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June 2012

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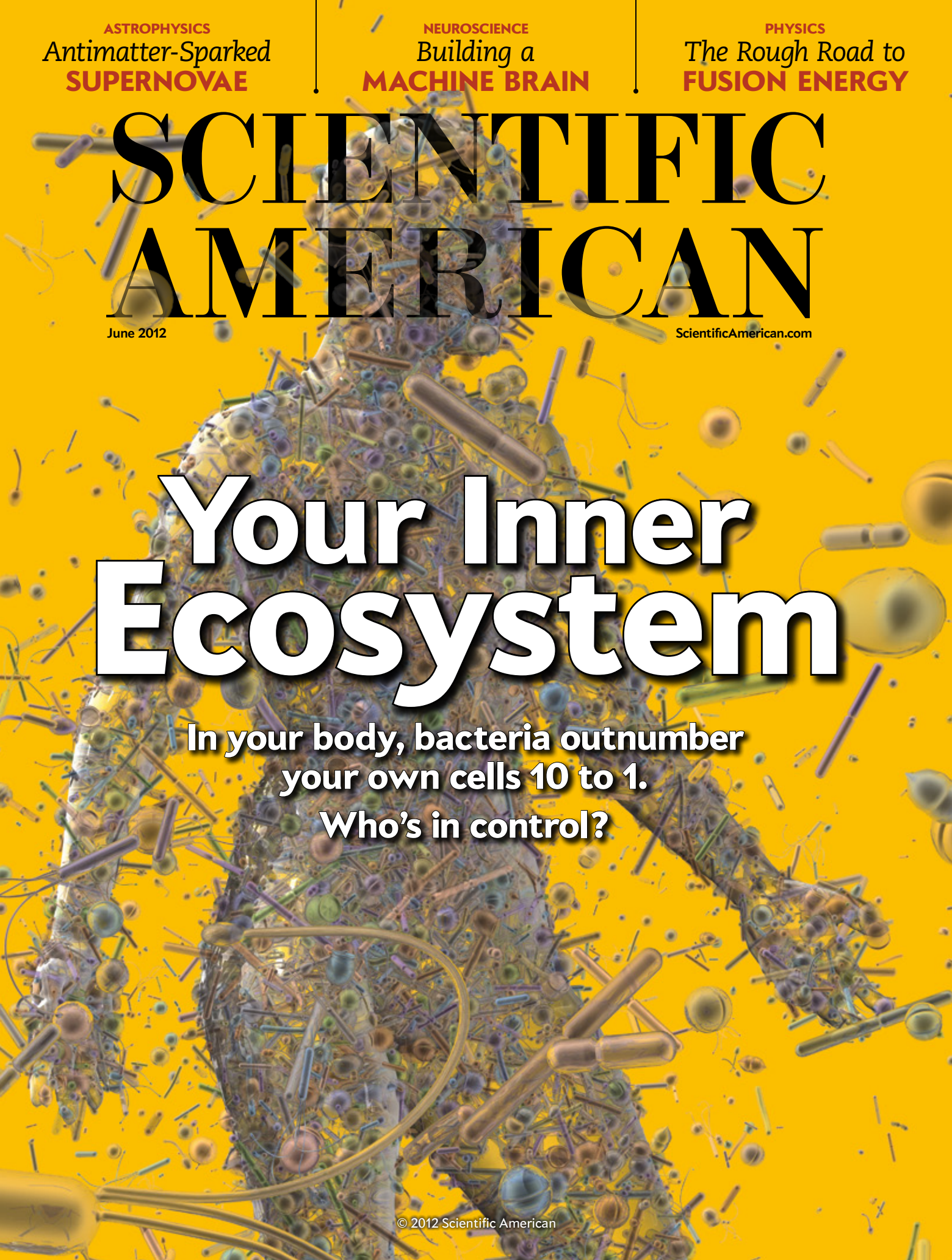

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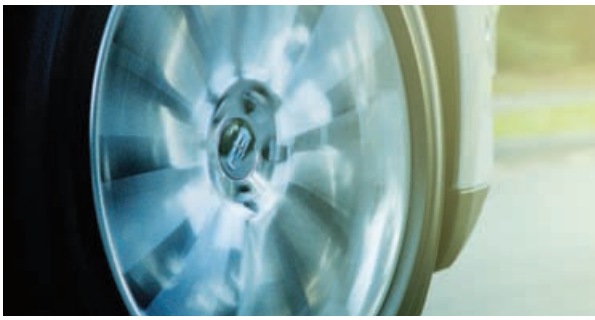

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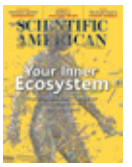


Trillions of beneficial microbes thrive on the surface of our bodies and deep within our tissues. By identifying the specific effects that some of these tiny denizens have on our health, researchers are gaining a new view of how our bodies function and how certain modern diseases, such as obesity and autoimmune disorders, can arise. Image by Bryan Christie.

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## FEATURES





*Photograph by David Liittschwager*


## WHO SAYS THE PARK HAS TO BE IN THE PARK?

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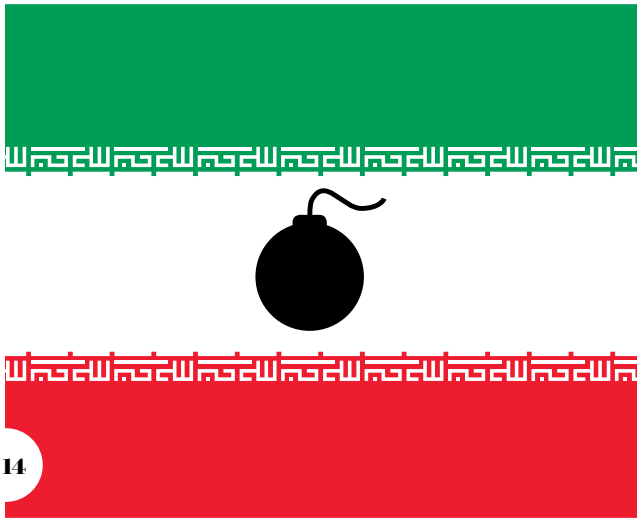

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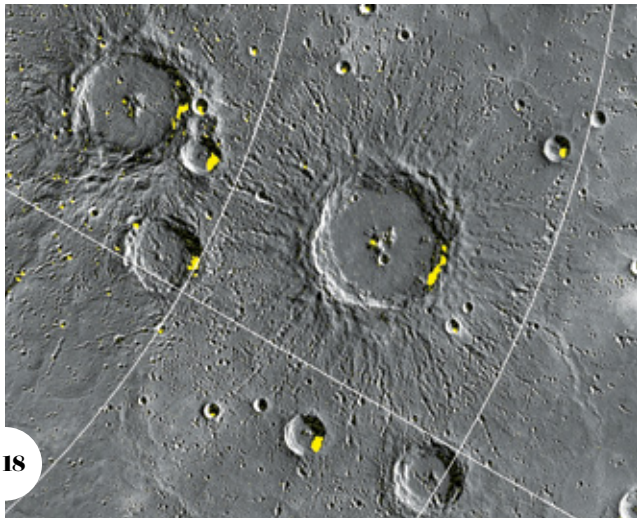

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30

# SCIENTIFIC AMERICAN

## DEPARTMENTS



## ON THE WEB

**The Future of Energy**
The race is on to reinvent the energy landscape. From mini nuclear reactors to better geothermal and from cleaner internal combustion to biofuels, the field has its established favorites—and plenty of long shots.
*Go to www.ScientificAmerican.com/jun2012/energy*


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

# We the People

"No man is an island, entire of itself," wrote English poet John Donne. Nearly four centuries later science is gaining a fuller appreciation of just how literally true that is.

In addition to the bacteria that can make us sick, researchers have known for a few decades that we play host to friendly microbes as well. They help our body by performing important tasks such as breaking down food components to make them digestible or processing nutrients so we can make use of them. Although the womb is sterile, we start acquiring our microscopic guests the minute we are born.

The sheer number and broader influence of these bugs may surprise you. For starters, microbes outnumber your body cells by 10 to 1. (The bacteria are much smaller than human cells, so their total weight is often estimated to be around two to five pounds.) In effect, we are each a walking superorganism, hosting our own unique microcommunity. No two individuals share the same makeup of microbes and their genes, not even identical twins. Nobel Prize winner Joshua Lederberg dubbed this inner ecosystem a microbiome, acknowledging its complexity and interconnectedness.

More to the point, your health, your life span—and even some of your actions—may have more to do with the genetic variation in those microorganisms you host than they do with your own genes. Our cover story, "The Ultimate Social Network," by Jennifer Ackerman, describes the efforts to map our human microbiome—no easy feat when certain critters, such as the gut bacteria that prosper in an oxygen-free environment, are challenging to grow in petri dishes in a laboratory. The results are illuminating. As you will learn when you turn to page 36, among other things, microorganism groups may influence not only how well we digest but also how much we eat. In addition, they have an important part in how well our immune system performs.

For a different kind of community effort—one involving teenagers and science that can benefit humankind—see the box at the left. SA

SCIENCE IN ACTION

## Award Winner

**Look for the announcement** of the winner of the Science in Action Award in June. *Scientific American* is sponsoring this $50,000 award, plus a year of mentoring, as part of the second annual Google Science Fair, a global online competition for students aged 13 to 18. The award will honor a project that addresses a social, environmental or health matter and could make a difference in the lives of a community or group. Find more information at www.google.com/sciencefair and at www.ScientificAmerican.com/science-in-action. —*M.D.*





*Illustration by Nick Higgins*

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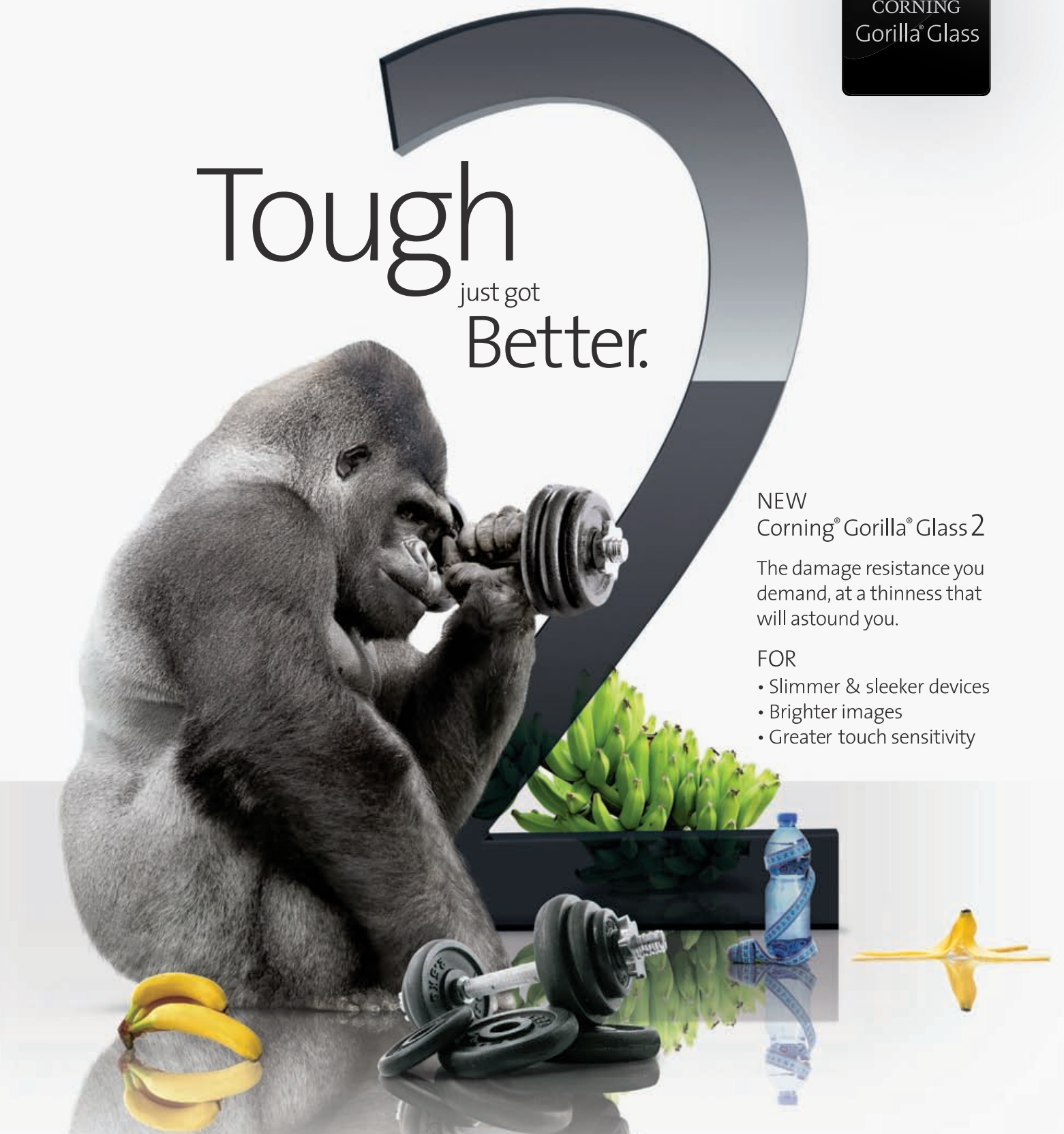

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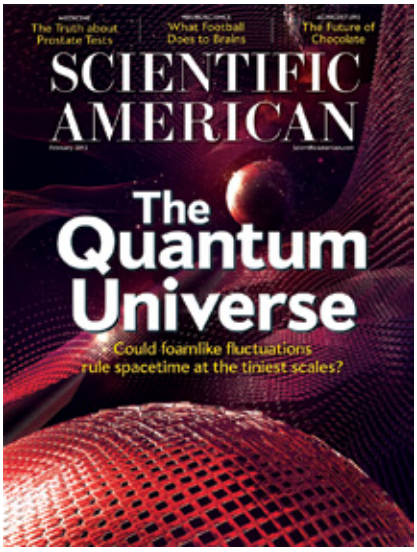


*February 2012*

**FLU SECURITY**

In "A Man-made Contagion," by Jeneen Interlandi [Advances], Michael T. Osterholm of the National Science Advisory Board for Biosecurity argues, regarding studies creating mutations that would allow the H5N1 virus to readily spread between humans, that "physicists have been doing ... classified work for 70 years. We have to find a way to do the same in the health sciences, without compromising our safety and security."

Classified physics work has put the future of our species in question, so not "compromising our safety and security" would require more stringent controls in the health sciences than were applied in the physical ones. Additionally, new life-forms can be created in an inexpensive lab with commercially available ingredients. Nuclear weapons materials are more difficult to obtain.

Martin Hellman
*Professor Emeritus, Electrical Engineering*
*Stanford University*

It would be best to destroy the existing mutated virus and place the information on creating it under the same kind of security as hydrogen bomb instructions. Freedom of information groups do not argue that thermonuclear weapons information be released to all; it is beyond foolishness to argue that infinitely more dangerous biological warfare information be made public.

Previously in biology, the benefits of publicly shared knowledge outweighed the dangers. This is no longer *always* the case. We have changed the terrain here, and our mind-set must change, too.

**"It is beyond foolishness to argue that biological warfare information be made public."**

David Green *Brookyln, N.Y.*

David Green
*Brooklyn, N.Y.*

**AMISS EXPERIMENT?**

"Is Space Digital?" by Michael Moyer, describes a proposed experiment by Craig Hogan of Fermilab near Batavia, Ill., that claims to test the holographic principle. The article quotes both of us, as theorists who played a central role in the discovery and general formulation of the holographic principle. But it fails to mention that we believe that Hogan's experiment does not actually test this principle.

The holographic principle asserts a fundamental relation between quantum information and the areas of spacetime's surfaces. Observation already supports it: no object in the universe is known to violate this relation. In fact, it could be ruled out by experiment: for example, if novel forms of matter were discovered that permitted violations of the holographic bound on information storage.

The principle, however, does not predict the quantum "jitters" that Hogan's experiment seeks to detect; it predicts their absence. They would conflict with Einstein's principle of relativity, which is central to the formulation of the holographic principle (and to our understanding of countless previous experimental results).

The holographic framework does make distinctive predictions. For an experiment occupying a region of space of about a meter in radius, it predicts subtle correlations that involve approximately $10^{70}$ photons. That is just about enough energy to make a black hole as big as the entire experiment. The length of time that it would take to accumulate the required information from the black hole would be around a quadrillion quadrillion quadrillion times the age of the universe.

The same is true for a larger or smaller experiment: the distinctive features of the principle always involve enough photons to create a black hole as big as the experiment and an extraordinary length of time to collect the required information. Hogan's experiment is absurdly far from this regime.

Raphael Bousso
*University of California, Berkeley*
Leonard Susskind
*Stanford University*

**TESTING POSITIVE**

Marc B. Garnick's fine article on prostate cancer ["The Great Prostate Cancer Debate"] neglects one very important consideration in its support of reduced screening: death from untreated cancer, though low, is quite often slow and very painful. I would much rather die of just about anything else.

In addition, treatment of advanced prostate cancer is no cakewalk. My prostate cancer was removed surgically after it was diagnosed, but my brother's was too far advanced. He is now being treated by hormones and other drugs, and his life is far from rosy: weight gain, hot flashes, heart problems and incontinence are not his only problems. For me, the prostate-specific antigen (PSA) test was a godsend.

Joe Cusack
*Scottsdale, Ariz.*

The discussion should not be about the many low-grade tumors that elevated PSA tests find but about how many mid- and high-grade tumors are discovered. The fact that elevated PSA scores can indicate the possibility of aggressive cancers in the prostate sooner than any other noninvasive test should justify some periodic PSA testing for men. How often these screenings should be done and at what age they should begin is the proper question, not whether they should be eliminated.

Henry Maze
*San Mateo, Calif.*

*GARNICK REPLIES: Whether prostate cancer screening will reduce the death rates and suffering from prostate cancer forms a key and critical question underlying any screening program. The thinking behind such programs hypothesizes that cancers*



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*start as a microscopic focus, turn into a localized cancer—becoming more regionally advanced in the organ from which they arose—then metastasize, eventually claiming the life of the individual. Thus, screening and finding these cancers "early" should result in saved lives. Yet although nearly every screening program finds seemingly less aggressive and earlier-stage cancers than those found later on, the expected improved survival rates have not materialized.*

*Although it is reassuring to think that "catching" prostate cancer early will save lives, the complexities and differing genetic makeup of prostate cancers that ultimately determine the disease's biological behavior are probably the most important factors. Oncologists remain hopeful that future biomarkers will be developed that will inform us not only of whether cancer is present but of what the behavior—and hence the need for treatment—of that cancer is likely to be.*

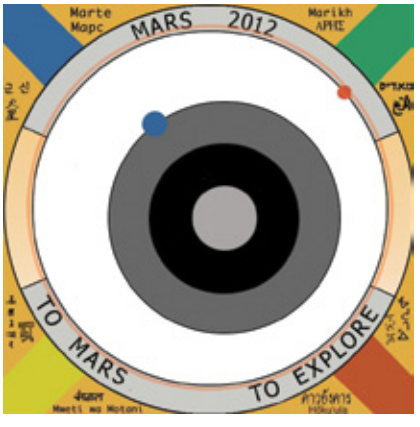
## CLARIFICATION

In "A Diabetes Cliffhanger," by Maryn McKenna [The Science of Health], Rebecca Lipton is described as an emeritus professor at the University of Chicago. She is a retired associate professor at that institution.

## ERRATA

"Is Space Digital?" by Michael Moyer, describes physicist Stephan Meyer of the University of Chicago as a veteran of the Laser Interferometer Gravitational-Wave Observatory (LIGO) detector. This is incorrect. His experience is in cosmic microwave background radiation experiments.

The corrected sundial image in "Storybook Wishes for Martian Rovers," by Glendon Mellow [Advances], appears below:

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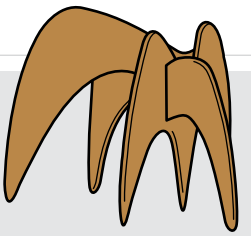

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Letters may be edited for length and clarity. We regret that we cannot answer each one. Post a comment on any article at ScientificAmerican.com/jun2012

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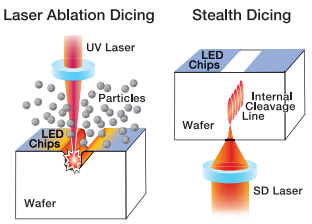


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# Protect Women's Health

## Political attacks on Planned Parenthood pose a threat to the well-being of millions of women in the U.S.

**Almost 100 years ago** Margaret Sanger opened a tiny birth-control clinic in the Brownsville section of Brooklyn, N.Y. Poor Yiddish- and Italian-speaking women, overwhelmed by large families that they could not support, would come for advice about how to avoid pregnancy and the dangers of horrific, sometimes life-threatening, self-administered abortions. The clinic taught women to use the diaphragm. Nine days after it opened, Sanger and two other women who ran the center were jailed for violating a New York State law that prohibited contraception.

This clinic eventually grew into Planned Parenthood, the nation's largest nonprofit supplier of reproductive health services to women and men. A century after its founding, the organization is again at the heart of one of the most divisive issues in American political life. It has come under attack by Republican presidential candidates seeking to revoke the group's federal funding—almost half of its $1-billion budget comes from federal and state sources. Last year the House of Representatives voted to withdraw some of its support, although the measure was not sustained in the Senate. (Backing for the group, initiated under the Nixon administration, has not always been a partisan issue.) In March, Mitt Romney, the GOP's presumptive presidential candidate, vowed to end federal funding if elected. This is a worrying prospect for both women and public health.

For some people, Planned Parenthood has come to symbolize abortion, which it has provided since 1970. But in all the rhetoric, facts have sometimes gone missing. For instance, Senator Jon Kyl of Arizona declared last year on the floor of the Senate that abortion accounts for "well over 90 percent" of what Planned Parenthood does. The actual figure is 3 percent. (Planned Parenthood clinics perform one in four abortions in the U.S. but use no federal funds for this practice.) To some abortion opponents, that 3 percent is reason enough to gut the organization. If a future Congress and White House were to do so, however, it would drive women once again into the back alleys, without necessarily decreasing the number of abortions.

Stripping Planned Parenthood of federal funding would also sacrifice the 97 percent of its public health work that has nothing to do with abortion, from which many people benefit directly. One in five American women have used the group's services, and three out of four of its patients are considered to have low incomes. In 2011 it carried out tests and treatment for more than four million individuals with sexually transmitted diseases. It supplied 750,000 exams to prevent breast cancer, the most common cancer among U.S. women. And it performed 770,000 Pap tests to prevent cervical cancer, which was a leading cause of death among women before this screen became widely available. Planned Parenthood is one of the most important public health care institutions in the country, even aside from its work in rational family planning.

Family planning has benefited society in numerous ways. It has saved lives, opened new horizons for women and kept populations from soaring. Since 1965, the year the Supreme Court struck down a Connecticut law that made access to contraception illegal, women's ability to plan and space out pregnancies has contributed to a 60 percent decline in maternal deaths. By 2002, moreover, only 9 percent of births were unwanted, compared with 20 percent in the early 1960s. As a major provider of contraceptives—it furnished birth control to two million Americans last year—Planned Parenthood serves as "America's largest abortion preventer," as one *Chicago Tribune* writer pointed out.

Access to birth control in the U.S. has helped narrow the income inequality gap between men and women by as much as 30 percent during the 1990s alone. The pill has given women greater choice about when to have children, freeing them up to acquire career skills. By 2009 women procured more than half of all U.S. doctoral degrees, compared with 10 percent in 1960. The health and well-being of a society correlates highly with the status of its women. In many parts of the Middle East, Asia and Africa, women are now making gains, to the betterment of all, in access to education and jobs—both contingent on family planning. Now is a particularly bad time for Americans, as citizens of the world, to forget what we have accomplished at home. SA

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*Illustration by Thomas Fuchs*

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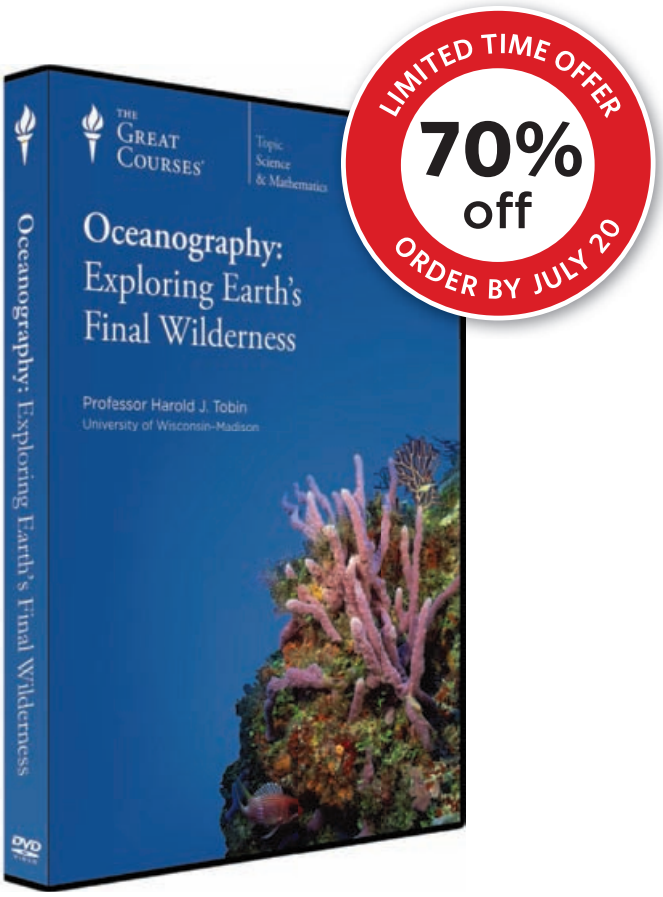


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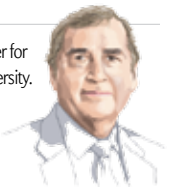
**Graham T. Allison** is director of the Belfer Center for Science and International Affairs at Harvard University. He is author of *Nuclear Terrorism: The Ultimate Preventable Catastrophe* (Henry Holt, 2005).

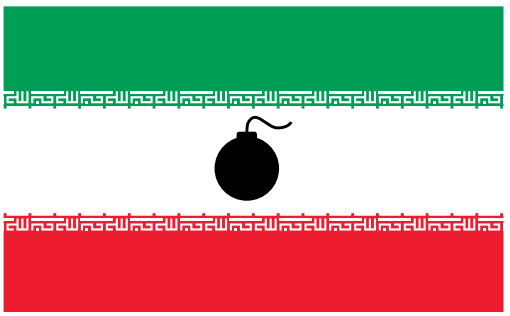


# Slinking toward the Bomb

## How close is Iran to acquiring a nuclear weapon?

**Over the past decade** Iran has been cautiously, but steadily, putting in place all the elements it needs to construct a nuclear weapon in short order. But as James R. Clapper, director of National Intelligence, told the U.S. Senate in January, while the Iranians are "moving on that path … we don't believe they have actually made the decision to go ahead with a nuclear weapon."

For several years experts have debated the possibility of a "breakout" scenario in which Iran makes a mad dash to complete and test its first bomb before other nations can act to stop it. That would require doing as much as possible to prepare for bomb making without tripping the alarms of the International Atomic Energy Agency (IAEA), the source of most good intelligence about Iran's declared program. From that point, Iran would then race to conduct a test quickly, perhaps in as little as several weeks. How close is Iran to achieving such an option?



Let us start with what we know. Since 2006 Iran has accumulated a stockpile of low-enriched uranium (LEU), containing 5 percent of the uranium 235 isotope, putatively to fuel future civilian nuclear reactors. If Iran were to enrich this material further, to the point at which 90 percent of it was uranium 235, it would provide the core of four nuclear bombs. Since February 2010 it has also been enriching uranium to 20 percent and has recently tripled the production rates of this material. It has also experimented with centrifuges that are three to six times more efficient than the first-generation centrifuges it is currently operating (the designs for which it got from Pakistan's nuclear godfather A. Q. Khan). These are significant steps toward making a bomb. Producing 20 percent enriched uranium requires nine tenths of the time and effort needed to make bomb-usable uranium. The IAEA suspects that although Iran may well have suspended its dedicated nuclear weapon research program in 2003, by that time it had already learned enough to be able to make such uranium into a simple, testable nuclear weapon.

