to bipedal humans—a time when our hominid ancestors were first beginning to adopt the use of stone tools. That finding lends credence to the notion that the L1 elements may have helped build brains that can process information about the environment rapidly and that can thus more readily meet the challenges of ever changing environmental and climatic conditions. L1 jumping genes seem to have been a collaborative partner in advancing the evolution of *Homo sapiens.* SA

MORE TO EXPLORE

L1 Retrotransposition in Human Neural Progenitor Cells. Nicole G. Coufal et al. in *Nature,* Vol. 460, pages 1127–1131; August 27, 2009.

LINE-1 Retrotransposons: Mediators of Somatic Variation in Neuronal Genomes? Tatjana Singer et al. in *Trends in Neurosciences,* Vol. 33, No. 8; August 2010. **www.ncbi.nlm.nih.gov/pmc/articles/PMC2916067/?tool=pubmed**

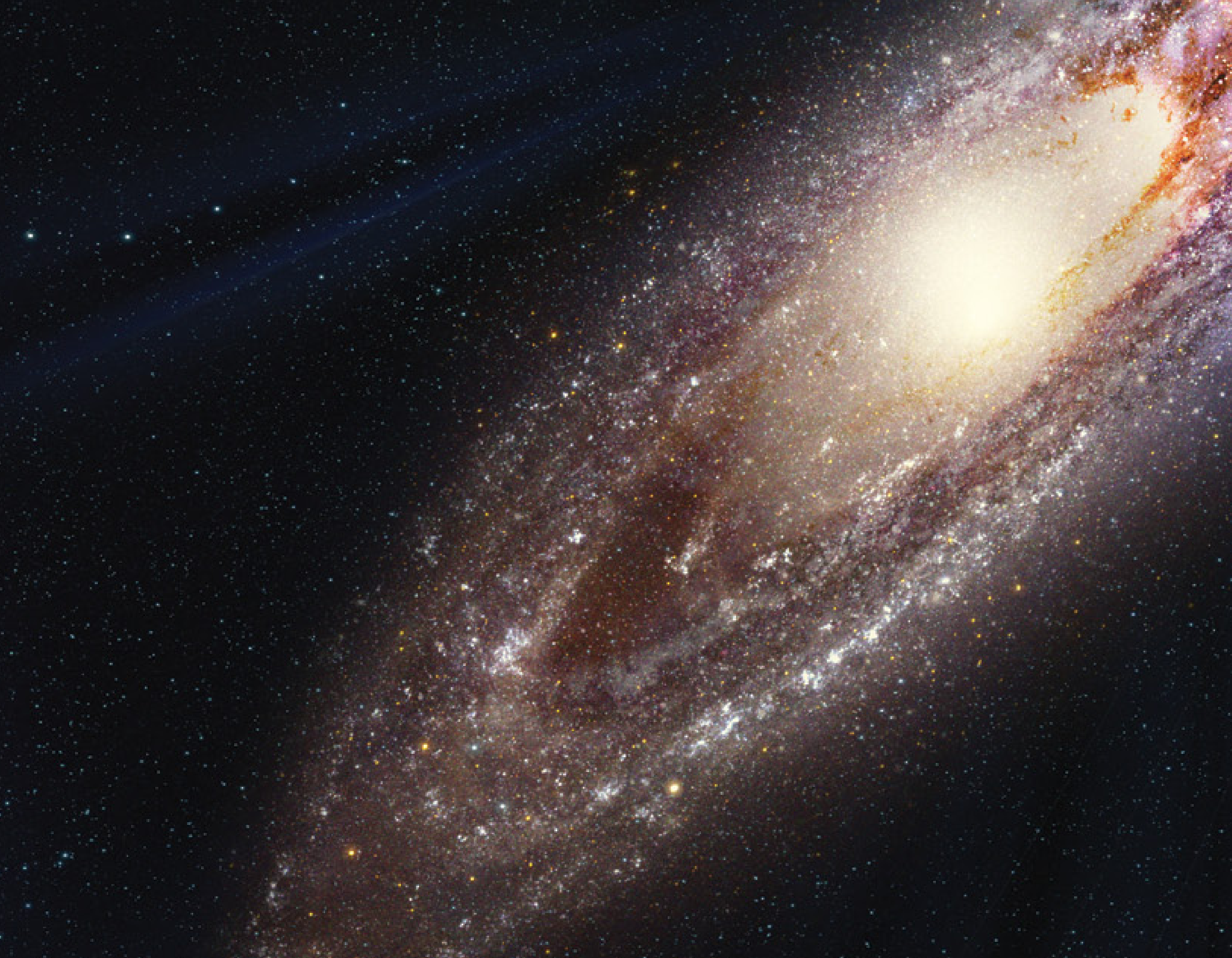
SCIENTIFIC AMERICAN ONLINE
A video of some of Gage's work on jumping genes can be found by going to **ScientificAmerican.com/mar2012/jumping-genes**

ASTROPHYSICS

THE FAR, FAR FUTURE OF STARS

Some say its glory days are long gone, but the universe has life in it yet. Brand-new types of celestial phenomena will unfold over the coming billions and trillions of years

By Donald Goldsmith



IN BRIEF

Although the grand era of galaxy and star formation is over, the universe remains a vigorous place. In the future stars will gradually shift their appearance as their composition changes. Star and planet systems will fall apart, and celestial objects that now are rare will become common, such as dense balls of helium. In some ways, the universe in the future may be more hospitable to life than it is today.

Considering the far future of the cosmos is more than inherently interesting. The far distant future provides astrophysicists with an intellectual sandbox, a way for them to grasp the implications of their theories and observations.

Illustration by Kenn Brown, Mondolithic Studios

Donald Goldsmith may well be the only astronomer who once worked as a tax attorney. That career was lucrative but short-lived. He received his Ph.D. in astronomy from the University of California, Berkeley, in 1969 and served as a consultant on Carl Sagan's *Cosmos* series. He was the principal writer for other shows such as NOVA's *Is Anybody Out There?* with Lily Tomlin and the series *The Astronomers.*

TIME'S SEEMINGLY INEXORABLE MARCH HAS ALWAYS PROVOKED INTEREST IN, AND SPECULATION about, the far future of the cosmos. The usual picture is grim. Five billion years from now the sun will puff itself into a red giant star and swallow the inner solar system before slowly fading to black. But this temporal frame captures only a tiny portion—in fact, an infinitesimal one—of the entire future. As astronomers look ahead, say, "five hundred and seventy-six thousand million years," as humorist Douglas Adams did in *The Restaurant at the End of the Universe,* they meet a cosmos replete with myriad slow fades to oblivion. By then the accelerating expansion of space will have already carried everything outside our galaxy beyond our view, leaving the night sky ever emptier. Lord Byron captured the prospect of such a celestial wasteland in his 1816 poem "Darkness": "The bright sun was extinguish'd, and the stars/Did wander darkling in the eternal space."

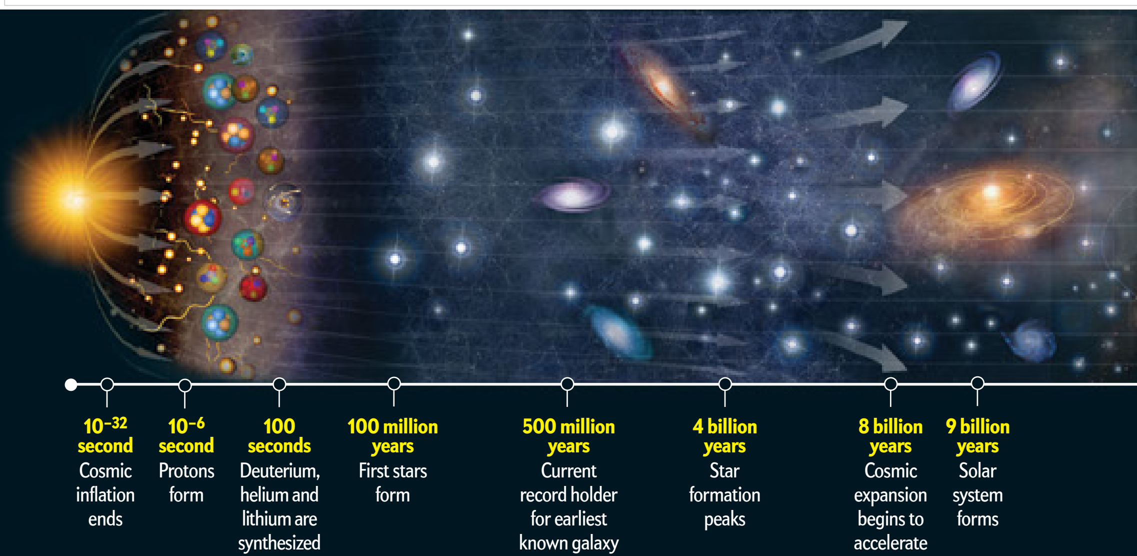
But here's the good news: oncoming darkness captures only half the story. Star formation has indeed long since passed through its most glorious epoch, but the universe has life in it yet. Strange new beasts will enter the astronomers' zoo. Outlandish phenomena that now occur rarely, if at all, will become routine. Cosmic conditions favorable to life may, if anything, become even more abundant.

Scientific eschatology—the study of the far future—has a dis-

COSMIC HISTORY

Dawn to Dusk

After the furies of birth, the mature cosmos now evolves more slowly. Stars will continue to form for as long as another 100 trillion years (about 10,000 times the present age of the universe), which leaves plenty of time for slow-building cosmic phenomena to occur.



Timeline not to scale

Illustrations by Malcolm Godwin

tinguished history in cosmology and physics. Fascinating in its own right, this endeavor also offers a conceptual testing ground for new theories, plus an opportunity to make abstract ideas more concrete. One of the most abstract ideas of all, the shape of space, may prove easier to grasp when cosmologists describe what it implies for the fate of the universe. Physicists who seek to reconcile their disparate theories about fundamental particles and forces predict processes that will occur only after trillions of years, or even longer, such as the decay of protons and the evaporation of black holes. Increasingly, astrophysicists bring the far future into their models of stellar and galactic evolution as well. During the past decade they have attempted to reconstruct the ways that the formation and composition of stars and galaxies have changed since the big bang. Their growing knowledge of the past allows them to extrapolate trends into the far future.

FORGOT TO TURN IT OFF

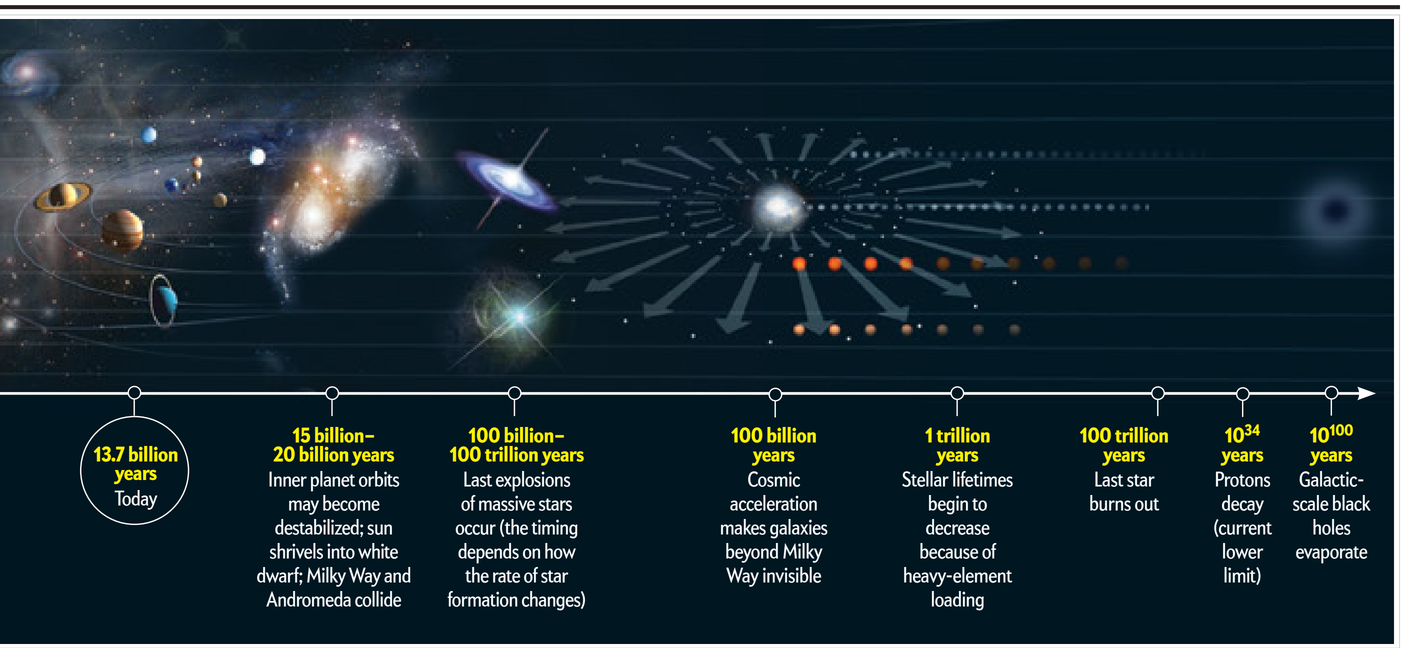
AMONG THIS SUBJECT'S PIONEERS is Greg Laughlin, an expert on star formation at the University of California, Santa Cruz. As a graduate student, he created a computer code to calculate the evolution of extremely low mass stars and forgot to flag it to turn off after reaching the present age of the universe. Left to its own devices, the program ran and ran, producing trillions of years of future predictions—quite wrong, as things turned out, but sufficient to get him hooked on the subject.

To know the future of stars requires understanding how they form. Stars are born within interstellar clouds of gas and dust, which contain hundreds of thousands to several million times the mass of our sun. Such stellar nurseries, sprinkled throughout the Milky Way, gave birth to its few hundred billion stars and will eventually produce tens of billions more. Yet this success consumes the future: the raw material for new stars is being used up. Even though massive stars die in supernova explosions that return some material into interstellar space and even though galaxies can also accrete fresh gas from intergalactic space, the new material cannot replenish all the gas that stars have locked up. The interstellar gas within our galaxy now totals only a tenth or so of the mass in stars.

Today stars form in the Milky Way at a rate close to one solar mass per year, but at its peak, eight to 10 billion years ago, the rate was at least 10 times higher. Laughlin estimates that star formation will decrease by approximately a factor of 10 for every factor of 10 in time, so that in 100 billion years it will slow to a tenth of its present rate, and a trillion years from now stars will form at only about one one-hundredth of the current rate.

That said, impressive changes could disrupt the steady march toward stellar obscurity. We in the Milky Way, for example, must soon—"soon," as in a few billion years—confront the arrival of the onrushing Andromeda system, the closest giant spiral galaxy to our own. The dense central regions of these two galaxies will either collide or begin to orbit their common center of mass. Their interaction will produce "Milkomeda." By churning and stirring the interstellar gas and dust, the creation of Milkomeda will reinvigorate star formation temporarily, producing what astronomers call a starburst. Once this growth spurt dies away, the merged system will closely resemble an elliptical galaxy, a mature system with a low density of star-forming material and a consequently low rate of star formation.

In addition to forming in smaller numbers, stars of the future will show the effects of the changes that will occur in their raw material. The fiery furnace of the big bang forged hydrogen, helium and lithium. All the heavier elements have been created by stars themselves, typically late in their lives—either within red giant stars, which shed their outer layers as they age, or during supernova explosions. Red giants provide most of the lighter and more abundant heavy elements, such as carbon, nitrogen and oxygen, whereas supernovae produce a wider range, all the way up to uranium. All of these mix into the existing elemental mulch of interstellar gas, allowing subsequent generations of stars to begin



life with more of these materials. The sun, a comparative youngster at five billion years old, has 100 times the heavy-element abundance of stars that formed over 10 billion years ago; indeed, some of the oldest stars contain almost no heavy elements at all. Coming generations of stars will be even more enriched, which will alter their inner workings and outward appearance.

NEW ABODES FOR LIFE

THE STEADILY INCREASING ABUNDANCE of heavy elements within newborn stars produces two noticeable effects. First, it augments the opacity of a star's outer layers. Hydrogen and helium are nearly transparent, but even a modest pinch of heavy elements traps radiation, lowering the star's luminosity. The balance of forces within the star shifts because the lower luminosity means that the star consumes its nuclear fuel at a lower rate. If only this effect were in operation, a star rich in heavy elements would live longer than a star of the same mass that lacks those elements. But a second effect counteracts the first: the heavy elements are nuclear deadweight. Because they do not participate in nuclear fusion, they reduce the amount of nuclear fuel available within a star of a given mass and tend to shorten its life.

Laughlin and his colleague Fred Adams of the University of Michigan made the initial study of these two effects in 1997. They found that the first will dominate for the next trillion years or so, as the increase in heavy elements within new stars raises their opacities and thus lengthens their lifetimes. Eventually, however, the heavy elements will constitute a significant fraction of stars' masses and will begin to shorten their lifetimes. The crossover point will occur when the heavy-element fraction within a newborn star reaches about four times the current value.

The extraheavy elements should also favor the birth of planets, along with stars, and thus the prospects for life in the universe. Astronomers have measured the elemental abundances in the stars around which more than 700 (and counting) Jupiter-like planets have now been discovered. Their results show that stars with greater heavy-element abundances are more likely to have one or more giant planets in orbit around them. "Jovian-type planets show a definite correlation with [heavy-element abundances]," says John Johnson, a planet-hunting expert at the California Institute of Technology. "Because the interstellar medium is getting steadily enriched [in heavy elements], planet occurrences will probably increase."

What about Earth-like planets? Although space-based telescopes are only now beginning to provide similar data for smaller worlds, their formation, too, should be correlated with their stars' heavy-element abundances, even more so as Earth-like planets consist almost entirely of the heavier elements. In short, the universe of the far future should be filled with planets. Despite the diminishing rate of star formation, perhaps half or two thirds of all the planets that will ever exist have yet to be born.

At first, the proliferation of planets does not seem promising for life. Most of the stars of the far future will be much less massive and less luminous than the sun. Fortunately, even a low-mass, dim star can allow life to flourish. A star with as little as one one-thousandth of the sun's luminosity can maintain temperatures that allow liquids to exist on close-in planets, satisfying what seems to be a requirement for living things to exist.

Planets should not only grow generally more common but also be enriched in the stuff of life. In addition to requiring a

FUTURE OF STELLAR EVOLUTION

The Meek Shall Inherit the Universe

In terms of raw brilliance, the glory days of the cosmos are already behind it. In subtler ways, though, it will remain vibrant for trillions of years to come. Red dwarfs, by far the most common type of star even today, have hardly even begun their life cycles and will eventually develop into novel stellar types. New generations of stars will incorporate the heavy elements forged by their predecessors, changing their appearance and life spans. Planets will, if anything, become even more abundant. Over the vastness of time, rare processes such as direct stellar collisions will become commonplace.

Slow but Steady Wins the Cosmic Race

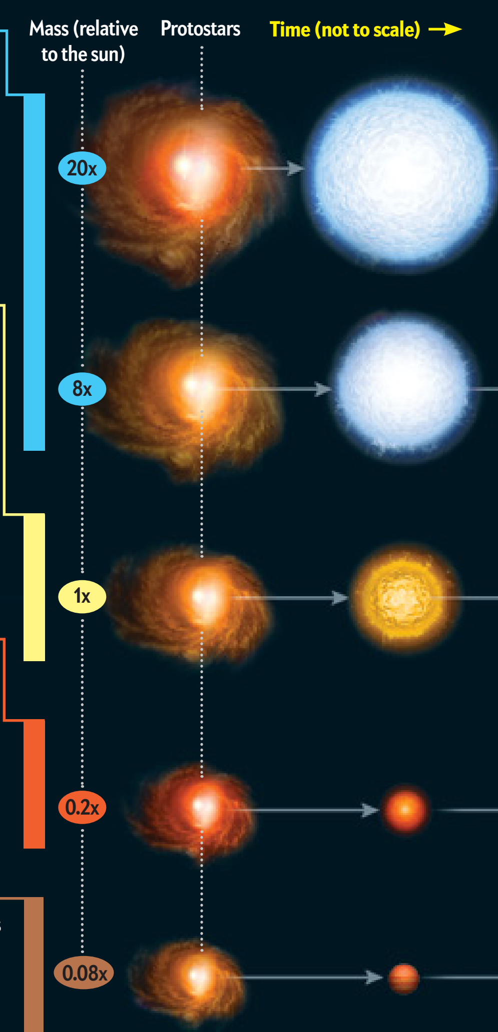
The life cycle of stars follows a simple rule: the bigger they come, the harder they fall. Massive stars have more fuel but consume it at a disproportionate rate and go out with a bang. Because they live for but a cosmic eyeblink, they rule the galaxy only as long as new ones are continually being born. The future belongs to lesser, longer-lasting stars.

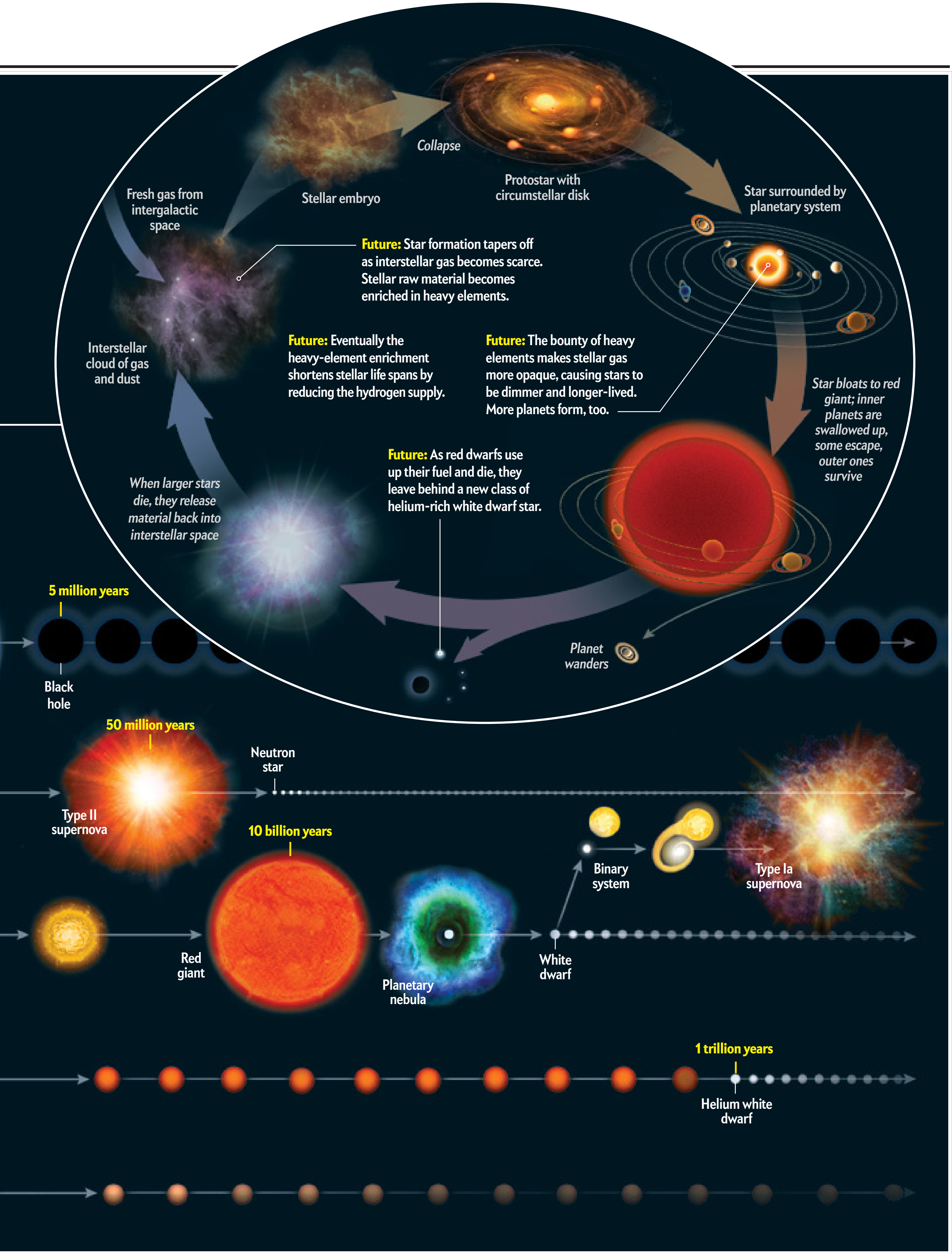
SUPERGIANTS When the mightiest stars cease to generate enough power to hold up their own weight, they collapse abruptly—which can trigger a supernova explosion or gamma-ray burst—and leave behind a neutron star or black hole.

SUNLIKE STARS Sunlike stars die by ejecting their outer layers as a colorful nebula, while their core collapses to a white dwarf star. The dwarf usually fades away like a burnt-out cinder but can blow up by merging with another white dwarf or cannibalizing a companion star.

RED DWARFS Red dwarfs, the most common type of star, keep on shining until they have converted every last drop of their hydrogen to helium. They turn into a special type of white dwarf.

BROWN DWARFS Stars below a certain mass threshold never get hot enough to ignite proton-proton fusion. They just cool off and fade away.





Collapse
Stellar embryo
Protostar with circumstellar disk
Star surrounded by planetary system
Fresh gas from intergalactic space
Future: Star formation tapers off as interstellar gas becomes scarce. Stellar raw material becomes enriched in heavy elements.
Interstellar cloud of gas and dust
Future: Eventually the heavy-element enrichment shortens stellar life spans by reducing the hydrogen supply.
Future: The bounty of heavy elements makes stellar gas more opaque, causing stars to be dimmer and longer-lived. More planets form, too.
Star bloats to red giant; inner planets are swallowed up, some escape, outer ones survive
When larger stars die, they release material back into interstellar space
Future: As red dwarfs use up their fuel and die, they leave behind a new class of helium-rich white dwarf star.
Planet wanders
5 million years
Black hole
50 million years
Neutron star
Type II supernova
10 billion years
Binary system
Type Ia supernova
Red giant
Planetary nebula
White dwarf
1 trillion years
Helium white dwarf

liquid bath, life on Earth, as well as almost all other forms of life that scientists speculate about, depends on the existence of carbon, nitrogen and oxygen. As time goes on, the increasing relative abundance of these elements should yield planets more hospitable to life. Therefore, as star formation steadily diminishes, every newborn star should appear with a progressively greater probability of lighting one or more potential life-bearing planets. Some of these new stars will have the low masses and tiny luminosities that allow them to last for hundreds or thousands of billions of years (not that such immense lifetimes seem necessary for the origin and evolution of life). However full or empty of life the universe may be today, it should teem with more abundant and more varied forms of life in the future.

WHEN WORLDS COLLIDE

PLANETARY SYSTEMS will endure so far into the future that new considerations will come into play. We take the stability of our solar system for granted; no one worries that Earth's orbit will soon grow chaotic and cause us to collide with Venus. That confidence evaporates when we look to multibillion-year timescales. In 2009 Jacques Laskar and Mickael Gastineau of the Paris Observatory conducted several thousand computer simulations of the future orbits of the sun's four inner planets, varying the planets' initial positions by a tiny amount—just a few meters—between each simulation. They found a probability of about 1 percent that Mercury would smack into Venus during the next five billion years, setting the stage for even more horrific collisions that would probably involve Earth. Over a trillion years such collisions would become highly probable.

Astronomers see no sign that life has affected the cosmos on a grand scale. That will change in the future. All the universe will become our garden.

The pot will be stirred when the Andromeda galaxy merges with the Milky Way, an event that will reconfigure both galaxies' gravitational fields and could well trigger a wholesale restructuring of the solar system. As Laughlin commented in reviewing Laskar and Gastineau's simulations, "What now remains is to understand the extent to which the hand of dynamical chaos that so lightly touches our solar system has molded the galactic planetary census."