The state of Iran's *declared* stockpile and production capabilities is fairly well known. But it may well have *undeclared* capabilities, materials and know-how. In addition to the facilities at Natanz and Fordow that the IAEA inspects regularly, it is reasonable to assume that Iran has invested in hidden enrichment facilities because both Israel and the U.S. have been threatening air strikes on these targets for many years. Although no one has reported evidence that Iran has bought nuclear weapons or material from the former arsenal of the Soviet Union or from North Korea, Iran's leaders must have considered this option as well. We know that more than one bomb's worth of fissile material went missing after the Soviet Union collapsed.

With the centrifuges now known to be operating, from where Iran stands today it would take at least five months to produce enough material for one bomb. As more centrifuges come online and production rates improve, this timeline will shorten. But any scenario that requires months between tripping the IAEA's alarm and testing a bomb would mean taking a huge risk of being attacked, something Iran's supreme leader Sayyid Ali Khamenei has so far assiduously avoided.

How then could Iran produce a nuclear bomb without getting bombed? The most worrisome scenario would be for it to "sneak out." Iran would complete the conversion of its low-enriched uranium stockpile to 20 percent at declared facilities, as it is now doing. Simultaneously, it would install advanced centrifuges at a secret facility. At the chosen moment, it would stage an incident—say, an explosion at Fordow—that it would claim had dispersed such high levels of radioactivity that the area had to be quarantined for several weeks, making inspections impossible. (It could even blame the incident on an Israeli covert attack.) Under this cover, Iran would move the 20 percent uranium to the secret facility and complete the enrichment to weapons-grade levels. Because the U.S., Israel and the IAEA would be unable to determine whether declared stockpiles had been moved or where they had been moved to, they might find themselves unable to act. In this scenario, Iran could produce enough weapons-usable uranium to conduct a test in as little as a few weeks.

The best way to deter Iran from making the decision to build a bomb in the short term is to maximize the likelihood that such a decision will be discovered and met by a devastating attack. The lower the level of enrichment of Iran's stockpile, the longer the timeline to weapons-grade material and greater the likelihood of discovery. The U.S. should thus aggressively explore the offer made by Iran's president Mahmoud Ahmadinejad last fall to end all enrichment beyond LEU in exchange for the purchase of fuel for its Tehran Research Reactor. SA

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CAREERS

# The Motherhood Gap

Family responsibilities, not discrimination, may explain why fewer women than men pursue tenure-track jobs in science

**Nearly half of all** college math majors are women, and females now score as well as males on standardized math tests. Yet only about 30 percent of Ph.D.s in mathematics—and fewer in computer science, physics and engineering—are awarded to women every year, and men far outnumber women in science- and math-related tenure-track positions at U.S. universities. Why? For decades researchers have blamed sex discrimination and bias, but research suggests that there may now be a less sinister culprit: motherhood.

There is no arguing that women in science have had to fight sex discrimination for decades. But Wendy Williams and Stephen Ceci, a husband-and-wife team of psychologists at Cornell University, recently reviewed the literature on whether female scientists still have more trouble landing jobs, publishing papers or winning grants when compared with men. They found no evidence of lingering bias. "The problem is that women don't apply for the jobs, not that they're discriminated against once they apply," explains Williams, who initially published the research in the *Proceedings of the National Academy of Sciences USA* last year and wrote a follow-up article in the March/April issue of *American Scientist*.

According to a report by the National Academy of Sciences, which Williams and Ceci cite, 27 percent of Ph.D.s in math are awarded to women, but females make up only 20 percent of the tenure-track applicant pool for positions in mathematics. In chemistry, the loss is greater: 32 percent of Ph.D.s are awarded to women, but only 18 percent of tenure-track chemistry job applicants are female.

What holds women back, Williams says, is the realization that they cannot juggle the many demands of an academic career and also have a family. The busiest years of a researcher's life are in her 20s and 30s, which corresponds with the time her biological clock is ticking most loudly. Men can put off having kids longer and can also more easily juggle career and family because women still "do the lion's share" of child care, Ceci adds. Recent research by Adam Maltese, a science education researcher at the University of Indiana, shows that men are 5 to 10 percent more likely than women to have kids while in graduate school.

Not everyone believes this is the whole story, however. "Motherhood and family do have an impact on women's career trajectories in the sciences, but I think that this is too simplistic," says Shirley Malcom, head of education and human resources at the American Association for the Advancement of Science. Plenty of successful female scientists have families, she notes.

But Malcom, Williams and Ceci agree that universities should give women the option of working part-time or flexible hours when they want to start families and "stopping the tenure clock" so that women can take more time with their careers. Many universities have started offering family leave to graduate students, extending stipends and health benefits while suspending academic deadlines for those expecting babies. Women should never be forced to pick between career and family, Malcom says, and institutions need to "create a climate that allows them to not have to make these really tough, terrible choices."

*—Melinda Wenner Moyer*

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*Journal of American Chemical Society, March 2011*

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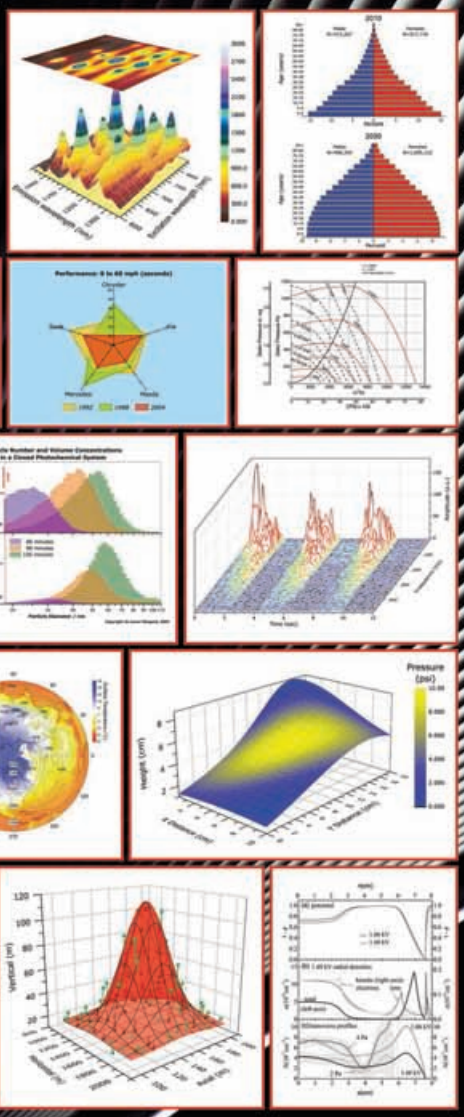

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ASTROPHYSICS

# Fire and Water

## Mercury shows new signs that it may harbor ice

**Mercury** is a world of extremes. Daytime temperature on the planet closest to the sun can soar as high as 400 degrees Celsius near the equator—hot enough to melt lead. When day turns to night, the planet's surface temperature plunges to below –150 degrees C.

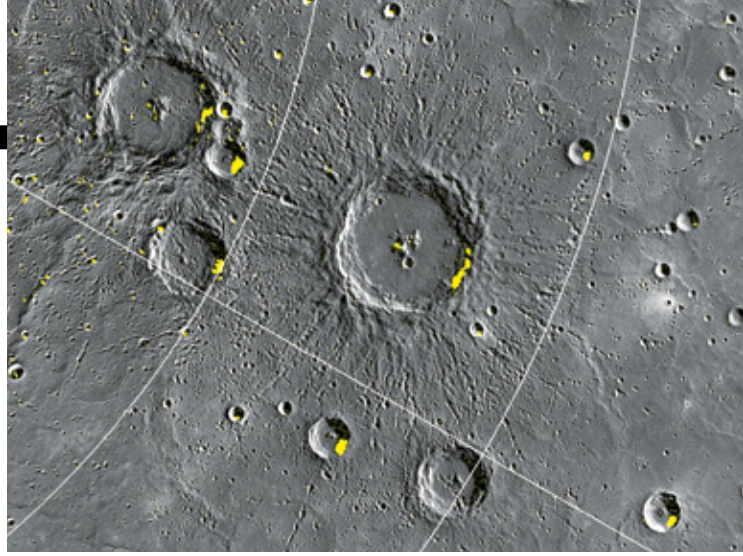
But some places on Mercury are slightly more stable. Inside polar craters on the diminutive planet are regions that never see the light of day, shaded as they are by the craters' rims. The temperature there remains cold throughout the Mercury day. Now new data from NASA's MESSENGER satellite, which were presented in March at the annual Lunar and Planetary Science Conference, corroborate a long-held hypothesis that Mercury has squirreled away pockets of water ice in those shadowy craters, despite the sun's proximity.

Since 2011 MESSENGER has orbited the innermost planet, charting Mercury's surface in unprecedented detail. MESSENGER's maps of polar craters match up nicely with earlier imagery of the poles, taken by Earth-based radars, which showed anomalously bright features—patches that reflected radio waves much better than the surrounding terrain, just as ice does.

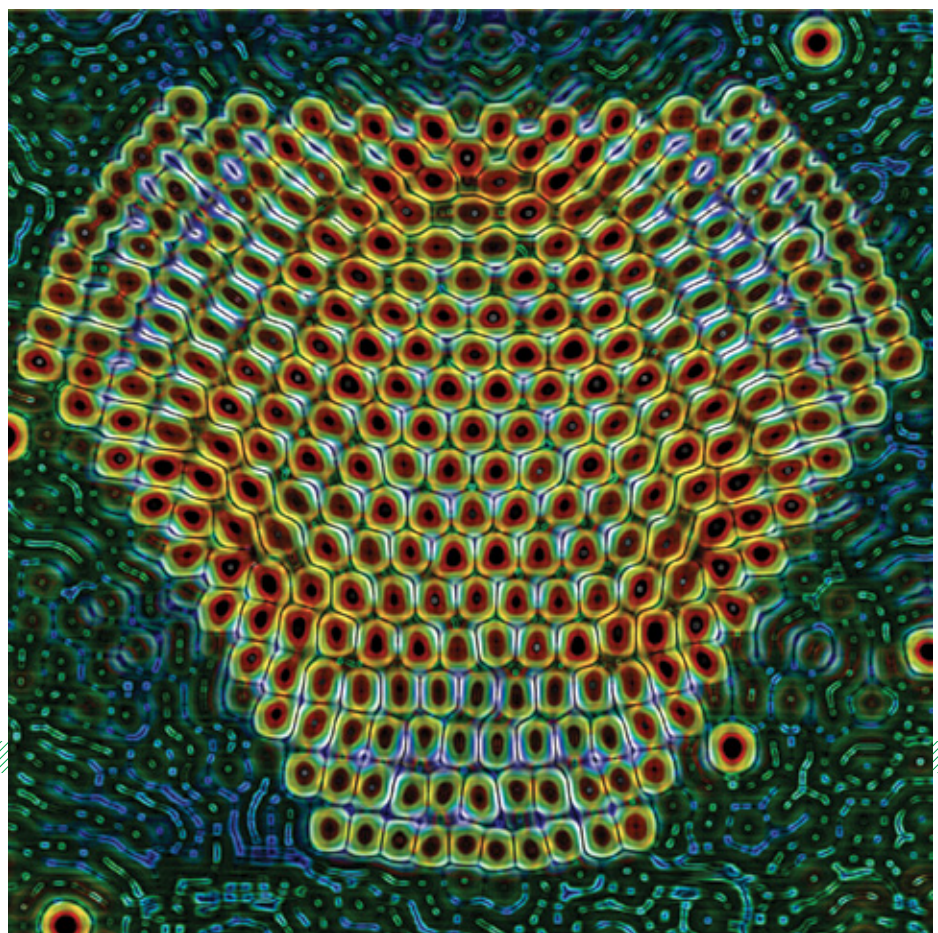
But the radar hotspots also line smaller craters and those at lower latitudes that would have less ice-friendly temperatures across the crater floor. These ice deposits would likely require a thin insulating blanket, perhaps a layer of fine-grained surface material, or regolith, to keep it from sublimating away.

In fact, MESSENGER's data seem to confirm that some insulating material blankets whatever ice may line the craters. The temperatures inside the shadowed craters are just right for ice deposits blanketed by regolith darkened by organic compounds, explained David Paige of the University of California, Los Angeles.

The new look at features spotted long ago by Earth-based radars, Paige said, shows "fairly conclusively that they are predominantly composed of thermally stable water ice." —*John Matson*



**CRATERS** on Mercury as mapped by MESSENGER. Radar bright spots, shown in yellow, may mark ice deposits.



### WHAT IS IT?

***The honeycomb lattice*** is one of nature's favorite patterns. In the two-dimensional crystal of carbon atoms known as graphene, for instance, the honeycomb structure arises from bonds among the atoms. Kenjiro K. Gomes of Stanford University and his colleagues have learned to make a honeycomb material in a striking new way. They place carbon monoxide molecules at regular intervals on the surface of a copper crystal, creating an imitation graphene layer. (The added molecules appear as black dots.)

By tweaking the pattern, the researchers can investigate how variations of small-scale structure change a material's electric properties. In the image at the left, a slightly deformed honeycomb lattice forces the electrons to behave as if they were subjected to intense magnetic fields. Such "designer materials" may lead to the discovery of new and exotic physics. —*Davide Castelvecchi*

COURTESY OF NASA/JOHNS HOPKINS UNIVERSITY APPLIED PHYSICS LABORATORY/CARNEGIE INSTITUTION OF WASHINGTON (*top*); COURTESY OF HARI MANOHARAN *Stanford University/SLAC, mota.stanford.edu* (*bottom*)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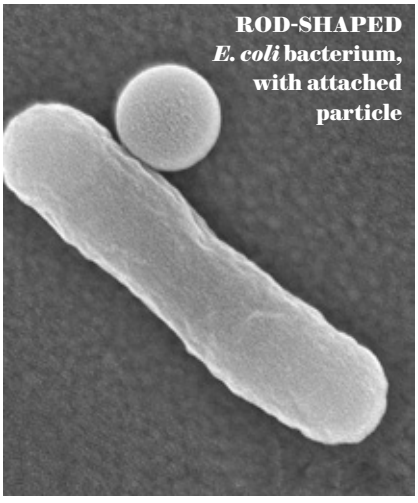
MEDICINE

# Microbial Mules

## Scientists are engineering bacteria to transport nanoparticles and drugs

**Tiny robots** that swim through our blood vessels attacking invaders have not quite crossed the line that separates science fiction from science—but there might be a way to jump-start their development.

Rather than designing such minuscule machines from scratch, some scientists have been experimenting with the idea of enlisting the thousands of species of bacteria swarming inside our bodies. In recent years researchers have saddled microorganisms with useful nanoparticles and bits of DNA. Although the research is preliminary, some engineers and microbiologists see potential. This past March, at the American Chemical Society's biannual National Meeting & Exposition in San Diego, biomolecular engineer David H. Gracias of Johns Hopkins University explained how he and his colleagues have decorated nonpathogenic *Escherichia coli* with tiny beads, rods and crescents made from nickel and tin coated in gold.



ROD-SHAPED *E. coli* bacterium, with attached particle

Once inside the body, such nanoparticles can be heated from afar with infrared light, thus destroying diseased tissue. Ultimately Gracias dreams of coaxing bacteria to ferry spongy nanoparticles soaked in drugs and outfitting bacteria with mini tools to perform surgery on a single cell.

Similar research by other scientists confirms that engineered bacteria can deliver medical packages directly into diseased or cancerous cells. In earlier work Demir Akin, now at Stanford University, and his colleagues attached the luciferase gene that makes fireflies glow to *Listeria monocytogenes,* a bacterium responsible for many cases of food poisoning. Three days after Akin injected the germs into living mice, the rodents glowed under a specialized camera, which confirmed not only that the bacteria had entered the mice's cells but that the cell nuclei had expressed the gene. Akin designed the living micro bots to release their DNA packages inside mammalian cells and replicated these results in human cancer cells in petri dishes.

The advantage of *L. monocytogenes* is that it has evolved ways to get inside animal cells—but it is not harmless. In contrast, many strains of *E. coli* are harmless but do not have specific adaptations for entering cells. The key, says Douglas Weibel of the University of Wisconsin–Madison, is working with a harmless microorganism that is a strong swimmer and has no problem butting its way into mammalian cells. In one study, Weibel yoked nanosize polystyrene beads to single-cell green algae and steered the "micro oxen" (algae move toward light)—an early experiment that inspired later work.

Weibel remains fascinated by ongoing research. "Bacteria have evolved amazing motility," he says. "They can sense changes in their environment and adapt not only on a short timescale but genetically, too. Even if we can't get them to deliver things in the human body, they could be useful for transporting nanoparticles in the lab. Who knows what advances we'll have 50 years from now?" —*Ferris Jabr*

COURTESY OF DAVID H. GRACIAS LABORATORY





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GEOLOGY

# Thar She Blows!

## New ways of modeling tremors that precede volcanic eruptions may help warn of impending disaster

**Earthquakes** often precede explosive volcanic eruptions such as the devastating outburst from Mount St. Helens in 1980. But attempts to use tremors to predict the timing and force of such explosions have proved unsuccessful for decades. Now multidisciplinary teams of researchers have developed models that could help warn of disastrous eruptions hours to days before they happen.

A group of scientists at the University of Leeds in England investigated the mystery of why volcanic tremors come in clusters and why they can occur at multiple depths within volcanoes. The answer may lie in how magma behaves: much like Silly Putty, it shatters if pulled apart quickly. When magma rising within a volcano's main conduit ruptures, the magma develops deep cracks. These cracks weaken the magma, helping it rupture at other points and flow more quickly, which causes still more shattering to occur.

Such a series of ruptures may explain the swarms of low-frequency earthquakes that past research has detected from volcanoes. Analysis of such tremors could determine how fast magma is ascending "and thus can be used to forecast explosions," says geophysicist Jürgen Neuberg of Leeds. Neuberg and his Leeds colleague Mark Thomas detailed their findings online March 2 in *Geology*.

A model developed by another team considers tremors created by columns of magma within a volcano that wag back and forth within its main conduit like a metronome rod. The rate at which the magma wagging occurs matches the dominant frequency of most volcanic tremors, reports volcanologist and geophysicist Mark Jellinek of the University of British Columbia, who described his team's work in the February 24, 2011, issue of *Nature*. (*Scientific American* is part of Nature Publishing Group.)

As explosive eruptions near, this model indicates the volcanic tremor frequency would rise in a predictable manner: explosive eruptions would generate gas that would constrict the magma column into a stiffer, thinner shape that would wobble faster. Both research teams say they need to further refine their models with additional data from volcanoes. Any future attempts to predict explosive eruptions will also need to look at changes in gas emissions and how volcanoes physically deform before explosions. "If we take all these data together, we might be able to prevent tragedies," Neuberg says. —*Charles Q. Choi*

MOUNT ST. HELENS, 1980

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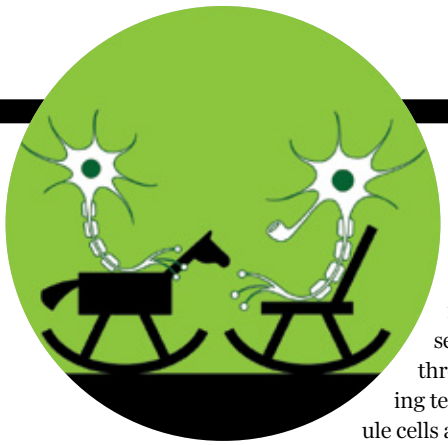

NEUROSCIENCE

# Old Neurons, New Tricks

## Brain cells help us recall the past by taking on new roles as they age

**For decades** researchers have known that our ability to remember everyday experiences depends on a slender belt of brain tissue called the hippocampus. Basic memory functions, such as forming new memories and recalling old ones, were thought to be performed along this belt by different sets of neurons. Now findings suggest that the same neurons in fact perform both these very different functions, changing from one role to another as they age.

The vast majority of these hippocampal neurons, called granule cells, develop when we are very young and remain in place throughout our lives. But about 5 percent develop in adulthood through the birth of new neurons, a process known as neurogenesis. Young granule cells help form new memories, but as they get older they switch roles to helping recall the past. Newer granule cells pick up the slack, taking on the role of helping to form new memories. Susumu Tonegawa of the Massachusetts Institute of Technology and his colleagues published the findings on March 30 in the journal *Cell*.

Tonegawa's team tested the role of these adult-born cells by genetically engineering mice in which the old cells could be selectively turned off. They then put the mice through a series of mazes and fear-conditioning tests, which demonstrated that young granule cells are essential to forming separate memories of similar events, whereas old granule cells are essential to recalling past events based on small cues. This discovery suggests that memory impairments common in aging and in post-traumatic stress disorder may be connected to an imbalance of old and new cells. "If you don't have a normal amount of young cells, you may have a problem distinguishing between two events that would be seen as different by healthy people," Tonegawa says. At the same time, the presence of too many old cells would make it easier to recall traumatic past experiences based on current cues.

Previous research has shown that both traumatic experiences and natural aging can lead to fewer new neurons being produced in the hippocampus. But a cause-and-effect relation between impaired neurogenesis and memory disorders has yet to be established. If such a connection is found, this research will have opened the door to a novel class of treatments aimed at stimulating neurogenesis. Already it is changing the way we think memory works. —*Meehan Crist*





*Illustrations by Thomas Fuchs*

SCIENTIST IN THE FIELD

# When Cockroach Legs Dance

## An educational entrepreneur talks about teaching neuroscience to high school students

**When I was** a graduate student in neuroscience at the University of Michigan, we would record the brains of animals and try to figure out what the brains were doing. At the same time, we were going into classrooms and teaching neuroscience to kids. Tim Marzullo—now my business partner—and I noticed that there was a big difference between what we were doing in the lab and what was being taught. They were using Ping-Pong balls and jump ropes to explain action potentials [electrical activity that occurs when neurons fire], but that's so far removed from what is really going on in the brain.

We came up with an idea to build a recording kit for $100. The SpikerBox is a bioamplifier. What's happening is that axons have electricity, and the electricity gets picked up by the pins on the machine. You're listening to what the brain is doing. In our example, we use cockroaches, but we'd like to get things going on vertebrates and sea animals in the future.

Although our assembled kit costs $100, if you build it yourself, the parts are $49. A lot of high schools have an engineering or a physics class where the students build the kit and then use it in that course or hand it off to another class, say, biology or physiology.

We wanted to do this because kids who could become the best neuroscientists in the world might never become neuroscientists because neuroscience is not taught in high school. They might teach about the nervous system or the brain, but it's very general. When you choose a career, you don't choose things you read about in books; you choose based on the experiences you have. Seeing that cockroach leg dance to music and being able to manipulate the leg and hear the spikes that come out of it are really compelling. Those are events in children's lives. *—As told to Rose Eveleth*

**PROFILE**

NAME
**Greg Gage**

POSITION
**Co-founder of Backyard Brains**

LOCATION
**Ann Arbor, Mich.**

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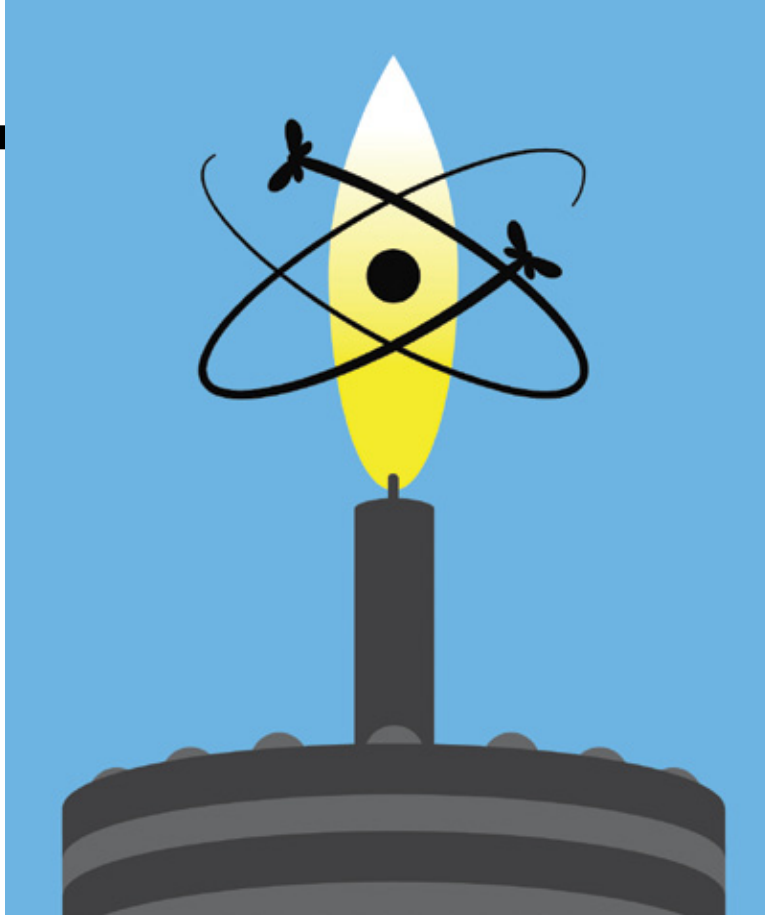

HISTORY OF SCIENCE

# Happy Birthday, Electron

## Lorentz's electron theory of 1892 bridges classical and modern physics

**Electrons rule our world,** but not so long ago they were only an idea. This month marks the 120th anniversary of a profound and influential creation, the electron theory of Dutch physicist Hendrik Antoon Lorentz. His electron was not merely a hypothesized elementary particle; it was the linchpin of an ambitious theory of nature. Today physicists are accustomed to the notion that a complete description of nature can rise out of simple, beautiful equations, yet prior to Lorentz that was a mystic vision.

For most physicists the memorable peak of 19th-century physics is the theory of electrical and magnetic fields, capped by James Clerk Maxwell's mathematical synthesis of 1864. Then a haze settles, until the 20th-century massifs of relativity and quantum theory poke through. That foggy folk history obscures the bridge between—itself a brilliant achievement, built through heroic labor.

To set the context, it is important to admit a blasphemy: Maxwell's own exposition of his equations is a mess. You will not find, in his writings, the clean, compact, elegant structure that students learn as "Maxwell's equations." Instead you discover a torrent of symbols and a sprawl of words and equations. Maxwell, a profoundly humble man, did not consider that he was producing poetry for the ages, suitable for engraving. Rather he simply set out to summarize, in mathematical form, everything then known about electricity and magnetism. In his presentation, fundamental equations mingle with makeshift phenomenology.

Lorentz's achievement was to purify the message of Maxwell's equations—to separate the signal from the noise. The signal: four equations that govern how electrical and magnetic fields respond to electric charge and its motion, plus one equation that specifies the force those fields exert on charge. The noise: everything else!

Now one had definite equations for the behavior of tiny bodies with specified mass and charge. Could one use those equations to rebuild the description of matter on a new foundation, starting from idealized "atoms" of charge? This was the burden of Lorentz's electron theory. Starting with his 1892 paper, Lorentz and his followers used the electron theory to explain one property of matter after another—conduction of electricity and of heat, dielectric behavior, reflection and refraction of light, and more. Thus, they laid the groundwork for the subjects we now call electronics and materials science. And in 1897 Joseph John Thomson showed experimentally that electrons really do exist. (One could say that the electron was conceived in 1892 and delivered in 1897.)

Much of Lorentz's 1892 paper deals with the seductive, though not unproblematic, idea that the mass of electrons could be a consequence of their electric charge. Moving charge generates both electrical and magnetic fields, which resist change and back-react on the electron's motion. Might that back-reaction account for the electron's inertia—hence its mass? Such ideas have an ancient history: Aristotle wanted to account for the inertia of matter through the back-reaction of air. Lorentz's vision of electromagnetic mass was immensely influential. It inspired hard technical work, notably by Lorentz himself and by Henri Poincaré, that anticipated major parts of Einstein's special theory of relativity.

Quantum mechanics changed the rules of the game, and the idea that electromagnetic back-reaction alone is responsible for the mass of the electron no longer appears viable. Remarkably, however, my colleagues and I have successfully explained the mass of protons, neutrons and other strongly interacting particles using a closely related idea. The inertia of those particles arises from back-reaction of the gluon fields of electromagnetism's big brother, quantum chromodynamics. Although the Higgs particle is sometimes credited with giving matter mass, its contribution to the mass of ordinary matter is actually quite small. Lorentz's beautiful idea, in modern form, accounts for most of it.

Lorentz's electron theory, though eventually superseded in detail, was pivotal. By recognizing the right answers and posing the right questions, he readied the path to relativity, quantum theory and the physics of today. Near the end of his own life, Albert Einstein penned Lorentz a memorable tribute: "For me personally he meant more than all the others I have met on my life's journey." —*Frank Wilczek*

*Wilczek, a professor of physics at the Massachusetts Institute of Technology, shared the 2004 Nobel Prize in Physics for his role in developing quantum chromodynamics, the theory of the strong nuclear interaction. His 2008 book,* The Lightness of Being *(Basic Books), points toward a unified theory of all fundamental forces.*



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DO THE MATH

# The Case of the Traveling Salesman

A seemingly unsolvable problem offers a glimpse at the limits of computation

**Is it hopeless** to try to compute the shortest route to visit a large number of cities? Not just a good route but the guaranteed shortest. The task is the long-standing challenge known as the traveling salesman problem, or TSP for short.

Finding a method that can quickly solve every example of the TSP would be a stunning breakthrough in mathematics. Using complexity theory, such a method would allow us to solve efficiently any computational problem for which answers can be easily verified. Most mathematicians expect this to be impossible.

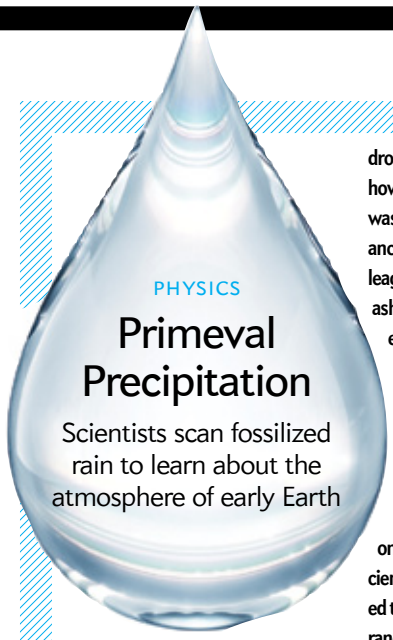
But suppose that you are handed the locations of 100,000 cities. Is it really impossible to find the shortest route? We are not asking for a solution to every instance of the TSP, just the quickest way around these specific locations.

To take up the challenge, your best bet is to follow Yogi Berra's advice: "When you come to a fork in the road, take it." A tool called linear programming allows us to do just that by assigning fractions to roads that join pairs of cities rather than deciding immediately whether to use a road or not. In this model, it is perfectly fine to send half a salesman along both branches of the fork. The process begins with the requirement that, for every city, the fractions assigned to the arriving and departing roads each sum to 1. Then, step by step, further restrictions are added, each involving sums of fractions assigned to roads. Linear programming eventually points us to the best decision for each road and thus the shortest possible route.

I should add that 100,000 cities is not a hypothetical challenge. Current computations are zeroing in on the solution to a pretty set of 100,000 points created by Robert Bosch of Oberlin College, where the tour traces out a drawing of the *Mona Lisa*. We may not be able to knock off every example of the TSP, but new ideas can push the frontiers of solvability.

Here is the big picture: complexity theory suggests there are limits to the power of general computational techniques in science and elsewhere. What are these limits and how widely do they constrain our quest for knowledge? That is what research into the TSP is all about. —*William J. Cook*

*Cook, a professor at the Georgia Institute of Technology, is author of* In Pursuit of the Traveling Salesman: Mathematics at the Limits of Computation *(Princeton University Press, 2012).*



PHYSICS

## Primeval Precipitation

Scientists scan fossilized rain to learn about the atmosphere of early Earth

**Some 2.7 billion years ago,** in what is now Omdraaisvlei farm near Prieska, South Africa, a brief storm dropped rain on a layer of ash from a recent volcanic eruption. The raindrops, which formed tiny craters, were buried by more ash and, over aeons, that ash hardened into rock. Closer to the present, other rainstorms eroded the rock, exposing a fossil record of raindrops from the Archean era. Researchers are now studying these fossilized raindrops to learn more about early Earth's atmosphere.

By using lasers to scan the craters—and comparing the indentations with those created today—astrobiologist Sanjoy Som of the NASA Ames Research Center and his colleagues have derived a measurement of the pressure exerted by the early atmosphere. The scientists reported online March 28 in *Nature* that the ancient air may have been less dense than the present-day atmosphere.

The key to that determination is raindrop size. Back in 1851 pioneering geologist Charles Lyell suggested that measuring the fossilized indentations of raindrops might reveal details about the ancient atmosphere. The atmosphere drags on each drop, constraining the speed of its descent based on its size. If one could determine an ancient raindrop's size, one could determine how thick the atmosphere likely was. To figure out the size of the ancient droplets, Som and his colleagues got creative. They collected ash from the 2010 Eyjafjallajökull eruption in Iceland, as well as from Hawaii, and released various-size droplets from 27 meters above it. They then turned these modern craters to "rock" by using hair spray and low-viscosity liquid urethane plastic. Based on comparisons between the ancient and new craters, they concluded that the size of ancient droplets ranged from 3.8 to 5.3 millimeters.

Plugging those numbers into the mathematical relations among raindrop size, speed and atmospheric density suggests that the early Earth's atmosphere probably exerted the same or as little as half the present pressure.

This finding sheds light on yet another early Earth mystery known as the "faint young sun" paradox: billions of years ago the sun emitted less radiation and therefore heated the planet less, yet the fossil record suggests that the climate was warm. But if the atmosphere was no denser than it is now how did it hold so much heat? The simplest explanation is that Earth boasted an atmosphere rich with greenhouse gases able to trap a large amount of heat per molecule. Those gases likely originated from volcanoes and microbial life. "The sky was probably hazy" from these gases, Som says.

Consistent with this scenario, research published online March 18 in *Nature Geoscience* suggests that the early atmosphere cycled through periods of a "hydrocarbon haze" that included potent greenhouse gases like methane. Such a haze—potentially being re-created today—helped to trap the young sun's heat, making life comfortable for microbes—and may offer a signal of life on other planets as well.

—*David Biello*

ISTOCKPHOTO (*raindrop*)



COMMENT AT ScientificAmerican.com/jun2012

TECHNOLOGY

# Go with the Flow

## A new app and Web site may make it easier to predict storm surges

COURTESY OF PROGRAM FOR THE STUDY OF DEVELOPED SHORELINES, WESTERN CAROLINA UNIVERSITY AND WCU MOBILE APP DEVELOPMENT TEAM (*screenshot*); MUTLU KURTBAS (*Stockphoto (iPhone)*; ANGELA COPPOLA *Corbis (bald head)*

**Researchers have had** a notoriously difficult time predicting how much flooding a given area will experience in the wake of a storm. Now a team led by researchers at Western Carolina University has developed a Web site and smartphone app that may help. The scientists gathered storm-surge data going back 65 years at more than 3,400 sites along the Atlantic and Gulf coasts and are making it available just in time for the June 1 start of the Atlantic hurricane season (see http://stormsurge.wcu.edu). Users can enter a zip code and view a map that shows all high-water measurements made in that area. Also shown are the paths of the hurricanes that caused those floods, along with other aspects that most likely influenced storm-surge height, including wind speed and barometric pressure.

The database, which the researchers continue to compile, will ultimately be maintained and archived at NOAA's National Climatic Data Center. Detailed analyses of this information may lead to a better understanding of the nonstorm-related factors that influence surges, including the slope of the seafloor immediately offshore, says Katie McDowell Peek, a member of the Western Carolina team. And scientists may be better able to forecast a storm's effects by comparing its projected path and strength with those of hurricanes that previously struck the coast.

*—Sid Perkins*

DERMATOLOGY

# It's Not "Like Growing Grass"

## Progress may seem slow, but new treatments for hair loss are under way

**More than 40 percent of men** in the U.S. will show signs of male-pattern baldness sometime between the ages of 18 and 49. But studies looking at the genomes of this group of men have failed to turn up a genetic cause, which makes a true cure seem an unlikely prospect.

Treatments for male-pattern baldness, also known as androgenic alopecia, may be forthcoming, however. Recent work is homing in on three types, including one that was reported in March in the journal *Science*. In the new paper, George Cotsarelis of the University of Pennsylvania and his team found that a compound known as prostaglandin $D_2$ ($PD_2$) was elevated in the blood of men with male-pattern baldness. When they blocked $PD_2$ receptors in mice, they ensured that the hair did not stop growing. Those blockers could be applied topically, Cotsarelis says.

He is also working on growing new hair. Researchers have noticed that if you wound a mouse, the animal generates new hair follicles as part of the healing process. The new follicles come from skin cells that turn into hair follicles through what is called the *Wnt*-mediated signaling pathway. It is the same pathway that helps you generate new hairs naturally as they fall out. Cotsarelis is working with a company to replicate that process.

A third approach, called follicular neogenesis, would allow doctors to remove, multiply and then reimplant the stem cells found inside a person's hair follicles. So far, though, when researchers remove the stem cells and culture them, the cells appear to "forget" they were ever hair cells. Researchers are now attempting to figure out how to restore their "memory."

As scientists continue to search for treatments to androgenic alopecia, they recommend patience. "People think of it like growing grass or something, but it's nothing like that," Cotsarelis says. "It's like trying to treat cancer; it's a complicated process." *—Rose Eveleth*

## *Best of the Blogs*

BIOLOGY

# Lice Don't Lie

### Parasites give clues to lemurs' social lives

**ITCHY?** A mouse lemur from Madagascar

**Weighing in** at only 40 grams, brown mouse lemurs are one of the smallest species of primate in the world. Their diminutive size, as well as their nocturnal, tree-dwelling lifestyle, makes them difficult to track and observe. Sarah Zohdy, then a graduate student at the University of Helsinki in Finland, and her colleagues came up with an ingenious way to study the interactions of these small lemurs: they followed their lice.

Scientists have estimated that lice originated at least 130 million years ago, when they fed off feathered dinosaurs, although they now live on just about all species of birds and mammals. They tend to be very host-specific, meaning they only live and feed on one species or a set of closely related species. And for lice to reproduce and spread, their hosts have to be in fairly close contact (like, as many parents know, kids in a kindergarten classroom). In wild species, lice rarely switch hosts unless the animals interact physically, whether through wrestling, nesting together or mating.

Zohdy and her colleagues had been studying lemurs in Madagascar, using traps to monitor their movement. The team tagged *Lemurpediculus verruculosus,* a species of lice that is specific to the brown mouse lemur, with a unique color code using nail polish. Over time the researchers continued to trap lemurs and look at their lice to see if any of the tagged ones had switched hosts.

They documented 76 transfers among 14 animals—all males—over the course of a month, which happened to be during the breeding season. The researchers hypothesized that the male-only transfers most likely occurred during fights over females. But perhaps more interestingly, the lice data found 13 new social interactions that the traps had failed to predict. Among these was the finding that lemurs travel more than had been thought: some lice transfers occurred between lemurs that had last been trapped more than 600 meters apart.

This is not the first study that used lice to look at a bigger scientific picture, but it is one of the first to use lice to study behavior in a living wild species. The team hopes its work shows the usefulness of this technique. —*Christie Wilcox*

*Adapted from the Science Sushi blog at blogs.ScientificAmerican.com/science-sushi*

BOTANY

# Beautiful Mutants

### Researchers discover the genetic secret behind van Gogh's famous sunflowers

**The word "sunflower" brings to mind a mane of vibrant yellow petals encircling a dark whorl of seeds. But not all sunflowers are alike. Some sunflowers have scraggly petals, for instance, or small centers. Many of the sunflowers Vincent van Gogh depicted in his famous series of oil paintings look rather unusual—they sport woolly, chrysanthemumlike blooms. Now scientists have pinpointed the genetic mutation responsible for these strange sunflowers' abundance of small yellow petals.**

**Van Gogh's paintings from the late 1880s clearly feature some typical sunflowers, but they are paired with what look like fuzzy pom-poms stuck on sunflower stems. Such double-flowered sunflowers, as they are known, have overlapping rows of supple yellow petals and a small, sometimes hidden, center. In a new study, John Burke of the University of Georgia and his co-workers traced the unusual floral arrangement of van Gogh's sunflowers to mutations of a single critical gene. The findings appear in the March 29 *PLoS Genetics.***

**Burke and his colleagues worked with typical sunflowers as well as double-flowered cultivars, such as the teddy bear sunflower, which looks like a giant dandelion. By crossing different varieties of sunflowers with one another and crossing their offspring with themselves, the researchers discovered that double-flowered cultivars have mutated forms of a gene called *HaCYC2c*.**

**For thousands of years people have been growing sunflowers for their seeds, oil and beauty. The first double-flowered sunflowers probably arose naturally as the result of a chance mutation. Breeders very likely seized the opportunity to preserve the mutants' unique qualities and offer customers a new kind of sunflower. Apparently van Gogh was one such customer.**

**—*Ferris Jabr***

***Adapted from the Observations staff blog at blogs.ScientificAmerican.com/observations***

MITSUYOSHI TATEMATSU *Minden Pictures*



COMMENT AT ScientificAmerican.com/jun2012

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**Philip T. B. Starks** is an associate professor of animal behavior at Tufts University. Every fall he teaches a Darwinian medicine class that explores the evolutionary reasons people are susceptible to diseases.

**Brittany L. Slabach** will be a Ph.D. student in the University of Kentucky's department of biology starting in August. While earning her M.S. in biology at Tufts University, she and Starks discovered a mutual fascination with geophagia.

# The Scoop on Eating Dirt

## New findings suggest that ingesting soil is adaptive, not necessarily pathological

THOMAS JACKSON *Getty Images*

**In the fall of 2009** a group of biology students at Tufts University sat down together and ate some dirt. They ground up small clay tablets and swallowed the powder to find out, firsthand, what clay tastes like. This unusual taste test was part of a Darwinian medicine class taught by one of us (Starks). The students were studying the evolution of geophagia—the practice of eating dirt, especially claylike soils, which is something animals and people have been doing for millennia.

The standard reference guide for psychiatrists—the fourth edition of the *Diagnostic and Statistical Manual for Mental Disorders* (*DSM-IV*)—classifies geophagia as a subtype of pica, an eating disorder in which people consume things that are not food, such as cigarette ash and paint chips. But as the students would learn, studies of animals and human cultures suggest that geophagia is not necessarily abnormal—in fact, it may well be adaptive. Researchers are taking another look at dirt eating and discovering that the behavior often provides people and animals with vital minerals and inactivates toxins from food and the environment.

### EVOLUTIONARY APPROACH

ONE WAY TO DECIDE whether geophagia is abnormal or adaptive is to determine how common the behavior is in animals and across human societies. If many different species and cultures demonstrate the same behavior, then it is probably beneficial in some way.

Today it is clear that geophagia is even more widespread in the animal kingdom than previously thought. Investigators have observed geophagia in more than 200 species of animals, including parrots, deer, elephants, bats, rabbits, baboons, gorillas and chimpanzees. Geophagia is also well documented in humans, with records dating to at least the time of Greek physician Hippocrates (460 B.C.). The Mesopotamians and ancient Egyptians used clay medicinally: they plastered wounds with mud and ate dirt to treat various ailments, especially of the gut. Some indigenous peoples in the Americas used dirt as a spice and prepared naturally bitter foods such as acorns and potatoes with a little clay to counteract the acerbic taste. Geophagia was a frequent practice in Europe until the 19th century, and some societies, such as the Tiv tribe of Nigeria, still rely on cravings for dirt as a sign of pregnancy.

A common explanation for why animals and people eat dirt is that soil contains minerals, such as calcium, sodium and iron, which support energy production and other vital biological processes. The fact that an animal's need for these minerals changes with the seasons, with age and with overall health may explain why geophagia is especially common when an animal's diet does not provide enough minerals or when the challenges of the environment demand extra energy. Mountain gorillas and African buffalo that live at high altitudes may, for example, ingest earth as a source of iron that promotes red blood cell development. Elephants, gorillas and bats eat sodium-rich clays when they do not get enough sodium in their diet. One elephant population is known to continually visit underground caves where the animals dig up and eat salt-enriched rock.

Among human populations in Africa, those who have ready access to calcium do not practice geophagia as often as those deprived of calcium. The need for calcium may also partly explain

why geophagia is most commonly associated with pregnancy: a mother needs extra calcium as the fetal skeleton develops.

Mineral acquisition does not fully explain geophagia, though. In an extensive review paper published in the 2011 *Quarterly Review of Biology,* Sera L. Young of Cornell University and her colleagues conclude that eating earth rarely adds significant amounts of minerals to one's diet and, in many cases, interferes with the absorption of digested food from the gut into the bloodstream, sometimes resulting in nutrient deficiency.

If animals and people are not getting much in the way of dietary minerals from dirt, what is the benefit of geophagia? A second explanation—that eating dirt is often a form of detoxification—is gaining credence.

## DIRT DETOX

THE IDEA THAT, IN MOST CASES, eating dirt is probably a way to get rid of toxins could explain why people and animals so often prefer claylike soils to other kinds of earth. Negatively charged clay molecules easily bind to positively charged toxins in the stomach and gut—preventing those toxins from entering the bloodstream by ferrying them through the intestines and out of the body in feces. Detoxification might also explain why some indigenous peoples prepare meals of potatoes and acorns with clay—these foods are bitter because they contain small amounts of toxins.

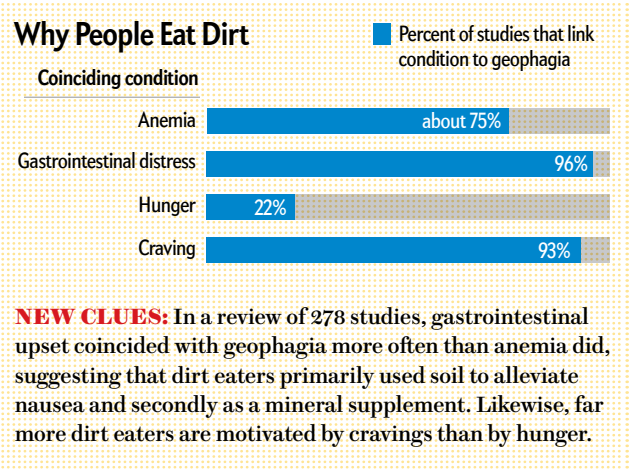
In the 1990s James Gilardi, executive director of the World Parrot Trust, found support for the detoxification hypothesis in one of the few experimental studies on geophagia. While observing a flock of Peruvian parrots foraging on a particular band of exposed soil along the Manu River, Gilardi noticed that the birds neglected nearby stretches of soil with far more minerals. He surmised that the parrots were not ingesting soil for minerals but rather to counteract toxic alkaloids in the seeds and unripe fruit that make up a large part of their diet. Toxins prevalent in plants (and meats) often irritate the gut. To test this idea, Gilardi fed some parrots the toxic alkaloid quinidine with and without their preferred dirt and measured how much alkaloid made it into the birds' blood after the meal. Birds that did not consume the soil had higher levels of quinidine in their blood, whereas a side dish of dirt reduced quinidine levels in the blood by 60 percent. Researchers have shown the same benefit in chimpanzees and baboons that supplement their diets with clay.

Further evidence of dirt detox comes from studies of bats. A 2011 study in *PLoS ONE* asked whether Amazonian bats visit clay licks—cliff sides of exposed clay—for nutrition or detoxification. Christian Voigt of the Leibniz Institute for Zoo and Wildlife Research in Berlin and his colleagues captured bats of two different species: one that eats mostly fruit and one that eats mostly insects. If the bats were eating clay for minerals, Voigt predicted, he would find fewer fruit-eating bats at the clay licks because fruits have more dietary minerals than insects. But most of the bats he captured at the clay lick were fruit-eating bats—and many of them were pregnant or lactating. Voigt concluded that the pregnant fruit bats visited the clay licks to detox because they were eating twice as much to feed their babies, which meant twice the dose of plant toxins from unripe fruits, seeds and leaves.

Like bats, pregnant women may also eat dirt for its detoxifying properties, in addition to using dirt as a supplemental source of minerals. The first trimester of pregnancy plagues many women with nausea and vomiting, and cross-cultural studies document geophagia early in pregnancies in response to morning sickness. Women in sub-Saharan nations and in the southern U.S. have reported that they consume clay to alleviate this discomfort. Some researchers have proposed that morning sickness purges the mother of toxins that might harm the fetus. Perhaps geophagia and morning sickness work together to protect the developing fetus. Because clay can bind bacteria and viruses, it may also protect both mother and fetus from food-borne pathogens such as *Escherichia coli* and *Vibrio cholerae*.

Although the scientific community has only recently accumulated enough evidence to argue that geophagia is an adaptive behavior, people—and not just pregnant women—have used clay minerals as remedies for nausea, vomiting and diarrhea for thousands of years. In the age of modern medicine, pharmaceutical companies harnessed the binding properties of kaolin, a clay mineral, to produce Kaopectate, a drug that treats diarrhea and other digestive issues. Eventually the synthetic chemical bismuth subsalicylate—also the key ingredient in Pepto-Bismol—replaced kaolin, but the clay is still used today in other ways. Kaolin and smectite bind not only harmful toxins but also pathogens. Ranchers use clay when preparing livestock feed to inhibit toxin transmission, and some researchers have proposed harnessing clay's pathogen-binding talents to purify water.

Of course, ingesting dirt can also be poisonous. Along with minerals and detoxifying materials, you might unintentionally ingest bacteria, viruses, parasitic worms, and dangerous amounts of lead or arsenic. Because of these risks, modern dirt eaters should stick with safe commercial products that have been heated or otherwise sterilized—but they should not be stigmatized for their behavior. Taken as a whole, the evidence argues that geophagia, in many cases, is not a sign of mental illness. It is a specific defense that has evolved to combat toxins and, possibly, ease mineral deficiencies. Although you may not be thinking about geophagia when you take vitamins or seek comfort from a swig of Kaopectate, you are in fact participating in the age-old practice of eating dirt. SA




**NEW CLUES: In a review of 278 studies, gastrointestinal upset coincided with geophagia more often than anemia did, suggesting that dirt eaters primarily used soil to alleviate nausea and secondly as a mineral supplement. Likewise, far more dirt eaters are motivated by cravings than by hunger.**

SOURCE: "WHY ON EARTH?: EVALUATING HYPOTHESES ABOUT THE PHYSIOLOGICAL FUNCTIONS OF HUMAN GEOPHAGY," BY SERA L. YOUNG ET AL., IN *QUARTERLY REVIEW OF BIOLOGY*, VOL. 86, NO. 2, JUNE 2011

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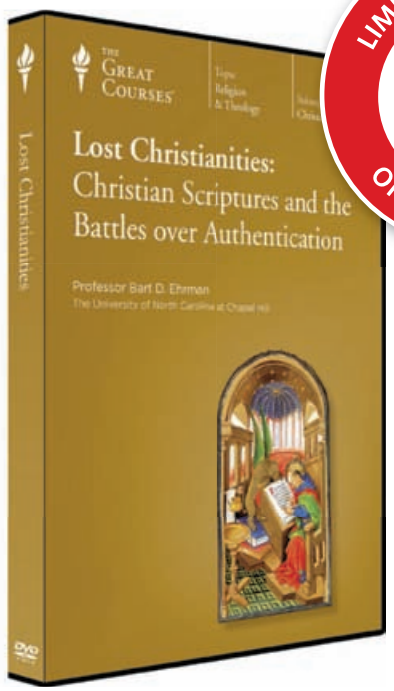


# How Has Christianity Changed over 2,000 Years?

In the first centuries after Christ, there was no "official" New Testament. Instead, early Christians read and fervently followed a wide variety of scriptures—many more than we have today.

Relying on these writings, Christians held beliefs that today would be considered bizarre. Some believed that there were 2, 12, or as many as 30 gods. Some thought that a malicious deity, rather than the true God, created the world. Some maintained that Christ's death and resurrection had nothing to do with salvation while others insisted that Christ never really died at all.

What did these "other" scriptures say? Do they exist today? How could such outlandish ideas ever be considered Christian? If such beliefs were once common, why do they no longer exist? These are just a few of the many provocative questions that arise from **Lost Christianities: Christian Scriptures and the Battles over Authentication**, an insightful 24-lecture course taught by Professor Bart D. Ehrman, the Chair of the Department of Religious Studies at the University of North Carolina at Chapel Hill and the author and editor of 17 books, including *The New York Times* bestseller *Misquoting Jesus*.

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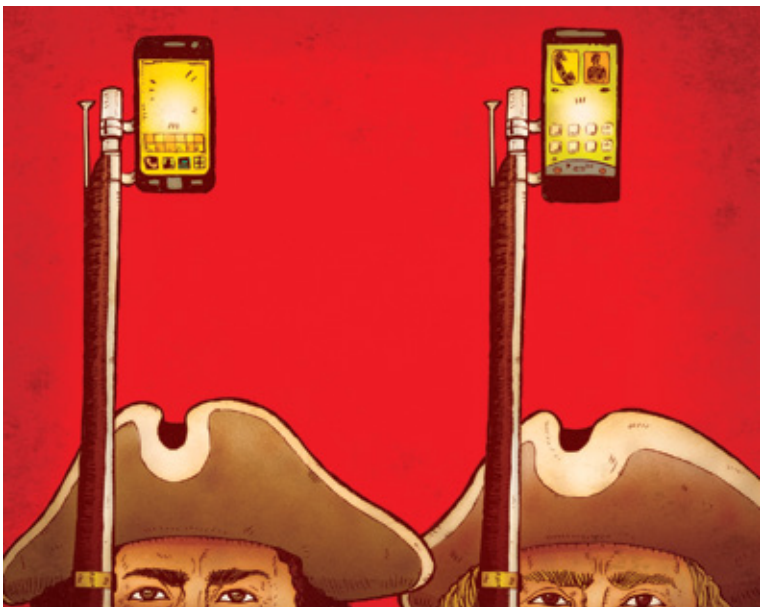
**David Pogue** is the personal-technology columnist for the *New York Times* and an Emmy Award–winning correspondent for *CBS News*.

# Down with Double Data Fees!

## And other proclamations that should be in a cell phone user's Bill of Rights



***We the People of the United States,*** *in Order to form a more perfect Lifestyle, establish Fairness, ensure blood pressure Tranquility, provide for the common Text Messager, promote less Outrage and secure Cell phone Service that's anywhere near as good as it is in Other Countries, do ordain and establish this Cellular Bill of Rights.*

**Article 1.** ***The Subsidy Repayment must end Sometime.***
The carriers (Verizon, AT&T, T-Mobile, Sprint) provide to us very inexpensive phones. We love getting a $650 iPhone 4S for $200!

But we get that handsome price only when we agree to a two-year contract. In other words, we're paying off the real price over two years of payments. The carriers are subsidizing the phones.

Which is a good system. Yet what happens once the subsidy has been repaid? After the two-year period, we're paying only for the service. Our monthly payment should therefore drop automatically.

**Article 2.** ***We need not Voicemail Instructions.***
When we leave a voicemail, we hear a greeting—then instructions. "To page this person, press 4. To leave a callback number, press 5. When you have finished recording, you may hang up."