The orbital chaos within a star's planetary family will also occur on much larger scales. The stars in closely bound double-, triple- and higher-multiple star systems orbit the center of mass of each system under their mutual gravitational influences. Much the same is true for star clusters and even entire galaxies. Stars in all these structures almost never make contact; huge expanses of space separate them despite their astronomical neighborliness.

Over long expanses of time, however, "almost never" ratchets up to "sometimes" and ultimately to "almost always." Every double-star system will eventually experience either disruption, as the result of external gravitational forces, or merger, if the two stars orbit so closely that gravitational radiation saps the system of energy. Naturally enough, widely separated double-star systems face the former fate, whereas close-in binaries confront the latter.

When two stars merge, they may temporarily produce a more massive, more luminous star [see "When Stars Collide," by Michael Shara; SCIENTIFIC AMERICAN, November 2002]. Even a planet such as Jupiter can cause a similar effect, though on a smaller scale. Consider a modest star, with just one tenth of the sun's mass and a lifetime close to a trillion years, and suppose it has a Jupiter-like planet. If the planet has an orbital period greater than few days, it will probably eventually be lost from the system. But if it moves on a tighter orbit, the planet could eventually merge with the star, contributing a fresh supply of hydrogen that would temporarily boost the star's energy output dramatically, producing a novalike outburst. In the future such stellar eruptions will punctuate the slow decline in star numbers and brightnesses. Astronomers even a trillion years from now will observe some strange events among the ever declining numbers of stars in their host galaxies.

LIVE SLOW, DIE OLD

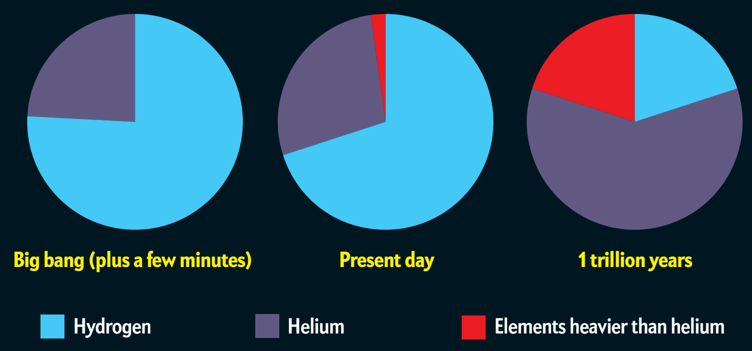
EVEN AFTER TENS AND HUNDREDS of billions of years have elapsed, even when star formation has slowed to a trickle, enormous numbers of stars will continue to shine. Most stars in the universe have low masses and extremely long life expectancies. Stars' lifetimes depend on their masses in a strikingly inverse manner. High-mass stars are so luminous that they burn themselves out quickly and explode after a few million years. Medium-mass stars such as our sun shine modestly and last for billions of years. Stars with significantly less than the sun's mass can endure for hundreds of billions of years or even longer. These stars consume their fuel so slowly that even their meager supplies can feed their nuclear fires through these immense spans of time.

Stars of different masses die in different ways. The sun will become a red giant and, as its outer layers dissipate completely into interstellar space, reveal its core as a white dwarf—a dense, Earth-size stellar corpse made almost entirely of carbon nuclei and electrons. But in stars with less than about 50 percent of the sun's mass, the core temperature never rises high enough to trigger the nuclear reactions that lead to the red-giant phase. Instead astronomers think these stars eventually become helium white dwarfs. Such beasts, as the name suggests, consist almost entirely of helium, with little if any hydrogen and just a smattering of other elements. In today's universe they are occasionally born when two close binary stars strip each other's outer layers before they can ignite their helium cores, but astronomers have yet to discover any that arose in the normal course of stellar evolution, because not enough time has passed since the big bang so far. Isolated helium dwarfs are a prime example of a novel phenomenon that our distant descendants (may they live in peace) will one day see for the first time.

Stars with larger masses undergo far more dramatic deaths. The collapse of a massive star core that forms either a neutron star or a black hole triggers a shock wave that blasts the star's overlying layers into space in a supernova explosion. As massive stars disappear from the skies, so, too, will most of these explosions that now punctuate the cosmos. But a second kind of supernova will still occasionally light the skies. This class, called type Ia supernovae, arises in binary-star systems in which one star has become a white dwarf. According to astronomers' most favored models, in some of these stellar pairs

Enriching the Cosmic Mulch

Stars shine by fusing hydrogen into helium and, toward the end of their lives, helium into still heavier elements. Each generation of stars starts life with a greater endowment of heavy elements than the previous one. This process gradually changes the appearance and longevity of stars. It may also increase the number of planets that form.



hydrogen-rich material from the companion star collects on the white dwarf's surface until its sudden nuclear fusion produces a supernova. Such events will take place as long as there are sufficiently massive companions, perhaps for another 100 billion years or so.

In another supernova model, which has been gaining in popularity, two white dwarfs orbit their common center of mass in close proximity. As they do so, their orbital motions cause the binary system to emit gravitational radiation. This emission robs the system of energy and shrinks the size of the white dwarfs' orbits. The approach of the dwarfs proceeds ever more rapidly, until their death spiral melds them in a brief, final paroxysm. Such events might continue to occur for trillions of years.

Even brighter than supernova explosions are gamma-ray bursts (GRBs). These megaexplosions come in two distinct varieties, which apparently originate in two entirely different scenarios. Long GRBs, those whose eruptions of energetic radiation last for two seconds or more, are believed to occur when a massive star's core collapses to form a neutron star. Short GRBs, whose outbursts last for less than two seconds, are thought to result from the merger of a neutron star with either another neutron star or a black hole. Over the coming eons the long variety will become exceedingly rare, as massive stars cease to form, but short bursts might punctuate the heavens for trillions of years.

TRILLIONS AND TRILLIONS

WHEN WE MEASURE COSMIC TIME not by billions but by trillions of years, we enter an epoch when star formation will have ended. All but the lowest-mass stars will have burned themselves out, ending their lives either by blowing up or by withering into white dwarfs. Not counting dark matter, whose composition remains a mystery, our galaxy—and all others in the universe—will then consist primarily of black holes, neutron stars, white dwarfs and extremely faint red stars, so dim that none of them would be visible without a telescope, even at distances less than the current distances from the sun to the nearest stars. How sad, how degenerate, how uninteresting.

And yet, among these dead or fading objects, nature will on occasion produce an enormous outburst, a brief reminder of the nuclear fury that once spangled the heavens with the light from billions of stellar furnaces. If the surviving stars have planets in close propinquity—and we may expect that many or most of them will—then liquid water, along with various forms of life, could appear and endure on their surfaces. Any life that might arise on those planets will have the possibility (already present around the faintest stars) of lasting for epochs well beyond easy imagination, provided they can avoid being blasted into eternity by nearby supernovae or GRBs.

This survey of the far future leaves a great and indeterminate issue. Could highly advanced civilizations, if they exist and persist, change the course of the cosmic history? More than 30 years ago Freeman Dyson of the Institute for Advanced Study in Princeton, N.J., reviewed the situation. The grand leader in this sort of cosmic speculation, he stated, "I think I have shown that there are good scientific reasons for taking seriously the possibility that life and intelligence can succeed in molding this universe of ours to their own purposes." In our present epoch, not even 14 billion years after the big bang, little evidence exists that living things have affected the cosmos on a grand scale. But time's train has barely left the station. In the future the survival of life will require that it commandeer an ever greater fraction of the cosmos's resources [see "The Fate of Life in the Universe," by Lawrence M. Krauss and Glenn D. Starkman; SCIENTIFIC AMERICAN, November 1999]. All of the universe will become our garden.

Bound on this journey for a brief moment, we have little chance of attaining absolute certainty about what will actually happen. Our unfettered minds remain free to roam as far into the future as we choose. As W. H. Auden wrote in his 1957 poem, in an entirely different context: "Were all stars to disappear or die/I should learn to look at an empty sky/And feel its total darkness sublime/Though this might take me a little time." SA

MORE TO EXPLORE

The Five Ages of the Universe: Inside the Physics of Eternity. Fred Adams and Greg Laughlin. Free Press, 2000.

The Runaway Universe: The Race to Find the Future of the Cosmos. Donald Goldsmith. Basic Books, 2000.

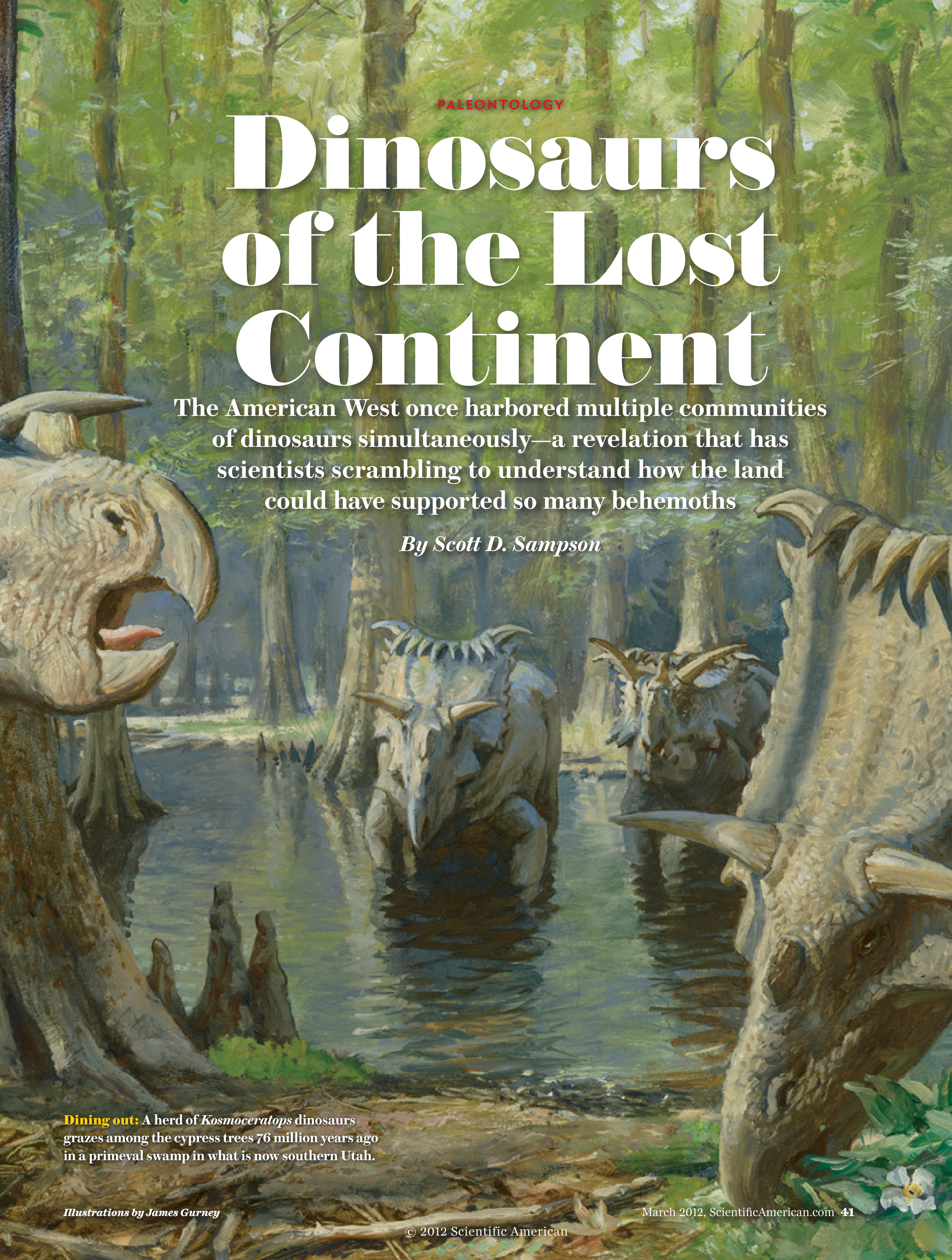
The Formation and Evolution of the Milky Way. Cristina Chiappini in *American Scientist,* Vol. 89, No. 6, pages 506–515; November/December 2001.

An Integrated Picture of Star Formation, Metallicity Evolution, and Galactic Stellar Mass Assembly. L. L. Cowie and A. J. Barger in *Astrophysical Journal,* Vol. 686, No. 1, pages 72–116; October 10, 2008. Preprint available at **arxiv.org/abs/0806.3457**

SCIENTIFIC AMERICAN ONLINE
For an animated timeline of the history of the universe from the big bang to the farthest future, visit **ScientificAmerican.com/mar2012/starlight-starbright**

Graphic by Jen Christiansen


GURNEY



PALEONTOLOGY

Dinosaurs of the Lost Continent

The American West once harbored multiple communities of dinosaurs simultaneously—a revelation that has scientists scrambling to understand how the land could have supported so many behemoths

By Scott D. Sampson

Dining out: A herd of *Kosmoceratops* dinosaurs grazes among the cypress trees 76 million years ago in a primeval swamp in what is now southern Utah.

Illustrations by James Gurney

Scott D. Sampson is a dinosaur paleontologist and a research curator at the Natural History Museum of Utah. He has been leading efforts to recover Late Cretaceous fossils from Grand Staircase-Escalante National Monument in Utah since 2000. Sampson is also the scientific adviser for and on-air host of the PBS KIDS television series *Dinosaur Train*.

ON A COOL SEPTEMBER MORNING IN 2010 MY CREW AND I BEGAN OUR DAILY DESCENT from camp back into deep time, walking single file down a steep, knife-edge ridge of sandstone and mudstone in southern Utah's Grand Staircase-Escalante National Monument. Each of us carried water, a field notebook, lunch, a rock hammer and other hand tools. Heavier tools and materials—rock saws, picks, shovels, bags of plaster and swaths of burlap—awaited us half a mile away at the dig site. Even from the hilltop we could easily see the plaster jackets down in the quarry—alabaster beacons in a wilderness of arid, gray-striped badlands. Some of the irregular lumps were not much bigger than a loaf of bread. Others spanned 10 feet and tipped the scales at more than a ton. All contained the bony remains of animals that coexisted here 76 million years ago.

Over the course of two field seasons this single quarry—one of many in the fossil-rich rocks of the Kaiparowits Formation—had yielded a striking array of creatures, including several dinosaurs. Most impressive was a largely complete skeleton of *Gryposaurus,* a massive, duck-billed plant eater approaching the size of *Tyrannosaurus*. The crew was now under pressure to finish excavating the remaining fossils before the helicopter came in a few days to airlift the priceless cargo to a nearby road. From there the fossils would travel by truck to the Natural History Museum of Utah in Salt Lake City, where trained volunteers would painstakingly open the jackets, remove the rock and glue the bones back together over a period of months.

Pausing on a sandstone ledge to soak in the sprawling vista below, I imagined for the umpteenth time how this place might have appeared when these dinosaurs roamed. Back then, much of the territory was an immense, waterlogged floodplain. Sluggish rivers from mountains to the west meandered across a verdant landscape interspersed with ponds and lakes. Cypress trees thrived in the swampy lowlands; better-drained settings supported forests of conifers and flowering trees. Vines draped the tree branches, and the buzzing of insects filled the humid air. The scene would have called to mind the swamplands of northern Louisiana today—but with the addition of more than a dozen dinosaur species, from herbivorous duck-billed hadrosaurs and horned dinosaurs (called ceratopsids) to carnivorous, sickle-clawed dromaeosaurs and a type of giant tyrannosaur.

IN BRIEF

Between 90 million and 70 million years ago, during the Late Cretaceous period, a shallow sea flooded the central region of North America, subdividing the continent into eastern and western landmasses. Scientists refer to the western landmass as Laramidia.

In the 1980s a researcher proposed that distinct dinosaur communities inhabited the northern and southern regions of Laramidia for several million years. Critics doubted that so many large animals could have shared this relatively small chunk of land, however.

But over the past decade discoveries in southern Utah have bolstered the notion of distinct dinosaur communities in the north and south, revealing a host of species new to science—including many giant varieties.

Exactly what enabled so many behemoths to coexist in such a small area remains unclear, but it may be that dinosaurs had lower energy requirements than today's large terrestrial animals do or that plants during the Late Cretaceous provided more food than their modern-day counterparts.

Uphill climb: **Members of the author's team scale a ridge out of the Kaiparowits badlands in Utah's Grand Staircase-Escalante National Monument (*1*), where they have discovered remains of a number of new dinosaur species. Fossils such as this skull of *Kosmoceratops* are brought to the Natural History Museum of Utah, where volunteers clean and reassemble them (*2*). Species found in that area include another horned dinosaur, *Utahceratops* (*3*).**

RICK WICKER Denver Museum of Nature and Science (Kaiparowits Formation); COURTESY OF MARK LOEWEN Natural History Museum of Utah (dinosaur heads)

Our excavations in this remote region over the past decade have opened a fascinating window on the mix of dinosaur species that lived during the so-called Campanian Stage of the Late Cretaceous period, between 83.5 million and 70.6 million years ago—a time when dinosaurs here were undergoing perhaps their greatest florescence. In a sense, the Kaiparowits fossil assemblage is unremarkable, preserving the same broad dinosaur groups unearthed from sediments of similar antiquity farther north in Montana and in Alberta, Canada. Yet the particular species in the Kaiparowits are unique, with many large-bodied forms—findings that are forcing us to reconsider much of what we thought we knew about dinosaur evolution and ecology. Let me explain.

SOUTH VS. NORTH

DURING THE LATE CRETACEOUS the earth was a hothouse world. The planet's polar regions were free of ice caps, and global sea levels tended to be exceptionally high. A warm, saltwater sea, the Western Interior Seaway, inundated the central region of

North America, connecting the Arctic Ocean with the Gulf of Mexico and dividing the continent into eastern and western portions: Appalachia and Laramidia, respectively. The dinosaurs, plants and other organisms we have been recovering from the Kaiparowits lived on Laramidia, a landmass less than one fifth of the size of its parent continent.

Beginning in the 1960s, fossil hunters working in the Western Interior began to notice that Late Cretaceous dinosaurs found in Montana and Alberta belonged to distinct species from those recovered from similarly aged rocks farther south in such places as New Mexico and Texas. In the 1980s Thomas Lehman of Texas Tech University tabulated the geographic occurrences of dinosaurs and other vertebrate creatures on Laramidia and found evidence of distinct northern and southern assemblages during the final 15 million years of the Cretaceous period, including the Campanian Stage. Lacking any indication of a physical barrier to north-south dispersal, Lehman hypothesized that a latitudinal climate gradient had produced distinct communities of plants and animals, including a bevy of big-bodied dinosaurs. His was a bold theory. Other researchers questioned the likelihood of multiple dinosaur communities coexisting on the diminutive landmass of Laramidia. It simply did not seem possible that so many kinds of giants could have shared such a small chunk of real estate.

Critics of Lehman's hypothesis pointed out that any apparent provincialism might be illusory, the result of uneven sampling of fossils through time. Given that the Late Cretaceous spans many millions of years, they noted, perhaps paleontologists working at different latitudes in the Western Interior have effectively been "time traveling" to different intervals. If so, this imbalanced sampling through time could generate the perception of distinct, coeval faunal provinces even if only a single cosmopolitan dinosaur fauna existed on Laramidia at any given geologic moment. Alternatively, skeptics observed, the seemingly distinct dinosaur communities could be the result of poor geographic sampling. Until recently, the vast majority of Laramidian dinosaurs were known from the north, particularly Alberta and Montana. Perhaps a more thorough sampling of dinosaurs from southern Laramidia would ultimately reveal a single, widespread community. These issues remained unresolved when my colleagues and I began our work in southern Utah in 2000.

The fossils that we have recovered from Grand Staircase-Escalante go a long way toward filling the southern dinosaur gap on Laramidia and bolstering Lehman's theory. Dating of the fossils has been essential to answering the question of whether distinct, coeval dinosaur provinces existed in the north and south. Team geologist Eric Roberts of James Cook University found layers of volcanic ash scattered throughout the Kaiparowits strata that he was able to date using radiometric techniques. The results indicated that the key, fossil-rich hot zone formed over a period of one million years between 76.5 million and 75.5 million years ago. Comparing these ash dates with those from other Laramidian formations revealed that the Kaiparowits Formation closely overlapped in time with the Dinosaur Park Formation in Alberta. We now had strong evidence that at least one pair of northern and southern dinosaur assemblages lived concurrently.

The next step was to assess whether the dinosaurs themselves differed from north to south. Of the 15 dinosaur varieties that the team has recovered so far from the one-million-year interval, a dozen are sufficiently complete to allow species-level identifications. Only one—a duck-billed hadrosaur in the *Gryposaurus* genus—was possibly present farther north. This species looks very similar to *G. notabilis* from Alberta, but the identification is currently uncertain, and investigations are under way to assess whether ours is a distinct species.

Outside of this single question mark, the emergent picture is clear. Every other Kaiparowits dinosaur species thus far identified differs from those found farther north. When small- to mid-size carnivores such as the oviraptorosaur *Hagryphus* and the troodont *Talos* prowled ancient Utah, the same groups were represented instead by *Chirostenotes* and *Troodon,* respectively, up in Alberta. Similarly, whereas a large-bodied, short-faced tyrannosaur named *Teratophoneus* was the top land carnivore in the Utah region, other tyrannosaurs such as *Gorgosaurus* filled this role in the north. Plant-eating dinosaurs in the Kaiparowits Formation are similarly distinct from the northern forms. One of these is *Parasaurolophus,* a bizarre hadrosaur with a long, tubular crest on the top of its head. Three species of *Parasaurolophus* have been found previously, one in Alberta and two in New Mexico; the Utah species appears to be new to science.

The pattern repeats among the ceratopsids. One type of ceratopsid that we recently dubbed *Utahceratops* possesses a long-frilled skull approaching seven feet in length. The skull of a second, shorter-frilled species, *Kosmoceratops,* is ornate in the extreme, bearing 15 horns on its head, the most of any dinosaur. While *Utahceratops, Kosmoceratops* and a third (as yet unnamed) ceratopsid dinosaur foraged in Utah, different species of horned dinosaurs munched on plants up north.

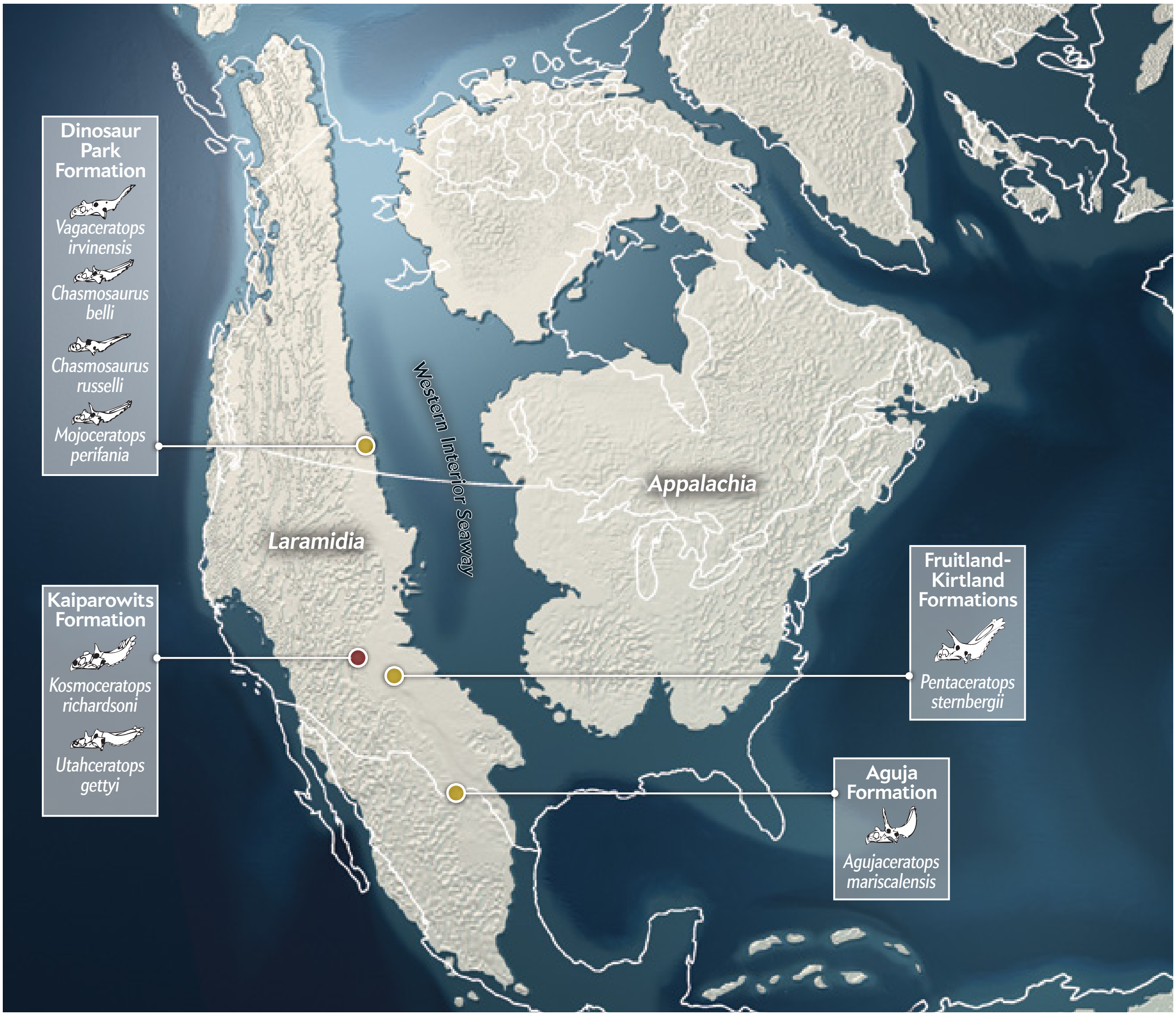
The newly discovered Kaiparowits dinosaur assemblage in Grand Staircase-Escalante provides by far the strongest evidence of isolated dinosaur provinces on Laramidia. Although the same major groupings of dinosaurs occurred in both the north and south, northerners and southerners were distinct species. None of the more than 50 Campanian dinosaur species from numerous formations can yet be confidently placed in both the north and south. These findings effectively refute the possibility that distinct northern and southern assemblages are merely an artifact of incomplete temporal or geographic sampling. Instead we must come to grips with the fact that at least two dinosaur communities coexisted on this landmass for about a million years of late Campanian time.

LAND OF GIANTS

THAT MANY OF THE DINOSAURS in these two communities were giants deepens the Laramidia mystery. Studies of modern-day terrestrial mammals show a tight connection between maximal body size and land area. Large-bodied forms tend to range farther, both as individuals and as species, because bigger animals require more area to obtain enough food. For the same reason, species with more extensive home ranges tend to have lower population densities. Maximum body size in giant terrestrial mammal species, then, reflects a balance between maintaining population densities low enough to avoid overexploitation of food resources yet high enough to avoid extinction. Ultimately, the upper limits of both body size and species diversity among megavertebrates are constrained by a combination of physiolo-

Dinosaur Diversity

Between about 90 million and 70 million years ago, during the Late Cretaceous, an interior sea isolated the western portion of what is now North America, turning that strip into a landmass called Laramidia. Researchers have long observed that northern and southern Laramidia seem to have hosted different communities of dinosaurs and other animals. But critics questioned whether the pattern might instead be the result of uneven sampling of fossils over time and space. Recently discovered fossils in the Kaiparowits Formation of Grand Staircase-Escalante National Monument have revealed a previously unknown assemblage of dinosaur species that lived at the same time as a different assemblage farther north, bolstering the theory of distinct northern and southern dinosaur provinces in Laramidia. The nature of the barrier that separated these northern and southern dinosaurs remains a mystery. The map below shows some of the horned dinosaurs (as represented by their skulls) from these northern and southern assemblages.



ADAPTED FROM RON BLAKEY *Northern Arizona University*

gy (higher metabolic rates demand greater food intake), food availability and landmass area, with more extensive landmass areas typically supporting more kinds of large-bodied species. This relationship places the severest demands on big-bodied carnivores, which must maintain relatively larger home ranges than herbivores because only a small fraction of an ecosystem's total energy budget reaches the top of the food chain.