The carriers say these instructions exist for the benefit of those who have never used voicemail (assuming they exist). The real reason for the instructions is, of course, to eat up our airtime and charge us more money. Verizon alone has 108 million customers. If they reach those infuriating messages twice a business day, they wind up paying Verizon about $1 billion a year.

Those pointless instructions should be optional.

**Article 3.** ***Text Messages being only Data, the Carriers should make them less Expensive.***
We can send all the e-mail we want, with no per-message charge—but we're still paying 20 cents for each text message. At that rate (20 cents per 160 characters), that's nearly $1,500 a megabyte.

Even if we sign up for unlimited texting, we're still paying way too much. Text messages should be included with our data plans.

**Article 4.** ***The People should decide how to Use the Data they've Bought.***
We can pay extra for tethering so that a laptop can get online wirelessly using our phone's data connection. It's great for anyone not in a Wi-Fi hotspot.

But we're already paying for a data plan. Why can't we use the data any way we want? Verizon's iPad plan has the right idea: you buy the data you need, and you can then tether several devices (via Wi-Fi) to get them online, too. It should work the same way with phone plans.

**Article 5.** ***We shall not be Double-Billed.***
When a person calls a friend, the carriers charge both of them. A 10-minute call costs 20 minutes. Isn't that called double billing?

Same thing with text messages. When I send you a text message, we're each charged for one message. How is that fair? In Europe, only the sender or the recipient pays. That's fair.

**Article 6.** ***International Calls should cost much Less.***
The carriers still charge us $2 or $5 a minute to make cell phone calls when we're out of the country. Hear me now, carrier people, we live in the age of Skype, iChat and Google Talk. We can make free calls from anywhere to anywhere on the Internet. How can you justify $5 a minute?

Listen: last year AT&T and Verizon alone made $14 billion in profits. How about sending us fewer bills for service—and more Bills of Rights? SA

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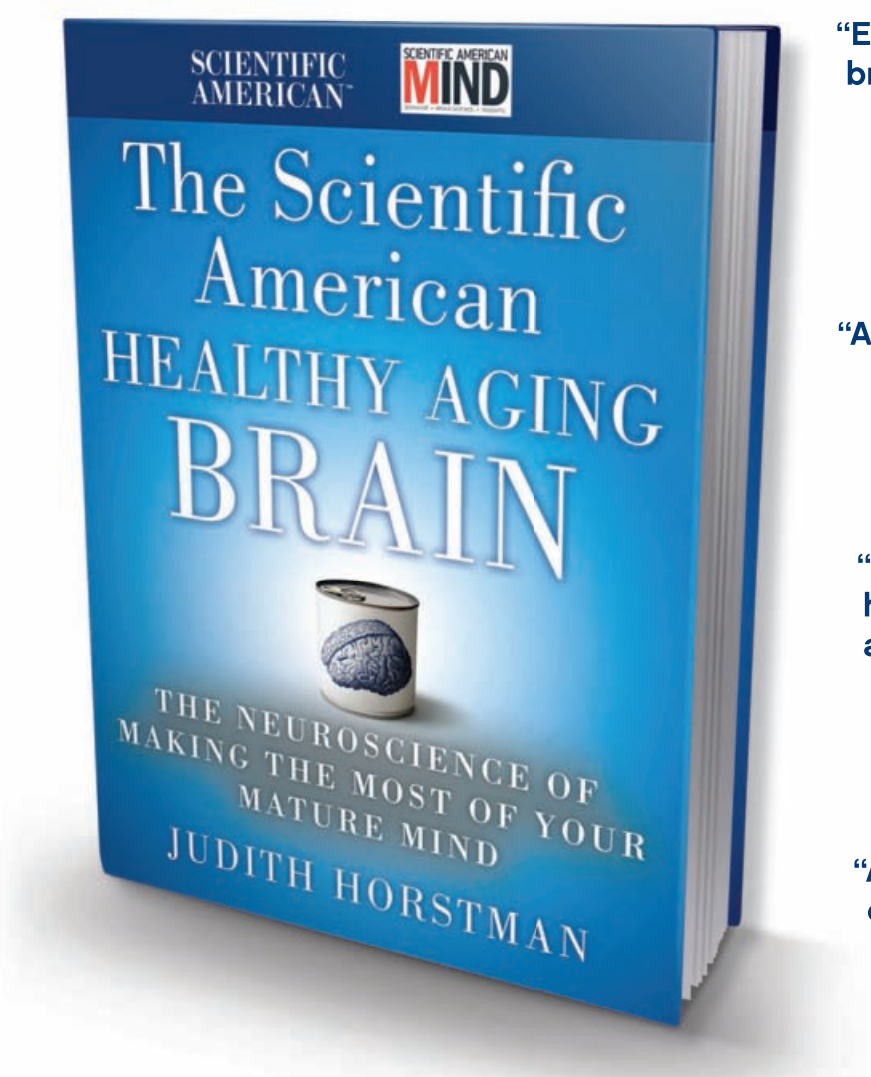
How to reclaim your voicemail: ScientificAmerican.com/jun2012/pogue



*Illustration by Brian Taylor*

# Discover why there's never been a better time, in all of history, to grow old.

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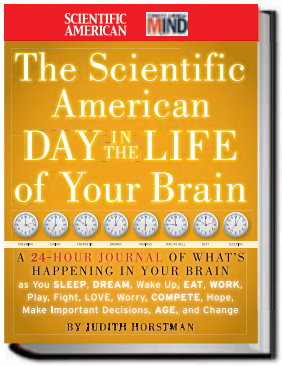


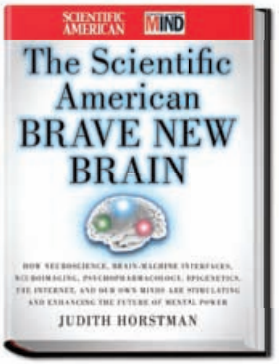


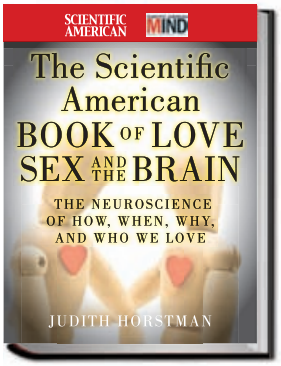


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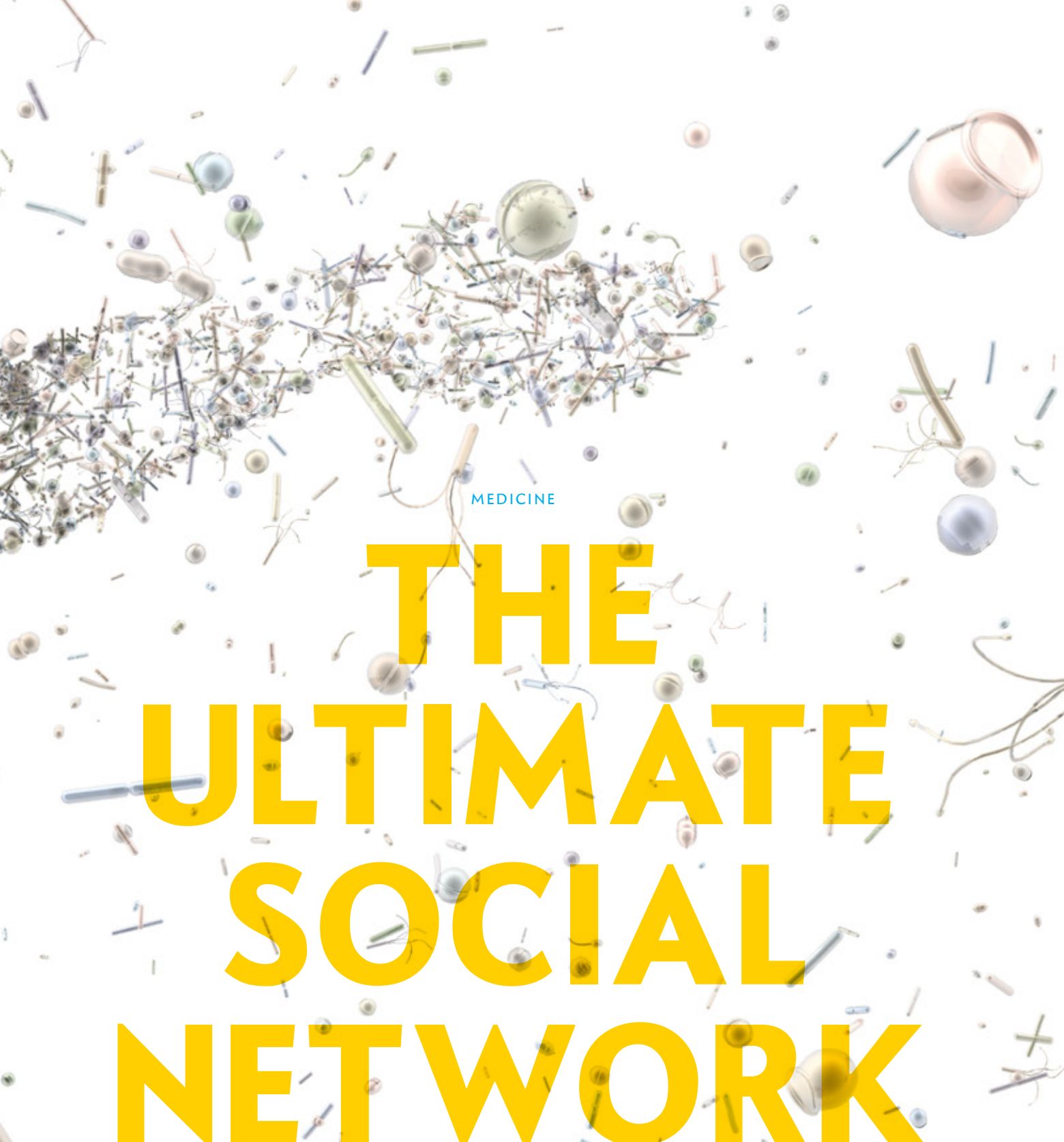


MEDICINE

# THE ULTIMATE SOCIAL NETWORK

Researchers who study the friendly bacteria that live inside all of us are starting to sort out who is in charge—microbes or people?

*By Jennifer Ackerman*

*Illustrations by Bryan Christie*

**Jennifer Ackerman** is an award-winning science writer and author of *Ah-Choo! The Uncommon Life of Your Common Cold* (Twelve, 2010). She is now writing a book about the intelligence of birds.

BIOLOGISTS ONCE THOUGHT THAT HUMAN BEINGS WERE physiological islands, entirely capable of regulating their own internal workings. Our bodies made all the enzymes needed for breaking down food and using its nutrients to power and repair our tissues and organs. Signals from our own tissues dictated body states such as hunger or satiety. The specialized cells of our immune system taught themselves how to recognize and attack dangerous microbes—pathogens—while at the same time sparing our own tissues.

Over the past 10 years or so, however, researchers have demonstrated that the human body is not such a neatly self-sufficient island after all. It is more like a complex ecosystem—a social network—containing trillions of bacteria and other microorganisms that inhabit our skin, genital areas, mouth and especially intestines. In fact, most of the cells in the human body are not human at all. Bacterial cells in the human body outnumber human cells 10 to one. Moreover, this mixed community of microbial cells and the genes they contain, collectively known as the microbiome, does not threaten us but offers vital help with basic physiological processes—from digestion to growth to self-defense.

So much for human autonomy.

Biologists have made good progress characterizing the most prevalent species of microbes in the body. More recently, they have begun to identify the specific effects of these residents. In so doing, they are gaining a new view of how our bodies function and why certain modern diseases, such as obesity and autoimmune disorders, are on the rise.

## OUT OF MANY, ONE

WHEN PEOPLE THINK of microbes in the body, they usually think of pathogens. Indeed, for a long time researchers focused solely on these harmful bugs and ignored the possible importance of more benign ones. The reason, argues biologist Sarkis K. Mazmanian of the California Institute of Technology, is our skewed view of the world. "Our narcissism held us back; we tended to think we had all the functions required for our health," he says. "But just because microbes are foreign, just because we acquire them throughout life, doesn't mean they're any less a fundamental part of us."

Indeed, all humans have a microbiome from very early in life, even though they do not start out with one. Each individual acquires his or her own community of commensals (from the Latin for "sharing a table") from the surrounding environment. Because the womb does not normally contain bacteria, newborns begin life as sterile, singular beings. But as they pass through the birth canal, they pick up some of Mom's commensal cells, which then begin to multiply. Breast-feeding and handling by proud parents, grandparents, siblings, and friends—not to mention ordinary contact with bedsheets, blankets, and even pets—quickly contribute to an expanding ark of microbes. By late infancy our bodies support one of the most complex microbial ecosystems on the planet.

For the past five years or so scientists have been working to characterize the nature of this ecosystem. The task has been devilishly difficult. The bacterial cells in the intestines, for example, have evolved to grow in the crowded, oxygen-free environment of the gut, so many species do not survive well in the lonely expanse of a petri dish. Researchers have gotten around this problem, however, by studying the genetic instructions, the strands of DNA and RNA, found within a microbe rather than the whole cell itself. Because DNA and RNA can be manipulated in a normal, oxygenated laboratory environment, investigators can take microbial samples from the body, extract the genomic material and analyze the results.

Each species of commensal bacteria has a signature, it turns out—its own unique version of a gene (known as the 16S ribo-

### IN BRIEF

**Bacterial cells** in the body outnumber human cells by a factor of 10 to 1. Yet only recently have researchers begun to elucidate the beneficial roles these microbes play in fostering health.

**Some of these bacteria** possess genes that encode for beneficial compounds that the body cannot make on its own. Other bacteria seem to train the body not to overreact to outside threats.

**Advances in computing** and gene sequencing are allowing investigators to create a detailed catalogue of all the bacterial genes that make up this so-called microbiome.

**Unfortunately**, the inadvertent destruction of beneficial microbes by the use of antibiotics, among other things, may be leading to an increase in autoimmune disorders and obesity.

SOURCE: ELINOR ACKERMAN

somal RNA gene) that codes for a particular RNA molecule found in the ribosomes, the protein-making machinery of cells. By determining the sequence of this gene, scientists are creating a catalogue of the entire human microbiome. In this way, they can glean which species exist in our bodies and how the precise combination of species may differ from one person to another.

The next step is to analyze other genes found in the microbial community to determine which ones are active in people and what functions they perform. Again, that chore is a tall order because of the great number of species and because their genes get mixed together in the extraction process. Determining whether a specific bacterial gene is active (or expressed) in the body is relatively straightforward; figuring out to which species that particular gene belongs is not. Fortunately, the development of ever more powerful computers and ultrafast gene sequencers in the first decade of the 21st century has turned what would once have been an impossible task of sorting and analysis into merely a very complicated one.

Two separate groups of scientists, one in the U.S. and the other in Europe, have harnessed this new technology to enumerate the bacterial genes within the human body. In early 2010 the European group published its census of microbial genes in the human digestive system—3.3 million genes (from more than 1,000 species)—about 150 times the 20,000 to 25,000 genes in the human genome.

Research into the nature of the human microbiome has yielded many surprises: no two people share the same microbial makeup, for instance—even identical twins. This finding may help unravel a mystery presented by the Human Genome Project, which confirmed that the human DNA of all people the world over is 99.9 percent alike. Our individual fates, health and perhaps even some of our actions may have much more to do with the variation in the genes found in our microbiome than in our own genes. And although the microbiomes of different people vary markedly in the relative number and types of species they contain, most people share a core complement of helpful bacterial genes, which may derive from different species. Even the most beneficial bacteria can cause serious illness, however, if they wind up somewhere they are not supposed to be—for example, in the blood (causing sepsis) or in the web of tissue between the abdominal organs (causing peritonitis).

### FRIENDS WITH BENEFITS

THE FIRST INKLING that beneficial bugs might do us good came decades ago during research on digestion and the production of vitamins in the guts of animals. By the 1980s investigators had learned that human tissue needs vitamin $B_{12}$ for, among other things, cellular energy production, DNA synthesis and the manufacture of fatty acids and had determined that only bacteria synthesize the enzymes needed to make the vitamin from scratch. Similarly, scientists have known for years that gut bacteria break down certain components of food that would otherwise be indigestible and would pass out of the body unused. Only in the past few years, however, have they learned the juicy details: two commensal species in particular play major roles in both digestion and the regulation of appetite.

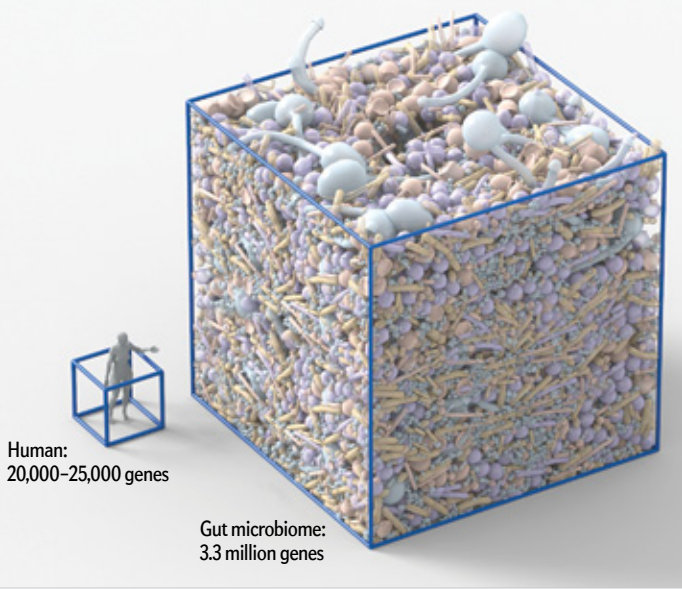
Perhaps the prime example of a helpful bug sounds like it was named after a Greek sorority or fraternity. *Bacteroides thetaiotaomicron* is a champion carbohydrate chomper, capable of breaking down the large, complex carbohydrates found in many plant foods into glucose and other small, simple, easily digestible sugars. The human genome lacks most of the genes required to make the enzymes that degrade these complex carbohydrates. *B. thetaiotaomicron,* on the other hand, has genes that code for more than 260 enzymes capable of digesting plant matter, thus providing humans with a way to efficiently extract nutrients from oranges, apples, potatoes and wheat germ, among other foods.

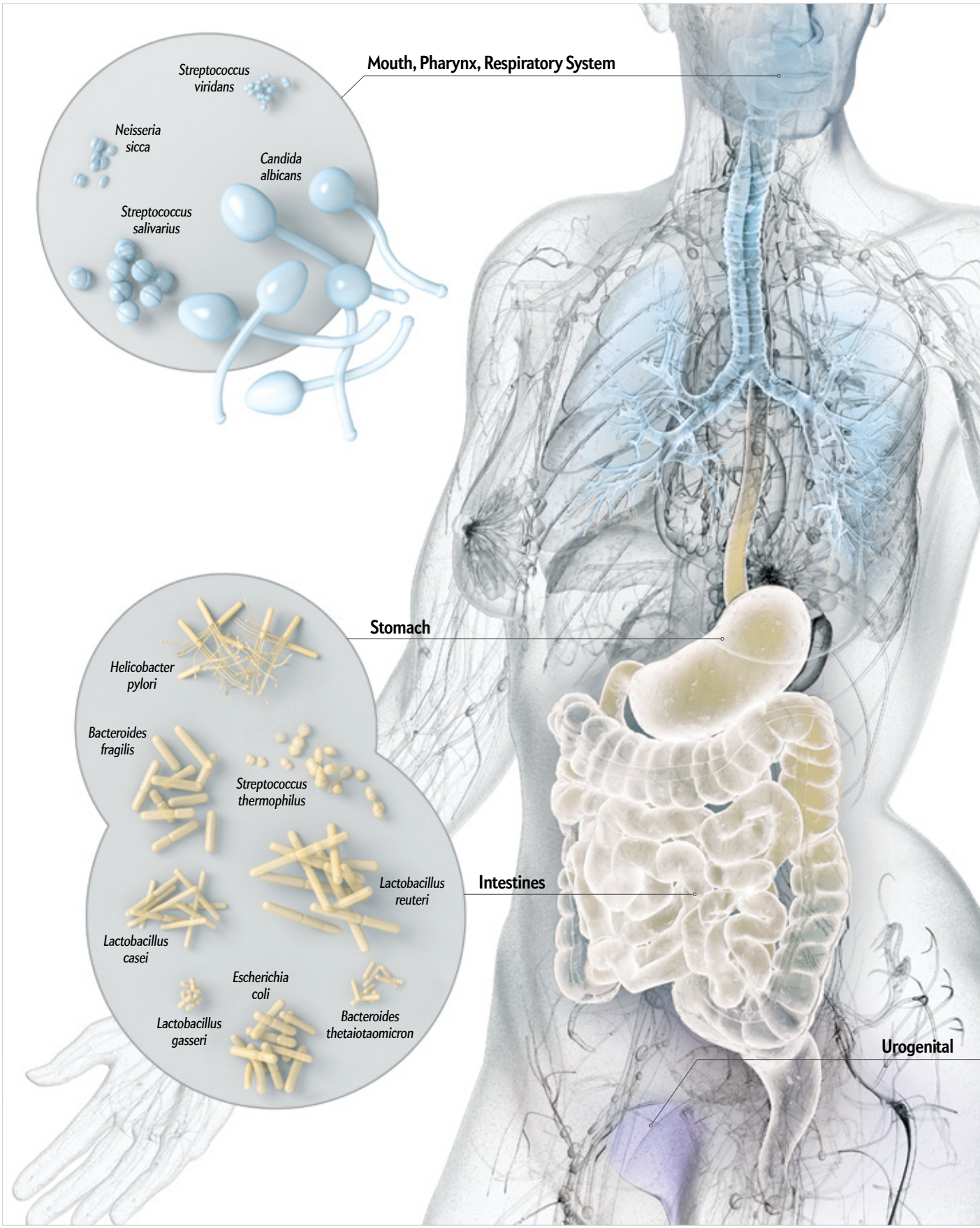
Fascinating details about how *B. thetaiotaomicron* interacts with, and provides sustenance to, its hosts come from studies of mice raised in a completely sterile environment (so they had no microbiome) and then exposed only to this particular strain of microbes. In 2005 researchers at Washington University in St. Louis reported that *B. thetaiotaomicron* survives by consuming complex carbohydrates known as polysaccharides. The bacteria ferment these substances, generating short-chain fatty acids (essentially their feces) that the mice can use as fuel. In this way, bacteria salvage calories from normally indigestible forms of carbohydrate, such as the dietary fiber in oat bran. (Indeed, rodents that are completely devoid of bacteria have to eat 30 per-

MORE THAN HUMAN

## Buddy, Can You Spare a Gene?

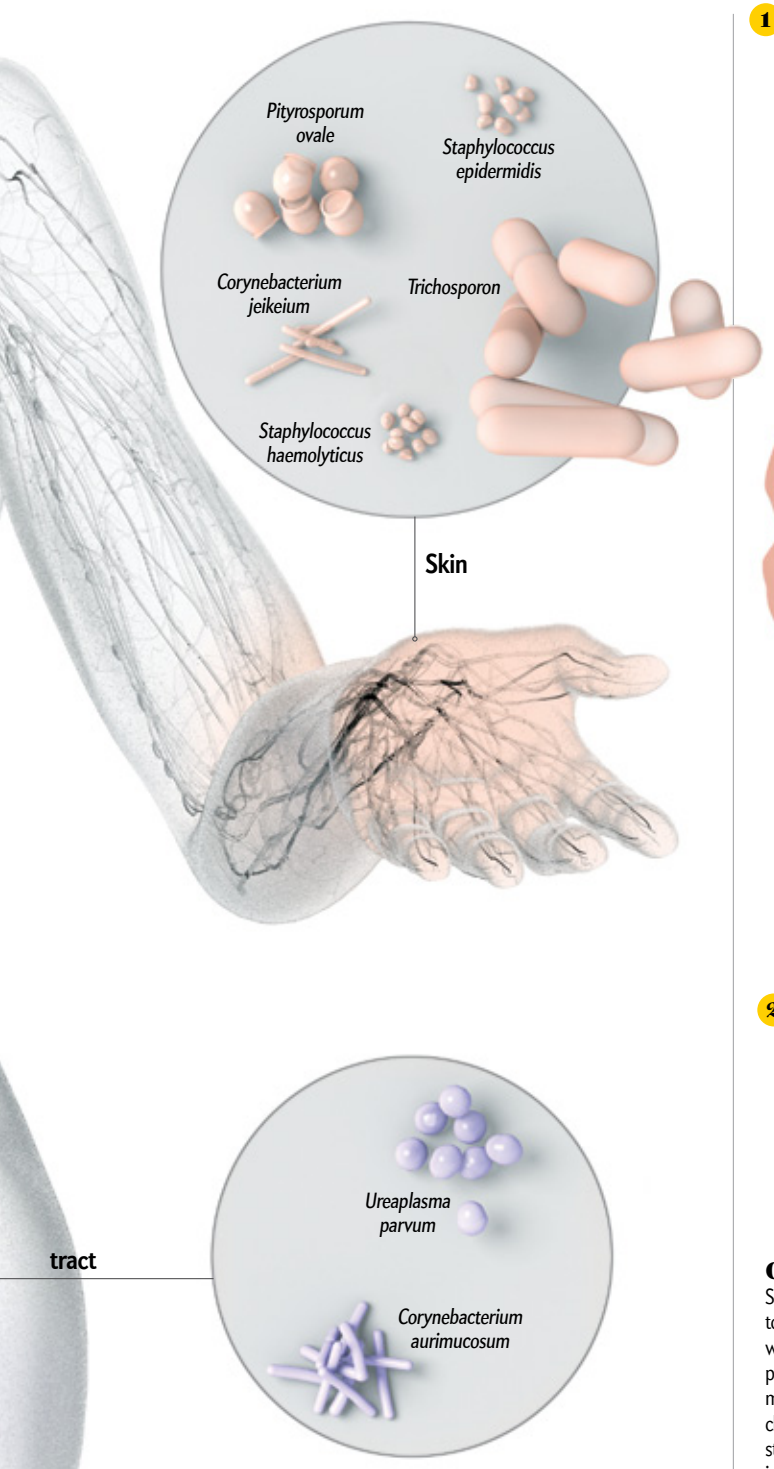
**Helping hands:** The number of genes distributed among the friendly bacteria that live inside people's bodies and on their skin far outnumbers the number of genes we inherit from our parents. Researchers are figuring out in greater detail which of these microbial genes benefit their human hosts and how.



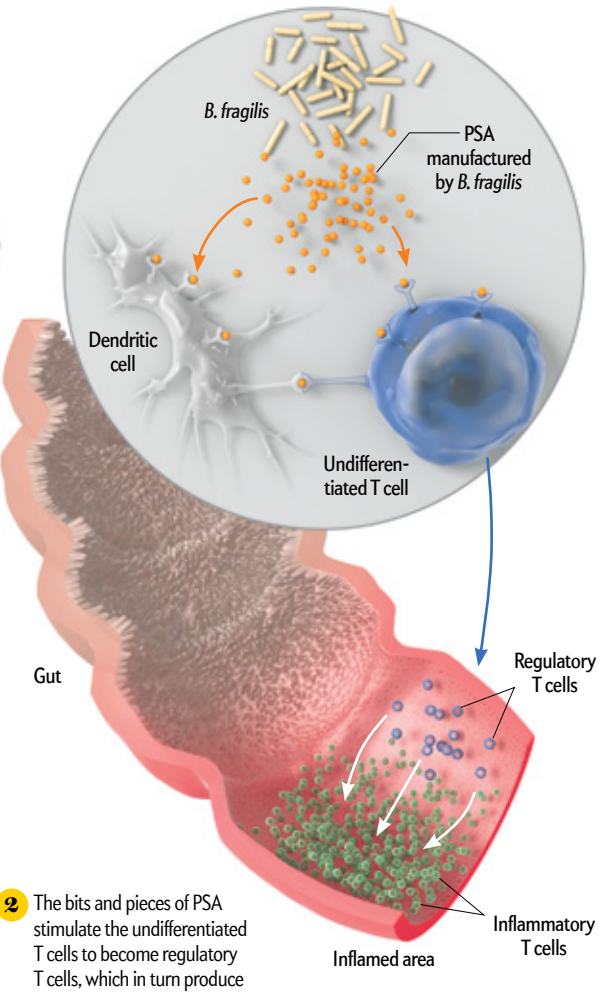


# Different Species for Different Reasons

**Various types of microbes** congregate everywhere in and on the human body. Their presence maintains their host's health in part by making it hard for disease-causing germs to gain access to the body. Several species, such as *Bacteroides fragilis,* also perform specific useful functions, including aiding in the development and regulation of the immune system (*below, right*).




**1** Immune cells called dendritic cells pick up a molecule called polysaccharide A (PSA) from the *B. fragilis* cells and present it to undifferentiated T cells.




**2** The bits and pieces of PSA stimulate the undifferentiated T cells to become regulatory T cells, which in turn produce substances that tamp down the aggressive efforts of inflammatory T cells.

## Case Study: How One Bacterial Species Helps

Studies on mice raised in sterile conditions reveal that *B. fragilis* bacteria are crucial to maintaining the health of the intestines. In one experiment, germ-free mice that were given a strain of *B. fragilis* bacteria that produced the complex carbohydrate polysaccharide A did not develop inflammation of the intestine (colitis), whereas mice that were given a strain of *B. fragilis* bacteria that did not make PSA developed chronic inflammation of the gut. Investigators showed that the presence of PSA stimulated the development of regulatory T cells that in turn switched off the inflammatory T cells, thereby restoring health.

SOURCE: "INSIDE THE MICROBIAL AND IMMUNE LABYRINTH: GUT MICROBES: FRIENDS OR FIENDS?" BY WARREN STROBER. IN *NATURE MEDICINE*, VOL. 16; 2010 (*B. fragilis case study*)

cent more calories than do rodents with an intact microbiome to gain the same amount of weight.)

The study of the microbiome has even partially rehabilitated the reputation of one disease-causing bacterium called *Helicobacter pylori*. Fingered by Australian physicians Barry Marshall and Robin Warren in the 1980s as the causative agent of peptic ulcers, *H. pylori* is one of the few bacteria that seem to thrive in the acidic environment of the stomach. While continued use of medicines known as nonsteroidal anti-inflammatory drugs, or NSAIDs, had long been known to be a common cause of peptic ulcers, the finding that bacteria contributed to the condition was remarkable news. After Marshall's discovery, it became standard practice to treat peptic ulcers with antibiotics. As a result, the rate of *H. pylori*–induced ulcers has dropped by more than 50 percent.

Yet the matter is not so simple, says Martin Blaser, now a professor of internal medicine and microbiology at New York University who has studied *H. pylori* for the past 25 years. "Like everyone, I started working on *H. pylori* as a simple pathogen," he says. "It took a few years for me to realize that it was actually a commensal." In 1998 Blaser and his colleagues published a study showing that in most people, *H. pylori* benefits the body by helping to regulate levels of stomach acids, thus creating an environment that suits itself and its host. If the stomach churns out too much acid for the bacteria to thrive, for example, strains of the bug that contain a gene called *cagA* start producing proteins that signal the stomach to tone down the flow of acid. In susceptible people, however, *cagA* has an unwelcome side effect: provoking the ulcers that earned *H. pylori* its nasty rap.

A decade later Blaser published a study suggesting that *H. pylori* has another job besides regulating acid. For years scientists have known that the stomach produces two hormones involved in appetite: ghrelin, which tells the brain that the body needs to eat, and leptin, which—among other things—signals that the stomach is full and no more food is needed. "When you wake up in the morning and you're hungry, it's because your ghrelin levels are high," Blaser says. "The hormone is telling you to eat. After you eat breakfast, ghrelin goes down," which scientists refer to as a postprandial (from the Latin word *prandium,* for "a meal") decrease.

In a study published last year, Blaser and his colleagues looked at what happens to ghrelin levels before and after meals in people with and without *H. pylori*. The results were clear: "When you have *H. pylori,* you have a postprandial decrease in ghrelin. When you eradicate *H. pylori,* you lose that," he says. "What that means, a priori, is that *H. pylori* is involved in regulating ghrelin"—and thus appetite. How it does so is still largely a mystery. The study of 92 veterans showed that those treated with antibiotics to eliminate *H. pylori* gained more weight in comparison to their uninfected peers—possibly because their ghrelin level stayed elevated when it should have dropped, causing them to feel hungry longer and to eat too much.

Two or three generations ago more than 80 percent of Americans played host to the hardy bug. Now less than 6 percent of American children test positive for it. "We have a whole generation of children who are growing up without *H. pylori* to regulate their gastric ghrelin," Blaser says. Moreover, children who are repeatedly exposed to high doses of antibiotics are likely experiencing other changes in their microbial makeup. By the age of 15, most children in the U.S. have had multiple rounds of antibiotic treatment for a single ailment—otitis media, or ear infection. Blaser speculates that this widespread treatment of young children with antibiotics has caused alterations in the compositions of their intestinal microbiome and that this change may help explain rising levels of childhood obesity. He believes that the various bacteria within the microbiome may influence whether a certain class of the body's stem cells, which are relatively unspecialized, differentiate into fat, muscle or bone. Giving antibiotics so early in life and thereby eliminating certain microbial species, he argues, interferes with normal signaling, thereby causing overproduction of fat cells.

Could the accelerating loss of *H. pylori* and other bacteria from the human microbiome, along with societal trends—such as the easy availability of high-calorie food and the continuing decline in manual labor—be enough to tip the balance in favor of a global obesity epidemic? "We don't know yet whether it's going to be a major or minor part of the obesity story, " he says, "but I'm betting it's not trivial."

The widespread use of antibiotics is not the only culprit in the unprecedented disruption of the human microbiome in Blaser's view. Major changes in human ecology over the past century have contributed as well. The dramatic increase in the past few decades in the number of deliveries by cesarean section obviously limits the transfer through the birth canal of those all-important strains from Mom. (In the U.S., more than 30 percent of all newborns are delivered by C-section, and in China—land of one child per couple—the operation is responsible for nearly two thirds of all births to women living in urban areas.) Smaller family sizes throughout the world mean fewer siblings, who are a prime source of microbial material to their younger siblings during early childhood years. Even cleaner water—which has saved the lives of untold millions—exacts a toll on the human microbiome, reducing the variety of bacteria to which we are exposed. The result: more and more people are born into and grow up in an increasingly impoverished microbial world.

## A DELICATE BALANCE

AS THE ONGOING STUDIES of *B. thetaiotaomicron* and *H. pylori* illustrate, even the most basic questions about what these bacterial species are doing in the body lead to complicated answers. Going one step further and asking how the body responds to the presence of all these foreign cells in its midst introduces even greater complexity. For one thing, the traditional understanding of how the immune system distinguishes the body's own cells (self) from genetically different cells (nonself) suggests that our molecular defenses should be in a constant state of war against these myriad interlopers. Why the intestines, for example, are not the scene of more pitched battles between human immune cells and the trillions of bacteria present is one of the great, as yet unsolved mysteries of immunology.

The few clues that exist offer tantalizing insights into the balancing act between the microbiome and human immune cells that has taken some 200,000 years to calibrate. Over the eons the immune system has evolved numerous checks and balances that generally prevent it from becoming either too aggressive (and attacking its own tissue) or too lax (and failing to recognize dangerous pathogens). For example, T cells play a major role in recognizing and attacking microbial invaders of the

body, as well as unleashing the characteristic swelling, redness and rising temperature of a generalized inflammatory response to infection by a pathogen. But soon after the body ramps up its production of T cells, it also starts producing so-called regulatory T cells, whose principal function seems to be to counteract the activity of the other, pro-inflammatory T cells.

Normally the regulatory T cells swing into action before the pro-inflammatory T cells get too carried away. "The problem is that many of the mechanisms that these proinflammatory T cells use to fight infection—for example, the release of toxic compounds—end up blasting our own tissues," says Caltech's Mazmanian. Fortunately, the regulatory T cells produce a protein that restrains the proinflammatory T cells. The net effect is to tamp down inflammation and prevent the immune system from attacking the body's own cells and tissues. As long as there is a good balance between belligerent T cells and more tolerant regulatory T cells, the body remains in good health.

For years researchers assumed that this system of checks and balances was generated entirely by the immune system. But in yet another example of how little we control our own fate, Mazmanian and others are starting to show that a healthy, mature immune system depends on the constant intervention of beneficial bacteria. "It goes against dogma to think that bacteria would make our immune systems function better," he says. "But the picture is getting very clear: the driving force behind the features of the immune system are commensals."

**WE HAVE COMPLETELY CHANGED OUR ASSOCIATION WITH THE MICROBIAL WORLD. THERE IS A PRICE TO PAY FOR OUR GOOD INTENTIONS.**

Mazmanian and his team at Caltech have discovered that a common microorganism called *Bacteroides fragilis,* which lives in some 70 to 80 percent of people, helps to keep the immune system in balance by boosting its anti-inflammatory arm. Their research began with observations that germ-free mice have defective immune systems, with diminished function of regulatory T cells. When the researchers introduced *B. fragilis* to the mice, the balance between the pro-inflammatory and anti-inflammatory T cells was restored, and the rodents' immune systems functioned normally.

But how? In the early 1990s researchers started characterizing several sugar molecules that protrude from the surface of *B. fragilis*—and by which the immune system recognizes its presence. In 2005 Mazmanian and his colleagues showed that one of these molecules, known as polysaccharide A, promotes maturation of the immune system. Subsequently, his laboratory revealed that polysaccharide A signals the immune system to make more regulatory T cells, which in turn tell the pro-inflammatory T cells to leave the bacterium alone. Strains of *B. fragilis* that lack polysaccharide A simply do not survive in the mucosal lining of the gut, where immune cells attack the microbe as if it were a pathogen.

In 2011 Mazmanian and his colleagues published a study in *Science* detailing the full molecular pathway that produces this effect—the first such illumination of a molecular pathway for mutualism between microbe and mammal. "*B. fragilis* provides us with a profoundly beneficial effect that our own DNA for some reason doesn't provide," Mazmanian says. "In many ways, it co-opts our immune system—hijacks it." Unlike pathogens, however, this hijacking does not inhibit or reduce our immune system performance but rather helps it to function. Other organisms may have similar effects on the immune system, he notes: "This is just the first example. There are, no doubt, many more to come."

Alas, because of lifestyle changes over the past century, *B. fragilis,* like *H. pylori,* is disappearing. "What we've done as a society over a short period is completely change our association with the microbial world," Mazmanian says. "In our efforts to distance ourselves from disease-causing infectious agents, we have probably also changed our associations with beneficial organisms. Our intentions are good, but there's a price to pay."

In the case of *B. fragilis,* the price may be a significant increase in the number of autoimmune disorders. Without polysaccharide A signaling the immune system to churn out more regulatory T cells, the belligerent T cells begin attacking everything in sight—including the body's own tissues. Mazmanian contends that the recent sevenfold to eightfold increase in rates of autoimmune disorders such as Crohn's disease, type 1 diabetes and multiple sclerosis is related to the decline in beneficial microbes. "All these diseases have both a genetic component and an environmental component," Mazmanian says. "I believe that the environmental component is microbiotic and that the changes are affecting our immune system." The microbial shift that comes with changes in how we live—including a decrease in *B. fragilis* and other anti-inflammatory microbes—results in the underdevelopment of regulatory T cells. In people who have a genetic susceptibility, this deviation may lead to autoimmunity and other disorders.

Or at least that is the hypothesis. At this stage in the research, the correlations in humans between lower microbial infections and increased rates of immune disease are only that—correlations. Just as with the obesity issue, teasing apart cause and effect can be difficult. Either the loss of humanity's indigenous bugs have forced rates of autoimmune diseases and obesity to shoot up or the increasing levels of autoimmunity and obesity have created an unfavorable climate for these native bugs. Mazmanian is convinced that the former is true—that changes in the intestinal microbiome are contributing significantly to rising rates of immune disorders. Yet "the burden of proof is on us, the scientists, to take these correlations and prove that there is cause and effect by deciphering the mechanisms underlying them," Mazmanian says. "That is the future of our work." SA

MORE TO EXPLORE


**Who Are We? Indigenous Microbes and the Ecology of Human Diseases.** Martin J. Blaster in *EMBO Reports,* Vol. 7, No. 10, pages 956–960; October 2006. www.ncbi.nlm.nih.gov/pmc/articles/PMC1618379

**A Human Gut Microbial Gene Catalogue Established by Metagenomic Sequencing.** Junjie Qin et al. in *Nature,* Vol. 464, pages 59–65; March 4, 2010.

**Has the Microbiota Played a Critical Role in the Evolution of the Adaptive Immune System?** Yun Kyung Lee and Sarkis K. Mazmanian in *Science,* Vol. 330, pages 1768–1773; December 24, 2010. www.ncbi.nlm.nih.gov/pmc/articles/PMC3159383


**SCIENTIFIC AMERICAN ONLINE**

For an interactive feature about some of the key microbial species found in and on the body, visit ScientificAmerican.com/jun2012/microbiome-graphic

**HIGHEST-ENERGY SUPERNOVAE** might look quite spectacular from a planet orbiting the exploding star, but any civilization would most likely be obliterated.

**Avishay Gal-Yam** graduated with a Ph.D. in astrophysics in 2004 at Tel Aviv University and has been a Hubble Postdoctoral Fellow at the California Institute of Technology. He is now a senior scientist at the Weizmann Institute of Science in Rehovot, Israel.

ASTROPHYSICS

# SUPER SUPERNOVAE

## The largest stars die in explosions more powerful than anyone thought possible—some triggered in part by the production of antimatter

*By Avishay Gal-Yam*

IN THE MIDDLE OF 2005 THE W. M. KECK OBSERVATORY ON MAUNA KEA IN Hawaii completed an upgrade of one of its giant twin telescopes. By automatically correcting for atmospheric turbulence, the instrument could now produce images as sharp as those from the Hubble Space Telescope. Shrinivas Kulkarni of the California Institute of Technology urged young Caltech researchers—myself among them—to apply for observing time. Once the rest of the astronomy community realized how terrific the telescopes were, he warned us, securing a slot would become very competitive.

Taking this advice, I teamed up with my then fellow postdocs Derek Fox and Doug Leonard to attempt a type of study that previously had been carried out almost solely with the Hubble: hunting for supernova progenitors. In other words, we wanted to know what stars look like when they are about to explode.

For decades theorists have been able to predict which celestial bodies are going to go supernova—for instance, they know that bright blue stars are due to explode soon. But "soon" to an astronomer means within the next million years or so. So, although observing the entire process unfold would enable us to understand it better, just patiently watching an individual star was not an option.

We thought that Keck could help us, and we were granted a single night of observing time in November 2005. As I flew in to the Big Island, I was anxious, hoping for good weather, as we had only one chance to try this new approach. Fortunately, the weather gods cooperated. That evening of observing set me on a research path that ultimately helped to overturn long-standing views of how large stars can become and how these giants die.

At the time, experts maintained that very large stars do not explode; rather they gradu-

*Illustration by Ron Miller*

ally shrink by shedding mass as stellar wind. Indeed, most theoretical astrophysicists would have said that because of these powerful winds, stars in the present-day universe cannot grow to a massive size in the first place—that they cannot become much heavier than, say, 100 times the mass of our sun.

As a result of our Hawaiian adventure, though, we gradually came to realize that stars of at least 200 solar masses do exist in our current universe and that they end their lives with the most energetic explosions in the universe. Equally surprising, we were also to discover that some of those stars explode in a way quite unlike anything astronomers had ever seen—in a process involving the generation of antimatter at the star's center.

Such enormous stars, and probably even larger ones, were the first celestial bodies to form from primordial gas in the universe's early history. Their way of exploding thus tells us how the elements they produced could spread around the cosmos and ultimately sow the seeds of today's suns, planets and people.

## AN UNLIKELY START

IN OUR ONE TIME at the telescope, Fox, Leonard and I hoped to observe an active supernova and then, by looking at archival images shot by the Hubble, find an image of the star before it exploded. We therefore needed to look for a supernova in one of the many galaxies the Hubble had imaged in the past. The difficult part of finding our target in a Hubble photograph would be figuring out which star, among the billions in a galaxy, was the one that blew up. To do so, we would need to measure the location of the supernova with great precision. Before the advent of adaptive-optics systems such as Keck's, that was possible only through the Hubble itself. Even then, the task was so challenging that astronomers had managed to positively identify only three progenitors.

Among the supernovae active at the time, we selected one named SN 2005gl. Other groups would have considered it a poor choice, and for good reason: researchers who seek supernovae progenitors typically look within a radius of about 60 million light-years of Earth; this one was more than three times farther than that—about 200 million light-years away. For us to find the progenitor of SN 2005gl in Hubble images, that star would have to have been among the most luminous ever observed. The likelihood of success was low, but we felt that sometimes only by aiming at long shots can you reap huge rewards.

Our gamble paid off. After measuring SN 2005gl's position with Keck data, we looked at a Hubble image and saw something there that looked like a star, although we could not be sure. If it was a single star, its brightness (perhaps a million times that of the sun) suggested it was massive—100 times the sun's mass. Yet given prevailing opinion that such a heavyweight should not explode at all, most astronomers would have thought it more plausible that the dot of light in the Hubble image came from a cluster of smaller, fainter stars that together produced the brightness we saw. And our data could not rule out this possibility—yet.

## ANOTHER STRANGE BLOWUP

EVEN THOUGH our result was inconclusive, I became increasingly interested in finding observational evidence speaking to the fate of the most massive stars. But science rarely follows a straight line from asking a question to finding an answer. I was thinking of stellar explosions of an entirely different kind—those called gamma-ray bursts—when a chance event in 2006 led to another surprising finding, which suggested not only that giant stars might go supernova but also that they could do so in a startling way.

This new chapter in the story began with another night at the Keck observatory in 2006. This time, however, the gods seemed much less kind: the weather was terrible. I sat by the control computer and waited, as hours went by. Just as I was beginning to wonder whether my long trip back had been in vain, the clouds thinned out. The sky did not exactly clear up, but you could see some stars. I decided to observe the brightest supernova explosion visible at that time, an unusually luminous event called SN 2006gy, which then University of Texas at Austin graduate student Robert Quimby had discovered eight days earlier using a telescope less than one-twentieth the size of the giant Keck reflectors. I managed to observe for 15 minutes until the clouds thickened again, this time for good. It seemed like the night was a total loss.

But later, a team led by my Caltech colleague Eran Ofek analyzed the data I had obtained, and SN 2006gy turned out to be the most luminous supernova explosion ever found to date. A parallel study led by Nathan Smith, then at the University of California, Berkeley, came to a similar conclusion. It made no sense. None of the types of supernovae we were aware of could generate so much light. SN 2006gy was in a galaxy that had not been imaged by Hubble before, so we also had no way of studying its progenitor star in detail. Judging from the violence of its explosion, though, the star probably weighed at least 100 solar masses.

We thought of several possible explanations for the luminosity, two of which seemed the least implausible. The first was that the extremely bright light was heat radiation from a shock wave that formed as the supernova's explosive debris caught up with the slower stellar wind that the star itself had emitted before exploding and swept that stellar wind away. The second option we considered was radioactivity. Supernovae synthesize new elements, largely in the form of radioactive isotopes that later decay into other, more stable ones. Perhaps this giant explosion synthesized a huge amount of radioactive material, whose slow decay injected energy into an expanding cloud of stellar debris and made the cloud glow in fluorescent light. But what could produce enough radioactive material to explain such outrageous luminosity?

That last question grabbed our interest. To try to answer it, we began to review past theoretical work. We stumbled on old, dusty theoretical papers from the late 1960s by three young astrophysicists—Gideon Rakavy, Giora Shaviv and Zalman Barkat. They had proposed a new way that a star could blow up.

Stars shine because their cores are dense and hot enough

### IN BRIEF

**In recent years** several supernovae have turned out to be more powerful and long-lasting than any observed before.

**Archival images** showed that the stars that gave rise to some supernovae were about 100 times as massive as the sun: according to accepted theory, stars this big were not supposed to explode.

**Some supernovae** may have been thermonuclear explosions triggered by the creation of pairs of particles of matter and antimatter.

**The first generation** of stars in the universe, which created the materials that later formed planets, may have exploded through a similar mechanism.

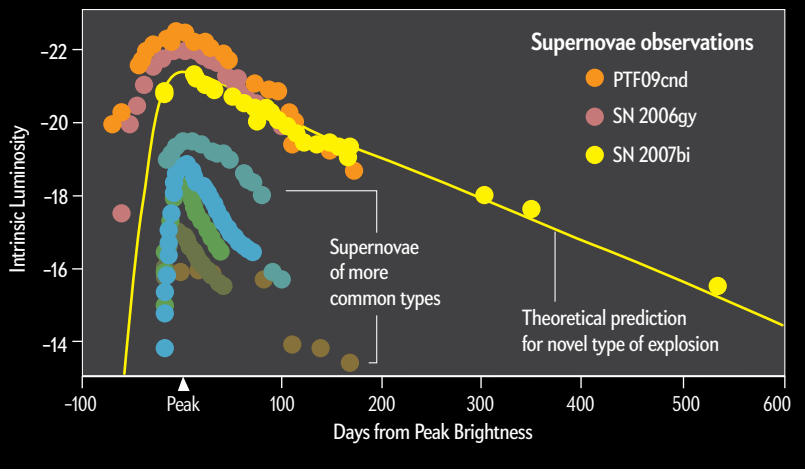
that hydrogen atoms fuse, turning into helium and heavier elements and releasing energy. Those two parameters—density and temperature—by and large control the physics of the core of a massive star and the star's evolution. In general, as time progresses, the core gets denser and hotter. The core then crosses successive thresholds toward the fusion of increasingly heavy elements—first helium to carbon, then carbon to oxygen, and so on. Each stage between thresholds may last thousands to billions of years, depending on how fast the star's nuclear burning affects its core temperature and pressure.

Rakavy and company calculated what would happen when a very massive star, perhaps hundreds of times more massive than the sun, reaches the stage at which its core is mostly oxygen. In lesser stars, we know what is next: the star contracts, and its core heats up until conditions allow the nuclear fusion of oxygen into silicon. But in a hypergiant, the theory said, the core would contract under gravity and heat up without becoming very dense. So instead of oxygen fusion, something else would happen: physicists call it pair production.

SUPERNOVA OBSERVATIONS

## The Brightest of the Bright

**Supernova explosions** studied by the author and his collaborators in the past few years have turned out to be the most energetic ever observed. One event, which began in 2006, reached record brightness (*pink*), beaten by another in 2009 (*orange*). But those died off relatively fast. Another one, from 2007, did not peak quite as high but released the most energy overall (*yellow*). It was the first example of a new type of explosion believed to occur in very massive stars [*see box on next two pages*].




In matter that is hot enough, energetic particles such as nuclei and electrons emit very powerful light—photons so energetic that they are in the gamma-ray spectrum. Because of Albert Einstein's famous equation relating mass and energy, $E = mc^2$, two very energetic photons can, if they collide, spontaneously convert into pairs of other particles; specifically, they can transform into a pair that consists of an electron and its antiparticle, the positron. Most of the energy of the photons thus gets locked up in the form of matter. Consequently, electrons and positrons exert much lower pressure than the photons they originated from: they are deadweight. If the core of a very massive star reaches these conditions, its pressure suddenly falls, almost as if the star had a release valve. Before, pressure was what kept the star from collapsing under its own weight; now the core becomes unstable and begins to rapidly contract.

As density shoots up, it ignites the fusion of oxygen. Because the threshold to fusing oxygen is crossed in a collapsing core rather than in a stable one, the ignition is explosive: fusion releases nuclear energy that heats the material further, which in turn speeds up the fusion, in a "runaway" reaction. The star can burn so much oxygen in such a short time—mere minutes—that the energy it releases is larger than the star's entire gravitational energy. Thus, whereas typical supernovae leave behind charred remains such as a neutron star or a black hole, in this type of explosion the object completely obliterates itself. All that is left is a fast-expanding cloud, much of it made of elements that were synthesized in the fury of the deflagration.

The theorists predicted that this type of event—called a pair-instability supernova because it destabilizes the star through the production of electron-positron pairs—would form a huge amount of nickel 56 in addition to other relatively heavy elements. Nickel 56 is an isotope with a tightly bound nucleus that nonetheless is radioactive, ultimately producing nonradioactive iron. If this scenario occurred in the precursor of SN 2006gy, we thought, the decay of nickel 56 might explain the supernova's intense luminosity.

Although the three astrophysicists' theory was correct, for decades common wisdom was that their hypothetical process would not actually take place in nature. Theorists who work on the formation and evolution of stellar bodies thought that such massive stars should not form at all, at least not in the present-day universe. And even if they did form, they would drive such strong stellar winds that they would rapidly lose most of their mass, leaving them unable to form cores massive enough to reach pair instability. The situation was different less than a billion years after the big bang. Then, the first stars might have been massive enough to explode as pair-instability supernovae. Perhaps.

Meanwhile the new record-smashing supernova, SN 2006gy, became a hit among astronomers, spurring more observational and theoretical studies. Ironically, even though SN 2006gy prompted us and others in the supernova community to reconsider the pair-instability model, this particular event did not, in the end, seem to have the right signature for nickel radioactivity—namely, a specific way the light dimmed with time. In a pair-instability explosion, most of the light should come not from the blast itself but from nickel 56 and the other radioactive isotopes it forges. Radioactivity is a well-studied process in which decay proceeds at a predictable, gradual rate. But SN 2006gy, after being bright for many months, quite suddenly disappeared, too quickly to have been powered by radioactivity. It was likely not a pair-instability supernova after all, and the other option we had considered—that the event's unusual brightness originated from

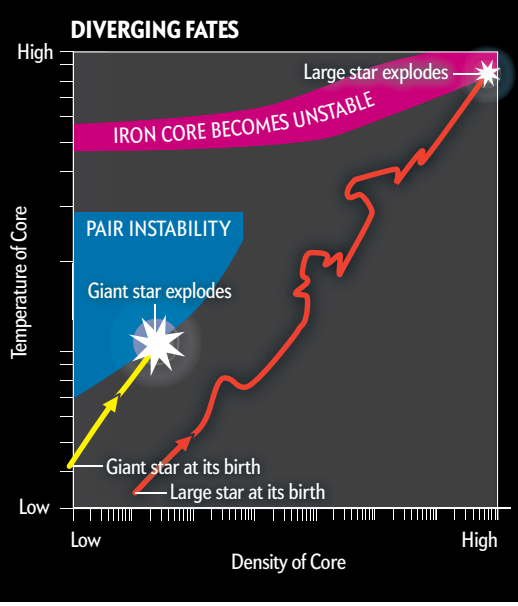
SOURCE: AVISHAY GAL-YAM

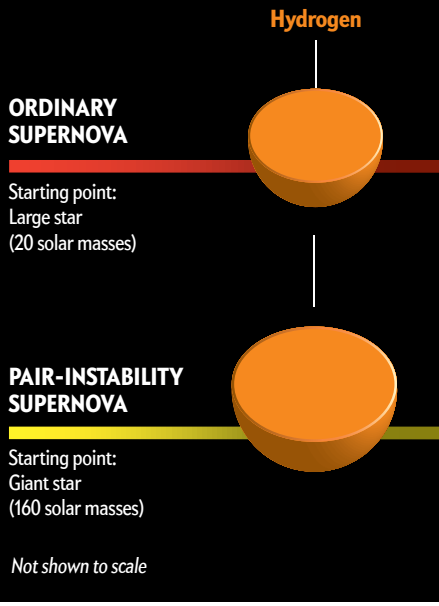
*Graphics by Jen Christiansen*

SUPERNOVAE COMPARED

# How Large Stars Die

**Stars forge** new elements by nuclear fusion, which is what makes them shine. As a star ages, its core gets hotter and denser (*graph*) and produces heavier and heavier elements, which tend to form onionlike layers (*diagram*). A relatively heavy star, such as one of 20 solar masses (*red in graph and diagram*), eventually becomes dense enough that it collapses, spewing out large amounts of energy and much of its mass. But a very heavy star, say, 160 solar masses (*yellow*), annihilates itself sooner in a recently discovered, even mightier type of blast.




a shock wave—became the accepted explanation. Still, the near miss had put me on the alert for signs of pair-instability events.