In theory, giant dinosaurs should have followed a pattern similar to that of today's large terrestrial mammals, with few species on the relatively small Laramidian landmass. Yet taken together, the animal communities represented in the Kaiparowits Formation and the Dinosaur Park Formation contain at least 17 to 20 coeval species of giant dinosaurs—that is, forms exceeding one ton in adult body mass—with most weighing in at more than two tons. By modern standards, that scenario seems downright bizarre. Today the only place on earth where

Illustration by George Retseck

Killer instinct: ***Teratophoneus,*** **a type of tyrannosaur, takes down a duck-billed hadrosaur called** ***Gryposaurus.*** **Remains of both types of dinosaurs have been recovered from deposits in Grand Staircase-Escalante National Monument dating to about 76 million years ago.**

you can find an abundance of giants is Africa, which harbors six mammals with a mean body mass in excess of one ton, all of them herbivores: the giraffe, the hippopotamus (which spends most of its time in freshwater rather than on land), and two species each of elephants and rhinoceroses.

It is true that Africa and some other landmasses housed considerably more large terrestrial species in the past. For example, during the early Pleistocene, between about 2.5 million and two million years ago, Africa supported on the order of 16 megaherbivore mammals: multiple varieties of giraffes, elephants, hippos and rhinos, plus several types of big-bodied antelope that weighed nearly a ton. Nevertheless, a number of lines of evidence indicate that the Laramidian dinosaur example is exceptional.

First, Laramidia was less than one fifth of the size of Pleistocene Africa, so those 17 to 20 dinosaur behemoths were confined to a much smaller area than their mammalian counterparts. Furthermore, abundant evidence from mass death accumulations, or bone beds, indicates that many species of hadrosaurs and ceratopsids congregated for at least part of every year in large "herds," numbering in the hundreds (and perhaps thousands) of animals. Second, mammal-dominated ecosystems from the Pleistocene onward have few terrestrial carnivores approaching a ton. Indeed, mammal evolution on land has yet to produce carnivores that even approach the magnitude of a tyrannosaur. Africa's largest predator, the lion, typically weighs less than 600 pounds; Laramidia, in contrast, was home to at least three giant tyrannosaurs, all of which apparently exceeded a ton. Third,

whereas paleontologists have found early Pleistocene fossils in multiple African countries, current sampling on Laramidia is limited to two coeval geologic formations. Given that Laramidian dinosaurs appear to have had considerably smaller species ranges than modern terrestrial mammals, with minimal overlap between concurrent communities, it seems highly probable that additional dinosaurs lived on this landmass during the Campanian. If so, the total number of contemporaneous giants on Laramidia may have far surpassed 20 species. In short, the new Kaiparowits evidence strongly suggests that dinosaurs exceeded known mammalian limits for species richness at large body sizes.

CONSERVATIVE DINOS OR PRODUCTIVE PLANTS?

THIS COMPARISON between African mammal giants and Laramidian dinosaur giants brings us back to the burning question elicited by Lehman's hypothesis. How did dinosaurs manage to squeeze so many varieties of giants into such a small area? Two major possibilities remain: either these dinosaurs got by on less food than modern giants do, or the environments they inhabited produced more food than we see in modern settings.

Scientists have long debated whether dinosaur metabolism was more like that of the cold-blooded ectotherms (such as amphibians and reptiles) or the warm-blooded endotherms (such as birds and mammals). If their metabolic rates were intermediate between these groups, causing them to have lower energy requirements than large mammals do, this difference could help explain how so many big-bodied species coexisted on the relatively tiny landmass of Laramidia. Recent research by Brian K. McNab of the University of Florida supports this notion of "Goldilocks" dinosaurs—not cold-blooded, not hot-blooded, but something in between. McNab has found a range of evidence indicating that lower energy expenditures of dinosaurs may have enabled their communities to support biomasses up to five times greater than those of mammalian herbivores in present-day Africa.

Alternatively, relative to present-day land ecosystems, Late Cretaceous plants may have offered megaherbivores foods that were more abundant or more nutritious, or both. Plant diversity and abundance are controlled by such factors as precipitation, temperature, length of growing season and availability of niches. Today the greatest diversity and biomass of plants tend to occur in the tropics, but during the hothouse of the Late Cretaceous high temperatures may have limited plant and animal diversity in the equatorial regions. At midlatitudes such as those occupied by much of Laramidia, in contrast, the climate was mild and the growing season long. To the west, Laramidian mountain ranges and rivers multiplied the number of available niches. To the east, the Western Interior Seaway ameliorated temperatures while providing a major source of precipitation. Paleobotanists Ian Miller and Kirk Johnson of the Denver Museum of Nature and Science have thus far recovered almost 100 different plant varieties from the Kaiparowits strata. Although much more work needs to be done, all indicators suggest that the dinosaur communities in Laramidia were founded on a great bounty and diversity of plants.

Figuring out whether slower metabolic rates or augmented food supplies enabled dinosaurs to reach such gargantuan proportions and high richness of species will require further testing. My hunch is that both factors were involved. One thing we can say with confidence is that the hothouse world of the dinosaurs was very different from the world of today. Many of the major biomes of our present-day icehouse Earth—for example, grasslands, tundra and rain forests—were absent during the dinosaurs' reign, and we are still trying to glean even a basic understanding of their hothouse predecessors. The good news is that paleontology is becoming increasingly interdisciplinary—involving collaborations with geologists, paleoecologists and paleoclimatologists, to name a few—increasing the odds that fruitful insights will emerge.

Meanwhile our work in the Kaiparowits Formation, like any scientific research worth its salt, is generating as many questions as answers. How many distinct dinosaur communities existed at any one time on the lost continent of Laramidia? What was the nature of the barrier separating the northern and southern communities? Was this boundary based solely on climatic variation between the north and south, as first thought? Or, as some geologists now suspect, was some kind of physical barrier present, perhaps a series of large rivers flowing from the mountains to the sea at the latitude of northern Utah and Colorado?

One final, intriguing implication is worth noting. If it turns out that dinosaurs tended toward much smaller species ranges than equivalent-size mammals, the richness of dinosaur species globally may have been far greater than previously anticipated. Which is to say that many, many more weird and wonderful dinosaurs are probably still buried out there, patiently awaiting discovery. SA

MORE TO EXPLORE

Dinosaurs, Dragons, and Dwarfs: The Evolution of Maximal Body Size. Gary P. Burness, Jared Diamond and Timothy Flannery in *Proceedings of the National Academy of Sciences USA,* Vol. 98, No. 25, pages 14518–14523; December 4, 2001.

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New Horned Dinosaurs from Utah Provide Evidence for Intracontinental Dinosaur Endemism. Scott D. Sampson et al. in *PLoS ONE,* Vol. 5, No. 9; September 22, 2010.

SCIENTIFIC AMERICAN ONLINE
To learn how paleoartist James Gurney created the dinosaur images in this article, visit **ScientificAmerican.com/mar2012/dinosaurs**

GATHER THE

If renewable energy is going to take off, we need good ways of storing it for the times when the sun isn't shining and the wind isn't blowing

By Davide Castelvecchi

TO SEE THE BIG OBSTACLE CONFRONTING renewable energy, look at Denmark. The small nation has some of the world's largest wind farms. Yet because consumer demand for electricity is often lowest when the winds blow hardest, Denmark has to sell its overflow of electrons to neighboring countries for pennies—only to buy energy back when demand rises, at much higher prices. As a result, Danish consumers pay some of the highest electricity rates on the planet.

IN BRIEF

The sun does not shine at night, and the wind does not always blow; methods to store large amounts of energy for downtimes are needed to make widespread solar and wind power more practical.

Some utility companies already use excess solar or wind power to pump water to uphill reservoirs, where it can later fall to turn turbines; this pumped-hydro approach could be installed in many more locations.

Other viable energy storage solutions include facilities that compress air into large underground caverns, that heat fluids or molten salts that later create steam to turn turbines, or that can charge advanced batteries. These methods require breakthroughs to make them more efficient so they can compete on price with the cost of electricity from traditional power plants.

WIND

Davide Castelvecchi is a contributing editor for *Scientific American*. He lives in Rome.

Utilities in Texas and California face a similar mismatch between supply and demand; they sometimes have to pay customers to take energy from their windmills and solar farms. On paper, wind and sun could supply the U.S. and some other countries with all the electricity they require. In practice, however, both sources are too erratic to supply more than about 20 percent of a region's total energy capacity, according to the U.S. Department of Energy. Beyond that point, balancing supply and demand becomes too difficult. What are needed are cheap and efficient ways of storing power, to be tapped later, that is generated when winds are howling and the sun is beating down.

Certain technologies such as superconducting magnets, supercapacitors and advanced flywheels are too expensive for that purpose or cannot efficiently hold power for extended periods. But SCIENTIFIC AMERICAN has examined five technologies that might do the trick. Each of them could possibly store, for days, the amounts of energy needed to keep an entire metropolis humming. We asked a panel of experts to rate each one based on three criteria: How well can the technology scale up? Is it cost-effective to build? Is it efficient to operate? No storage method can return the same amount of energy put into it, yet some systems do better than others.

The first two solutions—pumped hydro and compressed air—are somewhat mature and economically feasible. Each of the other contenders will require some kind of breakthrough, but the payoff could be huge. "Ten years from now I expect that we will see a lot of energy storage on the grid," says Imre Gyuk, a physicist who manages the DOE's storage program.

PUMPED **HYDRO**

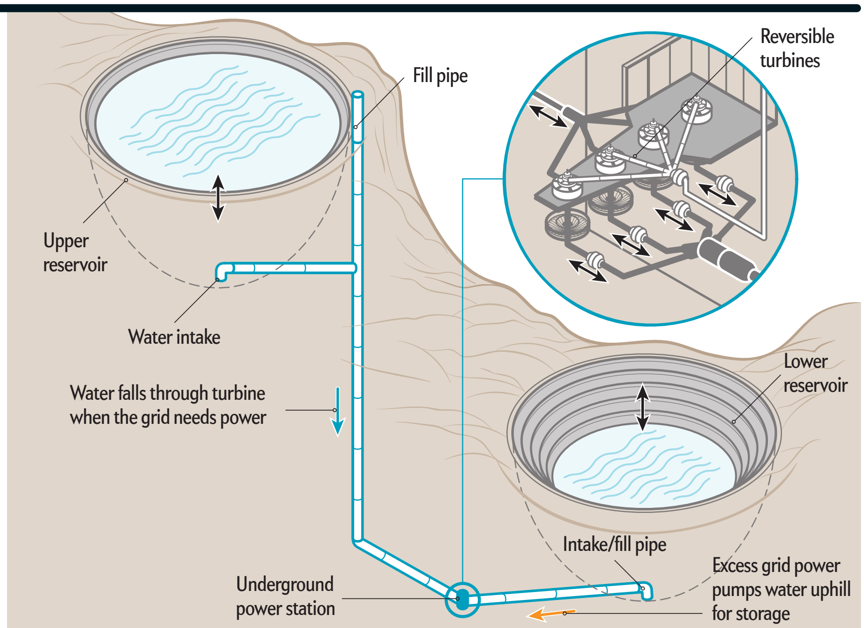
SCALABILITY 4.0

COST-EFFECTIVENESS 4.0

ENERGY EFFICIENCY 4.2*

PROS:	CON:
EFFICIENT, COST-EFFECTIVE, HIGHLY RELIABLE	LACK OF SUITABLE SITES

Average ratings, out of 5, by our panel of experts



SEVERAL COUNTRIES ALREADY STORE CONSIDERable power—about 20 gigawatts in the U.S.—using pumped hydro. This century-old technique is essentially a hydroelectric dam that can operate in reverse. Excess electricity is used to pump water from a low reservoir to one higher uphill. When the water falls back down to the lower reservoir, it passes through turbine blades that turn a generator to create electricity. Round-trip efficiency—the energy that can be recovered, minus losses—can be as high as 80 percent.

In the U.S., 38 pumped-hydro facilities can store the equivalent of just over 2 percent of the country's electrical generating capacity. That share is small compared with Europe's (nearly 5 percent) and Japan's (about 10 percent). But the industry has plans to build reservoirs close to existing power plants. "All you need is an elevation difference and some water," says Rick Miller, a senior vice president at HDR in Omaha. Enough projects are being considered to double existing capacity, he says.

Among the most ambitious plans is the Eagle Mountain Pumped Storage Project in southern California. It would carve two reservoirs out of an abandoned iron surface mine to store energy from regional wind and solar farms, and it could return 1.3 gigawatts of power—as much as a large nuclear power station. In Montana, Grasslands Renewable Energy's proposed hydro storage project would hold wind energy from the Great Plains in an artificial lake that would be built on top of a butte, with a drop of 400 meters.

Pumped hydro's growth is limited primarily by topography. Large, elevated basins must be flooded, which can damage the ecosystem. Some places, such as Denmark and the Netherlands, are just too flat. For those regions Dutch energy consulting company Kema has come up with a radical "energy island" alternative: an artificial lagoon—in a shallow sea—with a circular wall that would be built from landfill. Excess electricity would pump seawater out of the lagoon and into the surrounding ocean. When energy is needed, water from the sea would flow back inside, through tunnels in the wall, passing through turbines. The ocean acts as the "upper" reservoir.

Gravity Power in Santa Barbara, Calif., has an option that could be deployed almost anywhere: a deep vertical shaft would be dug into the ground, and a heavy cylinder would rest at the bottom. Water would be pumped underneath the cylinder, lifting it. To recover energy, tunnels at the base would open, and the water would rush into them through turbines.

OUR EXPERT PANEL

Imre Gyuk
U.S. Department of Energy

Ruth Howes
Ball State University

Haresh Kamath
Electric Power Research Institute

David J. C. MacKay
University of Cambridge

Ernest Moniz
Massachusetts Institute of Technology

CHRISTOPHER GRIFFITH *Trunk Archive (preceding pages)*

Illustrations by Jameson Simpson

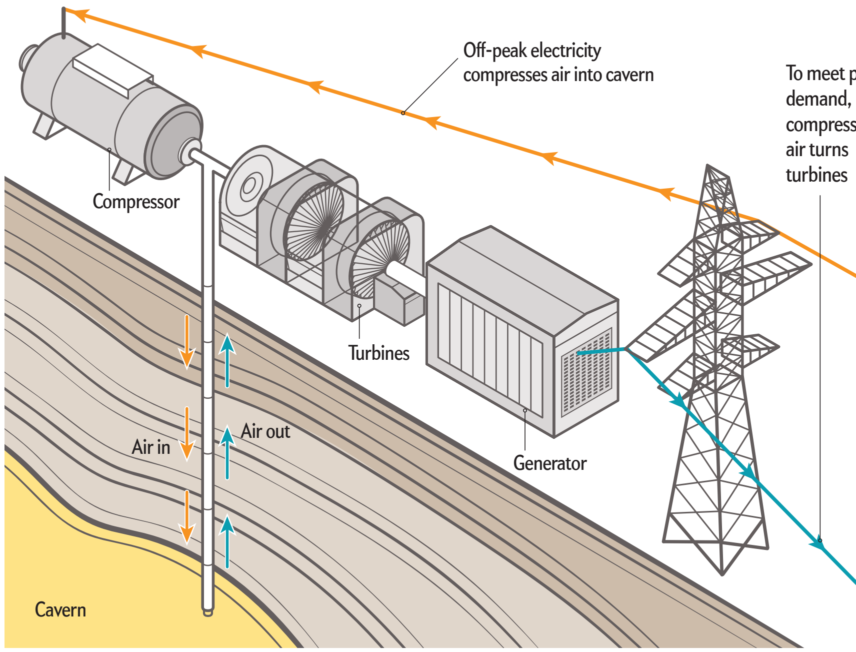
COMPRESSED **AIR**

SCALABILITY **4.0**

COST-EFFECTIVENESS **4.0**

ENERGY EFFICIENCY **3.4**

PROS:	CON:
COST-EFFECTIVE, TESTED	MAY NEED TO BURN SOME NATURAL GAS



DEEP UNDER THE GROUND IN RURAL ALABAMA, a cavern half as large as the Empire State Building holds what could be the quickest fix for the world's energy storage needs: air. Up on the surface, powerful electric pumps inject air at high pressure into the cavern when electricity supply exceeds demand. When the grid is running short, some of that compressed air is let out, blasting through turbines and spinning them. The facility, in McIntosh, Ala., run by the PowerSouth Energy Cooperative, can provide a respectable 110 megawatts for up to 26 hours. It is the only compressed-air operation in the U.S., but it has operated successfully for 20 years. German company E.ON Kraftwerke, based in Hannover, operates a similar plant in Huntorf in the state of Lower Saxony.

PowerSouth created the cavern by slowly dissolving a salt deposit with water, the same process that formed the U.S. Strategic Petroleum Reserve caverns. Salt deposits are plentiful throughout the southern U.S., and most states have geologic formations of one kind or another, including natural caverns and depleted gas fields, that could hold compressed air.

Proposals for compressed-air projects have popped up in several states, including New York and California. Yet recently a proposed $400-million Iowa Stored Energy Park near Des Moines was scrapped because detailed study showed that the permeability of the sandstone that would hold the air was unacceptable.

One practical hurdle is that air heats up when it is compressed and gets cold when it is allowed to expand. That means some of the energy that goes into compression is lost as waste heat. And if the air is simply let out, it can get so cold that it freezes everything it touches—including industrial-strength turbines. PowerSouth and E.ON therefore burn natural gas to create a hot gas stream that warms the cold air as it expands into the turbines, reducing overall energy efficiency and releasing carbon dioxide, which undermines some of the benefits of wind and solar power.

Because these complications limit the efficiency of compressed-air storage, engineers are devising countermeasures. One option is to insulate the cavern so that the air stays warm. The heat could also be transferred to a solid or liquid reservoir that could later reheat the expanding air. SustainX, a start-up based in Seabrook, N.H., sprays water droplets into the air during compression, which heat up and collect in a pool. The water is later sprayed back into expanding air, warming it. SustainX has demonstrated its process in above-ground tanks. General Compression in Newton, Mass., is developing a similar approach for underground storage and is planning a large demonstration plant in Texas. "We don't need to burn gas, ever," says president David Marcus.

ADVANCED **BATTERIES**

SCALABILITY **3.6**

COST-EFFECTIVENESS **2.0**

ENERGY EFFICIENCY **3.8**

PROS:	CON:
ENERGY-EFFICIENT, RELIABLE	EXPENSIVE

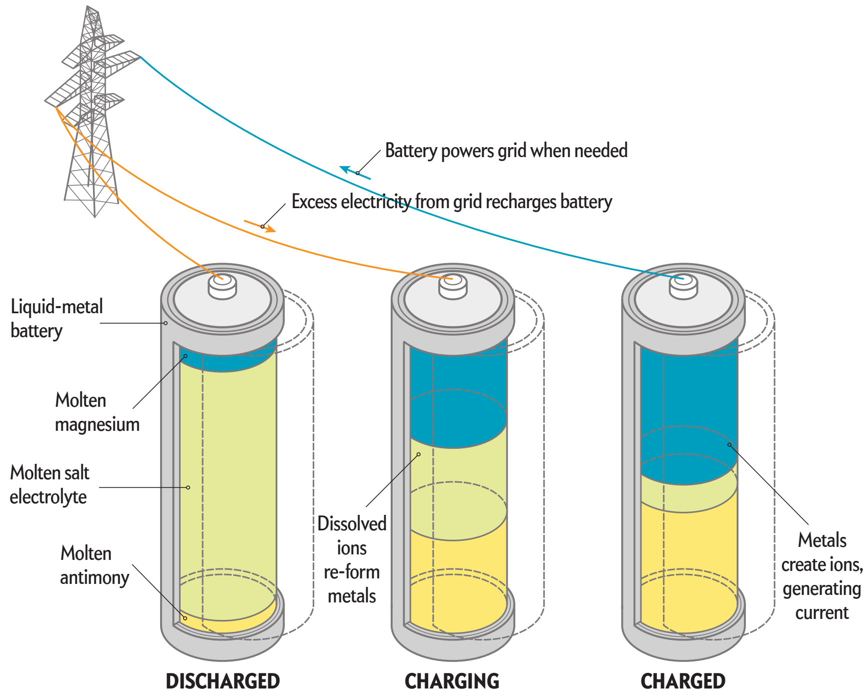
BATTERIES MAY BE THE IDEAL STORAGE MEDIUM for intermittent power sources, some experts say. They charge readily, turn on and off instantly, and can be scaled up easily. For decades utilities have provided backup power to remote recesses of the grid by stacking up racks of off-the-shelf batteries, including the lead-acid type found in cars. Some companies have experimented with molten sodium-sulfur batteries. Power company AES has installed more than 30 megawatts of lithium-ion batteries in Elkins, W.Va., to back up its 98 megawatts of wind turbines. Yet if batteries are to compete for large-scale storage, their cost must drop considerably.

A battery's expense is driven by materials—the positive and negative electrodes and the electrolyte that separates them—as well as the process of manufacturing them into a compact package. Radical redesigns may have a better shot at sharply cutting costs than incremental improvements to common battery types.

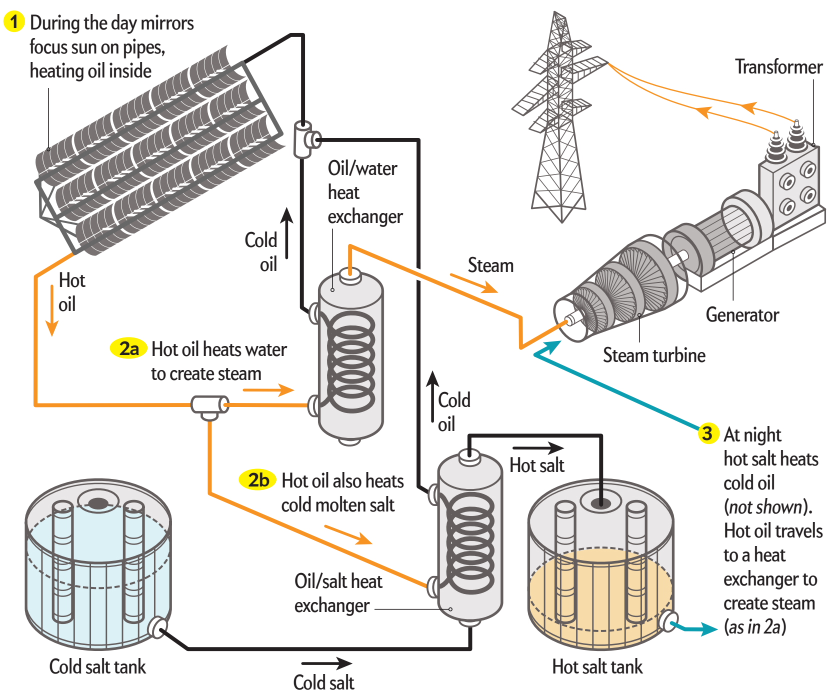
Donald R. Sadoway, a chemist at the Massachusetts Institute of Technology, is developing one unusual design that he calls a liquid-metal battery. Its promise lies in its simplicity: a cylindrical vat kept at high temperature is filled with two molten metals, separated by a molten salt between them. The liquid metals are immiscible with the salt—“like oil and vinegar,” Sadoway says—and have different densities, so they naturally stack on top of each other. When the two metals are connected via an external circuit, an electric current flows. Ions of each metal dissolve into the molten salt, thickening that layer. To recharge the battery, excess current from the grid runs the process in reverse, forcing the dissolved ions back into their respective layers.

Sadoway has so far made “pizza box–size” batteries in the lab, but he thinks that the design could scale up economically, perhaps even becoming cheaper than the $100 per kilowatt-hour of pumped hydro. Sadoway will not know for sure what issues may arise with scaling until he tries it, but he is enthusiastic because, unlike the painstaking, costly manufacture of traditional batteries, his can be built in bulk simply by pouring the materials into a tank.

A more tried-and-true design is the flow battery. A solid-state membrane inside a container separates two liquid electrodes, which can store a lot of energy. Flow batteries are similar in spirit to a more recent technology nicknamed “Cambridge crude,” which uses nanoparticles as electrodes that are suspended in a fluid [see “Liquid Fuel for Electric Cars,” by Christopher Mims; World Changing Ideas, Scientific American, December 2011].



The flow battery has several advantages. It operates at room temperature, unlike the liquid-metal battery, which must be heated. To scale up, just make larger electrodes or add more containers. A defunct start-up company, VRB Power Systems, installed two flow batteries with solutions based on the metal vanadium—one in Moab, Utah, and one on a small Australian island—before selling its technology to Prudent Energy in Bethesda, Md. Other companies are trying to improve on the idea by making the ion flow across the membrane more efficient. Mike Perry, a chemical engineer at United Technologies Corporation (UTC) in Hartford, Conn., says his company is investing millions of dollars and betting that within five years or so flow batteries can become competitive with gas-fired plants used to satisfy peak utility demand. UTC has focused on vanadium, too, because it is a plentiful and inexpensive by-product of petroleum extraction. Energizer Resources in Toronto is also developing a large vanadium mine in Madagascar, which would ensure supply.



THERMAL STORAGE

SCALABILITY 3.6

COST-EFFECTIVENESS 3.6

ENERGY EFFICIENCY 3.0

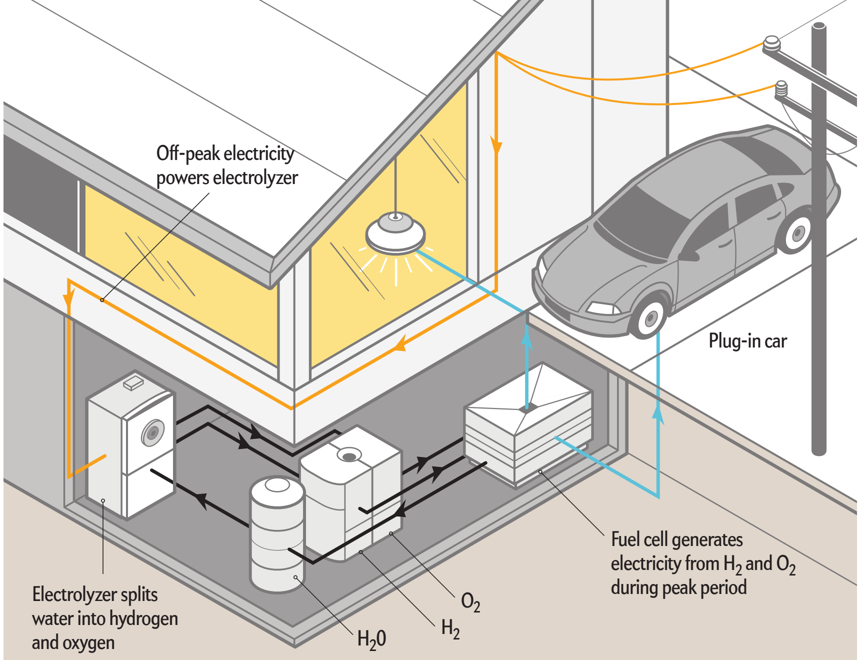
PRO:	CONS:
CAN BE SITED ANYWHERE	EXPENSIVE, HARD TO HOLD ENERGY FOR LONG PERIODS

In regions that have steady sunshine, concentrated solar power stations can be an economical way to generate power as well as to store the sun’s energy. Rows of parabolic mirrors focus sunlight on long pipes that run parallel to the rows, heating a fluid such as mineral oil inside the pipe. The oil travels to a building where its heat converts water into steam, which turns a turbine to generate electricity. When the sun goes down, the fluid can be stored in tanks to produce more steam for at least several hours, until it slowly cools.

A number of concentrated solar power stations operate in the U.S. and Europe. To retain heat energy longer, however, Archimede Solar Energy in Italy has built a demonstration plant near the town of Syracuse in Sicily that uses molten salt instead of oils. Molten salt can be heated to nearly 550 degrees Celsius, compared with 400 degrees C for oil, so it can create more steam for more hours after sundown, says Paolo Martini, Archimede's director of business development and sales. Five cubic meters of molten salt can store one megawatt-hour of energy, compared with 12 cubic meters of oil, Martini says. Solar Millennium in Germany has been operating the sizable Andasol 1 molten salt system in Andalusia, Spain, since 2008. And in June 2011 it achieved the milestone of 24-hour uninterrupted solar-electric generation.

Power from today's concentrated solar power plants is about twice as expensive as that from a natural gas plant. Yet an industry road map predicts that by tweaking plant designs—including the chemistry of the fluids—and introducing economies of scale, concentrated solar energy could become competitive with natural gas within 10 years. Success might be most likely for plants built in places that rarely see clouds, such as the Sahara Desert.

Of course, excess energy generated from wind farms or other sources can also heat fluids that generate power later on. Thermal storage can involve cold instead of hot, too. Ice Energy, a start-up based in Windsor, Colo., sells systems that produce ice during the night when power is plentiful. During the day the ice melts to feed cooling fluid to HVAC systems for air-conditioning. Some commercial utility customers such as big-box stores are beginning to install the units, thereby lessening demand on the grid for air-conditioning power during the hottest hours of the day.



HOME HYDROGEN

SCALABILITY 2.2

COST-EFFECTIVENESS 1.0

ENERGY EFFICIENCY 1.4

PROS:	CON:
EFFICIENT, LIGHTWEIGHT	BASIC MATERIALS BREAKTHROUGHS STILL NEEDED

ONE LONG-SHOT METHOD OF STORING ENERGY would rely on homeowners instead of utility installations. For more than two centuries scientists have split water into hydrogen and oxygen by running an electric current through it. The hydrogen can later be consumed in a fuel cell to generate electricity. The challenge is to both split water and "burn" hydrogen efficiently, without producing too much waste heat.

The efficiency of splitting hydrogen could be much higher if sunlight were used directly, instead of power from the grid, the way plants harness the sun for hydrolysis during photosynthesis. Man-made hydrolytic cells that can do the same have existed for years, but they are inefficient and expensive. Chemists such as Daniel Nocera of M.I.T. and Nathan S. Lewis of the California Institute of Technology have been developing novel materials that could perform better—cobalt-based catalysts in Nocera's case and nanorods in Lewis's—but costs remain very high.

Whether one is using electricity or the sun directly, hurdles on the reconversion side are enormous as well. Fuel cells burn hydrogen efficiently, but they rely on expensive catalytic materials such as platinum. A unit that can power a car or light a building can cost tens of thousands of dollars. Thus, scientists are seeking alternative materials. Storing hydrogen adds another difficulty because the gas is explosive and must be liquefied or compressed.

If all these challenges could be overcome, homeowners could have their own small hydrogen power stations on their premises. When the local utility has excess wind or solar energy, homeowners would use it to split hydrogen, which would later power the home when the sun or winds fade. And because hydrogen's energy density is even greater than that of gasoline, it could one day propel cars and trucks as well, leading to the long-envisioned hydrogen economy.

MORE TO EXPLORE

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The Role of Energy Storage with Renewable Electricity Generation. Paul Denholm et al. National Renewable Energy Laboratory, January 2010.

Integrating Renewable Electricity on the Grid. American Physical Society Panel on Public Affairs. American Physical Society, November 2010.

SCIENTIFIC AMERICAN ONLINE
For more discussion of storage options, see the author's blog at **ScientificAmerican.com/mar2012/castelvecchi**

Carl June is a physician and researcher at the University of Pennsylvania Perelman School of Medicine and studies ways that the immune system might be genetically modified to more effectively fight cancer and HIV.

Bruce Levine is an immunologist studying cell and gene therapies at the University of Pennsylvania Perelman School of Medicine, where he is director of the Clinical Cell and Vaccine Production Facility.

MEDICINE

Blocking HIV's Attack

Scientists have rid one man of HIV by preventing the virus from entering certain immune cells. But the treatment was dangerous and likely unrepeatable. Can they figure out a safer, more broadly achievable way to help millions more?

By Carl June and Bruce Levine

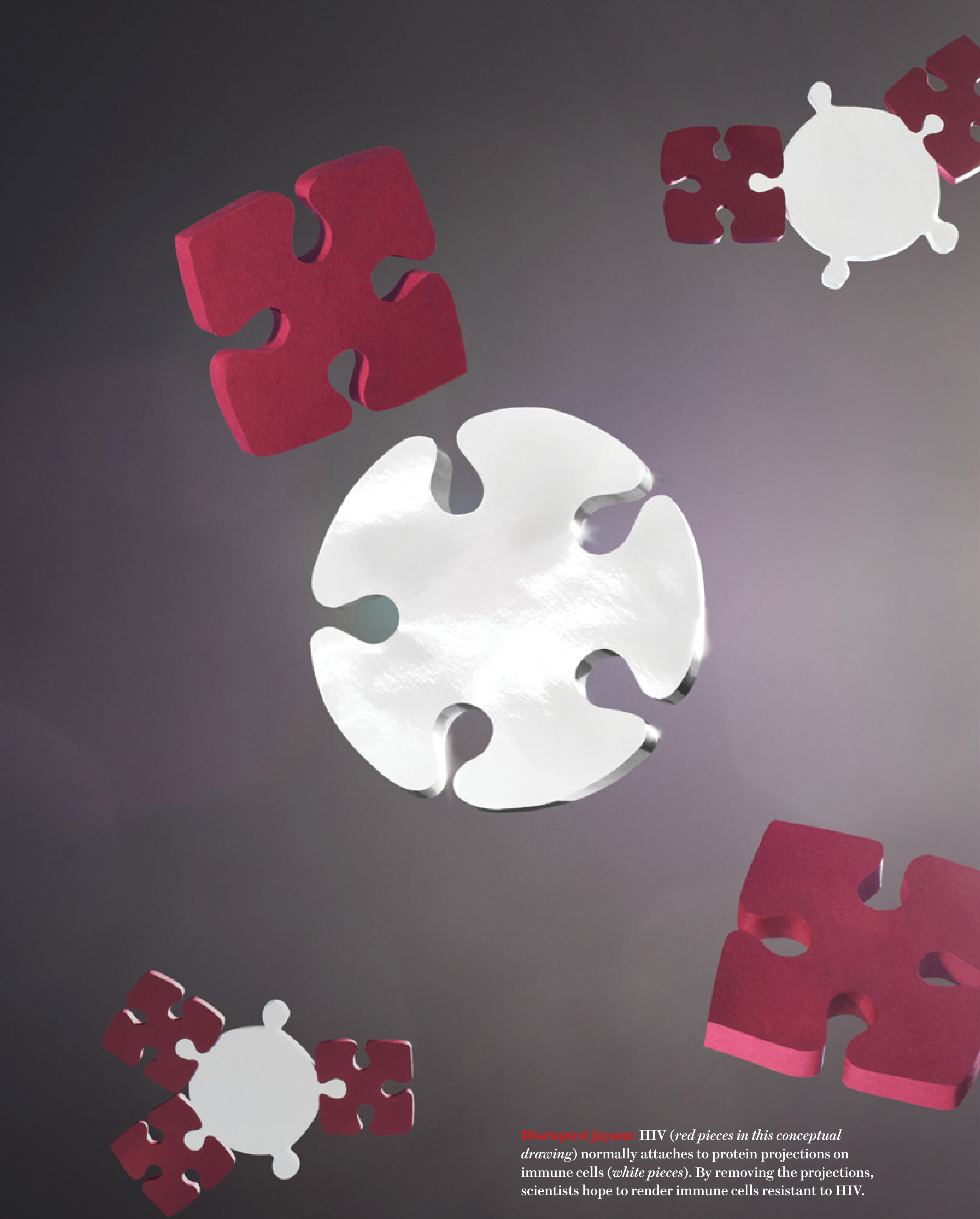
A LITTLE MORE THAN THREE YEARS AGO A MEDICAL TEAM FROM BERLIN PUBLISHED THE results of a unique experiment that astonished HIV researchers. The German group had taken bone marrow—the source of the body's immune cells—from an anonymous donor whose genetic inheritance made him or her naturally resistant to HIV. Then the researchers transplanted the cells into a man with leukemia who had been HIV-positive for more than 10 years. Although treatment of the patient's leukemia was the rationale for the bone marrow transplant therapy, the group also hoped that the transplant would provide enough HIV-resistant cells to control the man's infection. The therapy exceeded the team's expectations. Instead of just decreasing the amount of HIV in the patient's blood, the transplant wiped out all detectable traces of the virus from his body, including in multiple tissues where it could have lain dormant. The German researchers were so surprised by the spectacularly positive results that they waited nearly two years before publishing their data.

The news seemed too good to be true. And yet five years after undergoing his initial treatment, the so-called Berlin patient (who later disclosed his identity as Timothy Ray Brown of California) still shows no signs of harboring the AIDS virus—despite not taking HIV-fighting, antiretroviral drugs for all this time. Of the more than 60 million people who have been infected with HIV over the past few decades, Brown is so far the only individual who appears to have well-documented eradication of the infection.

The approach cannot be applied widely for many reasons, not

PHOTOGRAPH BY SAM HOFMAN

Illustration by Owen Gildersleeve



Disrupted jigsaw: HIV (*red pieces in this conceptual drawing*) normally attaches to protein projections on immune cells (*white pieces*). By removing the projections, scientists hope to render immune cells resistant to HIV.

the least of which is that the patient's own immune system has to be destroyed as a first step—a very risky undertaking. But the unexpected success has inspired researchers around the world to see if they can find safer and less expensive ways to give patients a new, HIV-resistant immune system like the one Brown received. Such a feat would allow doctors to essentially slam the door on HIV, so that it could no longer spread from cell to cell in the body. Eventually the modified immune system would also be likely to clear any remaining HIV from various hiding places in the body. Rather than following in the footsteps of previous therapies that merely suppress the virus, a new approach that mimics the Berlin treatment would—if successful—eliminate the virus and potentially cure the disease.

In fact, the two of us and our colleagues think we might have an easier way to give HIV patients an immune system like the one underlying the Berlin patient's successful treatment. The procedure has shown promise in the laboratory, and we are now carrying out early clinical trials in a small number of HIV-infected people. We have much work ahead of us and cannot be assured that the therapy will be effective, but the Berlin patient's continuing freedom from HIV and our own preliminary results make us feel the treatment we are developing could well be life-changing for millions of people infected with HIV today.

FINE-TUNING THE IMMUNE SYSTEM

OUR APPROACH TO ENGINEERING an immune system to fight HIV builds on research that addressed two related challenges. Scientists needed to figure out how to turbocharge the immune system against HIV. And they needed a way to keep HIV from being able to enter its favored cells, CD4+ cells, also known as helper T cells. These particular T cells serve as the quarterbacks of the immune response by coordinating the interaction among many different types of immune cells. When HIV first infects a helper T cell, the virus does not cause any real harm. Then later, when the immune cell is activated to fight an ongoing infection, it instead spits out more HIV copies. Even more unfortunate, HIV eventually kills these coordinating cells as well, depleting the immune system's ability to fight many other infections. In this way, HIV selectively eliminates the immune system's best-trained players. As they decline, so, too, does the body's ability to fight infections, until AIDS—the end stage marked by deadly infections—sets in.

Figuring out how to boost the immune system, let alone protect helper T cells, has not been easy. When news of the Berlin patient surfaced, however, progress had already been made on both fronts, albeit in separate lines of research.

For years scientists who study cancer, as well as those who investigate viral infections, have searched for ways to pump up the immune system—such as by taking T cells from a patient, exposing them to substances that cause them to both multiply and become more active against either cancer or viral infections, and then returning the juiced-up cells to the patient's body. The two of us joined the effort 20 years ago, when Levine came to work with June at what is now called the Walter Reed National Military Medical Center in Bethesda, Md. Building on the work of others—notably Philip Greenberg and Stanley Riddell of the Fred Hutchinson Cancer Research Center in Seattle and Malcolm Brenner and Cliona Rooney, now at the Baylor College of Medicine in Houston—we began experiments to improve methods for growing T cells outside the body. At that time, T cells from a donor could be cultured in the laboratory only by using complex cocktails of chemical messengers or by extracting from the donor's blood yet another type of cell, called dendritic cells, that normally instructs T cells to mature and multiply dramatically.

We thought we could simplify the process by creating artificial dendritic cells. Starting with tiny magnetic beads, slightly smaller than T cells, we attached to their surface two proteins that mimicked the molecules on dendritic cells. When mixed with T cells in laboratory flasks, the beads proved to be very efficient at their appointed task. By replenishing the beads every two weeks or so, we could keep a colony of active T cells multiplying happily for more than two months and increasing their numbers by a trillionfold.

When we began testing this approach using blood samples taken from HIV-positive volunteers, we discovered, much to our surprise, that the T cells we produced turned out to have a significant—albeit temporary—ability to deflect HIV's advances. We published our results in June 1996 while still not knowing why our magnetic bead method for growing T cells would boost their resistance to infection with HIV. But later that year an important clue emerged that would ultimately help explain the mystery.

A DOORWAY TO INFECTION

AT THE SAME TIME as we were developing our system for growing T cells, other researchers discovered a key flaw in HIV's method of attack. Very early on in the AIDS epidemic, investigators had identified a small number of individuals who appeared to be highly resistant to infection with HIV despite having been exposed to the virus multiple times. Toward the end of 1996, in a scientific publishing frenzy, several laboratories reported that a particular protein, known as CCR5, which sits on the surface of helper T cells and certain other cells, acts like a doorway, allowing HIV to gain entry. Furthermore, researchers showed that people who naturally lacked the protein did not become infected [see "In Search of AIDS-Resistance Genes," by Stephen J. O'Brien and Michael Dean; SCIENTIFIC AMERICAN, September 1997].

The absence of the doorway results from the deletion of 32 nucleotides (the A, T, C and G letters of the DNA alphabet) in the gene that codes for the cell-surface protein. The deletion results in a shortened CCR5 protein that is unable to make its way to the cell's surface. About 1 percent of Caucasians have inherited two copies of this defective gene, dubbed *CCR5-Delta32,* making their cells highly resistant to HIV infection. The mutation is rare in Native Americans, Asians and Africans, however. Apart from their genetic peculiarity, affected individuals appear to be heal-

IN BRIEF

HIV makes use of a particular protein called CCR5, which is found on the surface of some immune cells, to infect those cells.

Some people have inherited a specific mutation that disables their copies of the CCR5 protein, thus offering them greater protection against infection with HIV.

Investigators are trying gene-editing techniques to modify immune cells so that they lack the CCR5 protein, making them resistant to HIV as well.

Preliminary results from safety studies of the gene-editing approach in humans are encouraging, but there is still a long way to go.

thy, although they may be more vulnerable to West Nile virus.

People who have inherited just one copy of the *CCR5-Delta32* gene are still susceptible to HIV—but it takes longer on average for them to progress from initial infection to the later stages of disease. Investigators have shown that natural chemical messengers called beta-chemokines can block a normal CCR5 receptor—making it unavailable to HIV. Indeed, blocking the CCR5 receptor is the basis for an entire class of anti-HIV medications. Unfortunately, it is tough to keep all the CCR5 receptors on all cells that bear it continuously coated with enough of the drug so that HIV cannot gain entry to any of them. In addition, HIV can mutate to avoid the blockade, and these slightly altered viruses can still use the CCR5 doorway to get into T cells.

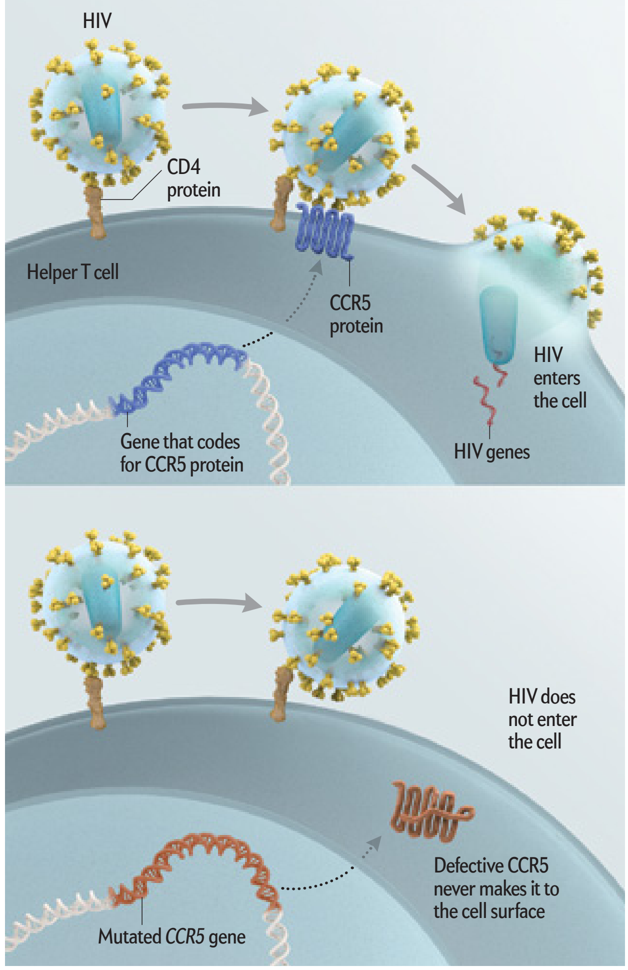
The discovery of CCR5's role in HIV infection helped to explain why our artificially grown T cells proved resistant. Somehow the activation of the T cells by the beads caused the cells to shut down their production of CCR5 proteins. Without a working doorway, HIV was unable to enter the cells.

At that point, we wondered if we could use the CCR5 discovery, together with our newly refined method of growing T cells, to create a novel treatment for HIV. This idea led to a collaboration with Kristen Hege and Dale Ando, both then at the San Francisco–based biotechnology company Cell Genesys, to take an early step: conducting human clinical trials to ascertain the safety of T cells that had been genetically modified to seek out and attack HIV-infected cells—T cells that had also been expanded using our magnetic bead techniques. The cells proved to be safe all right and survived for years after infusion. The specific genetic modification we studied had only a modest effect, however, on HIV replication in patients. Cell Genesys eventually shut down the effort.

DENYING ENTRY

How HIV Enters an Immune Cell

HIV destroys the immune system by targeting key cells called helper T cells. In the 1990s scientists learned that HIV gains entry to these cells by latching onto a protein on the cell's surface called CCR5 (*top panel*). A few people are able to withstand infection with HIV, however, because they lack a functional gene that codes for CCR5. Researchers hope that disabling the *CCR5* gene (*bottom panel*) in HIV-positive individuals might allow them to better control and perhaps even clear the infection.



ENGINEERING AN HIV-RESISTANT CELL

BY 2004, a few years after the two of us had moved to the University of Pennsylvania, Ando came to visit us in our new digs and to propose a second experiment. His new employer, Sangamo BioSciences, had recently developed a technique for cutting the DNA strands of genes in carefully selected places. This method was fundamentally different from and far more efficient than other approaches because it was able to target a specific gene sequence for editing. Previously researchers had no good way to control which genes, or sections of genes, were changed.

The Sangamo technology that Ando was talking about depends on two types of proteins to delete a section of a gene that is already in place. The first type are zinc finger proteins, which are naturally occurring molecules that bind to DNA during gene transcription, the process in which the information in the DNA molecule is converted into an RNA molecule needed for the synthesis of an encoded protein. Humans produce approximately 2,500 different zinc finger proteins, and each one binds to a different, specific nucleotide sequence on the DNA molecule.

Over a period of years scientists worked out a way to design and artificially construct zinc finger proteins able to latch onto any particular DNA sequence of interest—such as, for example, a section of the *CCR5* gene. Ando proposed that Sangamo create a customized set of DNA scissors first by creating zinc finger proteins that would attach to either end of a sequence that we wanted to delete. Then to each of these proteins, company scientists would add a second protein, an enzyme called a nuclease, able to cut DNA strands in two. The zinc finger part of this complex would identify the sections of the DNA to cut, and the nuclease would snip the genetic material. By developing the right pairs of zinc fingers, Sangamo could target just the particular section of the *CCR5* gene that we were interested in—without accidentally damaging other genes.

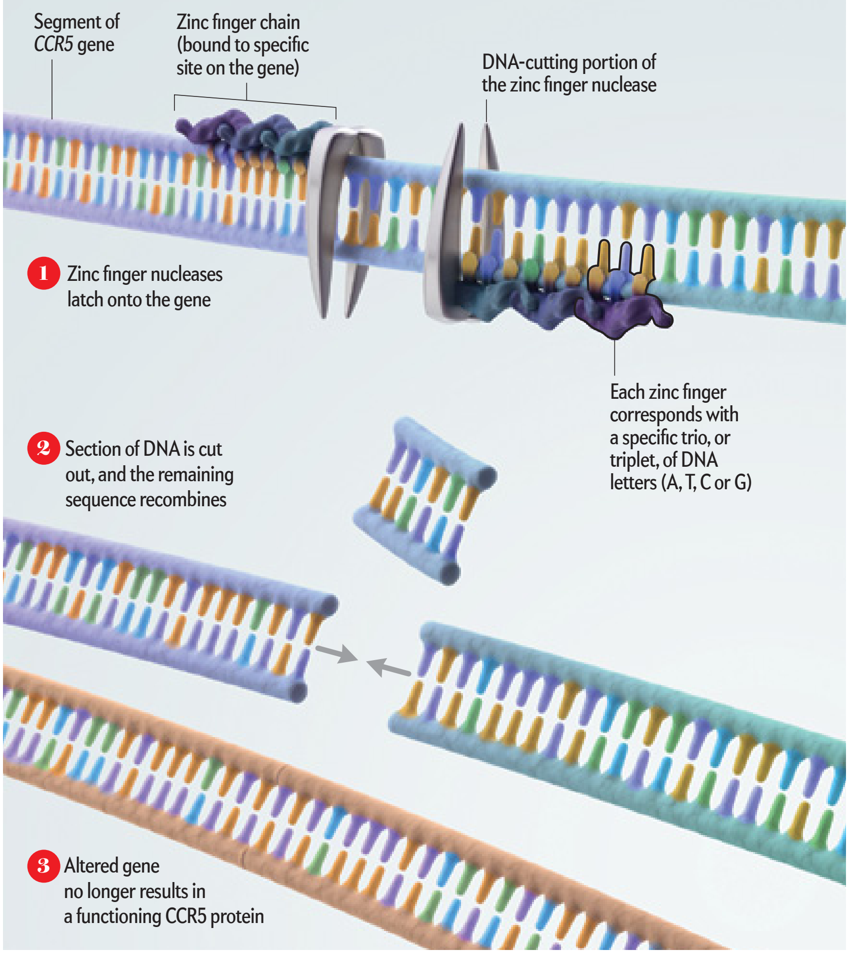
Once these designer zinc finger nucleases had bound to the DNA sequence in question, the cell's own repair machinery would take over. This machinery would recognize the break and rejoin the severed pieces of DNA, chewing up a few nucleotides or adding some extra ones in the process. Thus, the repair process itself

Illustrations by Anatomy Blue

DICING AND SPLICING

Careful Editing Disables a Key Gene

It may be possible to confer resistance to HIV in some individuals by disabling the gene that codes for the CCR5 gateway with compound proteins called zinc finger nucleases. One portion of the protein, made up of molecules called zinc fingers, latches onto the gene, while the second portion, called a nuclease, cuts the DNA ribbon. The body's repair mechanisms then take over, annealing the longer pieces together. Result: the broken gene no longer produces the CCR5 protein that HIV uses to enter immune cells.



would help to further ensure that the slit gene would be unable to give rise to a working copy of the CCR5 protein.

After Ando finished his proposal and left our lab, one of us (June, who is usually highly optimistic) turned to the other and said, "Yeah right, like that's gonna work!" But it was worth a try. Beyond being very specific for the *CCR5* deletion, the zinc finger system was appealing because the proteins need only a short time to function and leave no residual trace in the cell.

HOPES BOLSTERED BY BERLIN PATIENT

WE HAD ALREADY RECEIVED permission from the FDA and the National Institutes of Health to start safety studies in humans when news broke about the apparently successful treatment of the Berlin patient—giving us more reason to think that infusing T cells with mutated *CCR5* genes into patients could deal a significant blow to the HIV in their bodies. In particular, Gero Hütter and his colleagues reported that they had been able to conduct what was, perhaps, a once-in-a-lifetime experiment. One of their patients, who had been HIV-positive for more than 10 years and was doing well on antiviral drugs, developed acute myeloid leukemia, which was unrelated to his HIV infection. He underwent chemotherapy, but the cancer came back. Without a bone marrow transplant, in which the immune system of one person (including all the T cells) is essentially recreated in another person, he would die.

Hütter searched the European databases of potential bone marrow donors, looking for an individual who would match his patient's HLA markers, a group of proteins (the human leukocyte antigens) that the immune system uses to distinguish its own tissues from that of other creatures. Matching a transplant recipient's HLA type is vital to keep the transplanted cells from viewing the new host as foreign and attacking its tissues (a condition known as graft versus host disease) and to prevent rejection by any residual components of the patient's previous immune system.

Hütter did not stop there, however. He hoped to find someone with the right HLA markers whose cells also naturally carried two copies of the *CCR5-Delta32* mutation. A bone marrow transplant from such a person might conceivably provide an HIV-positive recipient with a new immune system that was resistant to virus that continued to persist.

Amazingly, after Hütter searched the databases and tested genes from more than 60 potential donors, he found a candidate who fit the bill. (The search was complicated by the fact that the HLA region varies so much from individual to individual and the HLA genes and the *CCR5* gene are on different chromosomes.) This discovery was a lucky break considering that so few people have the *CCR5-Delta32* mutation in both copies of their *CCR5* gene in the first place. Fortunately, the Berlin patient also had a very common HLA pattern. (To give an idea of just how rare this combination was, researchers across the globe have tried to replicate the German experiment and have yet to find any individuals with the right set of HLA markers and *CCR5* mutations.)

In the end, the Berlin patient needed two bone marrow transplants from the donor to cure his leukemia. Strikingly, more than five years after the transplant operation and in the continued absence of antiretroviral drug therapy, physicians have been unable to detect any HIV in his blood, liver, gut, brain, lymph tissues or plasma, using the most sensitive molecular tests available. No one knows whether HIV was truly eradicated from every tissue in the Berlin patient's body, achieving what is known as a "sterilizing cure," because HIV can insert its genes in the chromosomes of various cells [see "Can HIV Be Cured?" by Mario Stevenson; Scientific American, November 2008], allowing it to lie dormant for many years. Also unknown is whether total destruction of all HIV in his body is necessary if his immune system is now capable of dispatching any infection that might reemerge, meaning he is "functionally cured." At any rate, the patient no longer has to take antiretroviral drugs and is free of detectable virus. (Of course, he still has to take medication to maintain the health of his bone marrow transplant.)

Unfortunately, the German experiment may prove to be the sole example of a bone marrow cure for HIV for years to come. Not only is the right combination of HLA and genetic mutations in donor and recipient extremely rare, this particular approach is very expensive (bone marrow transplants incur minimum costs of $250,000 at our hospital), requires an intense regimen of chemotherapy, a risky bone marrow transplant and a lifelong regimen of antirejection drugs. In effect, the Berlin patient has traded one set of problems—HIV infection (and leukemia)—for another—being a transplant recipient. Most people who are able to lead more or less healthy, productive lives on anti-HIV drugs—albeit with significant side effects and lifetime costs—would hesitate to make a similar trade. Of course, because the Berlin patient had developed a deadly leukemia, he had no choice.

Although we were buoyed by the Berlin findings, we also knew that the *CCR5* deletion in the donated immune system might not have been the only reason for the patient's apparently HIV-free state. Perhaps the patient's reservoir of dormant HIV particles was drained during the years of treatment with antiretroviral drugs. Or perhaps the patient had no residual HIV left after his original immune system was destroyed in preparation for the transplant. Or perhaps the one instance of life-threatening graft versus host disease that the Berlin patient suffered during his treatment also destroyed any remaining HIV-infected cells before the reaction was brought under control with medication. (No HLA match is ever 100 percent perfect—except among identical twins.) Still, the *CCR5* deletion remained the most likely explanation for the transplant's success, and so we eagerly plowed on with our own experiments.