## THE REAL THING?

A FEW MONTHS AFTER our lucky break with the Hawaiian clouds, I went to Colorado on vacation. Soon, however, I was interrupted by an e-mail from Peter Nugent of Lawrence Berkeley National Laboratory. Nugent and I had just started a "practice run" for a big supernova search we had been planning. Now he sent me a supernova with a weird spectrum. I had never seen its like before.

Because atoms of each element in nature absorb and emit light at particular wavelengths, the spectrum of an astronomical source provides information about the chemical composition of the material emitting the light. The spectrum of Nugent's object—SN 2007bi—suggested that the elements that composed it were present in unusual proportions and that it was extremely hot.

After I got back to Caltech, I continued to track the evolution of this event. It emitted about 10 times more light than the typical supernova. And the amount of light declined very slowly: this source just refused to fade away, as days turned into weeks and weeks into months. I became more and more convinced that this was finally an example of a pair-instability supernova. It took more than a year before it finally disappeared from view. But I needed more data to be truly sure of my interpretation.

During 2007 and 2008 several collaborators and I continued to observe SN 2007bi using telescopes at Caltech's Palomar Observatory. As the light from this explosion finally grew fainter, about a year after we discovered it, I asked my Caltech colleagues Richard Ellis and Kulkarni to observe it with the large telescopes at Keck—promising in my e-mails that this was "the real deal."

In the meantime, I moved to Israel with my family and took up my current job at the Weizmann Institute of Science in Rehovot. In August 2008 Kulkarni and his graduate student Mansi Kasliwal sent me the latest spectrum for SN 2007bi. When I did a first, rough analysis, I could not believe what I saw. I analyzed the spectrum over and over, but the answer was the same: this explosion synthesized a staggering amount of nickel 56: between five and seven times the entire mass of our sun. It was 10 times more than we or anyone else had ever seen before—and just what you expect from a pair-instability supernova explosion. That night I paced back and forth in my apartment, thinking about this finding and its implications. When my wife gave me a strange look and asked what was going on, I said, "I think we've made a great discovery."

In late 2008 I traveled to Garching, Germany, to work with Paolo Mazzali at the Max Planck Institute for Astrophysics. Mazzali is a world expert in quantitative analysis of supernova spectra, so he could test the results of my rough analysis. He also had additional useful data he had obtained with another large instrument, the European Southern Observatory's Very Large Telescope in Chile. We sat together in his office as Mazzali ran his code. Yes! The results were consistent with my previous analyses: many solar masses of nickel 56, and a relative abundance of elements matching the predictions of pair-instability models.

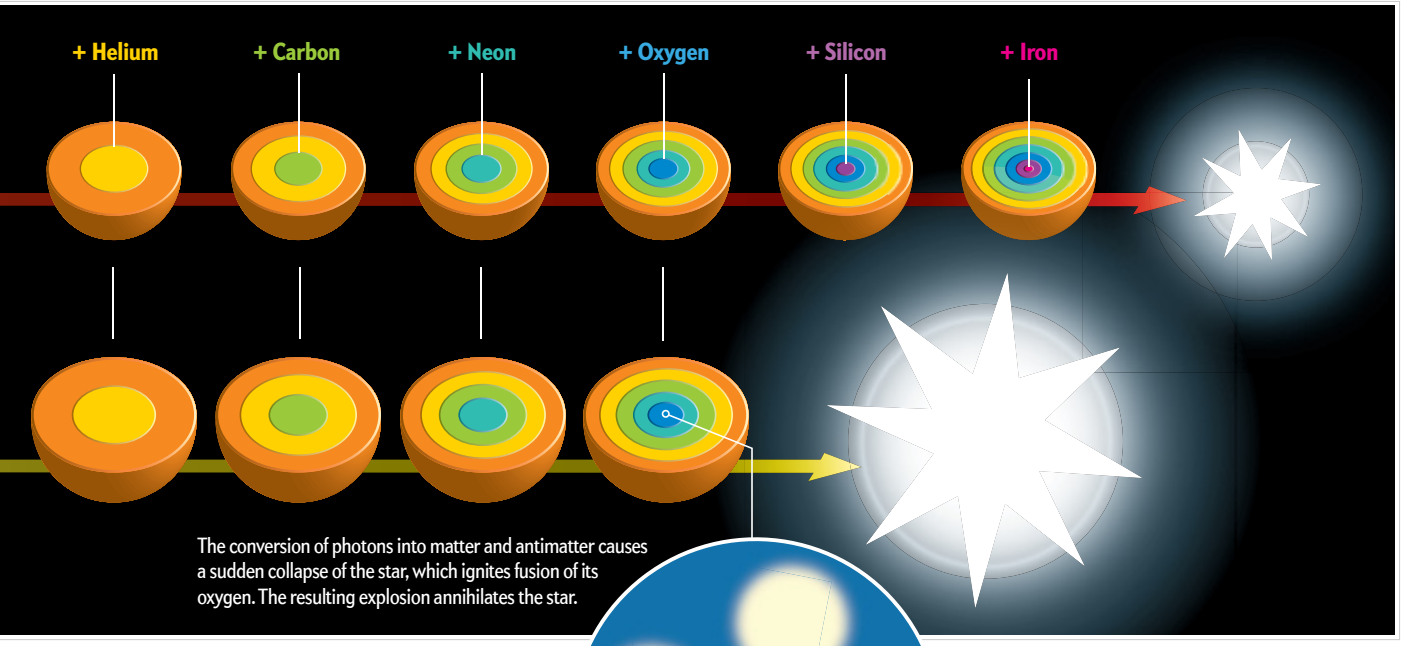
## DOUBLE TAKE

ALTHOUGH I WAS PRETTY CONFIDENT that we had identified a pair-instability supernova, when I returned to Israel I set the data aside for a few months while I was busy on another project involving the supernova that had set me on this journey in the first place: SN 2005gl. When Fox, Leonard and I found its putative progenitor star in late 2005, we could not be positive that it was indeed a single entity rather than a cluster of stars. Now, three years later, the supernova had disappeared, and I realized we could do a simple test: if our candidate was not the star that had blown up, it would still be there. Leonard and I returned to the Hubble to check.

By the end of 2008 we were finally sure: the star had disappeared. The progenitor of SN 2005gl was indeed very luminous and probably quite massive—a twin of Eta Carinae, one of the heftiest blue giants in our own galaxy.

Thus, the prevailing theory of hypergiant stars—that they

SOURCE: MODIFIED FROM "THE MOST MASSIVE CORE-COLLAPSE SUPERNOVA PROGENITORS," BY R. WALDMAN, IN *ASTROPHYSICAL JOURNAL*, VOL. 685: OCTOBER 1, 2008 (*graph*)




lose most of their mass before they explode—was wrong at least in this case. Some very luminous and massive stars do exist and explode before they lose all of their mass. And if the mass-loss theory was wrong, maybe some hypergiant stars still exist that can eventually explode as pair-instability supernovae.

Now I was ready to revisit SN 2007bi and to look for more conclusive evidence of a pair-instability explosion. A team of collaborators and I tested it in every way we could think of. We analyzed its spectra in detail and how its light evolved in time. We compared old models of stellar explosion and new ones. Near the end of 2009 all the evidence converged into a single conclusion: the most logical, almost inescapable way to explain SN 2007bi was that it was a pair-instability supernova. After more than two years of study, it was finally time to start publishing our results.

We have now collected three more events that are strong candidates for pair-instability supernovae. Overall, they appear to be exceedingly rare—constituting only one out of 100,000 supernovae—and to require a star of at least 140 solar masses and perhaps as many as 200. But they are huge factories of the elements, and they produce the most energetic explosions known to science. They might even deserve the name "hypernovae."

Perhaps the most fascinating aspect of this new type of supernova is that it gives us a glimpse into the early universe. The very first stars to light up, some 100 million years after the big bang, would have measured upward of 100 solar masses and maybe as much as 1,000 [see "The First Stars in the Universe," by Richard B. Larson and Volker Bromm; Scientific American, December 2001]. Some of those behemoths probably exploded via a pair-instability mechanism. Thus, the distant cousins of some of today's supernovae may have been the first explosions to seed the universe with heavier elements, thereby shaping the stars and planets that followed them—including our sun and Earth.

Not only do our observations suggest a novel way for stars to blow up, they also mean that the modern universe, contrary to earlier views, probably is sprinkled with hypergiant stars. Growth to extraordinary sizes for primordial stars was possible only in an environment made almost exclusively of hydrogen and helium. "Pollution" with the products of nuclear fusion then put a choke hold on stellar accretion: in the presence of heavier elements, stars collapse faster and thus ignite sooner, blowing off any residual gas around them before they can grow too heavy. But clearly, the heavier elements are less of a brake on stellar growth than astrophysicists used to believe.

The supernova survey Nugent and I began to plan in 2007 is now up and running: it is called the Palomar Transient Factory. As part of that project, we are searching for additional examples of pair-instability explosions; in fact, it enabled us to find one of our latest candidate events, which looks very much like SN 2007bi. As data accumulate, our understanding of these explosions and how they contribute to making the heavy elements in the universe deepens. Future instruments, such as NASA's next-generation observatory, the James Webb Space Telescope, will probably be able to detect very distant pair-instability explosions. Perhaps one day they will reveal the explosive deaths of the first stars to have ever formed in our universe. SA

## MORE TO EXPLORE

**How to Blow Up a Star.** Wolfgang Hillebrandt, Hans-Thomas Janka and Ewald Müller in *Scientific American*, Vol. 295, No. 4, pages 42–49; October 2006.

**A Massive Hypergiant Star as the Progenitor of the Supernova SN 2005gl.** A. Gal-Yam and D. C. Leonard in *Nature*, Vol. 458, pages 865–867; April 16, 2009.

**Supernova 2007bi as a Pair-Instability Explosion.** A. Gal-Yam et al. in *Nature*, Vol. 462, pages 624–627; December 3, 2009.

**SCIENTIFIC AMERICAN ONLINE**

See an interactive animation on stellar explosions at ScientificAmerican.com/jun2012/gal-yam

NEUROSCIENCE

# THE HUMAN BRAIN PROJECT

Building a vast digital simulation of the brain could transform neuroscience and medicine and reveal new ways of making more powerful computers

*By Henry Markram*

COURTESY OF ARTHUR W. TOGA *Laboratory of Neuro Imaging* AND RANDY BUCKNER *Martinos Center for Biomedical Imaging* (www.humanconnectomeproject.org)

## IT'S TIME TO CHANGE THE WAY WE STUDY THE BRAIN.

**Reductionist biology—examining individual brain parts, neural circuits and molecules—has brought us a long way, but it alone cannot explain the workings of the human brain, an information processor within our skull that is perhaps unparalleled anywhere in the universe. We must construct as well as reduce and build as well as dissect. To do that, we need a new paradigm that combines both analysis and synthesis. The father of reductionism, French philosopher René Descartes, wrote about the need to investigate the parts and then reassemble them to re-create the whole.**

**Putting things together to devise a complete simulation of the human brain is the goal of an undertaking that intends to construct a fantastic new scientific instrument. Nothing quite like it exists yet, but we have begun building it. One way to think of this instrument is as the most powerful flight simulator ever built—only rather than simulating flight through open air, it will simulate a voyage through the brain. This "virtual brain"**

### IN BRIEF

**Computer simulation** will introduce ever greater verisimilitude into digital depictions of the workings of the human brain.

**By the year 2020** digital brains may be able to represent the inner workings of a single brain cell or even the whole brain.

**A sim brain** can act as a stand-in for the genuine article, thus fostering a new understanding of autism or permitting virtual drug trials.

will run on supercomputers and incorporate all the data that neuroscience has generated to date.

A digital brain will be a resource for the entire scientific community: researchers will reserve time on it, as they do on the biggest telescopes, to conduct their experiments. They will use it to test theories of how the human brain works in health and in disease. They will recruit it to help them develop not only new diagnostic tests for autism or schizophrenia but also new therapies for depression and Alzheimer's disease. The wiring plan for tens of trillions of neural circuits will inspire the design of brainlike computers and intelligent robots. In short, it will transform neuroscience, medicine and information technology.

**Henry Markram** directs the Blue Brain Project at the Swiss Federal Institute of Technology in Lausanne. He has done extensive work on how neurons interconnect, communicate and learn. He also discovered fundamental principles of brain plasticity and is co-discoverer of the intense world theory of autism and the theory of how the brain computes as a liquid that is constantly perturbed.

## BRAIN IN A BOX

SCIENTISTS could be running the first simulations of the human brain by the end of this decade, when supercomputers will be powerful enough to support the massive number of calculations needed. The instrument will not require that all mysteries of the brain be unraveled first. Instead it will furnish a framework to accommodate what we do know, while enabling us to make predictions about what we do not. Those predictions will show us where to target our future experiments to prevent wasted effort. The knowledge we generate will be integrated with existing knowledge, and the "holes" in the framework will be filled in with increasingly realistic detail until, eventually, we will have a unified working model of the brain—one that reproduces it accurately from the whole brain down to the level of molecules.

Building this instrument is the goal of the Human Brain Project (HBP), an initiative involving about 130 universities around the world. The HBP is one of six projects competing for a glittering prize, up to €1 billion to be provided over 10 years by the European Union to each of two winners, who will be announced in February 2013.

We need the simulator for at least two reasons. In Europe alone, brain diseases affect 180 million people, or roughly one in three—a number that is set to grow as the population ages. At the same time, pharmaceutical companies are not investing in new treatments for the ailing nervous system. A holistic view of the brain would enable us to reclassify such diseases in biological terms rather than looking at them simply as sets of symptoms. The breadth of this perspective would allow us to move forward to develop a generation of treatments that selectively target the underlying abnormalities.

The second reason is that computing is fast approaching barriers to further development. Computers cannot do many tasks that animal brains do effortlessly, despite the inexorable increase in processing power. For instance, although computer scientists have made huge progress in visual recognition, the machines still struggle to make use of context in a scene or to use arbitrary scraps of information to predict future events in the way the brain can.

Moreover, because more powerful computers require more energy, supplying their needs will one day no longer be feasible. The performance of today's supercomputers is measured in petaflops—quadrillions of logic operations per second. The next generation, due around 2020, will be 1,000 times faster and will be measured in exaflops—quintillions of operations per second. By itself, the first exa-scale machine will probably consume around 20 megawatts, roughly the energy requirement of a small town in winter. To create increasingly powerful computers that perform some of the simple but useful things that humans are capable of in an energy-efficient way, we need a radically new strategy.

We could do worse than take inspiration from the human brain, which performs a range of intelligent functions on a mere 20 or so watts—a million times fewer than an exa-scale machine and equivalent to a weak lightbulb. For that, we need to understand the multilevel organization of the brain, from genes to behavior. The knowledge is out there, but we need to bring it together—and our instrument will provide the platform on which to do that.

Critics say that the goal of modeling the human brain is unachievable. One of their principal objections is that it is impossible to reproduce the connectivity among the brain's 100 trillion synapses because we cannot measure it. They are correct that we cannot measure the web of connections, which is why we are not going to—at least, not all of it. We intend to reproduce the myriad connections among brain cells by different means.

The key to our approach is to craft the basic blueprint according to which the brain is built: the set of rules that has guided its construction over evolution and does so anew in each developing fetus. In theory, those rules are all the information we need to start building a brain. The skeptics are right: the complexity they generate is daunting—hence our need for supercomputers to capture it. But unraveling the rules themselves is a far more tractable problem. If we pull it off, there is no logical reason why we cannot apply the blueprint in the same way that biology does and build an "in silico" brain.

The kind of rules we are talking about are ones that govern the genes that lead to the types of cells there are in the brain and the underlying plan for the way those cells are distributed and how they are connected. We know that such rules exist because we discovered some of them while laying the groundwork for the HBP. We started doing that almost 20 years ago by measuring the characteristics of individual neurons. We collected vast amounts of data about the geometric properties of different neuronal types and digitally reconstructed hundreds of them in three dimensions. Using a painstaking method called patch clamping, which involves placing the tip of a microscopic glass pipette up against a cell membrane to measure the voltage across its ion channels, we also recorded the neurons' electrical properties.

In 2005 modeling a single neuron took a powerful computer and a three-year Ph.D. project. It was clear that more ambitious goals would soon become achievable, however, and that we could model larger elements of brain circuitry even if our knowledge of those elements was incomplete. At the Brain Mind Institute at the Swiss Federal Institute of Technology in Lausanne, we launched one of the HBP's predecessors, the Blue Brain Project. We would build what we call "unifying computer models"—models that integrate all existing data and hypotheses about a

given brain circuit, while reconciling conflicts in that information and highlighting where knowledge is lacking.

### SYNTHESIS BIOLOGY

AS A TEST CASE, we set out to build a unifying model of a brain structure called the cortical column. The column is the equivalent of a processor in your laptop. To use a crude metaphor, if you were to put a miniature apple corer through the cortex and pull out a cylinder of tissue about half a millimeter in diameter and 1.5 mm in height, that would be a column. Within that tissue core, you would find a very dense network consisting of a few tens of thousands of cells. The column is such an efficient design for an information-processing element that once evolution had hit on the formula, it kept applying this recipe again and again until no more space was left in the skull and the cortex had to fold in on itself to create more room—hence, your convoluted brain.

The column penetrates the six vertical layers of the neocortex, the cortex's outer layer, and the neural connections between it and the rest of the brain are organized differently in each layer. The organization of these connections resembles the way telephone calls are assigned a numerical address and routed through an exchange. A few hundred neuron types reside in a column, and using our IBM Blue Gene supercomputer, we integrated all the available information about how those types mix in each layer until we had a "recipe" for a column in a newborn rat. We also instructed the computer to allow the virtual neurons to connect in all the ways that real neurons do—but only in those ways. It took us three years to build the software facility that, in turn, allowed us to construct this first unifying model of a column. And with it we had our proof of concept of what we call synthesis biology—a simulation of the brain from the full diversity of biological knowledge—and how it can serve as both a feasible and an inventive new way of doing research.

At that point, we had a static model—the equivalent of a column in a comatose brain. We wanted to know whether it would start to behave like a real column, albeit one isolated from the rest of the brain in a slice of living brain tissue, so we gave it a jolt—some external stimulation. In 2008 we applied a simulated electrical pulse to our virtual column. As we watched, the neurons began to speak to one another. "Spikes," or action potentials—the language of the brain—spread through the column as it began to work as an integrated circuit. The spikes flowed between the layers and oscillated back and forth, just as they do in living brain slices. This was behavior we had not programmed into the model; it emerged spontaneously because of the way the circuit was built. And the circuit stayed active even after the stimulation had stopped and briefly developed its own internal dynamics, its own way of representing information.

Since then, we have been gradually integrating more of the information generated by laboratories around the world into this unifying model of the column. The software we have developed is also being refined continuously so that each week we rebuild the column, we do so with more data, more rules and more accuracy. The next step is to integrate data for an entire brain region and then for an entire brain—to begin with, a rodent brain.

Our effort will depend heavily on a discipline called neuroinformatics. Vast quantities of brain-related data from all over the world need to be brought together in a coherent way, then mined for patterns or rules that describe how the brain is organized. We need to capture the biological processes those rules describe in sets of mathematical equations, while developing the software that will enable us to solve the equations on supercomputers. We also need to create software that will construct a brain that conforms to the inherent biology. We call it the "brain builder."

The predictions of how the brain operates offered up by neuroinformatics—and refined by new data—will accelerate our understanding of brain function without measuring every aspect of it. We can make predictions based on the rules we are uncovering and then test those predictions against reality. One of our current goals is to use knowledge of genes that give rise to the proteins for certain types of neurons to predict the structure and behavior of those cells. The link between genes and actual neurons constitutes what we call an "informatics bridge," the kind of shortcut that synthesis biology offers us.

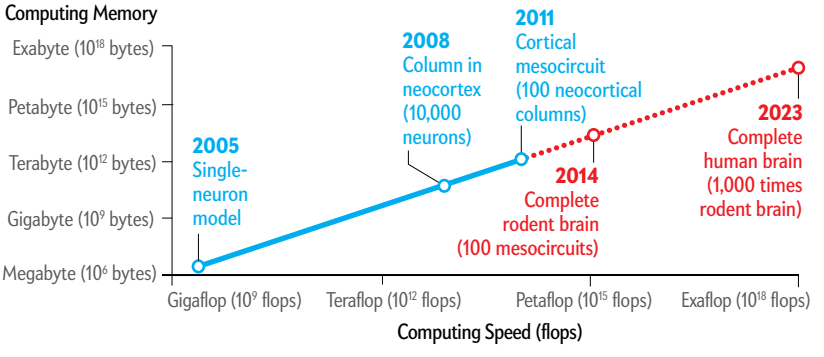
Another kind of informatics bridge that scientists have made use of for years has to do with genetic mutations and their link to disease: specifically, how mutation changes the proteins that cells manufacture, which in turn affect the geometry and electrical characteristics of neurons, the synapses they form and the electrical activity that emerges locally, in microcircuits, before spreading in a wide swath across whole brain regions.

In theory, for example, we could program a certain mutation into the model and then observe how that mutation affects it at each step along the biological chain. If the resulting symptom, or con-

POWER OF THE EXAFLOP

## More Computer = More Brain

**The ability to simulate** the brain in enough detail to carry out vital scientific research will grow with computer power. A digital facsimile of a cylindrical piece of tissue in the rat cortex became a reality in 2008, when speed was clocked in teraflops. As computers climb to the peta and exa scales, the Human Brain Project envisages full-brain simulations of a mouse and of the same species that conceived *Hamlet* and Einstein's general theory of relativity.

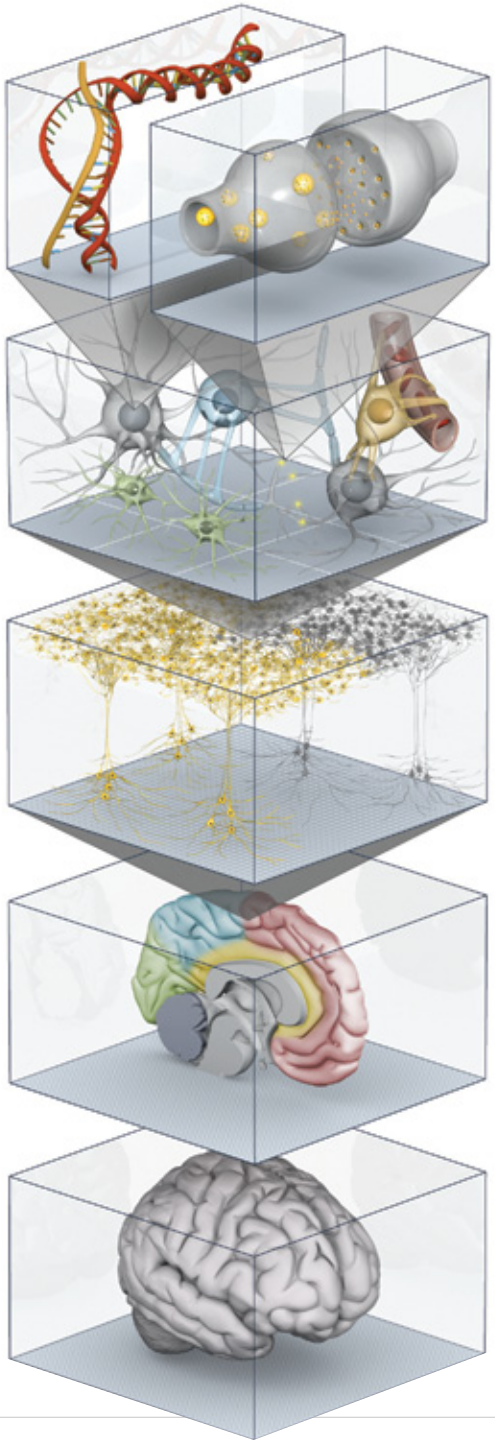



SOURCE: "BRAIN IN A BOX" BY M. MITCHELL WALDROP, IN *NATURE*, VOL. 482, FEBRUARY 23, 2012

LAYER BY LAYER

# Deconstructing the Brain

**The Human Brain Project** intends to create a computer simulation of the 89 billion neurons inside our skull and the 100 trillion connections that wire those cells together. A meticulous virtual copy of the human brain would potentially enable basic research on brain cells and circuits or computer-based drug trials. The project, which is seeking €1 billion in funding from the European Union, would model each level of brain function, from chemical and electrical signaling up to the cognitive traits that underlie intelligent behaviors.



### Molecular

A century of research, beginning with the first inspection of a brain cell under a microscope, would translate into a digital facsimile that combines component molecular parts to assemble a cell that demonstrates the essential properties of a neuron—the transmission of electrical and chemical signals.

### Cellular

A brain-in-a-box simulation will have to capture every detail of neurons and nonneuronal glial cells, including the exact geometric shapes of the dendrites and axons that receive and send information.

### Circuits

A model of the neural connections between different brain areas and among neighboring cells may furnish clues to the origins of complex brain diseases such as autism and schizophrenia.

### Regions

Major neural substructures—the amygdala (emotions), the hippocampus (memory), the frontal lobes (executive control)—can be inspected alone or as they interact with one another.

### Whole Organ

An in silico brain might substitute for the actual organ. By removing the computer code for a "gene," the virtual system can, for instance, mimic the effects of a mutation, as scientists do today by "knocking out" a gene in mice. The tool would avoid the lengthy breeding process and could simulate a multitude of experimental conditions.

stellation of symptoms, matches what we see in real life, that virtual chain of events becomes a candidate for a disease mechanism, and we can even begin to look for potential therapeutic targets along it.

This process is intensely iterative. We integrate all the data we can find and program the model to obey certain biological rules, then run a simulation and compare the "output," or resulting behavior of proteins, cells and circuits, with relevant experimental data. If they do not match, we go back and check the accuracy of the data and refine the biological rules. If they do match, we bring in more data, adding ever more detail while expanding our model to a larger portion of the brain. As the software improves, data integration becomes faster and automatic, and the model behaves more like the actual biology. Modeling the whole brain, when our knowledge of cells and synapses is still incomplete, no longer seems an impossible dream.

To feed this enterprise, we need data and lots of them. Ethical concerns restrict the experiments that neuroscientists can perform on the human brain, but fortunately the brains of all mammals are built according to common rules, with species-specific variations. Most of what we know about the genetics of the mammalian brain comes from mice, while monkeys have given us valuable insights into cognition. We can therefore begin by building a unifying model of a rodent brain and then using it as a starting template from which to develop our human brain model—gradually integrating detail after detail. Thus, the models of mouse, rat and human brains will develop in parallel.

The data that neuroscientists generate will help us identify the rules that govern brain organization and verify experimentally that our extrapolations—those predicted chains of causation—match the biological truth. At the level of cognition, we know that very young babies have some grasp of the numerical concepts 1, 2 and 3 but not of higher numbers. When we are finally able to model the brain of a newborn, that model must recapitulate both what the baby can do and what it cannot.

A great deal of the data we need already exist, but they are not easily accessible. One major challenge for the HBP will be to pool and organize them. Take the medical arena: those data are going to be immensely valuable to us not only because dysfunction tells us about normal



*Illustration by Emily Cooper*

function but also because any model we produce must behave like a healthy brain and later get sick in the same way that a real brain does. Patients' brain scans will therefore be a rich source of information.