CLINICAL TRIALS ARE UNDER WAY

When news of the Berlin patient came out, Sangamo had, as promised, developed a set of zinc finger nucleases that targeted a spot near the key 32-nucleotide sequence of the *CCR5* gene. (Because the goal was to disable *CCR5,* it did not matter if we reproduced the naturally occurring genetic mutation exactly as long as the resulting protein stopped functioning.) With Elena Perez, then a postdoctoral fellow in the lab, we had shown that the HIV infection itself could, ironically, aid the process of reshaping the immune system to become more resistant to the virus. Our laboratory experiments demonstrated that even when T cells whose *CCR5* genes had been disabled by zinc finger nucleases were initially present at low frequency in cultures, the altered cells were able to replenish and stabilize the T cell population after exposure to HIV; in contrast, nonedited T cells that still contained CCR5 receptors were destroyed by HIV. In other words, HIV killed the vulnerable T cells, leaving behind more and more of the CCR5-deficient T cells, which are exactly the cells that are resistant to HIV and can thus do their job as immune cells and provide protection from infections.

Our preliminary results in a safety trial in people have also been encouraging. Under the guidance of Pablo Tebas, the physician leading our trial in Philadelphia, the first patient received his CCR5-modified T cell reinfusion in the summer of 2009. Since then, we have treated an 11 additional HIV-positive volunteers in a study sponsored by the NIH. Sangamo is conducting a similar study on the West Coast. Although these safety studies by their very nature are not designed to prove whether a treatment is effective, we have observed that the number of helper T cells measured in ongoing blood tests has increased from baseline in all patients to date, a sign that the treatment probably is protecting T cells. In addition, helper T cells that lack a functioning CCR5 receptor have been detected in the lymphatic tissue of the intestines and in the blood. (These cells could have derived only from the reimplanted cells that were modified by the zinc finger nucleases.)

The next step is to test the ability of the newly altered immune cells to fight off the HIV particles that are already present in the body. We are employing a well-accepted, if nonetheless daunting, strategy to do so. Under close monitoring by study physicians, we plan to stop our volunteers' anti-HIV medications to see what happens. When we did this for 12 weeks with one of our treated subjects, who had inherited a single *CCR5-Delta32* gene (thus giving him a slight natural advantage), we found no evidence of the virus in his blood or lymph tissues at the conclusion of the three-month interruption of antiviral medications. The more recently treated patients are in the midst of their postinfusion regimen and follow-up, with completion of these visits over the next year. Additional clinical trials to test the efficacy of this novel technology are planned. If we are ultimately successful, the zinc finger nuclease approach could be significantly less expensive than either the rare CCR5-deficient bone marrow transplant or a lifetime of anti-HIV drug therapy.

Only a few years ago the idea of developing safe, effective and less expensive therapies that offer long-term, drug-free control of HIV was a vision that few of us even dared to dream. Even if our custom-designed zinc finger nucleases are not a cure, we believe they could be the closest anyone has come to locking out HIV in 30 years. SA

MORE TO EXPLORE

Establishment of HIV-1 Resistance in CD4+ T Cells by Genome Editing Using Zinc-Finger Nucleases. Elena E. Perez et al. in *Nature Biotechnology,* Vol. 26, pages 808–816; 2008.

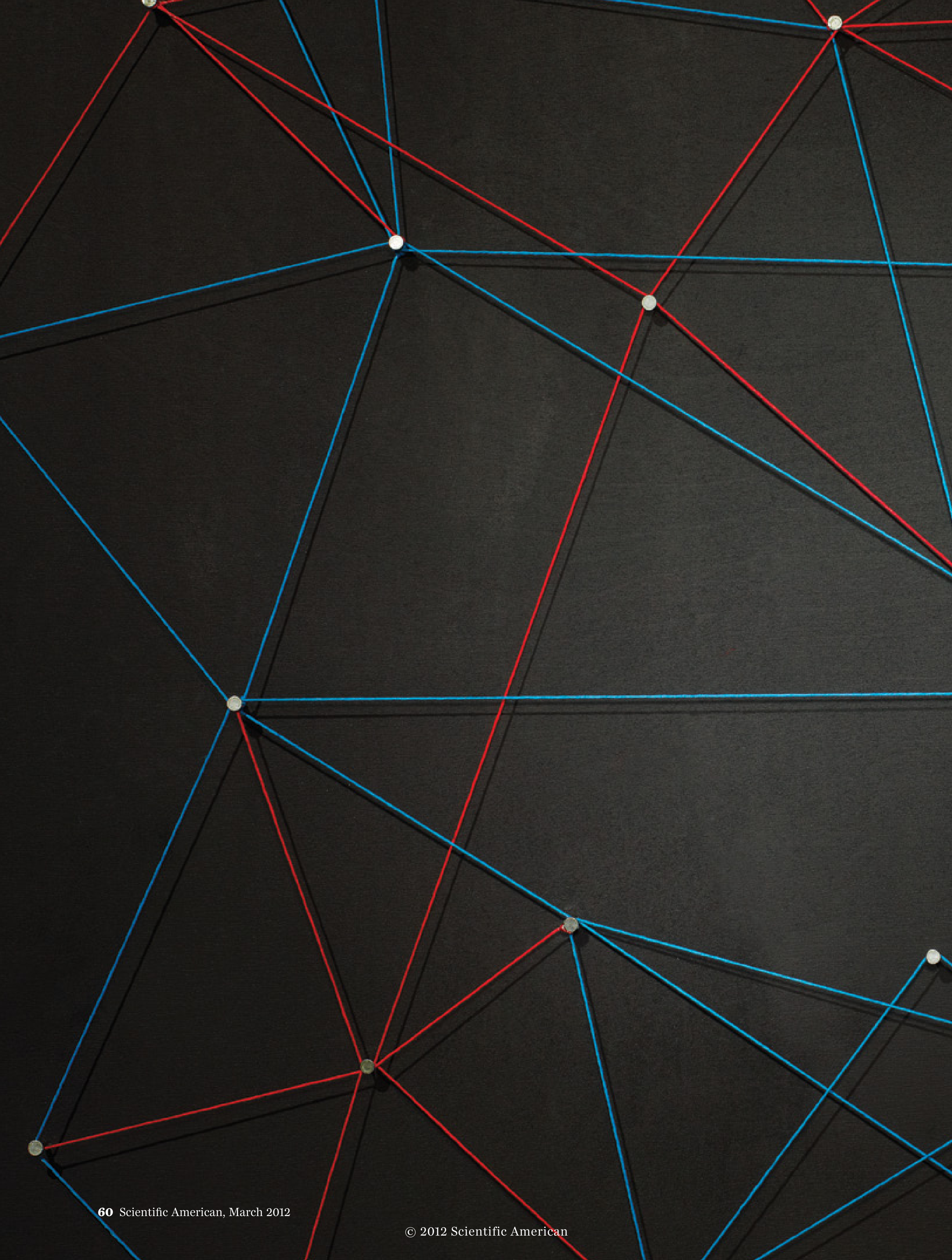
Long-Term Control of HIV by *CCR5 Delta32/Delta32* Stem-Cell Transplantation. Gero Hütter et al. in *New England Journal of Medicine,* Vol. 360, No. 7, pages 692–698; February 12, 2009.

Chemokine Receptor 5 Knockout Strategies. Paula Cannon and Carl June in *Current Opinions in HIV and AIDS,* Vol. 6, No. 1, pages 74–79; January 2011.

The Man Who Had HIV and Now Does Not. Tina Rosenberg in *New York Magazine;* May 29, 2011.

Cell and gene therapy professional societies: American Society of Gene and Cell Therapy (**www.asgt.org**) and International Society for Cellular Therapy (**www.celltherapysociety.org**)

SCIENTIFIC AMERICAN ONLINE
Follow the ups and downs of the search for AIDS treatments over the past three decades at **ScientificAmerican.com/mar2012/hiv-timeline**



INFORMATION TECHNOLOGY

THE SHADOW WEB

Governments and corporations have more control over the Internet than ever. Now digital activists want to build an alternative network that can never be blocked, filtered or shut down

By Julian Dibbell

IN BRIEF

The Internet was designed to be a decentralized system: every node should connect to many others. This design helped to make the system resistant to censorship or outside attack.

Yet in practice, most individual users exist at the edges of the network, connected to others only through their Internet service provider (ISP). Block this link, and Internet access disappears.

An alternative option is beginning to emerge in the form of wireless mesh networks, simple systems that connect end users to one another and automatically route around blocks and censors.

Yet any mesh network needs to hit a critical mass of users before it functions well; developers must convince potential users to trade off ease of use for added freedom and privacy.

Photograph by Dan Saelinger

Julian Dibbell has been writing about the Internet and digital culture for nearly two decades. He is author of *Play Money: Or How I Quit My Day Job and Made Millions Trading Virtual Loot* and editor of *The Best Technology Writing 2010*.

JUST AFTER MIDNIGHT ON JANUARY 28, 2011,

the government of Egypt, rocked by three straight days of massive antiregime protests organized in part through Facebook and other online social networks, did something unprecedented in the history of 21st-century telecommunications: it turned off the Internet. Exactly how it did this remains unclear, but the evidence suggests that five well-placed phone calls—one to each of the country's biggest Internet service providers (ISPs)—may have been all it took. At 12:12 A.M. Cairo time, network routing records show, the leading ISP, Telecom Egypt, began shutting down its customers' connections to the rest of the Internet, and in the course of the next 13 minutes, four other providers followed suit. By 12:40 A.M. the operation was complete. An estimated 93 percent of the Egyptian Internet was now unreachable. When the sun rose the next morning, the protesters made their way to Tahrir Square in almost total digital darkness.

Both strategically and tactically, the Internet blackout accomplished little—the crowds that day were the biggest yet, and in the end, the demonstrators prevailed. But as an object lesson in the Internet's vulnerability to top-down control, the shutdown was alarmingly instructive and perhaps long overdue.

Much has been made of the Internet's ability to resist such control. The network's technological origins, we are sometimes told, lie in the cold war–era quest for a communications infrastructure so robust that even a nuclear attack could not shut it down. Although that is only partly true, it conveys something of the strength inherent in the Internet's elegantly decentralized design. With its multiple, redundant pathways between any two network nodes and its ability to accommodate new nodes on the fly, the TCP/IP protocol that defines the Internet should ensure that it can keep on carrying data no matter how many nodes are blocked and whether it's an atom bomb or a repressive regime that does it. As digital-rights activist John Gilmore once famously said, "The Internet interprets censorship as damage and routes around it."

That is what it was designed to do anyway. And yet if five phone calls can cut off the Internet access of 80 million Egyptians, things have not worked quite that way in practice. The Egyptian cutoff was only the starkest of a growing list of examples that demonstrate how susceptible the Internet can be to top-down control. During the Tunisian revolution the month before, authorities had taken a more targeted approach, blocking only some sites from the national Internet. In the Iranian post-election protests of 2009, Iran's government slowed nationwide Internet traffic rather than stopping it altogether. And for years China's "great firewall" has given the government the ability to block whatever sites it chooses. In Western democracies, consolidation of Internet service providers has put a shrinking number of corporate entities in control of growing shares of Internet traffic, giving companies such as Comcast and AT&T both the incentive and the power to speed traffic served by their own media partners at the expense of competitors.

What happened, and can it be fixed? Can an Internet as dynamically resilient as the one Gilmore idealized—an Internet that structurally resists government and corporate throttles and kill switches—be recovered? A small but dedicated community of digital activists are working on it. Here is what it might look like.

IT'S A DAZZLING SUMMER AFTERNOON AT THE WIEN-SEMMERING power plant in Vienna, Austria. Aaron Kaplan has spent the past seven minutes caged inside a dark, cramped utility elevator headed for the top of the plant's 200-meter-high exhaust stack, the tallest structure in the city. When Kaplan finally steps out onto the platform at its summit, the surrounding view is a panorama that takes in Alpine foothills to the west, green Slovakian borderlands in the east and the glittering Danube straight below. But Kaplan did not come here for the

PROP STYLING BY LAUREN SHIELDS *(preceding pages)* view. He walks straight to the platform's edge to look instead at four small, weatherized Wi-Fi routers bolted to the guardrail.

These routers form one node in a nonprofit community network called FunkFeuer, of which Kaplan is a co-founder and lead developer. The signals that the routers beam and pick up link them, directly or indirectly, to some 200 similar nodes on rooftops all over greater Vienna, each one owned and maintained by the user who installed it and each contributing its bandwidth to a communal, high-speed Internet connection shared almost as far and wide as Kaplan, from the top of the smokestack, can see.

FunkFeuer is what is known as a wireless mesh network. No fees are charged for connecting to it; all you need is a $150 hardware setup ("a Linksys router in a Tupperware box, basically," Kaplan says), a roof to put your equipment on and a line-of-sight connection to at least one other node. Direct radio contact with more than a few other nodes isn't necessary, because each node relies on its immediate neighbors to pass along any data meant for nodes it cannot directly reach. In the network's early months, soon after Kaplan and his friend Michael Bauer started it in 2003, the total number of nodes was only about a dozen, and this bucket brigade transmission scheme was a sometimes spotty affair: if even one node went down, there was a good chance the remainder could be cut off from one another or, crucially, from the network's uplink, the one node connecting it to the Internet at large. Keeping the network viable around the clock back then "was a battle," Kaplan recalls. He and Bauer made frequent house calls to help fix ailing user nodes, including one 2 A.M. rooftop session in the middle of a –15 degree Celsius snowstorm, made bearable only by the mugs of hot wine ferried over by Kaplan's wife.

As the local do-it-yourself tech scene learned what FunkFeuer offered, however, the network grew. At somewhere between 30 and 40 nodes, it became self-sustaining. The network's topology was rich enough that if any one node dropped out, any others that had been relying on it could always find a new path. The network had reached that critical density at which, as Kaplan puts it, "the magic of mesh networking kicks in."

Mesh networking is a relatively young technology, but the "magic" Kaplan talks about is nothing new: it is the same principle that has long underpinned the Internet's reputation for infrastructural resilience. Packet-switched store-and-forward routing—in which every computer connected to the network is capable not just of sending and receiving information but of *relaying* it on behalf of other connected computers—has been a defining architectural feature of the Internet since its conception. It is what creates the profusion of available transmission routes that lets the network simply "route around damage." It is what makes the Internet, theoretically at least, so hard to kill.

If the reality of the Internet today more closely matched the theory, mesh networks would be superfluous. But in the two decades since the Internet outgrew its academic origins and started becoming the ubiquitous commercial service it is now, the store-and-forward principle has come to play a steadily less meaningful role. The vast majority of new nodes added to the network in this period have been the home and business computers brought online by Internet service providers. And in the ISP's connection model, the customer's machine is never a relay point; it's an end point, a terminal node, configured only to send and receive and only to do so via machines owned by the ISP. The Internet's explosive growth, in other words, has not added new routes to the network map so much as it has added cul-de-sacs, turning ISPs and other traffic aggregators into focal points of control over the hundreds of millions of nodes they serve. For those nodes there is no routing around the damage if their ISP goes down or shuts them off. Far from keeping the Internet tough to kill, the ISP, in effect, becomes the kill switch.

What mesh networks do, on the other hand, is precisely what an ISP does not: they let the end user's machine act as a data relay. In less technical terms, they let users stop being merely Internet consumers and start being their own Internet providers [*see box on next page*]. If you want a better sense of what that means, consider how things might have happened on January 28 if Egypt's citizens communicated not through a few ISPs but by way of mesh networks. At the very least, it would have taken a lot more than five phone calls to shut that network down. Because each user of a mesh network owns and controls his or her own small piece of the network infrastructure, it might have taken as many phone calls as there were users—and much more persuading, for most of those users, than the ISPs' executives needed.

AT 37 YEARS OLD, SASCHA MEINRATH HAS BEEN A KEY player in the community mesh-networking scene for about as long as there has been a scene. As a graduate student at the University of Illinois, he helped to start the Champaign-Urbana Community Wireless Network (CUWiN), one of the first such networks in the U.S. Later, he co-organized a post-Katrina volunteer response team that set up an ad hoc mesh network that spanned 60 kilometers of the disaster area, restoring telecommunications in the first weeks after the hurricane. Along the way, he moved to Washington, D.C., intent on starting a community wireless business but instead ending up being "headhunted," as he puts it, by the New America Foundation, a high-powered think tank that hired Meinrath to generate and oversee technology initiatives. It was there, early last year, that he launched the Commotion wireless project, an open-source wireless mesh-networking venture backed by a $2-million grant from the U.S. State Department.

The near-term goal of the project is to develop technology that "circumvents any kill switch and any sort of central surveillance," Meinrath says. To illustrate the idea, he and other core Commotion developers put together what has been called a prototype "Internet in a suitcase": a small, integrated package of wireless communications hardware, suitable for smuggling into a repressive government's territory. From there, dissidents and activists could provide unblockable Internet coverage. The suitcase system is really just a rough-and-ready assemblage of technologies already well known to mesh-networking enthusiasts. Any sufficiently motivated geek could set one up and keep it working.

The long-term question for Meinrath and his colleagues is, "How do you make it so easy to configure that the other 99.9 percent of nongeek humanity can do it?" Because the more people use a mesh network, the harder it is to kill.

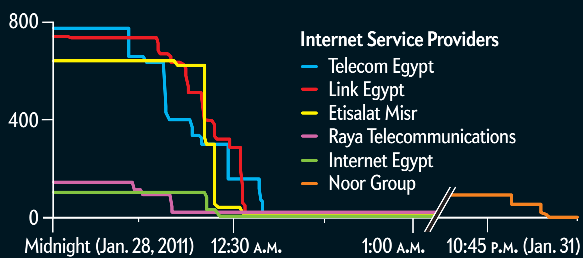
In one way, this is numerically self-evident: a mesh network of 100 nodes takes less effort to shut down, node by node, than a mesh of 1,000 nodes. Perhaps more important, a larger mesh network will tend to contain more links to the broader Internet. These uplinks—the sparsely distributed portal nodes stand-

HOW IT WORKS

The Perils of Centralized Networks

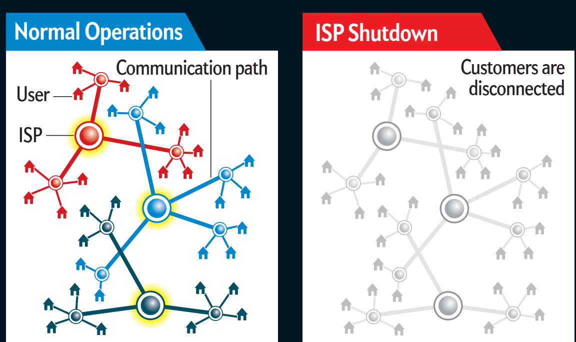
As Facebook-fueled protests threatened the Egyptian government last year, the Internet disappeared. Records show that each of Egypt's major Internet providers dropped users' connections within a few minutes of one another. The only system that did not disappear was the Noor Group, which happens to serve the Egyptian stock exchange. It was shut down four days later.

Active Internet Connections



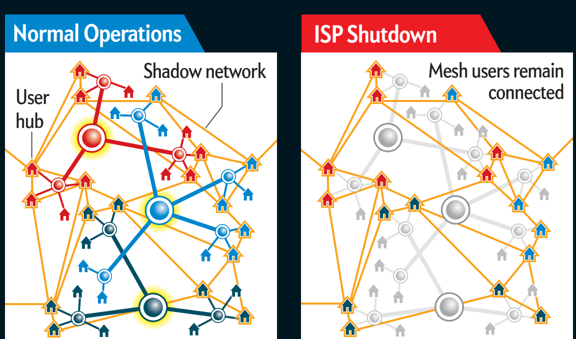
Traditional Hub-and-Spoke Networks

Nowadays individual Internet users depend on a single connection to reach the global network: that of their Internet service provider (ISP), any one of which might serve millions of individuals. If a single ISP goes down, all its customers will find themselves in digital darkness.



Decentralized Mesh Networks

In a mesh network, each user has the capability to receive and send information and to relay information on behalf of other connected computers. In this setup, an ISP shutdown might slow communications, but the shadow network would keep them alive, routing information around the primary hubs.



ing as choke points between the mesh and the rest of the Internet—become less of a vulnerability as the mesh gets bigger. With more uplinks safely inside the local mesh, fewer everyday communications face disruption should any one link to the global network get cut. And because any node in the mesh could in principle become an uplink using any external Internet connection it can find (dial-up ISP, tethered mobile phone), more mesh nodes also mean a greater likelihood of quickly restoring contact with the outside world.

Size matters, in a word. Thus, in mesh-networking circles, the open question of mesh networks' scalability—of just what size they can grow to—has tended to be a pressing one. Whether it is even theoretically possible for mesh networks to absorb significant numbers of nodes without significantly bogging down remains controversial, depending on what kind of numbers count as significant. Just a few years ago some network engineers were arguing that mesh sizes could never grow past the low hundreds of nodes. Yet currently the largest pure-mesh networks have node counts in the low four digits, and dozens of community networks thrive, with the biggest of them using hybrid mesh-and-backbone infrastructures to reach node counts as high as 5,000 (like the Athens Wireless Metropolitan Network in Greece) and even 15,000 (like Guifi.net in and around Barcelona). The doubt that lingers is whether it is *humanly* possible for mesh networks to grow much bigger, given how most humans feel about dealing with technologies as finicky and complicated as mesh networks.

Unlike most open-source technologies, which tend to downplay the importance of a user-friendly interface, the mesh movement is beginning to realize how critical it is for its equipment to be simple. But if Commotion is not alone in seeking to make mesh networks simpler to use, the key simplification it proposes is a uniquely radical one: instead of making it easier to install and run mesh-node equipment in the user's home or business, Commotion aims to make it unnecessary. "The notion is that you can repurpose cell phones, laptops, existing wireless routers, et cetera," Meinrath explains, "and build a network out of what's already in people's pockets and book bags." He calls it a "device as infrastructure" network, and in the version he envisions, adding one more node to the mesh would require all the effort of flipping a switch. "So in essence, on your iPhone or your Android phone, you would push a button and say, yes, join this network," he says. "It needs to be that level of ease."

IMAGINE A WORLD, THEN, IN WHICH MESH NETWORKS HAVE FINALLY reached that level—finally cleared the hurdle of mass usability to become, more or less, just another app running in the background. What happens next? Does the low cost of do-it-yourself Internet service squeeze the commercial options out of the market until the last of the ISPs' hub-and-spoke fiefdoms give way to a single, world-blanketing mesh?

Even the most committed supporters of network decentralization aren't betting on it. "This type of system, I think, will always be a poor man's Internet," says Jonathan Zittrain, a Harvard Law School professor and author of *The Future of the Internet: And How to Stop It.* Zittrain would be happy to see the mesh approach succeed, but he recognizes it may never match some of the efficiencies of more centrally controlled networks. "There are real benefits to centralization," he says, "including ease of use." Ramon Roca, founder of Guifi.net, likewise doubts mesh net-

SOURCE: JAMES COWIE *Renesys blog (Egyptian Internet data)*

Graphics by Brown Bird Design

works will ever put the ISPs out of business—and for that matter, doubts such networks will ever take much more than 15 percent of the market from them. Even at that low a rate of penetration, however, mesh networks can serve to "sanitize the market," Roca argues, opening up the Internet to lower-income households that otherwise could not afford it and spurring the dominant ISPs to bring down prices for everybody else.

As welcome as those economic effects might be, the far more important civic effects—mesh networking's built-in resistances to censorship and surveillance—need a lot more than a 15 percent market share to thrive. And if it is clear that market forces alone are not going to get that number up much higher, then the question is, What will?

Typically, when markets fail to deliver a social good, the first place that gets looked to for a fix is government. In this case particularly, that is not a bad place to start looking. The same mesh network that routes around censorship as if it were damage can just as effectively route around actual damage, which makes mesh networks an ideal communications channel in the face of hurricanes, earthquakes and other natural disasters of the kind that governments are charged with protecting against. Zittrain contends, therefore, that it would be good policy for governments to take an active hand in spreading mesh networks not just among foreign dissidents but among their own citizens. All it might take is a requirement that cell phones sold in the U.S. come equipped with emergency mesh-networking capabilities so that they are ready to turn themselves into relay-capable nodes at the press of a button. From a public policy perspective, Zittrain says, "it's a no-brainer to build that. And the national security and law-enforcement establishments should generally cheer it on."

The hitch, of course, is that it is just as easy to picture law-enforcement agencies denouncing any national mesh network as a place for criminals and terrorists to communicate out of earshot of the telephone and ISP companies that facilitate surveillance. Such are the complications of counting on government to support mesh networking when it is governments, often enough, that do the kind of damage mesh networks promise to help fix.

It is doubtful, then, that governments can be relied on to do the job any more than markets can. But Eben Moglen has some thoughts about what might. Moglen is a law professor at Columbia University and for many years has been the lawyer for the Free Software Foundation, a nonprofit group of digital activists. Last February, inspired partly by the news from Tunisia, he announced a project called FreedomBox. He also announced he was seeking start-up money for the project on the crowdsourced funding site Kickstarter, and he went on to raise $60,000 in five days.

As a project, FreedomBox has a number of similarities to Commotion, few of them entirely coincidental (Meinrath has a seat on the FreedomBox Foundation's technical advisory committee). Like Commotion, the project broke ground with an illustrative prototype—in this case, the FreedomBox, a networking device about the size of a small brick that costs "$149, in small quantity, and will ultimately be replaced by a bunch of hardware that is half that cost or less," Moglen says.

Again like Commotion, FreedomBox is not tied to the form of any specific gadget. Rather it's a stack of code that can go into the increasing number of networked CPUs that are piling up in our homes and lives, like "dust bunnies under people's couches," as Moglen puts it. All of these can become the infrastructure of an Internet that "rebalances privacy" and restores the vision of "a decentralized network of peers." There are IP addresses in television set-top boxes, in refrigerators—any of these, Moglen says, could be a FreedomBox. And it is not just about decentralizing the infrastructure. It is about decentralizing data, too. For Moglen, for example, the concentration of user data in cloud services such as Facebook and Google is just as much a threat to privacy and freedom of expression as the concentration of traffic in ISPs. To counteract this trend, FreedomBox will be optimized to run alternative social networks such as Diaspora that store your personal data on your machine, sharing it only with the people you choose via peer-to-peer networks.

Still, the key element in the project, Moglen says, is "the political will that is being displayed by a generation of young people who, because of their dependence on social networking, are increasingly aware of their and other people's vulnerability online." It is this earnestness he is counting on to motivate, in part, the many coders who are contributing labor to the project. It is also the one thing likeliest to push users to adopt the technology. Short of a sustained campaign of techno-activism, Moglen suggests, it's not clear what will ever wake the average user to the broad costs in eroded freedom and privacy that we pay for ease of use and other, more immediately tangible benefits.

"People underestimate the harm being done by the death of privacy pretty much in the same way that they underestimate the extraordinary multiplicative consequences of other ecologically destructive acts," such as littering and polluting, Moglen says. "It's hard for human beings to calculate ecologically. It's not a thing that the primate brain evolved to do."

This suggests that the reinvention of the Internet can never be just a matter of tweaking the technologies. It may require a political movement as broad-based and long-ranged as the environmental movement. If neither government nor markets can lead us there, maybe only a collective change of awareness will do, like the kind of change that the green movement brought about by force of will. Nobody recycled before. Now we do. Nobody uses mesh infrastructure now. Someday we might.

Even then, no single technical measure would be enough to preserve the freedoms that the Internet both evokes and embodies. That's because, ultimately, even the ideal, unkillable Internet can't, on its own, resist the social and economic forces that push to recentralize it. Mesh networking is just one way to help push back. "These mesh networks are good for communities, and the bigger they are, the better," Funkfeuer's Kaplan says. But even a single, worldwide mesh would still be at risk of retracing the evolutionary steps that led to the compromised Internet we have now. "Mesh networking is not a replacement for the Internet. It's just part of it," he says. "There's no place for utopia here." SA

MORE TO EXPLORE

A Survey on Wireless Mesh Networks. I. F. Akyildiz and Xudong Wang. *IEEE Communications Magazine,* Vol. 43, No. 9, pages S23–S30; September 2005.

Freedombox: **http://freedomboxfoundation.org**

Funkfeuer: **www.funkfeuer.at/index.php?L=1**

The Mesh Networks Research Group: **www.mesh-networks.org**

SCIENTIFIC AMERICAN ONLINE
Bill Joy talks about the importance of mesh networks at **ScientificAmerican.com/mar2012/mesh**

BIOTECHNOLOGY

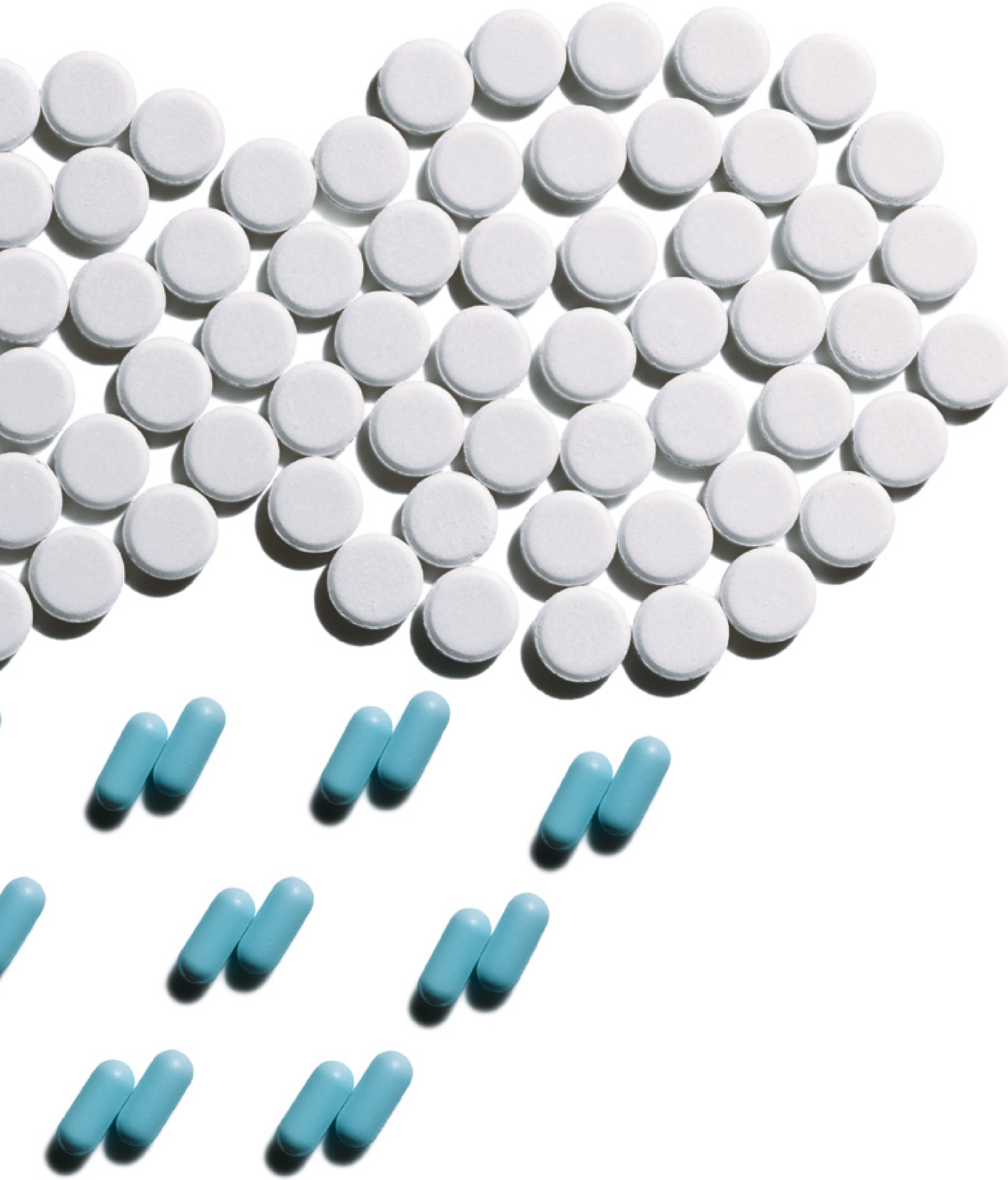
LIFTING THE BLACK CLOUD

TOM SCHIERLITZ *Trunk Archive*

Existing antidepressants leave a lot to be desired. They can take weeks to start working, and they fail many people. Researchers are scouting for better options

By Robin Marantz Henig

A YOUNG WOMAN WHO CALLS HERSELF blueberryoctopus had been taking antidepressants for three years, mostly for anxiety and panic attacks, when she recounted her struggles with them on the Web site Experience Project. She said she had spent a year on Paxil, one of the popular SSRIs (selective serotonin reuptake inhibitors), but finally stopped because it destroyed her sex drive. She switched to Xanax, an antianxiety drug, which brought back her libido but at the cost of renewed symptoms. Then Paxil again, then Lexapro (another SSRI), then Pristiq, a member of a related class of antidepressants, the SNRIs (serotonin and norepinephrine reuptake inhibitors). At the time of the post, she was on yet another SSRI, Zoloft, plus Wellbutrin (a cousin of SNRIs that affects the activity of dopamine as well as norepinephrine), which was intended to counteract the sexual side effects of Zoloft. "I don't notice much of a difference with the Wellbutrin, but I'm



on the lowest dose now," she wrote. "I'm going back to my psychiatrist next week, so maybe he'll up it. Who knows."

This is the typical trial-and-error approach to prescribing antidepressants, not only for depression per se but also for related disorders such as blueberryoctopus's. The tactic, Andrew Solomon wrote in *The Noonday Demon,* his landmark book about depression, "makes you feel like a dartboard."

Troubling side effects are not the only reason for the dartboard approach. The SSRIs and SNRIs that have dominated the antidepressant market since their introduction in the 1980s and 1990s do not help everyone and eventually fail in more than a third of users. A pill that seems to be working today might well stop helping tomorrow. And the drugs can take several weeks to start having a marked effect, a waiting period that can be especially perilous. According to a 2006 report in the *American Journal of Psychiatry,* among depressed older adults (age 66 and older) taking SSRIs, the risk of suicide was fivefold higher during the first month of treatment than in subsequent months.

Clearly, patients critically need antidepressants that work faster and better, yet the pipeline for novel drugs is drying up. In fact, in the past couple of years such pharmaceutical giants as GlaxoSmithKline have announced their intention to abandon psychiatric drug development, finding it too expensive, too hard and too much of a long shot.

Some scientists in government and academic laboratories and at small pharmaceutical companies are trying to pick up the slack. Whether their efforts will succeed remains an open question. But new drugs cannot come too fast for the nation's approximately 15 million depressed patients. Many remain unhelped by talk therapy and medicines and are desperate to try anything to relieve the psychic pain, including such experimental treatments as putting electrodes in their head or burning holes in their brain.

IN SEARCH OF SPEED

INVESTIGATORS aiming to find faster-acting antidepressants have been studying compounds known to be lightning-quick mood lifters, hoping to figure out why they work so much more rapidly than the SSRIs, which enhance levels of serotonin, a signaling molecule, in the brain. One such compound is ketamine.

Ketamine is an anesthetic, an analgesic and a recreational drug known on the street as Special K. It can, among other things, affect consciousness and cause hallucinations, and experiments in rodents show it can be toxic to nerve cells—all of which make it a less than ideal candidate for an antidepressant. But it has proved to be a fascinating compound to study for ideas about how to make antidepressants reduce symptoms faster. As Ronald Duman and George Aghajanian of Yale University and their colleagues have demonstrated, within only two hours after an injection of ketamine lab rats start increasing production of proteins needed to build new synapses—the contact points through which signals flow between nerve cells—in the prefrontal cortex. This region of the brain, located right behind the eyes, is known to behave abnormally in depressed individuals. By 24 hours after the ketamine shot, the rats also start sprouting new synaptic spines, like cloves in a Christmas orange, along dendrites, which are the nerve cell projections that receive signals from other neurons. The more spines, the quicker the transmission. And in Duman and Aghajanian's experiments, the more synaptic spines, the less the animals display depressionlike behavior (such as abandoning activities they would normally engage in).

"A lot of work over the past 10 years or so has shown that in depression, there is atrophy, not growth, in the prefrontal cortex and also the hippocampus," says Duman, who directs Yale's Laboratory of Molecular Psychiatry. "Ketamine can rapidly reverse that atrophy" and restore normalcy. Just how rapidly is the subject of current research, as the Yale scientists examine rat brains only a few hours after the ketamine injection to see if the increase in synaptic spines occurs even sooner than 24 hours.

Additional research in a different group of depressed rats has revealed how ketamine makes these synaptic spines grow: by activating an enzyme in neurons known as mTOR. Duman and his colleagues discovered this connection by giving rats a drug that blocks the enzyme's action. Then they gave ketamine to the mTOR-blocked rats. Nothing happened, which meant that when mTOR was inhibited, ketamine had no effect on synaptic spine proliferation or reversal of depressionlike behavior. In other words, mTOR needs to be functioning for the ketamine to do its spine-sprouting work.

Given that ketamine is too risky to use routinely as a medicine, the researchers began searching for other mTOR activators. They knew that ketamine stimulates the enzyme by preventing glutamate (the main excitatory neurotransmitter in the brain) from acting on a particular docking molecule—termed an NMDA receptor—on the surface of neurons. They therefore tested another NMDA blocker and found that it, too, led to mTOR activity and quickly promoted spine formation and produced antidepressant effects in rats. Now, Duman says, he and his co-workers are examining other compounds that block NMDA receptors to see if any have promise as safe, fast-acting antidepressants.

Another compound that elevates mood swiftly is, like ketamine, already on the market for another purpose: scopolamine, sold as a skin patch for treating motion sickness. Scopolamine influences a different brain circuitry than ketamine does: it impedes binding of the neurotransmitter acetylcholine—involved in attention and memory—to molecules known as muscarinic receptors.

Robin Marantz Henig is a contributing writer at the *New York Times Magazine* and author, most recently, of *Pandora's Baby: How the First Test Tube Babies Sparked the Reproductive Revolution.* She is working on a book about twentysomethings, which she is writing with her daughter Samantha.

IN BRIEF

Current antidepressants can take weeks to ease depression. In certain people, they do not work at all, and if they do work now, they may stop tomorrow.

Faster-acting agents and those with new mechanisms of action are needed, yet Big Pharma's pipeline of such drugs is limited.

Government and university laboratories and some small pharmaceutical companies are trying to fill in the gap and have some promising leads.

As far back as the 1970s, investigators knew that manipulating acetylcholine activity in the brain could lead to depression. When bipolar patients, who swing between mania and depression, were in their manic phase and were given a drug that enhances acetylcholine signaling, they developed symptoms of depression, such as sad mood and lethargy, within one hour. And when depressed patients were given a drug that increased the level of acetylcholine in the brain, the depression got worse.

You might assume, then, that scientists looking for new antidepressants would investigate ways to inactivate acetylcholine. Early interest got derailed, however, by that era's A-list neurotransmitter, serotonin. In fact, many psychiatrists thought that what made SSRIs so useful was specifically that they did not target brain circuits employing acetylcholine. They ignored acetylcholine after that, thinking that the older antidepressants had so many side effects because, unlike SSRIs, they acted on the cholinergic system, in particular on muscarinic receptors, which compose a subset of the acetylcholine receptors distributed throughout the brain.

Therefore, it goes against conventional wisdom to find a drug acting specifically on the muscarinic receptors that not only has relatively few side effects but is a fast-acting and effective antidepressant. Yet that is what some scientists are seeing in scopolamine.

In a trial involving 22 patients diagnosed with depression, Maura Furey, a staff scientist in the Experimental Therapeutics and Pathophysiology Branch at the National Institute of Mental Health, and her colleagues found that intravenous scopolamine relieved symptoms within three days. In fact, she says, patients typically reported waking up feeling better the very next day. At the end of the four-week trial, nearly two thirds of the subjects showed significant improvement in their symptoms, and one half achieved remission. These benefits lasted for two weeks after the final dose. The effects were later replicated in another 22 depressed patients.

The NIMH is hoping to find a pharmaceutical company to do the testing and clinical trials needed to bring scopolamine to market as a fast-acting antidepressant. Furey is "extremely disappointed" that there have been no takers so far because, she says, "I see how well this works for people."

Drug delivery is one stumbling block. Giving scopolamine intravenously, as is done by some anesthesiologists as part of an anesthetic mixture, is impractical. With a skin patch, blood levels of the drug do not get high enough; with an oral formulation, most of the scopolamine gets eliminated through the digestive system. Furey is now working on finding a method of administration that is both practical and effective.

A SOLUTION FOR THE REST

THE OTHER MAJOR DRAWBACK to current-generation antidepressants, in addition to how long they take to start helping, is that they do not work for everyone. To address that problem, researchers are focusing on several novel mechanisms of actions. Some are investigating a second class of acetylcholine receptors, known as nicotinic receptors (so named because they also respond to nicotine). In particular, scientists at Targacept, a small biopharmaceutical company in Winston-Salem, N.C., are looking at an experimental drug called TC-5214 that blocks a specific nicotinic receptor; they hope to market the compound as an add-on therapy when a single antidepressant does not reduce symptoms enough.

In early trials involving 265 subjects, patients who did not respond to the SSRI citalopram (Celexa) alone had either TC-5214 or a placebo added to the regimen. In 2009 Targacept reported that subjects taking citalopram plus placebo improved by 7.75 points on a standard assessment tool (the Hamilton Rating Scale for Depression), while those taking citalopram plus the experimental drug improved by 13.75 points.

AstraZeneca then signed on with Targacept to conduct more extensive efficacy studies (phase III trials) in which subjects receive either a placebo or TC-5214 in addition to the original antidepressant. The first two trials, involving a total of 614 subjects, yielded disappointing results (no improvement, when compared with placebo, in depression scores after eight weeks). But Targa-

NUMERICAL PICTURE

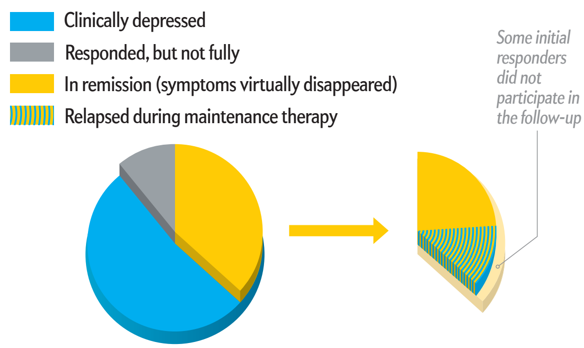
A Huge Gap

The need for better antidepressants is underscored by data from the Star*D trial, which monitored the effects of drug therapy in about 3,000 patients. The results, published in 2006, show that although medications do help many people, a large fraction of patients do not respond fully or relapse even when the agents work for a time. The drugs can also take weeks to become maximally effective.

The trial was complex, but in essence, patients initially received citalopram (Celexa), a selective serotonin reuptake inhibitor—the class of agents most widely prescribed today. Those who did not find relief were given any of several alternative treatments, generally switching up to three times in total. Subjects who did well were followed for a year while on maintenance therapy.

The data below come from the trial's first stage of treatment, with citalopram. Overall, 67 percent of patients who went through all stages of the trial achieved remission (at least for a time), but with each successive stage the percentage of patients who were helped declined and the likelihood of relapse increased.

The Best Case: Results from the First Treatment Stage of Star*D



Response to antidepressant
37 percent of treated subjects went into remission, doing so on average at 6.3 weeks. (The remitters were among the 49 percent who "responded"—had symptoms decline by at least half.)

Relapse rate
34 percent of patients who were in remission when they began maintenance therapy became symptomatic within 12 months.

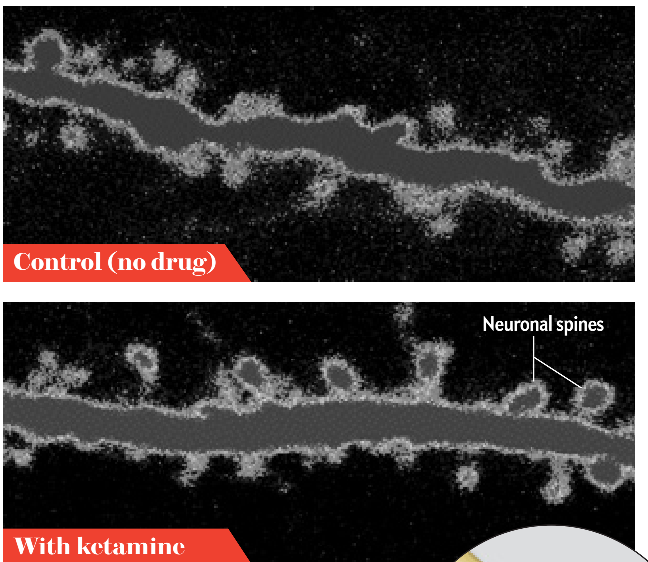
SOURCE: "ACUTE AND LONGER-TERM OUTCOMES IN DEPRESSED OUTPATIENTS REQUIRING ONE OR SEVERAL TREATMENT STEPS: A STAR*D REPORT," BY A. JOHN RUSH ET AL., IN *AMERICAN JOURNAL OF PSYCHIATRY*, VOL. 163, NO. 11; NOVEMBER 2006

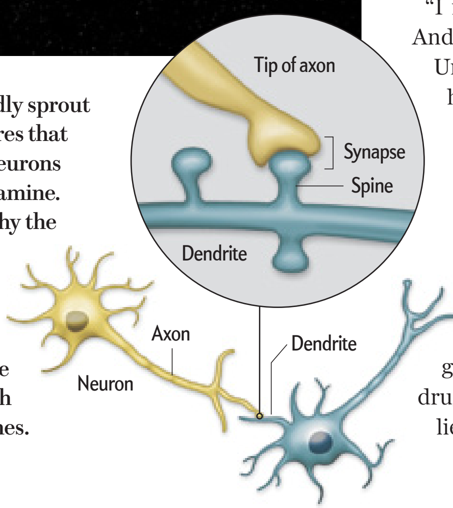
Graphic by Jen Christiansen

cept and AstraZeneca officials are continuing with two more planned efficacy trials, involving more than 1,300 subjects at centers around the world, as well as with a long-term safety study. They say they hope to file a new-drug application for TC-5214 with the Food and Drug Administration in the second half of 2012.

With a mechanism of action unrelated to its effect on serotonin or norepinephrine, Targacept's nicotinic receptor antagonist aims to assist depressed patients who are not being helped by drugs now on the market. Another way to target nonresponders is to shift gears even more radically—not by targeting signaling through this or that receptor but by acting on a different biological process. That process is neurogenesis (the growth of new neurons), in particular in the hippocampus, a small structure at the base of the brain thought to be one of two regions in the adult human brain where neurogenesis occurs.

Structural changes in the hippocampus have long been implicated in depression. Brain autopsies of clinically depressed people often show atrophy in that region and a significant reduction in volume. The SSRIs and SNRIs already in use ease depression not only by manipulating serotonin levels but also by increasing new hippocampal cell growth. That growth happens slowly, though, which is probably part of why the pills' benefits take so long to kick in. Scientists at the small pharmaceutical company Neuralstem in Rockville, Md., are hoping they have found a different way to spark neurogenesis—and to maintain it even after the drug has been stopped.





Dendrites on neurons rapidly sprout new spines (*above*)—structures that pick up signals from other neurons (*diagram*)—in rats given ketamine. The response may explain why the substance lifts mood in depressed individuals within hours of administration. Ketamine is too risky for routine use, but scientists are seeking safer substances with the same quick effect on spines.

To find their spark, Neuralstem researchers relied on cultures of neural stem cells derived from human hippocampal cells—the only such cultures in the world, according to the company. First, they screened some 10,000 compounds for their effect on the hippocampal cells in culture. The goal, chief scientific officer Karl Johe says, was to see which compounds increased the rate of cell proliferation after seven days. Fewer than 200 made the cut, he says, and from those the Neuralstem team devised a dozen candidate compounds that seemed most likely to stimulate hippocampal neurogenesis. In 2004 the workers began animal testing, injecting the preparations into healthy normal mice. The compounds best at provoking growth of new hippocampal cells were given to mice with depressive behavior, and from this protocol the single most promising one emerged.

Now Neuralstem is conducting early safety tests (phase I trials) of a pill form of the substance, called NSI-189, in humans. If all goes as planned, Neuralstem officials expect to begin tests of efficacy later this year. These studies will use magnetic resonance imaging to determine whether the drug increases neurogenesis and will use other measures to determine whether it relieves symptoms of depression. Even if NSI-189 works, though, it will not have rapid effects. "It's not like somebody having epilepsy, where you give a drug to stop the epilepsy instantaneously," Johe says. "This treatment requires changes in the cell at the genetic level." Hippocampal atrophy takes years to occur, he adds, and "to reverse the process will also require a long period of time." He hopes, however, that the effect will be long-lasting, so that NSI-189 may be needed only intermittently. That notion still has to be demonstrated, but it is "an exciting possibility," Johe says.

DIGGING DEEPER

RECENTLY INVESTIGATORS have realized that chronic inflammation—which has been linked to such diverse diseases as cancer, atherosclerosis and diabetes—contributes to depression, and the insight has opened yet another avenue of attack.

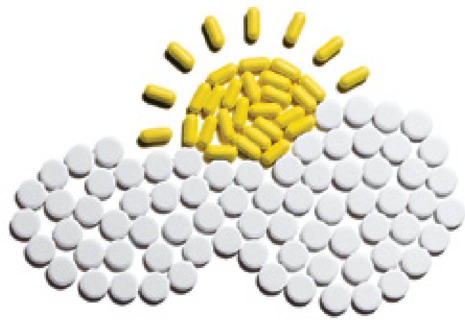
Several lines of research have made the connection between depression and inflammation, which more typically is the body's response to a perceived invader. Some studies have shown that depressed people have high circulating levels of small proteins called cytokines that orchestrate inflammatory processes; the cytokines go by such names as interleukin-6 and TNF-alpha. In addition, about a decade ago scientists observed that when skin cancer patients received inflammatory cytokines as a treatment, they became depressed.

"I interviewed one of these cancer patients early on," says Andrew Miller, director of psychiatric oncology at Emory University's Winship Cancer Institute, "and was struck by how similar the depression was to depression I might see in my office as a psychiatrist."

The particular nefariousness of cytokines is that they interfere with the neurogenesis prompted by SSRIs and SNRIs. "If you knock out neurogenesis, you're almost pulling the rug out from under these antidepressants," Miller says. This effect helps to explain why depressed people with the highest level of chronic inflammation are also the ones most likely to be hard to help. In 2006 a group of scientists reported in the *Lancet* that etanercept, a drug being tested to treat psoriasis in 618 subjects, often relieved depression, even in those for whom the psoriasis did

COURTESY OF GEORGE AGHAJANIAN AND RONG-JIAN LIU *Yale University*

Illustration by George Retseck



not improve. That effect apparently stems from neutralization of the inflammatory cytokine TNF-alpha. "At this point, no one should run to their doctor and ask for this drug for depression," said one of the team members, Ranga Krishnan of Duke University, at the time, noting that the depression results were anecdotal. "But the science is very exciting to us."

Miller also found the science exciting and contacted Krishnan to discuss a depression trial of a cytokine antagonist: Remicade, an anti-inflammatory already on the market to treat rheumatoid arthritis and other autoimmune diseases. It took more than five years, but Miller and his Emory colleague Charles Raison finally got funding from the NIMH to conduct the study. They have completed a trial of Remicade on 60 treatment-resistant depressed patients and say they will be releasing some promising findings soon.

Some researchers are training their sights on serotonin again but are looking to pump up its activity in a fresh way: by enhancing the number of serotonin receptors available to respond to the neurotransmitter in synapses. Even more radical, the investigators intend to achieve that effect through gene therapy.

Mention gene therapy to biologists, and you are likely to get an eye roll and a dismissive shrug. Recently, though, scientists announced preliminary success with gene therapy for one brain disorder, Parkinson's disease. And an investigator involved in the Parkinson's research wants to try something similar for depression.

The candidate gene for depression therapy is *p11,* which codes for a protein needed to move certain serotonin receptors to the cell surface; without *p11,* the receptors remain trapped inside the cell, which renders cells less able to respond to serotonin's messages. In 2006 Paul Greengard and his colleagues at the Rockefeller University demonstrated that rodents with depressionlike behavior (such as giving up formerly pleasurable activities) had low levels of *p11;* depressed humans, too, were shown on autopsy to have lower than normal levels.

"Knockout mice" developed in Greengard's lab—mice in which the *p11* gene had been destroyed—were then shown to develop depressionlike behavior. The next step was to see if delivering a functional *p11* gene to mice that lacked it would relieve the symptoms. That work was done by Michael Kaplitt, director of the Laboratory of Molecular Neurosurgery at Weill Cornell Medical College, and his colleagues; he was already conducting similar studies on gene therapy for Parkinson's. Using the same defanged adeno-associated virus he relied on to deliver a gene to Parkinson's patients, the team put the *p11* gene directly into the nucleus accumbens of *p11*-deficient mice, and their depressive behavior decreased.

Every neuroscientist has a favorite brain region, and Kaplitt's is the nucleus accumbens. "The reason I like it is that it's considered an important center in the brain for reward and satisfaction, where dopamine acts," he says. One common symptom of depression, anhedonia—an inability to get pleasure from life—is among the most devastating, Kaplitt says, and is probably related to dopamine signaling. Another reason he likes the nucleus accumbens is that functional MRI studies in animals and humans show that it is widely connected to many regions of the brain known to be involved in depression.

A third reason he likes the nucleus accumbens is that it has already been the surgical target for another experimental treatment for depression, a technique called deep-brain stimulation (DBS). An electrode is permanently implanted into the nucleus accumbens, and periodic electrical impulses are delivered through it [see "Depression's Wiring Diagram," by David Dobbs; Head Lines, Scientific American Mind, March/April 2009].

In Kaplitt's view, gene therapy performed directly on the brain will be simpler than deep-brain stimulation because "instead of an electrode for DBS, you'd be putting in this little catheter and leaving no hardware behind." (In deep-brain stimulation, not only is the electrode permanently in place, so is the neurostimulator, a pacemakerlike device implanted near the collarbone that generates the electrical impulses.) He and his colleagues have shown, in their work on Parkinson's, that the viral vector is safe and that the correct gene can be delivered through a catheter to the intended brain target, resulting in improved symptoms.

Now studies are in progress at the NIMH, under the direction of Elisabeth A. Murray of the Laboratory of Neuropsychology and Pam Noble of the primate care facility, to test *p11* gene therapy for safety and efficacy in monkeys. Success there would bolster a case for trials in humans.

As for blueberryoctopus, better treatments cannot come too soon. "Antidepressants definitely changed my life," she wrote on the Experience Project Web site, "but I'm dismayed that it was at the expense of my sex life." She was not yet 25 years old. "Eventually I'd like to come off [antidepressants] and resume having a normal sex life. I just don't think I'm ready yet." There should be better options. No one should have to choose between libido and despair; no one should be told, after trying and rejecting a series of depression therapies, that there is nothing left to try. If the promise of next-generation antidepressants comes to fruition, maybe the trade-offs will someday be less grim. SA

TOM SCHIERLITZ *Trunk Archive*

MORE TO EXPLORE

Breaking Ground, Breaking Through: The Strategic Plan for Mood Disorders Research of the National Institute of Mental Health. 2001 report. 136-page PDF available at the NIMH Web site, which also has some good depression basics: **www.nimh.nih.gov/about/strategic-planning-reports/breaking-ground-breaking-through-the-strategic-plan-for-mood-disorders-research.shtml**

The Noonday Demon: An Atlas of Depression. Andrew Solomon. Scribner, 2002.