Currently every time a patient has a scan, that scan resides in a digital archive. The world's hospitals stock millions of scans, and although they are already used for research purposes, that research happens in such a piecemeal way they remain a largely untapped resource. If we could bring together those scans on Internet-accessible "clouds," collecting them with patients' records and biochemical and genetic information, doctors could look across vast populations of patients for patterns that define disease. The power of this strategy will come from being able to mathematically pinpoint the differences and similarities among all diseases. A multiuniversity endeavor called the Alzheimer's Disease Neuroimaging Initiative is trying to do just that by collecting neuroimaging, cerebrospinal fluid and blood records from large numbers of dementia patients and healthy control subjects.

## THE FUTURE OF COMPUTING

LAST BUT NOT LEAST, there is the computing issue. The latest generation of Blue Gene is a peta-scale beast consisting of close to 300,000 processors packed into the space of 72 fridges. Petaflops are sufficient to model a rat brain of 200 million neurons at a cellular level of detail but not a human brain of 89 billion neurons. For that achievement, we need an exa-scale supercomputer, and even then a molecular-level simulation of the human brain will be beyond our reach.

Teams worldwide are racing to build such computers. When they arrive, like previous generations of supercomputers, they are likely to be adapted to simulating physical processes, such as those used in nuclear physics. Biological simulations have different requirements, and in collaboration with large computer manufacturers and other industrial partners, our consortium of high-performance-computing experts will configure one such machine for the task of simulating a brain. They will also develop the software that will allow us to build unifying models from the lowest to the highest resolution so that it will be possible, within our simulator, to zoom in and out among molecules, cells and the entire brain.

Once our brain simulator has been built, researchers will be able to set up in silico experiments using the software specimen much as they would a biological specimen, with certain key differences. To give you an idea of what these might be, think about how scientists currently search for the roots of disease by using mice in which a gene has been "knocked out." They have to breed the mice, which takes time, is expensive and is not always possible—for example, if the knockout is lethal to the embryo—even if one lays aside ethical concerns surrounding animal experimentation.

With the in silico brain, they will be able to knock out a virtual gene and see the results in "human" brains that are different ages and that function in distinctive ways. They will be able to repeat the experiment under as many different conditions as they like, using the same model, thus ensuring a thoroughness that is not obtainable in animals. Not only could this accelerate the process by which pharmaceutical researchers identify potential drug targets, it will also change the way clinical trials are conducted. It will be much easier to select a target population, and drugs that do not work or that have unacceptable side effects will be filtered out more quickly, with the result that the entire R&D pipeline will be accelerated and made more efficient.

What we learn from such simulations will also feed back into the design of computers by revealing how evolution produced a brain that is resilient, that performs multiple tasks rapidly and simultaneously on a massive scale—while consuming the same amount of energy as a lightbulb—and that has a huge memory capacity.

Brainlike computer chips will be used to build so-called neuromorphic computers. The HBP will print brain circuits on silicon chips, building on technology developed in the European Union projects BrainScaleS and SpiNNaker.

The first whole-brain simulations we run on our instrument will lack a fundamental feature of the human brain: they will not develop as a child does. From birth onward, the cortex forms as a result of the proliferation, migration and pruning of neurons and of a process we call plasticity that is highly dependent on experience. Our models will instead begin at any arbitrary age, leapfrogging years of development, and continue from there to capture experiences. We will need to build the machinery to allow the model to change in response to input from the environment.

The litmus test of the virtual brain will come when we connect it up to a virtual software representation of a body and place it in a realistic virtual environment. Then the in silico brain will be capable of receiving information from the environment and acting on it. Only after this achievement will we be able to teach it skills and judge if it is truly intelligent. Because we know there is redundancy in the human brain—that is, one neural system can compensate for another—we can begin to find which aspects of brain function are essential to intelligent behavior.

The HBP raises important ethical issues. Even if a tool that simulates the human brain is a long way off, it is legitimate to ask whether it would be responsible to build a virtual brain that possessed more cortical columns than a human brain or that combined humanlike intelligence with a capacity for number crunching a million times greater than that of IBM's Deep Blue, its chess-playing computer.

We are not the only ones setting the bar high in attempting to reverse the fragmentation of brain research. In May 2010 the Seattle-based Allen Institute for Brain Science launched its Allen Human Brain Atlas, with the goal of mapping all the genes that are active in the human brain.

Funding is likely to be the main limiting factor for any group making an attempt of this kind. In our case, the goal will be achievable only if we obtain the support we need. Supercomputers are expensive, and the final cost of the HBP is likely to match or exceed that of the Human Genome Project. In February 2013 we will know if we have the green light. Meanwhile we press ahead with an enterprise we believe will give us unparalleled insight into our own identities as creatures capable of contemplating the chiaroscuro of a Caravaggio painting or the paradoxes of quantum physics. SA

### MORE TO EXPLORE

Links to a few Human Brain Project sites:
Human Brain Project: www.humanbrainproject.eu
BrainScaleS: http://brainscales.kip.uni-heidelberg.de
SpiNNaker:http://apt.cs.man.ac.uk/projects/SpiNNaker

**SCIENTIFIC AMERICAN ONLINE**
Watch a video of a brain network in operation at ScientificAmerican.com/jun2012/brain-project

TECHNOLOGY

# Fusion's Missing Pieces

On the road to unlimited energy, the world's most complex science experiment encounters a few potholes

*By Geoff Brumfiel*

*Sculpture by Sachiko Akinaga*

**Geoff Brumfiel** is a staff reporter for *Nature* in London, where, for more than a decade, he has covered the ITER project.

GENEVA WAS COLD AND GRAY WHEN AIR FORCE ONE TOUCHED down in November 1985. President Ronald Reagan had come to meet Mikhail Gorbachev, the newly appointed leader of the Soviet Union. Reagan was convinced that the risk of catastrophic nuclear war was high, and he wanted to reduce the two superpowers' swollen arsenals. Gorbachev also recognized that the arms race was strangling the Soviet economy.

Yet the tête-à-tête quickly degenerated. Reagan lectured Gorbachev on the history of Soviet aggression. Gorbachev attacked Reagan's Strategic Defense Initiative, an ambitious plan to knock incoming nuclear weapons out of the sky. Negotiations nearly broke down. At five in the morning, the two sides agreed to a joint statement with no firm commitments. At the bottom—almost as a footnote—Reagan and Gorbachev inserted a gauzy pledge to develop a new source of energy "for the benefit of all mankind."

That note set in motion a project that has evolved into arguably the most ambitious scientific undertaking of the 21st century—a mash-up of complex experimental technologies that will, if all goes well, underpin the final solution to humanity's energy crisis.

ITER (formerly the International Thermonuclear Experimental Reactor) will attempt to reproduce the sun's power here on earth. It will generate around 500 megawatts of power, 10 times the energy needed to run it, using little more than hydrogen, the most abundant element in the universe. The project will illustrate a proof of principle for a technology that could lead to a nearly unlimited supply of energy for the power-hungry world. Politicians from seven participating members, including the U.S. and Russia, have enthusiastically enlisted their nations in the effort.

Yet like the summit that birthed it, ITER (pronounced "eater") has not lived up to expectations. Cost estimates have doubled and doubled again as engineering problems find bureaucratically expedient solutions. For instance, rather than pooling resources, the seven partners are producing bits and pieces in their home countries, then assembling them at ITER's building site in the south of France. The process is akin to ordering nuts, bolts and brackets from a catalogue, then trying to build a 747 in your backyard. Progress is glacial. Less than a year ago ITER was a 56-foot-deep hole in the ground, which has only recently been filled with nearly four million cubic feet of concrete. The start date has slipped from 2016 to 2018 to late 2020. The first real energy-producing experiments will not come before 2026—two decades after the start of construction.

IN BRIEF

**The ITER fusion reactor** promises to be a landmark step on the road toward unlimited clean energy. Once running, the machine will produce 10 times the amount of energy needed to power it.

**Yet for all its promise**, the ITER project is in trouble. Billions of dollars over budget and years behind schedule, the reactor will not start power-production experiments until 2026 at the earliest.

**The complex reasons** behind the troubles include unforeseen engineering difficulties and the baroque bureaucratic squabbles of a global partnership of seven major stakeholders.

**Critics contend** that ITER has become a pie-in-the-sky boondoggle whose only purpose is to suck money away from productive clean-energy research projects like wind and solar energy.

PRECEDING PAGES: HIRONOBU MAEDA (*photograph of Lego sculpture*)

And ITER is just the beginning of this putative new source of energy. Even if it is successful, another generation of test reactors will have to follow it, and only after these have run their course will local municipalities begin to build fusion plants to supply the grid. ITER is but one step in a project that will continue for decades, if not centuries.

Supporters argue that ITER is the only hope, in the long term, of meeting the world's unquenchable demand for power. But even they have been forced to recalibrate their utopian expectations. The project now seems to be propelled by institutional inertia—it is easier for individual governments to stay the course rather than be the lone pariah who pulls out early. Critics, meanwhile, have more ammunition with each delay and cost overrun. ITER, they say, is a colossal waste of money at a time when funding is desperately needed in other areas of energy research. Both sides agree: when the project is finally completed, it had better work.

## BOTTLED SUN

IN THEORY, fusion is the perfect energy source. It depends on the one thing in physics that everyone has heard of: energy equals mass times the speed of light, squared ($E = mc^2$). Because the speed of light is so great, $E = mc^2$ means that a very small amount of mass can generate an enormous quantity of energy.

All nuclear reactions exploit this basic law of the universe. In the case of ordinary nuclear power plants, heavy uranium nuclei split apart to create lighter elements. During this fission, a tiny fraction of the uranium's mass turns directly into energy. Fusion is the same, except backwards. When light nuclei such as hydrogen come together, they create helium ions that weigh slightly less than their parents. Per unit mass, fusion fuel can release around three times the energy of uranium fission. Even more important, hydrogen is far more abundant than uranium, and fusion's helium waste products are not radioactive.

"Fusion is seductive," says Gyung-Su Lee, a South Korean scientist who has devoted years to ITER negotiations. "It's like people searching for ways to make gold in the Middle Ages. It's the holy grail of energy research."

Lee is a fierce believer in fusion's power. In 1980 he arrived as a graduate student at the University of Chicago to study quantum field theory, one of the toughest corners of physics. But America changed Lee's thinking. "In the U.S., money is everything," he says, and quantum field theory offers only intellectual riches. He began to look for something more practical to study and eventually settled on fusion. "It's very difficult, scientifically and also in engineering," he notes. Yet if it worked, the payoff would be huge: energy would be widely available and cheap; fossil fuels would become irrelevant. The world would be transformed.

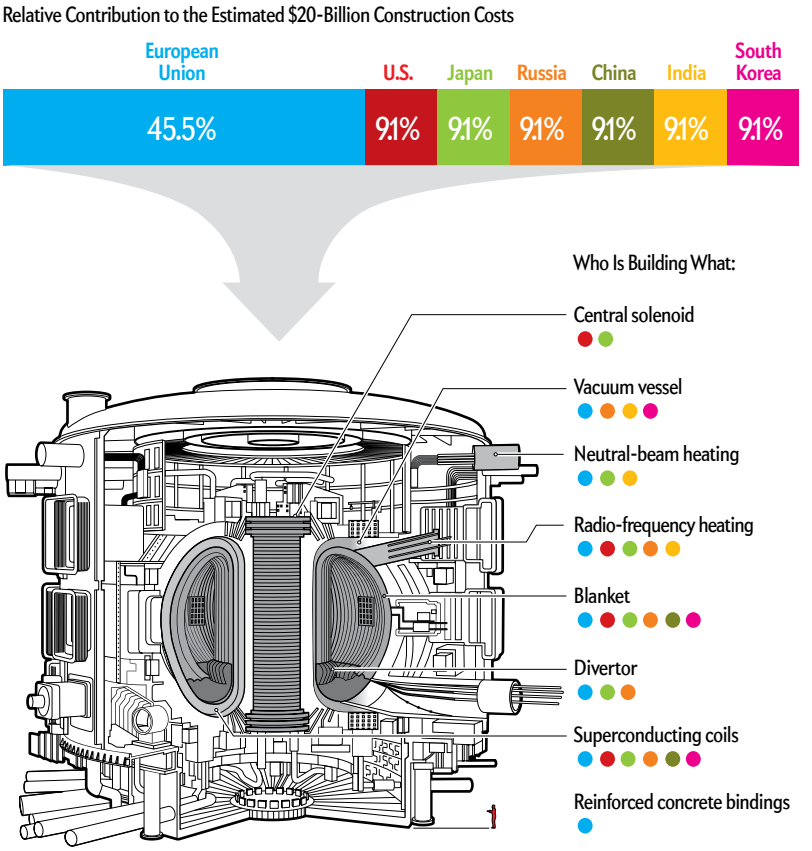
Scientists such as Lee have been seduced by fusion for half a century. Many before him have promised its impending arrival. Although some of those researchers were charlatans, the vast majority of them turned out to be plain wrong. Fusion is tough, and nature breaks promises.

Here is the core challenge: because hydrogen ions repel one another, scientists must slam them together to make them fuse. ITER's strategy is to heat the hydrogen inside a magnetic cage. The particular type of magnetic cage it employs is called a tokamak—a metal doughnut circled by loops of coil that generate magnetic fields. These magnetic cuffs squeeze a charged plasma of hydrogen ions as it warms to hundreds of millions of degrees—temperatures no solid material can withstand.

CONSTRUCTION CHALLENGES

# Fusion's Global Bazaar

**Six countries** and the European Union have joined together to build ITER, the world's largest experimental fusion reactor. Individual member states are responsible for supplying critical parts and in turn contract with homegrown industries to build the needed equipment. This means that a given superconducting coil, for instance, may come from Japan, China or Russia. The scientists building ITER must ensure that the all these parts work together with exquisite precision in an exceedingly demanding environment.




SOURCE: ITER

*Illustration by George Retseck*

In the 1970s tokamaks looked so promising that some researchers predicted they could build fusion electricity plants by the mid-1990s. The only challenge was scaling research reactors up to sufficient size—in general, the bigger the tokamak, the hotter the plasma can get, and the more efficient fusion becomes.

Then problems arose. Plasma conducts electricity and so can suffer from self-generated currents that make it buck and writhe. Violent turbulence snaps the plasma out of its cage, firing it toward the machine's wall. As the temperature rises, the tokamak grows to give the plasma space, and the magnetic fields need to be stronger to hold it. Extra room and stronger magnetic fields require higher electric current in the doughnut's copper coils. And higher current requires more power. Put simply: the larger and more powerful a machine becomes, the more energy it consumes trying to hold everything together.

This feedback meant that conventional tokamaks would never produce more energy than they consumed. Lee and others knew of only one solution: superconductors—special materials that, at very low temperatures, can carry extremely high current with no resistance. If a tokamak's magnets were superconducting, they could be pumped up with current and left to run indefinitely. It would solve the energy problem but would not be cheap. Superconductors are exotic, expensive materials. And to work, they need to be constantly cooled with liquid helium to just four kelvins above absolute zero.

Even in 1985 it was clear that neither Russia nor America could build a tokamak large enough to produce net energy. When ITER officially began, it was as a joint project among the U.S., the Soviet Union, Japan and Europe. The design was enormous and used the latest technology of the time. In addition to superconductors, ITER incorporated advanced accelerators to fire neutral beams of atoms into the core to heat it, along with sophisticated antennas that would act something like a microwave for plasmas. Rather than using plain hydrogen for fuel, ITER would use deuterium and tritium, two hydrogen isotopes that fuse at lower temperatures and pressures. Deuterium is relatively common—a drop of ocean water contains many trillions of deuterium atoms—but tritium is rare, radioactive and pricey. The original construction costs were estimated at $5 billion, but by the mid-1990s a more thorough accounting of the machine's complexities had doubled the price. In 1998, in large part because of the expense, the U.S. left the project.

Shortly thereafter, a small team desperate to keep the project alive hastily redesigned it at half the size and half the cost. Unfortunately, because of "the limited time to finish the design, some things were forgotten," admits Gunther Janeschitz, a senior scientist with ITER and a member of the original redesign team. The member states fought over all the big bits of the machine, but some of the little things—feedthroughs, connections—never got assigned. "There were holes between two of the components, and none of the procurement packages really described it," he says.

These gaps are the scourge of ITER because the machine is not really being manufactured by the ITER organization itself. Established nations such as Russia and Japan want their investment in ITER to go to scientists in their state-run laboratories, whereas newcomers such as India and China want to give their burgeoning industry a chance to learn advanced new technologies. Therefore, member states contribute fully built units to the enterprise (along with a small financial contribution to the central organization). Superconducting cables for its magnets will arrive from Hitachi in Japan, but they will also be supplied by Western Superconducting Technologies Company in China and the Efremov Scientific Research Institute of Electrophysical Apparatus in Russia. The machine's giant vacuum vessel will be constructed in Europe, India, Korea and Russia; the heating systems will come by way of Europe, Japan, India and the U.S., which rejoined the project in 2003. The central ITER organization must take these parts, figure out what is missing, then cobble everything together into the most sophisticated experiment ever built.

**A small team desperate to keep the project alive hastily redesigned it at half the size and half the cost. Unfortunately, because of "the limited time to finish the design, some things were forgotten."**

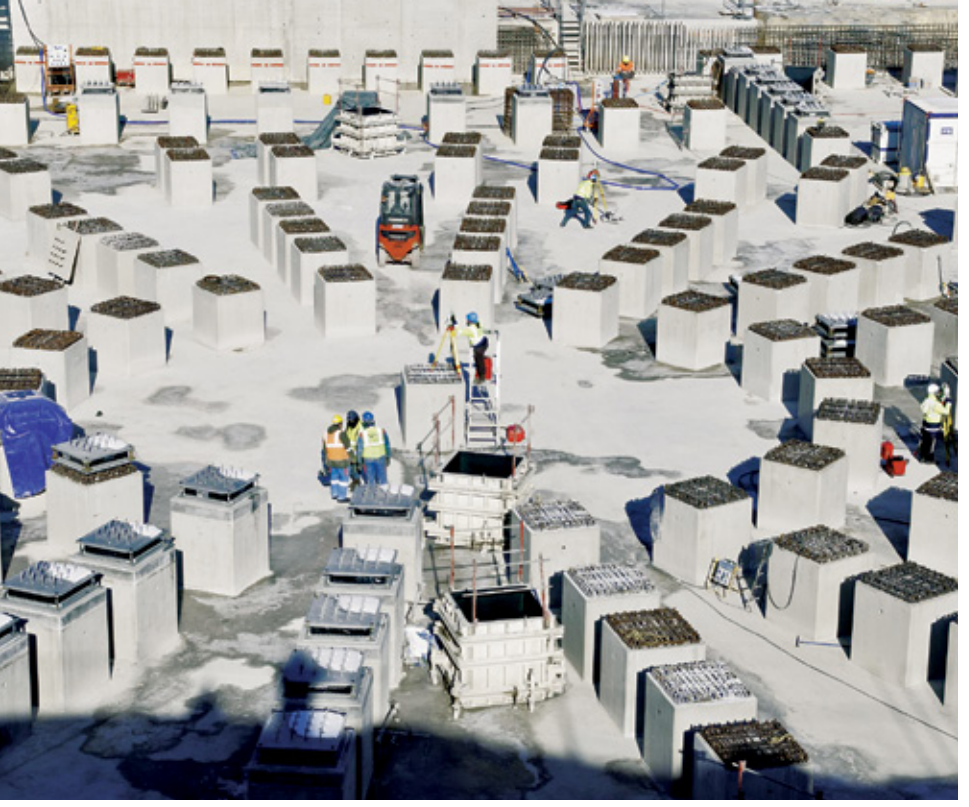
The challenge becomes clear at a medieval château overlooking the Durance River on the other side of a two-lane highway from ITER's temporary headquarters. Here ITER's members gather inside a purpose-built meeting room crammed with flat screens and microphones. The partners have no interest in letting a reporter in on the negotiations, but during a coffee break, Lee tells me a minor crisis is unfolding behind closed doors. "The Indians think a pipe should end here, and others think it should end there," he says, gesturing to opposite ends of the room with a small chocolate tart from the pastry table. "The obvious solution is to meet in the middle, but this is not technically possible. So we hand it on to the DG."

Until 2010 the DG, or director general, was a soporific Japanese diplomat named Kaname Ikeda. As these kinds of problems mounted, Ikeda resigned under pressure from ITER's council and was replaced by Osamu Motojima, a veteran Japanese fusion researcher whose quiet nature belies what insiders describe as a tough and sometimes autocratic personality. Motojima and his deputies, veterans of the U.S. and European programs, sit down to work out a deal with the Indians in a converted stable next to the conference room. While the team haggles, Harry Tuinder, at the time ITER's chief legal adviser (he has since left the organization for the European Commission), sits in the courtyard and lights a cigarette. I ask him if it would not make more sense if Motojima had the authority to force every nation to contribute the parts he needs. "That would basically be degrading all the relationships you try to reinforce," Tuinder says, leaning back in his chair. At the end of the day, it is members' willing participation, not the power of ITER's director general, that will make the project come together.

## ROAD TO POWER

AS NEGOTIATIONS DRAG ON, ITER's costs have doubled yet again to an estimated $20 billion, although the piecemeal way in which it is being built means that the actual cost may never be known. Its completion date has slipped by another couple of years.

The soaring price and lengthening delays have been fueling opposition to the giant tokamak, particularly in Europe, which



**SOLID FOUNDATION:** The reactor will sit on 493 columns topped by steel-and-rubber bearings to isolate the 400,000-ton structure from seismic vibrations.

COURTESY OF ITER ORGANIZATION www.iter.org

is supplying around 45 percent of its construction costs. "If we really want to put money to save the climate and have energy independence, then obviously this experiment is nonsense," says Michel Raquet, energy adviser to the Green Party of the European Parliament. The European Union is currently working on a budget that will accommodate the estimated €2.7 billion that ITER requires to complete construction by 2020. The Greens, ITER's chief opponents in Europe, fear that the money will come at the expense of such renewables as wind and solar.

In the U.S., which will pay just 9 percent of the cost, opposition is more muted. "It's not threatening—it's just a waste of money," says Thomas Cochran, a nuclear campaigner with the Natural Resources Defense Council. Cochran asserts that he would rather devote his energy to fighting other nuclear research programs that generate long-term waste or spread nuclear weapons technology. The U.S. Congress seems similarly indifferent about the program. "All I can say is that there's no move to kill it," says Stephen Dean, president of Fusion Power Associates, which advocates for the development of fusion energy. But that may change. The budget President Barack Obama presented this year funds a steep rise in ITER costs by slashing spending on domestic fusion research. Even then, the $150 million ITER will receive is 25 percent less than the U.S.'s scheduled contribution.

Other nations are also encountering trouble with their commitments to ITER. India has struggled to hand out contracts, and last March's massive earthquake off the coast of Japan damaged key facilities there. "Every country has its own reasons for delays," says Vladimir Vlasenkov, a member of the Russian delegation. Russia, he hastens to add, is on track.

ITER will prove whether fusion is achievable. It will not prove whether it is commercially viable. There is good reason to think it might not be. For starters, the radiation from fusion is very intense and will damage ordinary material such as steel. A power plant will have to incorporate some as yet undeveloped materials that can withstand years of bombardment from the plasma—otherwise the reactor will be constantly down for servicing. Then there is the problem of tritium fuel, which must be made on-site, probably by using the reactor's own radiation.

Arguably the greatest obstacle to building a reactor based on ITER is the machine's incredible complexity. All the specialized heating systems and custom-built parts are fine in an experiment, but a power plant will need to be simpler, says Steve Cowley, CEO of the U.K.'s Atomic Energy Authority. "You can't imagine producing power day in and day out on a machine that's all bells and whistles," he says. Another generation of expensive demonstration reactors must be built before fusion can come onto the grid. Given ITER's lumbering development, none of these will be up and running before the middle of the century.

Despite these setbacks and the uncertain future of fusion energy as a whole, it is difficult to find anyone familiar with ITER who thinks the machine will not get built. Peer pressure is one reason: "The French are in it and won't back out because the U.S. is in it and won't back out," Cochran says. Political visibility for the countries involved—and substantial penalties for pulling out early—also serves to keep the project moving, Tuinder observes.

Those legitimate, if cynical, reasons for staying the course aside, many scientists genuinely feel that fusion is the only hope to meet the world's energy demands. "I was scared about the future energy of the world—I didn't know where it would come from," says Raymond Orbach, chief scientist at the Department of Energy at the time the U.S. rejoined the project. "It's $CO_2$-free, it's essentially unlimited, it has no environmental impact—come up with an alternative." Most fusion scientists think a climate crisis is inevitable anyway. Further down the line, after humanity has learned its lesson, "we'd better have a set of technologies ready," Cowley admonishes. It is going to work, this line of thinking goes, because it must. SA

MORE TO EXPLORE


**The International Thermonuclear Experimental Reactor.** Robert W. Conn et al. in *Scientific American,* Vol. 266, No. 4; pages 102–110; April 1992.

**Fusion Energy: Just around the Corner.** Geoff Brumfiel in *Nature,* Vol. 436, pages 318–320; July 21, 2005.

**Sun in a Bottle: The Strange History of Fusion and the Science of Wishful Thinking.** Charles Seife. Viking, 2008.

**Fusion as an Energy Source: Challenges and Opportunities.** W. J. Nuttall. Report of the Institute of Physics, September 2008.

**Fusion's False Dawn.** Michael Moyer in *Scientific American,* Vol. 302, No. 3, pages 50–57; March 2010.


SCIENTIFIC AMERICAN ONLINE

The difference between fusion and fission: ScientificAmerican.com/jun2012/fusion

ECOLOGY

# BUSY BEE

## Orchid pollinators are surprisingly promiscuous about the plants they like

*By Rose Eveleth*

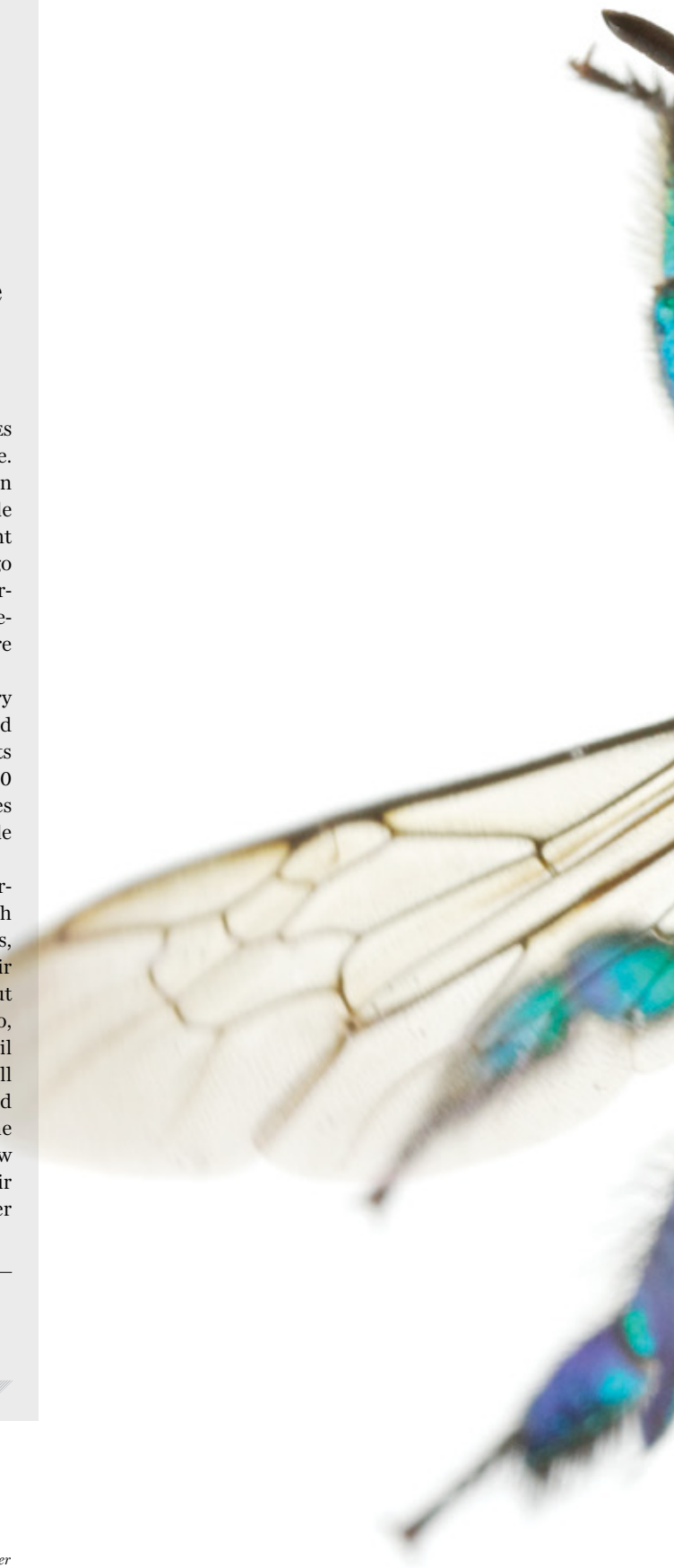
BIOLOGISTS HAVE LONG BELIEVED THAT ORCHID BEES and orchids rely on each other in equal measure. The shimmering bees pollinate orchids in return for the flowers' donation of perfumes, which male bees use to attract females. And so it was thought that the two organisms co-evolved. But a study led by Santiago Ramírez, an evolutionary biologist at the University of California, Berkeley, that was published in *Science* in late 2011 revealed that the bees arose first, thus suggesting that the two are more independent than previously thought.