Depression: Out of the Shadows. A PBS documentary that aired in 2008, which has a comprehensive Web site where you can watch the program and find further information: **www.pbs.org/wgbh/takeonestep/depression/index.html**

Stress, Depression, and Neuroplasticity: A Convergence of Mechanisms. Christopher Pittinger and Ronald S. Duman in *Neuropsychopharmacology Reviews,* Vol. 33, pages 88–109; 2008.

Stuck in a Rut: Rethinking Depression and Its Treatment. Paul E. Holtzheimer and Helen S. Mayberg in *Trends in Neuroscience,* Vol. 34, No. 1, pages 1–9; November 2010.

The NIMH has an interesting interactive on its Web site about the prevalence of depression and a variety of other mental illnesses, as well as treatment options: **www.nimh.nih.gov/statistics/index.shtml**

Sherwin Nuland gives a TED talk about depression (largely his own) and electroshock therapy (his own): **www.ted.com/talks/lang/eng/sherwin_nuland_on_electroshock_therapy.html**

SCIENTIFICAMERICAN ONLINE
Learn how researchers model depression in animals at **ScientificAmerican.com/mar2012/depression**

CLIMATE

Hit Them with the Hockey Stick

Michael E. Mann set out looking for a big scientific problem and wound up at the center of a political storm over climate change. Now he tells his side of the story

Interview by David Biello

CLIMATOLOGIST MICHAEL E. MANN IS MOST FAMOUS FOR WHAT HE CALLS ONE of the "least interesting" aspects of his work. In the 1990s he used data from tree rings, coral growth bands and ice cores as proxies for ancient temperatures, combining them with modern thermometer readings. This annual record of temperature variations over the past millennium offered insights into natural climate cycles. As an "afterthought," he included a graph of average temperatures in the Northern Hemisphere going back to the 1400s in a 1998 paper (he later extended it to A.D. 1000). That "hockey stick" graph, which shows temperatures bouncing up and down before rapidly rising more recently, became an icon of climate change.

It was also a focus of controversy. Although the U.S. National Research Council reviewed the hockey stick and endorsed its conclusions in 2006, Mann and his research came under often hostile public scrutiny, culminating in "Climategate"—the theft and publication of his and his colleagues' personal e-mails in 2009. Mann's employer, Pennsylvania State University, subsequently investigated him for research misconduct (and cleared him in 2010). And Virginia Attorney General Ken

IN BRIEF

WHO
MICHAEL E. MANN

VOCATION | AVOCATION
Climate modeler and scourge/target of climate change contrarians

WHERE
Pennsylvania State University

RESEARCH FOCUS
Improving climate models and climate communications

BIG PICTURE
"Being a climate scientist these days is not a 9 to 5 job. It's a 0 to 24 job."

Photographs by Chris Crisman

Cuccinelli has filed suit against the University of Virginia, Mann's former employer, to investigate his work there (at press time, the case is still pending). His detractors, Mann says, "never stop."

Mann is now hitting back with his own account, *The Hockey Stick and the Climate Wars*. Scientific American spoke with Mann about his research, the controversy and his hope for averting catastrophic climate change. Excerpts follow.

Scientific American: What first drew you to climate studies?

MANN: My undergraduate degrees were in applied math and physics, and I went off to graduate school to study theoretical physics. When I realized that the opportunities were becoming quite limited, I started looking to see where I could use the physics and math that I had learned to work on a big problem—one that had some real-world implications. I opened up the catalogue of applied science at Yale University and came upon the section that described some of the work that folks in the department of geology and geophysics were doing on developing theoretical models of the climate system. And that just sounded fascinating to me.

At that time, there was a legitimate scientific debate about the reality of human-caused climate change having yet been observed. My work actually had little do with that debate.

You started studying natural variability in temperature, right?

There's an irony there. Some of my early research was celebrated by contrarians in the climate change debate—I coined the term "Atlantic multidecadal oscillation" [AMO]. They love to argue that it's responsible for just about everything, when, in fact, the reality is far more nuanced. These oscillations do appear to exist, but they can't explain climate change.

Think of the AMO as a really long-term cousin of El Niño. This oscillation in the climate system takes several decades to go from one phase into the other. That's actually what got me interested in proxy data [such as tree rings]—because if you're trying to tease out a 50- to 70-year oscillation and you've only got 100 to 150 years of instrumental observations, you run into obvious problems.

These proxy data are natural archives that, by their nature, record some attribute about the climate. The thickness, for example, of trees rings is a function of the warmth of the growing season or, in some circumstances, the wetness of the growing season. So you can potentially tease climate information out of tree rings.

By combining the information from lots of different proxy data, you start to put together a more global picture of what's going on, and you can immunize yourself from the danger of relying entirely on any one type of proxy. Each has its own strengths and weaknesses.

The most famous outcome of that work is, of course, the hockey stick graph. How did that come about?

These are very imperfect thermometers provided by nature. Probably the main challenge was figuring out a way to relate that very noisy information to the modern surface-temperature record in a way that would then allow us to estimate temperatures back in time over the surface of the globe. It's only from looking at the relative pattern of temperature around the world that you can get insight, for example, into the history of El Niño.

The least interesting thing you could do with these spatial patterns once you built them was to average all those data to get a single number for each year—the average temperature of the Northern Hemisphere—and plot that back in time, which is what yielded this hockey stick curve.

The long-term temperature slowly declined from what is sometimes referred to as the Medieval Warm Period, a relatively warm time about 1,000 years ago, into the depths of the Little Ice Age of the 17th, 18th and early 19th centuries. That's the handle, if you will, of the hockey stick.

Then, at the end, that rapid rise is the blade of the hockey stick: the warming of the past 150 years, which takes temperatures beyond anything that we had reconstructed as far back as we could go. That single result got all the attention.

Who first called it the "hockey stick"?

It was Jerry Mahlman, who used to direct NOAA's Geophysical Fluid Dynamics Laboratory in Princeton, N.J. It turns out the term was actually used previously in the context of ozone depletion. There was some history of using the term "hockey stick" to describe the sort of data series where you're going along, and all of a sudden there's a huge spike at the end.

Do you regret the name?

There's always the danger that applying a simple term like that to something that's complicated creates a caricature of the science. There's a veritable hockey league now of reconstructions like ours that shows the same basic pattern.

The United Nations Intergovernmental Panel on Climate Change (IPCC) featured the hockey stick prominently in its 2001 report. Was that wise?

In retrospect, it probably wasn't the most prudent decision, because it played right into the argument that contrarians like to use: that somehow the science depends on one particular study or even one particular author of one particular study. And if you can somehow discredit that one study or that one person, the entire scientific case collapses.

There had, in fact, been several reconstructions that told a similar story in the technical report. By the time the IPCC report came out, there were three [additional] reconstructions that came to more or less the same conclusion.

How do you feel about being called the whipping boy of climate science?

At times I felt like: "Bring it on." I'm confident about the robustness of our scientific work. I think that if the climate change deniers thought they had found an area of the science that they could discredit by trying to go after a single scientist—me—I think they've been in for a disappointment.

The e-mails stolen in 2009 included some of yours, though they weren't the most controversial. What was that like?

The people who stole these e-mails and

Climate proxy: Natural archives such as tree rings provide clues to past climates.

posted them: How would they like someone to take their diaries, their private communications and expose them to the world out of context? The fact that climate change deniers needed to resort to criminal activity to try to discredit our science on the one hand disgusted me. It angered me. It angered, I think, many of us in the scientific community.

There was a concerted campaign to use these stolen e-mails to manufacture an echo chamber of climate change denial propaganda in the lead up to the Copenhagen summit. There was an attempt to use misrepresentations, false allegations, smears based on these out-of-context e-mails to have scientists fired.

At one point, an influential Republican legislator in the state of Pennsylvania threatened to withhold funding for Penn State if the university didn't take some sort of action against me because of the purported improprieties. So it was ugly.

We've lost three years to do something about climate change, and that's a huge opportunity cost. Each year we wait, it gets that much more difficult to stabilize carbon dioxide concentrations below levels that might very well be dangerous. I think that [Climategate] was a crime against humanity. It's a crime against the planet.

How do you respond to claims that there was a "trick to hide the decline?"

There are at least five things that are false about that statement, but the most obvious is that there was no reference to a "trick to hide the decline." That was taking two different parts of an e-mail and merging them together in a way that completely changes the sense of what was actually being discussed.

What's especially ironic about the claim that [climate scientists] were trying to hide the decline in global temperatures was that this e-mail was written in early 1999. It was on the heels of, by far, the warmest year we had ever seen, 1998. So if you were a scientist writing an e-mail at that time, you couldn't possibly imagine there was anything approaching a decline. If anything, there was an apparent acceleration of warming taking place. The "decline" simply referred to some bad tree ring data.

How does the opposition to climate science compare with past anti-scientific crusades?

It's hard to believe that in the 21st century we are still confronting rejectionism of science when so much of modern life depends so critically on the technological infrastructure that we've developed because of science. The very people who are denouncing what science has to offer in a wide variety of areas [benefit from] the contributions of modern science.

What effect has this had on scientists?

Maybe it's emboldened other scientists to fight the disinformation effort afoot in our field and also in many other fields of science. No longer can scientists stay isolated in their laboratories and trust that the impact of their work will percolate honestly and productively into the public discourse. Scientists need to be proactive in ensuring that their science is communicated as accurately as possible.

Any comment on the lawsuit against you and the University of Virginia?

It's really unfortunate that people with antiscientific views, who regard science with disdain, can rise to the highest levels of government in this country. That's very scary.

What role does politics play in science?

It's perfectly appropriate for science to inform one's view of policy matters. What's wrong is for one's policy views to influence the way one does science.

Years ago climate change was not a political issue. My colleague [Ohio State University glaciologist] Lonnie Thompson puts it very well when he talks about the loss of mountain glaciers. The ice has no agenda. It doesn't matter if you're a Republican or a Democrat. The ice is retreating. Sea levels are rising. They're not happening for political reasons. What we do about it is, of course, a political matter.

Are the impacts of climate change showing up faster than predicted?

Changes have been taking place faster than the models projected. With respect to sea-level rise, with respect to temperature changes, with respect to carbon emissions, and in just about every case, the changes have occurred either at the upper end of the projections or even above the range of the projections.

Arctic sea ice might be the most profound example, where the observed decline in summer Arctic sea ice is way outside the projected range. The great irony is that the climate scientists, if anything, have been too cautious and too conservative.

You say you still have hope. Why?

If we look to history, in the end, science and honesty won out—perhaps later than we would have liked.

We acted later than we should have with tobacco. We acted later than we should have with ozone depletion and the banning of chlorofluorocarbons. We presumably suffered far greater damage and loss of life because we delayed action. But we did take action. SA

David Biello is an associate editor.

MORE TO EXPLORE

Surface Temperature Reconstructions for the Last 2,000 Years. National Research Council. National Academies Press, 2006. www.nap.edu/catalog/11676.html

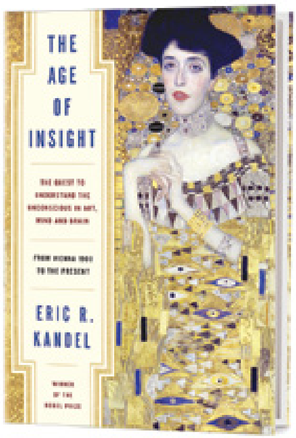
Dire Predictions: Understanding Global Warming. Michael E. Mann and Lee R. Kump. Prentice Hall, 2008.

The Hockey Stick and the Climate Wars: Dispatches from the Front Lines. Michael E. Mann. Columbia University Press, 2012.

SCIENTIFIC AMERICAN ONLINE
To hear a portion of the interview as a podcast, visit ScientificAmerican.com/mar2012/mann

Recommended by Anna Kuchment

BOOKS



The Age of Insight: The Quest to Understand the Unconscious in Art, Mind, and Brain, from Vienna 1900 to the Present

by Eric R. Kandel. Random House, 2012 ($40)

Neuroscientist and Nobel laureate Kandel has crafted a fascinating meditation on the interplay among art, psychology and brain science. The author, who fled Vienna as a child, has remained captivated by Austrian artists Gustav Klimt, Oskar Kokoschka and Egon Schiele, each of whom was profoundly influenced by Sigmund Freud and by the emerging scientific approach to medicine in their day. Kandel describes the psychological and biological insights reflected in their paintings, as well as the neuroscience behind how the beholder perceives the paintings. He concludes by calling for a new, interdisciplinary approach to understanding the mind, one that combines the humanities with the natural and social sciences.

BY THE NUMBERS

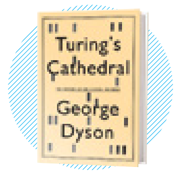
380

The shortest wavelength of light that humans can see, in nanometers. It appears deep violet.

SOURCE: The Age of Insight

The Idea Factory: Bell Labs and the Great Age of American Innovation

by Jon Gertner. Penguin Press, 2012 ($29.95)



Turing's Cathedral: The Origins of the Digital Universe

by George Dyson. Pantheon Books, 2012 ($29.95)

These two books on the mid-20th-century information revolution take readers back to a time when New Jersey, not Silicon Valley, was the center of American innovation. Gertner's *The Idea Factory* is a lively account of the minds behind Bell Labs, then the research and development wing of AT&T, and how the scientists created the network of copper cables, microwave links and glass fibers that made the company's dream of "universal" connectivity a reality. Dyson's *Turing's Cathedral* focuses on the creative geniuses at the Institute for Advanced Study in Princeton who invented computer code. In doing so, they realized the theoretical construct that mathematician Alan Turing dubbed

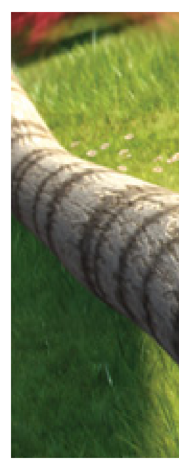
COURTESY OF ILLUMINATION ENTERTAINMENT/UNIVERSAL PICTURES (*Lorax* movie still)

MULTIMEDIA

Dr. Seuss' The Lorax. Universal Pictures, March 2. This animated feature voiced by Danny DeVito, Zac Efron, Taylor Swift and others brings to life the classic Seussian parable of greed and environmental destruction.

Frozen Planet. Discovery Channel/BBC, March 18. Alec Baldwin narrates the highly anticipated seven-part documentary about life at Earth's two poles.

Animation. New York Hall of Science, March 31–September 2. Kids can explore the math, science and technology behind cartoons.



the universal machine. Together they would pave the way for today's digital universe.

Imagine: How Creativity Works

by Jonah Lehrer. Houghton Mifflin Harcourt, 2012 ($26)

Imagine argues that modern science allows us to identify and harness the many different thought processes from which creativity emerges. The book is least convincing when Lehrer makes sweeping claims: he fixates on Elizabethan England as an age of "excess genius," as though no artists have equaled its accomplishments since, and he relies too heavily on patents as measures of creativity. The book's strength lies in specific examples—detailed stories about 3M, Pixar, Bob Dylan and Don Lee, the computer programmer who became a master mixer of quirky cocktails. These insightful tales make *Imagine* well worth the read. —*Ferris Jabr*

Viewing the world with a rational eye

Michael Shermer is publisher of *Skeptic* magazine (www.skeptic.com). His new book is *The Believing Brain.* Follow him on Twitter @michaelshermer

Opting Out of Overoptimism

The willful distortion of reality to extremes can be harmful

Are you better than average as a driver? I know I am. I'll bet 90 percent of you think you are, too, because this is the well-documented phenomenon known as the above-average effect, part of the psychology of optimism.

According to psychologist Daniel Kahneman, in his 2011 book *Thinking, Fast and Slow,* "people tend to be overly optimistic about their relative standing on any activity in which they do moderately well." But optimism can slide dangerously into overoptimism. Research shows that chief financial officers, for example, "were grossly overconfident about their ability to forecast the market" when tested by Duke University professors who collected 11,600 CFO forecasts and matched them to market outcomes and found a correlation of less than zero. Such overconfidence can be costly. "The study of CFOs showed that those who were most confident and optimistic about the S&P index were also overconfident and optimistic about the prospects of their own firm, which went on to take more risk than others," Kahneman notes.

Isn't optimistic risk taking integral to building a successful business? Yes, to a point. "One of the benefits of an optimistic temperament is that it encourages persistence in the face of obstacles," Kahneman explains. But "pervasive optimistic bias" can be detrimental: "Most of us view the world as more benign than it really is, our own attributes as more favorable than they truly are, and the goals we adopt as more achievable than they are likely to be." For example, only 35 percent of small businesses survive in the U.S. When surveyed, however, 81 percent of entrepreneurs assessed their odds of success at 70 percent, and 33 percent of them went so far as to put their chances at 100 percent. So what? In a Canadian study Kahneman cites, 47 percent of inventors participating in the Inventor's Assistance Program, in which they paid for objective evaluations of their invention on 37 criteria, "continued development efforts even after being told that their project was hopeless, and on average these persistent (or obstinate) individuals doubled their initial losses before giving up." Failure may not be an option in the mind of an entrepreneur, but it is all too frequent in reality. High-risk-taking entrepreneurs override such loss aversion, a phenomenon most of us succumb to—in which losses hurt twice as much as gains feel good—that we developed in our evolutionary environment of scarcity and uncertainty.

This loss-aversion override by those with pervasive optimistic bias seems to work because of what I call biographical selection bias: the few entrepreneurs who succeed spectacularly have biographies (and autobiographies), whereas the many who fail do not.

Think Steve Jobs, whose pervasive optimistic bias was channeled through something a co-worker called Jobs's "reality distortion field." According to his biographer Walter Isaacson, "at the root of the reality distortion was Jobs's belief that the rules didn't apply to him.... He had the sense that he was special, a chosen one, an enlightened one." Jobs's optimism morphed into a reality-distorting will to power over rules that applied only to others and was reflected in numerous ways: legal (parking in handicapped spaces, driving without a license plate), moral (accusing Microsoft of ripping off Apple when both took from Xerox the idea of the mouse and the graphical user interface), personal (refusing to acknowledge his daughter Lisa even after an irrefutable paternity test), and practical (besting resource-heavy giant IBM in the computer market).

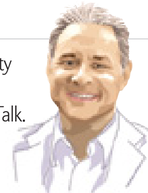
There was one reality Jobs's distortion field optimism could not completely bend to his will: cancer. After he was diagnosed with a treatable form of pancreatic cancer, Jobs initially refused surgery. "I really didn't want them to open up my body, so I tried to see if a few other things would work," he admitted to Isaacson. Those other things included consuming large quantities of carrot and fruit juices, bowel cleansings, hydrotherapy, acupuncture and herbal remedies, a vegan diet, and, Isaacson says, "a few other treatments he found on the Internet or by consulting people around the country, including a psychic." They didn't work.

Out of this heroic tragedy a lesson emerges—reality must take precedence over willful optimism. Nature cannot be distorted. SA

SCIENTIFIC AMERICAN ONLINE
Comment on this article at ScientificAmerican.com/mar2012

Illustration by Francesco Bongiorni

The ongoing search for fundamental farces



Steve Mirsky has been writing the Anti Gravity column since the DVD was invented. He also hosts the *Scientific American* podcast Science Talk.

The Unkindest Cut

Memo pads, printouts, the daily mail—they lie in wait for their next attack

It is, of course, the most agonizing injury known. The thought of it makes the strong tremble and the weak pass out. Its brutality can be unbounded—a loose page will suffice. It is the paper cut.

My thoughts went to the cruelest cut when a friend showed me a particularly vicious one she'd received on her fingertip. Most paper cuts I'd seen or suffered were straight slices less than a centimeter across. Hers was at least twice the normal length and zagged in the middle, as if some invisible assailant decided to twist a miniature knife. In the midst of my horror, I wondered what modern medicine has to say about the paper cut.

Surprisingly little, I discovered. Studies mentioning paper cuts that I found in medical journals were almost uniformly concerned with the possibility of infection, especially by the superscary methicillin-resistant *Staphylococcus aureus* bug, aka MRSA. A few sources noted that a hemophiliac will not in fact bleed to death from a paper cut, thereby dispelling a piece of playground wisdom widely disseminated among the community of eight-year-old amateur hematologists.

An irony of paper cuts, contends the Wisegeek Web site, is that they are more likely to occur when the paper is high quality. "When glossy sheets of paper are cut very thin, they are uniquely good at causing paper cuts," the site explains. Grab a ream of tightly bound paper with one interior sheet protruding slightly, and you have a serious weapon on your soon-to-be-bloody hands. "The other papers hold the dislocated paper in position, giving it enough stiffness to cut like a razor's edge," Wisegeek says. Which is why there may be a trail of blood leading from the office copier to the desk of whatever unfortunate soul did the good deed of filling up an empty paper tray.

Paper cuts do indeed bring on outsize pain. Fingertips, the most likely site of damage, are loaded with the nerve endings—including the pain-interpreting nociceptors—necessary for the constant exploration of the environment. Take a gander at a cortical homunculus, a representation of how much of the brain is devoted to dealing with signals from individual body parts: I can't hold a basketball with one hand, but my homunculus could palm a beach ball. So a tiny tip rip gets a disproportionate number of nociceptors, none of which knows the difference between a vacation brochure and a samurai sword.

The fear of a specific kind of paper cut overwhelms me whenever I'm about to send snail mail. In the movie *Swimming with Sharks,* the cowering assistant to misanthropic film executive Kevin Spacey reaches his breaking point. He ties up the exec and administers facial slices with the edge of an office envelope. Watching this scene instilled such terror that I changed my conventional east-west style of envelope licking, for fear of a tongue slash, to a series of north-south dabs.

The homunculus's crazy-big tongue supports my decision. It also shows why another fictional entertainment industry giant, Alec Baldwin's *30 Rock* kingpin Jack Donaghy, was probably wasting his time when he took lessons on "how to avoid getting paper cuts while making love in a pile of money." The legs and torso together take up less brain space than the tongue or fingers.

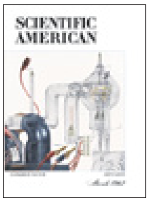
Also, Benjamins are soft. And soft paper is safer. Wisegeek points out that "newspaper may be the least likely to inflict a paper cut." I can offer anecdotal evidence in support of that claim. In my first job in journalism—as a paper boy delivering thousands of copies of the *New York Post*—I did not receive a single paper cut. Then again, the last time the *Post* contained anything sharp it was still being edited by William Cullen Bryant. SA

***Editors' note:** While opening reader mail just five hours after filing this column, Mirsky suffered a nasty paper cut.*

SCIENTIFIC AMERICAN ONLINE
Comment on this article at ScientificAmerican.com/mar2012

Illustration by Matt Collins

Innovation and discovery as chronicled in *Scientific American*



March 1962

Red Shift

"A recent paper by French astronomers has apparently laid to rest a skeleton that has been rattling in the closet of physics for more than 40 years. In a measurement of unprecedented accuracy they found a gravitational red shift in light from the sun almost exactly equal to that predicted by the general theory of relativity. The prediction is a consequence of Albert Einstein's principle of equivalence, which states that the effects of accelerated motion are indistinguishable from those of a gravitational field."

March 1912

Lighter Than Air

"Mr. Joseph Brucker's attempt to cross the Atlantic in a dirigible, from the Verde Islands to Barbados, is especially characterized by its business-like methods. Their airship *Suchard* has now been reconstructed three times to keep abreast of the most recent advances and experiences in dirigible navigation. From the outset they trusted only to a perfected and well-tested type and so built their ship after the *Parseval* model."

Brucker never followed through on his attempt. For a look into our archives at the technology of lighter-than-air flight in 1912, see the slideshow at www.ScientificAmerican.com/mar2012/dirigibles

Relativity Pondered

"To some people it seems that modern scientific concepts border very closely upon, if they do not actually invade, the realm of metaphysics. We have said that the mass of an electron increases with its velocity. It increases in such a way that at the velocity of light the mass becomes infinite. In other words, motion at a speed greater than that of light is impossible in nature. Before this result was fully established [by James Clerk Maxwell and others] an eminent German scientist [Arnold Sommerfeld] worked out the dynamics of systems moving at a speed greater than that of light [hypothetical particles later called tachyons]. We have here a result, a paradox, which many people find difficult to accept and to which objections at once present themselves. It is by pondering over these objections that scientific men [Albert Einstein and others] have been led to enunciate the 'Principle of Relativity.' This great principle is the most fundamental doctrine of modern physics. It asserts that mass, length, and time are all relative.—John W. N. Sullivan"

Radio Communication

"Within a few years practically every vessel of our navy, including colliers,

SCIENTIFIC AMERICAN, VOL. CVI, NO. 12; MARCH 23, 1912

In the wireless room of the *Gresham*, listening for distress calls off the rocky New England coast, 1912

tugs and the boats of the Revenue Cutter Service [later called the Coast Guard], has been equipped with wireless apparatus. A very important part of their work became the control of the revenue cutters [patrol boats] while on duty at sea. The ship *Gresham* [*see photograph*] has a record of over three score lives saved, and more than forty vessels towed from dangerous positions when out of control."

March 1862

Ironclads—The First Duel

"While the iron-plated *Merrimac* [CSS *Virginia*] was carrying destruction among the old wooden vessels of our navy, and spreading consternation throughout the land, the little *Monitor* with her two guns arrived upon the scene of conflict, and soon changed disaster and defeat into the most triumphant victory. For several hours she sailed around the *Merrimac,* sending her shot into any selected part of her antagonist with perfect precision, sustaining an unprecedented cannonade with absolute impunity, and finally succeeded in driving her formidable foe disabled away from the field of battle. It was stipulated in the contract for the *Monitor* that she should be tried under the guns of the enemy before being accepted by the Department of the Navy, but it could not have been anticipated that she would be subjected to so severe a trial as that which she has endured. This trial puts the final seal to the fate of all wooden ships of war."

Horrid Writing

"Has not the curse of steel pens swept over the land until decent handwriting is almost unknown? Do not ninety-nine persons in a hundred use steel pens, and has more than one out of the ninety-nine the effrontery to say he can write with them? Lord Palmerston was quite right—the handwriting of this generation is abominable; and as new improvements in steel pens go on, that of the next will be worse."

Cognitive Neuroscience, cont.

Windows on the Mind

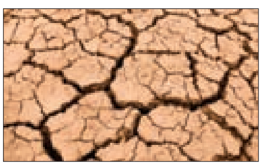
What's the connection behind eye movements and subliminal thought? Join Dr. Macknik and Dr. Martinez-Conde in a look at the latest neurobiology behind microsaccades, the involuntary eye movements that relate to perception and cognition. Learn how microsaccades suggest bias toward certain objects, their relationship to visual illusions, and the pressing questions spurring visual neurophysiologists onward.

Champions of Illusion

The study of visual illusions is critical to understanding the basic mechanisms of sensory perception and advancing cures for visual and neurological diseases. Connoisseurs of illusion, Dr. Macknik and Dr. Martinez-Conde produce the annual Best Illusion of the Year Contest. Study the most exciting novel illusions with them and learn what makes these brain tricks work.

Sleights of Mind

Magic fools us because humans have hardwired processes of attention and awareness that can be "hacked." A good magician employs the mind's own intrinsic properties. Magicians' insights, gained over centuries of informal experimentation, have led to new discoveries in the cognitive sciences, and reveal how our brains work in everyday situations. Get a front-row seat as the key connections between magic and the mind are unveiled!



CLIMATOLOGY

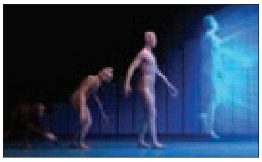
Speaker: Yohay Carmel, Ph.D.

Prioritizing Land for Nature Conservation: Theory and Practice

Forest clearing, climate change, and urban sprawl are transforming our planet at an accelerating rate. Conservation planning prescribes principles and practical solutions for selecting land for protection, assigning land for development, and minimizing the negative impact on nature. Taking a bird's-eye view of approaches to conservation, we'll put the hot topics and tough questions in perspective through an insightful discussion.

Facing a New Mega-Fire Reality

Worldwide, the area, number, and intensity of wildland fires has grown significantly in the past decade. Fire-protection strategies used in the past may not work in the future. Learn the roots and causes of wildfires and recent efforts to predict, manage, and mitigate fire risk. Gain food for thought about the complex interface between science and policy.



HUMAN EVOLUTION

Speaker: Chris Stringer, Ph.D.

Human Evolution: the Big Picture

Time-travel through 6 million years of human evolution, from the divergence from African apes to the emergence of humans. In 1871, Charles Darwin suggested that human evolution had begun in Africa. Learn how Darwin's ideas stand up to the latest discoveries, putting his tenets into context and perspective.

The First Humans

About 2 million years ago the first humans appeared in Africa, distinctly different from their more ancient African ancestors. Discover what drove their evolution and led to a spread from their evolutionary homeland to Asia and Europe. Explore current thinking on the early stages of human evolution.

The Neanderthals: Another Kind of Human

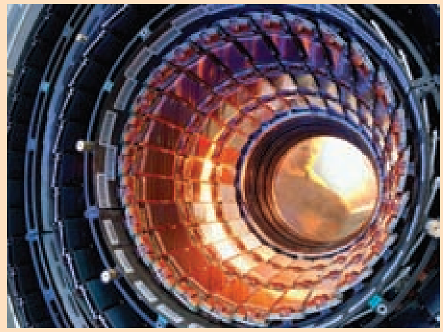
Our close relatives, the Neanderthals, evolved in parallel with *Homo sapiens*. Often depicted as bestial ape-men, in reality they walked upright as well as we do, and their brains were as large as ours. So how much like us were they? What was their fate? Track the evolution of the Neanderthals in light of the latest discoveries.

The Rise of *Homo Sapiens*

Modern humans are characterized by large brains and creativity. How did our species arise and spread across the world? How did we interact with other human species? We will examine theories about modern human origins, including Recent African Origin ("Out of Africa"), Assimilation, and Multiregional Evolution, and delve in to the origins of human behavioral traits.

SCIENTIFIC AMERICAN Travel HIGHLIGHTS

INSIDER'S TOUR OF CERN



Pre-cruise: October 22, 2012—From the tiniest constituents of matter to the immensity of the cosmos, discover the wonders of science and technology at CERN. Join Bright Horizons for a private full-day tour of this iconic nuclear-research facility.

Whether you lean toward concept or application, there's much to pique your curiosity. Discover the excitement of fundamental research and get an insider's look at the world's largest particle physics laboratory.

Our full-day tour will be led by a CERN physicist. We'll have an orientation, visit an accelerator and experiment, get a sense of the mechanics of the Large Hadron Collider (LHC), make a refueling stop for lunch, and have time to peruse exhibits and media on the history of CERN and the nature of its work.

This tour includes: Bus transfer from Geneva, Switzerland to our Genoa, Italy hotel (October 23) • 3 nights' hotel (October 20, 21, 22) • 3 full breakfasts (October 21, 22, 23) • Transfers to and from the hotel on tour day (October 22) • Lunch at CERN • Cocktail party following our CERN visit • Do-as-you-please day in Geneva, including transfers to and from downtown (October 21) • Transfer from airport to our Geneva hotel

The price is $899 per person (based on double occupancy). This trip is limited to 50 people. NOTE: CERN charges no entrance fee to visitors.

EPHESUS

November 1, 2012—Many civilizations have left their mark at Ephesus. It's a complex and many-splendored history, often oversimplified. Bright Horizons pulls together three important aspects of understanding Ephesus that are rarely presented together. You'll meander the Marble Road, visit the legendary latrines, check out the Library, and visit the political and commercial centers of the city. A visit to the Terrace Houses will enhance your picture of Roman-era Ephesus.

We'll take a break for Mediterranean cuisine in the Selcuk countryside, then visit the Ephesus Museum in Selcuk, where city excavation finds are showcased, and you'll get a fuller look at local history, from the Lydians to the Byzantines.

ATHENS

November 1, 2012—The Parthenon and its Acropolis setting are stunning, no doubt about it. Requiring no interpretation, they are ideal for a DIY Athens excursion. On the other hand, visiting the new Acropolis Museum and the National Archaeological Museum with a skilled guide who's on your wavelength adds immeasurably to the experience. We suggest you join Bright Horizons on a focused trip. You'll see the Parthenon frieze, exquisite sanctuary relics, and Archaic sculpture at the Acropolis Museum (as you can see from the picture, the museum sits just below the Acropolis).

Lunch is tucked away at a taverna favored by Athenian families. For dessert, we'll visit the richest array of Greek antiquities anywhere—at the National Archaeological Museum.

SCIENTIFIC AMERICAN Travel

BRIGHT HORIZONS™ 16

JANUARY 30–FEBRUARY 12, 2013 ✷ PATAGONIA ✷ www.InsightCruises.com/sciam16

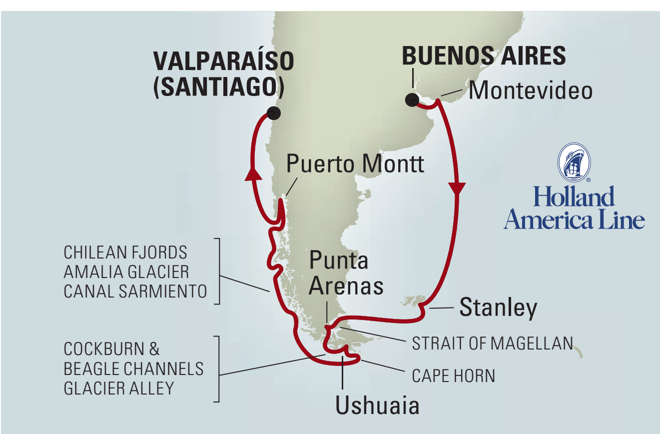
Explore the far horizons of science while living the dream of rounding Cape Horn. Gather indelible images of the uttermost ends of the Earth in the company of fellow citizens of science. Venture about South America's uniquely beautiful terrain with Scientific American Travel on the Bright Horizons 16 cruise conference on Holland America's Veendam, Buenos Aires, Argentina to Santiago, Chile, January 30 – February 12, 2013. An abundance of cultural, natural, and scientific riches await you.

Embrace the elemental suspense of Patagonia. Absorb the latest on neutrinos with Dr. Lawrence Krauss. Immerse yourself in oceanography with Dr. Gary Lagerloef. Survey South America's deep origins with Dr. Victor A. Ramos. Take a scientific look at beliefs, ethics, and morals with Dr. Michael Shermer. Ponder key questions about extraterrestrial life with Dr. Seth Shostak. See the world in a grain of soot and the future in nanotechnology with Dr. Christopher Sorenson.

You have pre- and post-cruise options to peer into the Devil's Throat at Iguazu Falls (a great wonder of the natural world), visit Easter Island or the Galapagos, or ascend Machu Picchu.

Savor South America with a friend. The potential of science beckons, and adventure calls on Bright Horizons 16. Please join us! We take care of the arrangements so you can relax and enjoy the natural and cultural splendor of South America. For the full details, email Concierge@insightcruises.com, or call 650-787-5665.

Cruise prices vary from $1,599 for an Interior Stateroom to $5,599 for a Deluxe Suite, per person. For those attending our SEMINARS, there is a $1,575 fee. Taxes, Port Charges, and an Insight Cruises fee are $336 per person. Program subject to change. **For more info please call 650-787-5665 or email us at Concierge@InsightCruises.com**



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THE EARTH FROM SPACE

Gary Lagerloef, Ph.D.

Earth From Space: A Dynamic Planet

The world's space programs have long focused on measurements of Earth. NASA has more than a dozen satellites collecting data on weather, climate change, the land, ocean and polar regions. They reveal Earth's dynamic biosphere, atmosphere, oceans and ice. Get a guided tour of an active and dynamic Earth with amazing and astonishing images and videos.

The Oceans Defined

Satellites have greatly enhanced the exploration & understanding of our oceans. From early weather satellite images detailing ocean currents to views of the marine biosphere, new satellite technologies have revolutionized our scientific understanding of the oceans. Find out what we can measure from space today, objectives of measurement, the amazing technology behind these abilities, and the latest compelling discoveries.

Climate Science in the Space Age

Climate variability and change are among the most important societal issues of our time. Signs of rising global temperatures are obvious in meteorology and oceanography. We'll discuss short, medium and long-term climate variability & change. You'll gain perspectives to effectively sort through contemporary debate about climate change.

The Aquarius/SAC-D Satellite Mission

Take an in-depth look at the Aquarius/SAC-D mission, an oceanographic partnership between the United States and Argentina. Get a behind-the-scenes look at the process of developing and launching a new satellite mission, a briefing on the core scientific mission, and a look at initial findings. Dive into a session that ties together mission, data, and applied science.

GEOLOGY

Speaker: Victor A. Ramos, Ph.D.

The Patagonia Terrain's Exotic Origins

Did Patagonia evolve as an independent microcontinent that fused with South America 265 million years ago? Dr. Ramos will give you the latest theory on the complex development of Patagonia. We'll look at the geologic evidence of Patagonia's close relationships with Antarctica, Africa, and South America, plus archaeological evidence suggestive of Patagonia's origins.

The Islands of the Scotia Arc

Delve into the dynamic nature of South Georgia and the South Sandwich and South Orkney Islands on the Scotia Plate, one of the youngest, and most active tectonic plates. Deepen your understanding of the geology, ecosystems, and history of the Scotia Arc, part of the backbone of the Americas.

The Andes: A History of Earthquakes and Volcanoes

Unfold deep time and learn how South America took shape. Get the details on how the Andes formed, how active Andean volcanoes are, the Andes as a unique climate change laboratory, and lessons learned from the Chilean earthquakes of 1960 and 2011. All certain to give you geologic food for thought on your voyage around the Horn.

Darwin in Southern South America

Darwin's voyage on the Beagle is an incredibly rich scientific and human adventure. Learn the highlights of HMS Beagle's mission in South America in 1833-1835, including Darwin's geological and biological observations. Gain a sense of South America's role in Darwin's life work, and an understanding of his contribution in the context of contemporary science.

PHYSICS

Speaker: Lawrence Krauss, Ph.D.

The Elusive Neutrino

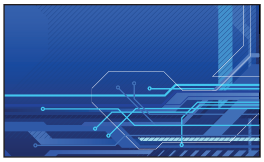
Neutrinos are the most remarkable elementary particles we know about. They are remarkable probes of the Universe, revealing information about everything from exploding stars to the fundamental structure of matter. Dr. Krauss will present a historical review of these elusive and exciting objects, and leave you with some of the most remarkable unsolved mysteries in physics.

The Physics of Star Trek

Join Lawrence Krauss for a whirlwind tour of the Star Trek Universe and the Real Universe — find out why the latter is even more exotic than the former. Dr. Krauss, the author of The Physics of Star Trek, will guide you through the Star Trek universe, which he uses as a launching pad to the fascinating world of modern physics.

Space Travel: Why Humans Aren't Meant for Space

The stars have beckoned humans since we first looked at the night sky. Humans set foot on the Moon over 40 years ago, so why aren't we now roaming our solar system or the galaxy in spacecraft? Dr. Krauss describes the daunting challenges facing human space exploration, and explores the realities surrounding our hopes for reaching the stars.



NANOSCIENCE
Chris Sorensen, Ph.D.

Fire, Fractals and the Divine Proportion
Physicist Chris Sorenson discusses the mysteries, beauties, and curiosities of soot. Take an unlikely journey of discovery of soot to find fractal structures with non-Euclidian dimensionality, networks that tenuously span space and commonalities among spirals, sunflowers and soot. Gain an appreciation for the unity of Nature, and the profound lessons in the commonplace as well as the sublime through soot!

Light Scattering
Take a *particle* physics perspective and ask: how do particles scatter light and why does light scatter in the first place? What are the effects of scattering on the polarization? How do rainbows, glories and sundogs work? How do light scattering and absorption effect the environment? Get the latest on scattering and see your universe in a new light.

Nanoparticles: The Technology.
Nanoscience has spawned a significant nanotechnology. Explore new nanomaterials such as self cleaning surfaces and fibers stronger yet lighter than steel. Then we'll do some informed daydreaming about far reaching possibilities like nanobots that could take a "fantastic voyage" inside your body or stealth materials for the invisible man. Enjoy reality science fiction at its best!

Nanoparticles: The Science.
What makes "nano" so special? Why does nano hold such great promise? Take a look at the clever chemistry that creates the nanoparticle building blocks of the new nanomaterials. Find out why physical properties of nanoparticles differ from larger particles. When this session is over, you'll understand why small can be better.

ASTROBIOLOGY
Speaker: Seth Shostak, Ph.D.

Hunting for Life Beyond Earth
Is Earth the only planet to sport life? Researchers are hot on the trail of biology beyond Earth, and there's good reason to think that we might find it within a decade or two. How will we find alien biology, and what would it mean to learn that life is not a miracle, but as common as cheap motels?

Finding E.T.
Life might be commonplace, but what about intelligent life? What's being done to find our cosmic confreres, and what are the chances we'll discover them soon? While most people expect that the cosmos is populated with anthropomorphic aliens aka "little gray guys with large eyes and no hair" you'll hear that the truth could be enormously different.

What Happens If We Find the Aliens?
One-third of the public believes that aliens are visiting Earth, pirouetting across the skies in their saucers. Few scientists agree, but researchers may soon discover intelligent beings sharing our part of the galaxy. Could we handle the news? What facts could be gleaned

immediately, and what would be the long-term effects such a discovery would have on us and our institutions, such as religion?

The Entire History of the Universe
Where and when did the cosmos begin, and what's our deep, deep future? The book of Genesis gives only a short description of the birth of the cosmos, but modern science can tell a more complex tale. How did the universe get started, and could there be other universes? And how does it all end, or does it end at all?

SKEPTICISM
Speaker: Michael Shermer, Ph.D.

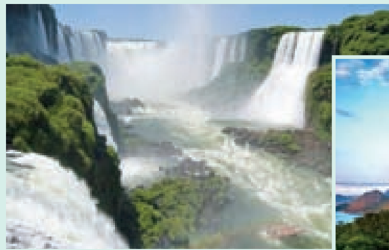
The Believing Brain: From Ghosts and Gods to Politics and Conspiracies — How We Construct Beliefs and Reinforce Them as Truths
The brain as a "belief engine"? Learn how our brains' pattern-recognition and confirmation bias help form and reinforce beliefs. Dr. Shermer provides real-world examples of the process from politics, economics, and religion to conspiracy theories, the supernatural, and the paranormal. This discussion will leave you confident that science is the best tool to determine whether beliefs match reality.

Skepticism 101: How to Think Like a Scientist
Harvest decades of insights for skeptical thinking and brush up on critical analysis skills in a lively session that addresses the most mysterious, controversial, and contentious issues in science and skepticism. Learn how to think scientifically and skeptically. You'll see how to be open-minded enough to accept new ideas without being *too* open-minded.

The Science of Good and Evil: The Origins of Morality and How to be Good Without God
Tackle two challenging questions of our age with Michael Shermer: (1) The origins of morality and (2) the foundations of ethics. Dr. Shermer peels back the inner layers covering our core being to reveal complex human motives — good and evil. Gain an understanding of the evolutionary and cultural underpinnings of morality and ethics and how these motives came into being.

The Mind of the Market: Compassionate Apes, Competitive Humans, and Other Lessons from Evolutionary Economics
How did we evolve from ancient hunter-gatherers to modern consumer-traders? Why are people so irrational when it comes to money and business? Michael Shermer argues that evolution provides an answer to both of these questions through the new science of evolutionary economics. Learn how evolution and economics are both examples of complex adaptive systems. Get your evolutionary economics tools together.

SCIENTIFIC AMERICAN Travel HIGHLIGHTS



IGUAZU FALLS AND RIO
January 25 – 30, 2013 — Surround yourself with 260 degrees of 240 foot-high walls of water at Iguazu Falls. Straddling the Argentinian-Brazilian border, Iguazu Falls is split into about 270 discrete falls and at peak flow has a surface area of 1.3 million square feet. (By comparison, Niagara Falls has a surface area of under 600,000 square feet.) Iguazu is famous for its panoramic views and breath-taking vistas of huge sprays of water, lush rainforest, and diverse wildlife.

We'll walk Iguazu National Park's extensive and well-engineered circuit paths over the Falls, go on a boat ride under the Falls, be bowled over by the massiveness and eco-beauty, and take a bazillion pictures.

MACHU PICCHU

February 12–15, 2013 — Scale the Andes and absorb Machu Picchu's aura. Visit this legendary site of the Inca World, draped over the Eastern slopes of the Peruvian, wrapped in mystery. Whether it was an estate for the Inca emperor Pachacuti or a site for astronomical calculations, it captures the imagination. Visit Machu Picchu, and see for yourself the massive polished dry-stone structures, the Intihuatana ("Hitching Post of the Sun"), the Temple of the Sun, and the Room of the Three Windows. Iconic ruins, rich flora and fauna, and incomparable views await your eye (and your lens).

EASTER ISLAND

February 12–17, 2013 — The moai of Easter Island linger in many a mind's eye, monumental statues gazing inland, away from the South Pacific. Join Bright Horizons on a six-day post-cruise excursion to explore the mysteries of Rapa Nui. Visit archaeological sites, learn about the complex cultural and natural history of the island, and absorb the ambiance of one of the most remote communities on Earth. Come along on an adventure where archaeology and environment create memories and food for thought.

GALAPAGOS

February 12–19, 2013 — Enter an unearthly natural world in an eight-day post-cruise excursion to the Galapagos Islands. "See the world in a grain of sand" and hone your knowledge of evolution with your observations in the Galapagos, a self-contained natural history laboratory. We'll tour Santiago, Chile, and straddle the Equator at the "Middle of the World" complex in Quito, Ecuador. Then off to the Galapagos for a four-day expedition on the MS Explorer II. Accompanied by certified naturalists see the incredibly diverse flora and fauna up close. You'll have the opportunity to swim and snorkel, and photograph legendary wildlife and wild landscapes. Join Bright Horizons in the Galapagos for all the intangibles that communing with nature provides.

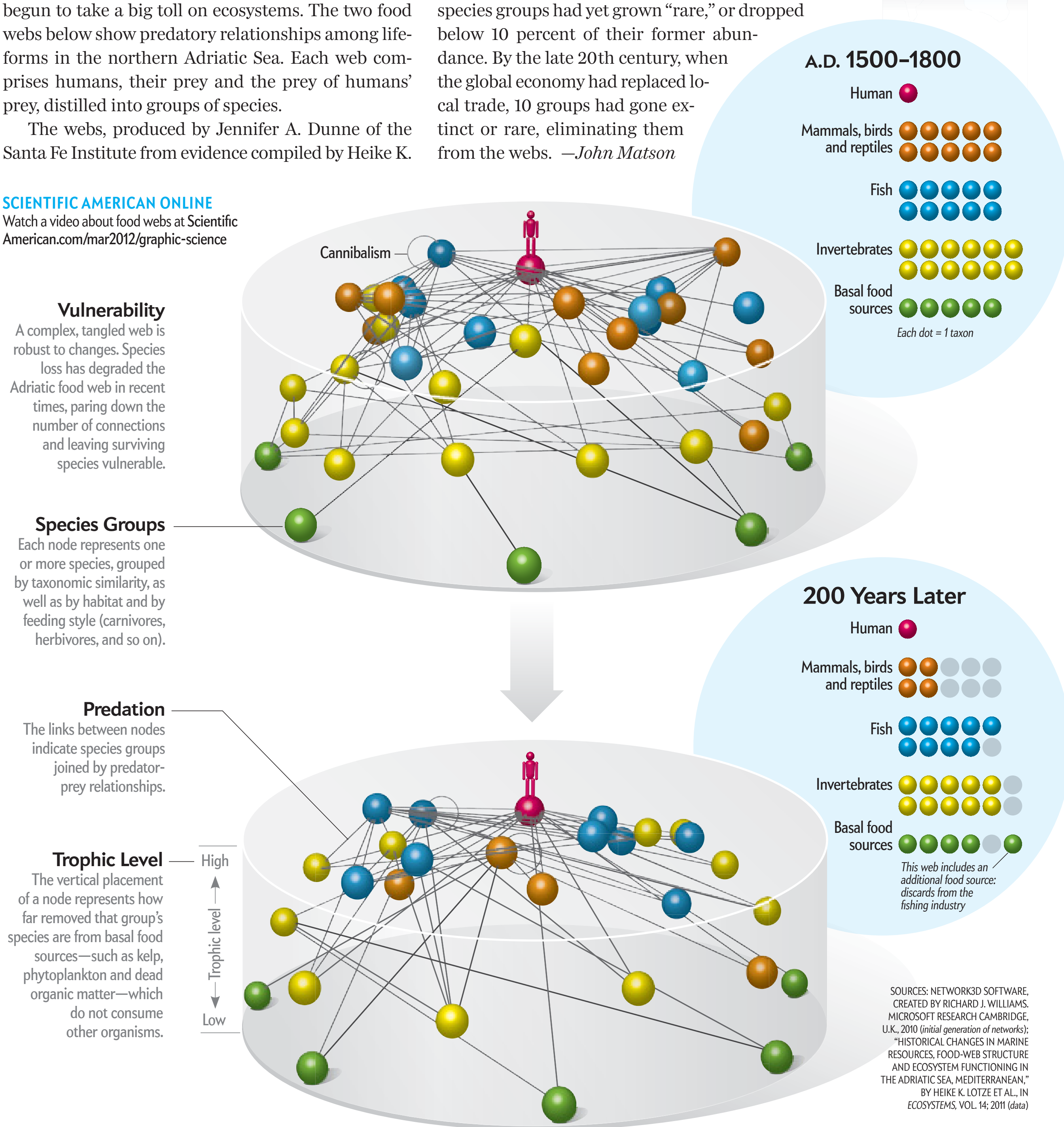
The Dwindling Web

How human exploitation has reshaped a marine ecosystem

Humans have harvested the sea for tens of thousands of years, but only in the past few centuries have we begun to take a big toll on ecosystems. The two food webs below show predatory relationships among life-forms in the northern Adriatic Sea. Each web comprises humans, their prey and the prey of humans' prey, distilled into groups of species.

The webs, produced by Jennifer A. Dunne of the Santa Fe Institute from evidence compiled by Heike K. Lotze and Marta Coll of Dalhousie University in Halifax, show that as recently as 1800 none of the Adriatic species groups had yet grown "rare," or dropped below 10 percent of their former abundance. By the late 20th century, when the global economy had replaced local trade, 10 groups had gone extinct or rare, eliminating them from the webs. *—John Matson*

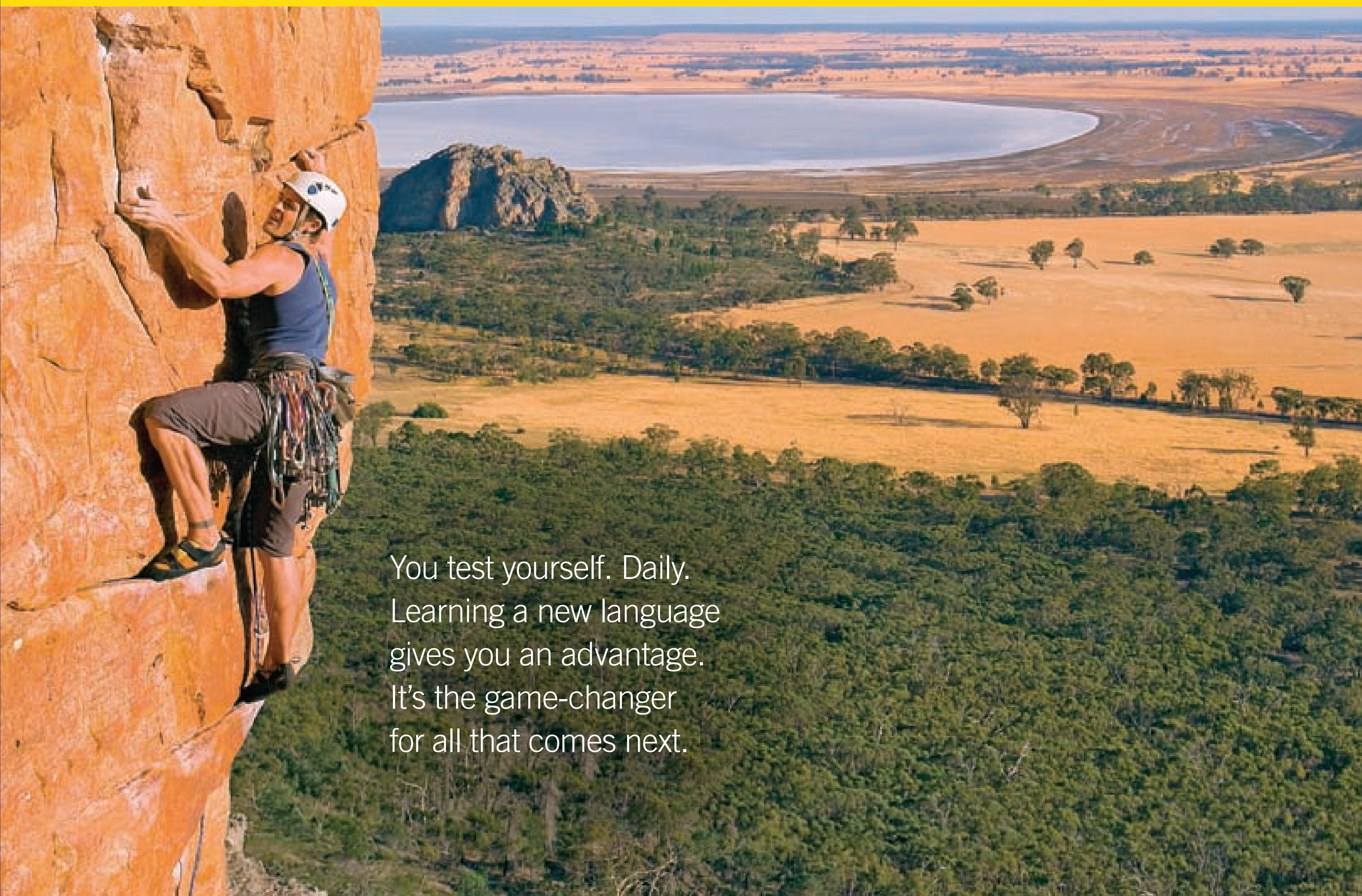
SCIENTIFIC AMERICAN ONLINE
Watch a video about food webs at ScientificAmerican.com/mar2012/graphic-science



SOURCES: NETWORK3D SOFTWARE, CREATED BY RICHARD J. WILLIAMS. MICROSOFT RESEARCH CAMBRIDGE, U.K., 2010 (*initial generation of networks*); "HISTORICAL CHANGES IN MARINE RESOURCES, FOOD-WEB STRUCTURE AND ECOSYSTEM FUNCTIONING IN THE ADRIATIC SEA, MEDITERRANEAN," BY HEIKE K. LOTZE ET AL., IN *ECOSYSTEMS*, VOL. 14; 2011 (*data*)

Graphic by Jennifer A. Dunne

More than words.
Drive.



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An underground substation built by Siemens helps make Anaheim a city worth building a future in.

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The station under Roosevelt Park delivers much-needed power to 25,000 people. It's the first underground substation in America, a feat made possible by an advanced design that makes it 70 percent smaller than traditional substations.

It seems like such a simple idea. But by putting the substation beneath the ground instead of above it, Siemens helped make life in Anaheim a little bit better.

Today, cities across the nation face countless choices about how to generate, distribute, and use electricity. Those choices call for unconventional thinking — because that's the kind of thinking that leads to truly lasting answers.

Somewhere in America, our team of more than 60,000 employees spends every day creating answers that will last for years to come.

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