Ramírez's work shows that although the orchids seem very adapted to the bees—having developed scents that bees like and mechanisms to deposit pollen onto the bees' body—the insects are far less specialized. They collect scents from more than 700 species of plants, and they pollinate an array of them. "The bees and plants all interact," Ramírez says, "and we know very little about how those networks of interactions evolve."

Learning more about the bees could help scientists understand their role in pollinating tropical orchids, many of which are in danger of extinction. The bees are in danger themselves, threatened by deforestation and land fragmentation in their native Central and South America, which has been wiping out the bees' habitat and food sources. As a result, André Nemésio, a researcher at the Federal University of Uberlândia in Brazil who studies the elusive creatures, worries that scientists will not learn about the bees quickly enough to save them. "Orchid bees are solitary, very shy, and you almost never see them in the forest," he says. Moreover, because no one knows exactly how important the bees are to the plants they pollinate or to their predators, the consequences of losing them present yet another mystery. SA

***Rose Eveleth** is a New York City–based freelance writer.*

**SCIENTIFIC AMERICAN ONLINE**
For an audio slide show, see ScientificAmerican.com/jun2012/orchid-bee



*Photograph by David Liittschwager*

INFECTIOUS DISEASE

# WAITING TO *Explode*

By concocting bird flu viruses that could potentially spread easily among humans, researchers have ignited a debate about the need for safety versus open inquiry

*By Fred Guterl*



*Photoillustration by Kyle Bean and Sam Hofman*

THE CHICKENS WERE ALREADY GETTING SICK WHEN Yoshihiro Kawaoka arrived in the U.S. in August 1983. A few months before, in April, a bird flu virus had arisen in the poultry farms of eastern Pennsylvania, but veterinarians had deemed it to be "low pathogenic"—meaning it made chickens sick but did not kill many of them. As the virus swept through the poultry farms, however, a new strain developed. Chickens began to die in large numbers, and farmers started to fear for their livelihoods. The state called in the U.S. Department of Agriculture, which set up a temporary command and control center in a strip mall outside of Lancaster. To contain the epidemic, it culled 17 million birds from Pennsylvania down through Virginia.

Kawaoka was a young researcher from Japan who was starting work at St. Jude Children's Research Hospital in Memphis. His boss, virologist Robert Webster, had a theory that human influenza viruses originate in bird populations—that they circulate harmlessly among ducks and geese and that, every once in a while, a strain will evolve the ability to live in the human upper respiratory tract. To combat human influenza, Webster asserted, you first had to understand bird flu. In November, when Webster heard that the outbreak had become serious, he dropped everything and headed to its epicenter.

Kawaoka stayed behind and watched the crisis unfold from behind the air lock of the Memphis hospital's biocontainment laboratory. He took samples sent back to him from the field, extracted the virus and cultured it. He then infected chickens that he kept in cages along a wall and waited to see what happened. What he found disturbed him: each and every chicken died—a mortality rate of 100 percent. In autopsies, he found that the virus was a ruthless pathogen, attacking almost every organ—similar to what some strains of Ebola do to humans.

In the months after the crisis, Kawaoka puzzled over why the April strain of the virus was so mild and why the strain that it evolved into by November was so deadly. He decided to compare the two. The difference, he discovered, came down to relatively small changes in the virus. "What this tells you," Kawaoka told me in an interview in 2010, "is that a highly pathogenic virus was generated from a single mutation. And it tells you there are many sources of highly pathogenic influenza viruses. It's all out there in birds."

The experience brought home to Kawaoka the urgency for scientists to figure out how bird flu can cause trouble for humans—the better to detect it early or to prepare effective vaccines and treatments. In particular, he wanted to know if a lethal bird flu akin to the one that burned through poultry farms in 1983 could turn into a human disease. And if so, what sequence of genetic code would the virus have to acquire?

Nearly three decades later Kawaoka got an answer. He took an avian flu—an H5N1 type—that lives in birds and combined it with the H1N1 pandemic virus of 2009. Then he tested his hybrid virus on ferrets—a common research stand-in for humans—and found that it spread easily by airborne droplets. With this result, the notion that an H5N1 influenza virus could become a human pathogen was no longer hypothetical. If he could do it in a lab, nature could do it, too.

Kawaoka submitted his paper to the journal *Nature,* which then sent it out to his peers for review, a standard practice. (*Scientific American* is part of Nature Publishing Group.) Virologist Ron Fouchier of Erasmus Medical Center in Rotterdam also independently concocted a potentially human transmissible H5N1 virus and tested it on ferrets; he submitted his paper to the jour-

IN BRIEF

**Birds** are a natural reservoir for influenza viruses that sometimes jump to humans.
**H5N1** strains in particular have some virologists worried because mortality may be high among the few people who have been infected, mainly from direct contact with birds.
**After the September 11 attacks,** biodefense spending soared, leading to recent research on H5N1 lab-made strains that are transmissible among mammals.
**This work set off** a debate between biodefense experts, who argue that the new H5N1 strains are potentially dangerous and want restrictions on research, and scientists, who argue that research on dangerous pathogens is important for improving surveillance of natural outbreaks and that hampering such work would do more harm than good.

nal *Science*. At some point, the White House got wind of the studies. By December 2011 biosecurity officials were pushing for a delay in publication and a moratorium on the research.

What had biosecurity experts worried is that one of these viruses could possibly do to people what the 1983 virus did to chickens. If that were the case, the research might serve as a blueprint for a bioweapon. Or perhaps the virus itself could escape from a lab via a worker who became infected accidentally. For the months after the submission of the papers, scientists argued publicly and often vociferously with one another about whether the new viruses were potentially lethal and what kinds of restraints, if any, should be applied to work on H5N1 influenza viruses. The practice of science, which thrives on the free flow of information and the propensity of scientists to follow their curiosity wherever it may lead, collided with the need to keep people safe from a pathogen that could arguably be considered a potential weapon of mass destruction—every bit as devastating, and troublesome to manage, as nuclear weapons.

## THE NATURAL THREAT

THE FIRST RECORDED instance of a "fowl plague" on poultry farms occurred in the countryside of northern Italy in 1878. It was thought to be a particularly virulent form of cholera. By 1901 scientists had pegged it to a virus of some kind. By 1955 they realized it was type A influenza, similar to strains that infect humans, which later led Webster and others to wonder if there was some relation between influenza in birds and human outbreaks.

Webster's hunch about birds being a reservoir for precursors to human viruses is now conventional wisdom. Wild birds carry such viruses around in their gastrointestinal tract without becoming sick and transmit the virus through feces. If a wild bird infects a chicken on a poultry farm, the virus may get opportunities to interact with a range of additional viruses through close contact with pigs and other animals. This is indeed what has happened in the live animal markets and backyard farms of China and southern Asia. Influenza viruses are notorious for their ability to change, through a combination of mutation and "reassortment"—a borrowing of genes from other viruses. An open farm acts like a virus convention, where different strains swap genetic material like conventioneers swap business cards.

In the past few decades influenza specialists have focused their worry on the H5N1 strains circulating on Asian farms. Type A influenza viruses are categorized by their surface proteins hemagglutinin and neuraminidase—the "H" and "N" in the species designations. (The 1983 virus was an H5N2.) If a virus can be said to have a personality, the H5N1 virus seems restless and unpredictable. For instance, the virus was thought to be benign in wild birds, but in 2005 thousands of ducks, geese, gulls and cormorants were found dead in Qinghai Lake in Central China, apparently killed by H5N1. In the past decade H5N1 has killed civets in Vietnam and tigers in a Thai zoo.

It has killed people, too. During the outbreak among poultry in Asia in 1997, a three-year-old boy in Hong Kong became the first known human fatality. By year's end the death toll was six. To stem the outbreak, authorities in China and neighboring countries oversaw the culling of millions of birds. Still, the virus came surging back in 2004 in Thailand, Vietnam, China and Indonesia.

All told, around 350 people have died from H5N1, most from contact with birds. The absolute number is not high, but the virus, according to the World Health Organization, has a mortality rate of about 60 percent. In contrast, the 1918 influenza virus, which killed 20 million to 50 million people, had a mortality rate of about 2 percent. Since the Kawaoka and Fouchier papers surfaced last fall, the actual mortality rate of H5N1 has been the subject of intense debate. Some scientists—notably, Peter Palese, professor of infectious diseases and chair of microbiology at the Mount Sinai School of Medicine—argue that mild cases of H5N1 have gone underreported or do not register in tests, which has artificially driven up the mortality rate. Others argue that deaths from H5N1 have gone underreported, which may make the mortality rate appear lower than it actually is. Kawaoka and Fouchier have reported low mortality among ferrets for their lab-made viruses. Whatever the danger these particular viruses might or might not pose, the fact that H5N1 could potentially spread easily among humans is not good news.

In September 2001 anthrax that had been weaponized as a fine white powder made its way through the U.S. mail, killing five people and terrorizing a nation already skittish from the World Trade Center and Pentagon attacks on 9/11. Spending on biodefense soared. Since 2001 the U.S. government has plowed more than $60 billion into vaccine stockpiling, disease surveillance and basic research into potential bioweapons agents, including influenza. The National Institute of Allergy and Infectious Disease (NIAID), the major source of funds in the U.S., nearly tripled its budget on influenza research in fiscal year 2003—from $17 million to $50 million—and doubled it again to $100 million in 2004. In 2009 funding hit a peak of nearly $300 million, from which it has come down slightly. Kawaoka was the recipient of some of that largesse. Since 2006 he has received nearly $500,000 a year from NIAID for research on the "pandemic potential of H5N1 influenza viruses," according to the National Institutes of Health Web site. Fouchier got his funding from Palese's group at Mount Sinai, which subcontracted the work from a grant from NIAID. Fouchier's lab made mutations to an H5N1 virus to enhance transmissibility and then passed the virus to ferrets until it spread via airborne droplets among them. The Centers of Disease Control and Prevention also had a group investigating transmissibility of H5N1, but it was not as successful as Kawaoka's and Fouchier's groups.

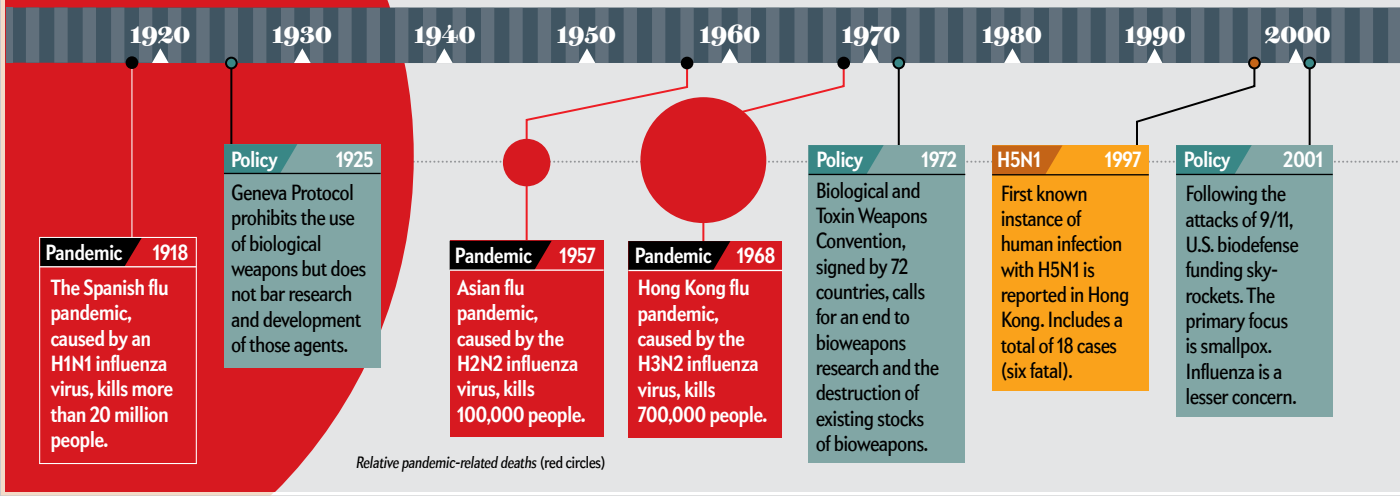
## THE WEAPON

FOR YEARS AFTER 9/11, however, concerns over smallpox as a potential bioweapon eclipsed those of influenza. The variola virus that causes smallpox kills one in three people infected and persists for years between hosts. It was declared eradicated in 1979. Although officially only two samples are kept under lock and key in Atlanta and in Koltsovo, Russia, there have been persistent rumors of other, illicit samples. In response to heightened fears after the 9/11 attacks, the U.S. stockpiled about 300,000 doses of smallpox vaccine, which now sit in secret warehouses throughout the country.

Influenza made it onto the bioweapons agenda in 2005, but biosecurity officials gave it a pass. Scientists had succeeded in reconstructing the 1918 pandemic flu virus from tissue samples of human remains that had been frozen in Arctic ice. The National Science Advisory Board for Biosecurity (NSABB) conferred and decided that the benefits to science and public health outweighed the security risk. Current NSABB chair Paul Keim

# Evolution of a Bioweapon

Influenza has long caused pandemics, but H5N1 bird flu has not been able to spread readily from one human to another. New findings suggest that nature or terrorists could change that, thus paving the way for a bird flu bioweapon. Outbreaks of the H5N1 strain among poultry in Asia in the 1990s alerted health officials to the potential for a human pandemic strain. If a highly pathogenic flu virus were to spread as rapidly as the 2009 H1N1 virus, health officials would have little time to respond. Since the September 11 attacks in 2001, influenza (including the 1918 pandemic strain) has been considered a potential bioweapon.




recently called that decision "a mistake." The 2009 pandemic virus, an H1N1 type with low pathogenicity, made the issue moot by conferring at least partial immunity to the 1918 virus to much of the world's population. Since H5N1 is novel to the human immune system, there is no natural resistance.

Some defense experts now consider Kawaoka's and Fouchier's lab-made H5N1 viruses to be potentially more dangerous than smallpox. Influenza viruses are more contagious than variola and move more quickly through human populations, which gives public health officials less time to marshal vaccines and treatments. "Influenza is the lion king of transmissibility," says Michael Osterholm, director of the Center for Infectious Disease Research and Policy at the University of Minnesota and an outspoken member of the NSABB. A highly transmissible H5N1 virus with a human mortality rate even approaching the 60 percent observed so far among bird flu victims is a terrifying prospect. As Osterholm has pointed out, even at one-twentieth the pathogenicity, H5N1 would be deadlier than the 1918 pandemic virus. NSABB called for a withholding of details in the Kawaoka and Fouchier papers last December but gave the go-ahead for full publication in March.

There is general agreement in the biosecurity community that bird flu—or, to be specific, H5N1 viruses made in the laboratory to be transmissible among mammals—is a potential bioweapon, which, like smallpox, has to be managed. "The very fact that this virus exists creates a risk," says Richard H. Ebright, a biodefense expert and chemical biologist at Rutgers University. "It creates the risk of accidental release, and it creates the risk that someone will turn it into a weapon."

What has defense experts, as well as many scientists, miffed is that the research proceeded without any analysis of the benefits and the risks beforehand. The NSABB, purely an advisory board with no oversight responsibility, got involved only after prodding by the White House. In 2007 John Steinbruner and his colleagues at the Center for International and Security Studies at Maryland wrote a report recommending "some constraint on freedom of action at the level of fundamental research, where individual autonomy has traditionally been highly valued for the best of reasons." The report was largely ignored. After the Fouchier and Kawaoka papers came to light, however, the U.S. government called on funding agencies to perform risk assessments on research involving the H5N1 and 1918 flu viruses.

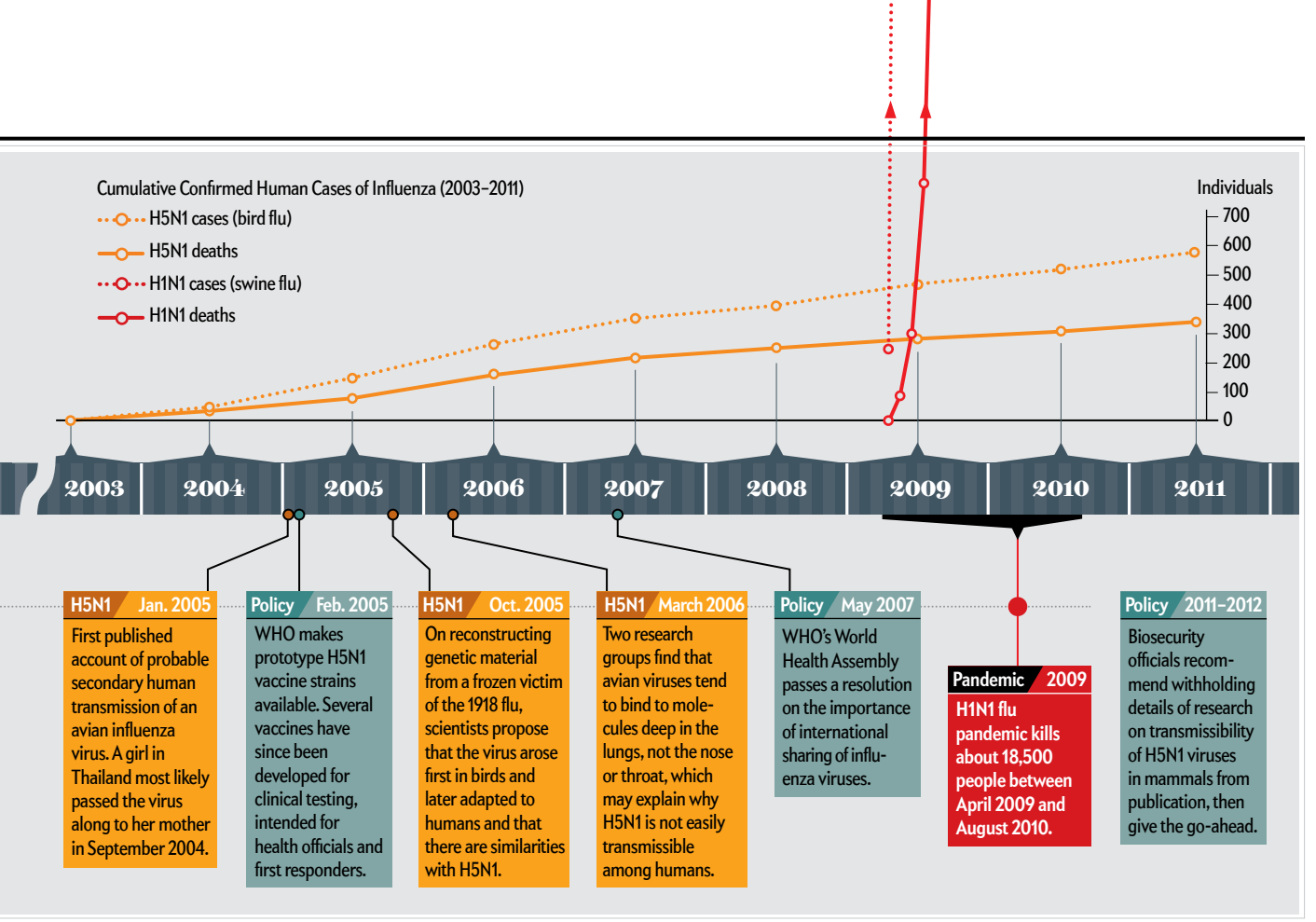
Steinbruner and others recommend some kind of international oversight group with some power to impose mandatory constraints on potentially dangerous research and oversee it, much as the WHO does now with smallpox. "It wouldn't be an airtight protection, but it would establish the norm that nobody can go off into a closet and do these experiments," Steinbruner says. An H5N1 virus engineered to spread among mammals "is an agent of mass destruction that gets into the nuclear weapons league and even exceeds it," he adds. "It is a very dangerous pathogen. It's not a matter of [scientists] being personally careful. There's got to be some institutional safety procedure."

How restrictive should those procedures be? Nuclear weapons technology is subject to military classification, which means some research can only be conducted in secret. Unlike nuclear weapons, however, influenza is a matter of global public health. Classifying some aspects of H5N1 research would leave scientists and health officials in the dark about one of the world's bigger public health threats. In contrast, many security experts argue in favor of restricting research on mammal-trans-

SOURCES: "H5N1 AVIAN INFLUENZA: TIMELINE OF MAJOR EVENTS," BY WORLD HEALTH ORGANIZATION, DECEMBER 13, 2011 (*H5N1 timeline entries*); WHO (*H5N1 and H1N1 human case rates*)



*Graphic by Jen Christiansen*




missible viruses to only the most secure labs—more secure than the labs Kawaoka and Fouchier did their work in. Such restrictions would put the research out of reach of many scientists.

Many investigators have been passionate in their defense of the kind of work Kawaoka and Fouchier have done on the grounds that the more we know about H5N1, the better we can protect ourselves from the natural threat. Science, the argument goes, advances best when research activities are unfettered. Pinning down precisely what genetic components are needed to confer traits such as lethality and transmissibility on H5N1 would allow health experts to be on the watch for dangerous new strains that emerge in the wild and prepare for them in advance. Once a novel human flu virus crops up and begins to spread, it is too late to stop the first wave of infection. Flu vaccine production typically takes six months to complete, sometimes more. For instance, by the time the H1N1 virus came to the attention of health officials in April 2009, it had spread widely in Mexico and the U.S. and was well on its way to becoming a pandemic.

Moreover, one of the genetic components Kawaoka identified as conferring transmissibility on H5N1 has been observed in natural viruses, which suggests that the roulette wheel is already in spin. "Because H5N1 mutations that confer transmissibility in mammals may emerge in nature, I believe that it would be irresponsible not to study the underlying mechanism," Kawaoka wrote in an essay in *Nature*. (He declined to be interviewed for this article.) Fouchier has defended his work on the same grounds.

Having the genetic details of potentially deadly flu viruses is of little use, however, without the funding, networks and access to animals out in the field. During the H5N1 outbreaks, virologists began rigorous monitoring of the live animal markets in southern China, but those measures have not been applied consistently elsewhere in China or Southeast Asia. In the U.S., livestock farms often bar health officials from testing their pigs even though precursors of the 2009 H1N1 pandemic are thought to have kicked around U.S. pig farms for years before emerging in Mexico [see "Flu Factories," by Helen Branswell; Scientific American, January 2011].

Surveillance may never be good enough to forestall human pandemics. "We're better prepared now than we were prior to the H1N1 pandemic," says Nancy Cox, director of the Influenza Division of the CDC, "but the world is not prepared for the emergence of highly transmissible, highly pathogenic influenza virus in humans. Honestly, I don't think the world ever will be unless we have a universal vaccine that protects against all strains." A universal vaccine is not in sight, which leaves us in the uncomfortable position of having too much knowledge and too little. SA

***Fred Guterl*** *is executive editor of* Scientific American *and author of* The Fate of the Species, *which Bloomsbury releases this month.*

MORE TO EXPLORE

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**The History of Avian Influenza.** Blanca Lupiani and Sanjay M. Reddy in *Comparative Immunology, Microbiology and Infectious Disease*, Vol. 32, No. 4, pages 311–323; July 2009.

**SCIENTIFIC AMERICAN ONLINE**

See an expanded timeline on the history of avian influenza and other potential bioweapons agents at ScientificAmerican.com/jun2012/bird-flu

HISTORY OF SCIENCE

# THE RIGHT WAY TO GET IT WRONG

*Most errors are quickly forgotten. Others end up remaking the face of science*

*By David Kaiser and Angela N. H. Creager*

*Photograph by Dan Saelinger*

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**Angela N. H. Creager** is a professor of history at Princeton University who studies the history of biology. She received her Ph.D. in biochemistry at the University of California, Berkeley, before training in the history of science at Harvard and M.I.T.

PERHAPS MORE THAN ANY OTHER PROFESSION, SCIENCE PLACES A PREMIUM ON BEING CORRECT. Of course, most scientists—like most living humans—make plenty of mistakes along the way. Yet not all errors are created equal. Historians have unearthed a number of instances in which an incorrect idea proved far more potent than thousands of others that were trivially mistaken or narrowly correct. These are the productive mistakes: errors that touch on deep, fundamental features of the world around us and prompt further research that leads to major breakthroughs. Mistakes they certainly are. But science would be far worse off without them.

Niels Bohr, for example, created a model of the atom that was wrong in nearly every way, yet it inspired the quantum-mechanical revolution. In the face of enormous skepticism, Alfred Wegener argued that centrifugal forces make the continents move (or "drift") along the surface of the earth. He had the right phenomenon, albeit the wrong mechanism. And Enrico Fermi thought that he had created nuclei heavier than uranium, rather than (as we now know) having stumbled on nuclear fission.

Two instances of productive mistakes, one from physics in the 1970s and one from biology in the 1940s, illustrate this point dramatically. The authors of the mistakes were not hapless bumblers who happened, in retrospect, to get lucky. Rather they steadfastly asked questions that few of their colleagues broached and combined ideas that not many at the time had considered. In the process, they laid critical groundwork for today's burgeoning fields of biotechnology and quantum information science. They were wrong, and the world should be thankful for their errors.

## THE PHANTOM PHOTON CLONE

OUR FIRST MISTAKE helped to illuminate a dispute that had begun during the early days of quantum mechanics, when Albert Einstein and Bohr engaged in a series of spirited debates over the nature and ultimate implications of quantum theory. Einstein famously railed against several strange features. Using the equations of quantum mechanics, for example, physicists could predict only probabilities for various occurrences, not definite outcomes. "I, at any rate, am convinced that *He* [God] is not playing at dice," came Einstein's rejoinder. There the matter stood for 30 years. Neither Einstein nor Bohr managed to convince the other side.

Decades later a young physicist from Northern Ireland, John Bell, returned to Einstein and Bohr's exchanges. Bell revisited a thought experiment that Einstein had published back in 1935. Einstein had imagined a source that spat out pairs of quantum particles, such as electrons or photons, moving in opposite directions. Physicists could measure certain properties of each particle after it had traveled far apart from the other. Bell wondered about correlations between the outcomes of those measurements.

In 1964 he published a remarkably brief and elegant article demonstrating that, according to quantum mechanics, the outcome of one of those measurements—say, the spin of the right-moving particle along a given direction—must depend on the choice of which property to measure of the left-moving particle. Indeed, Bell deduced, any theory that reproduced the same empirical predictions as quantum mechanics must incorporate a signal or "mechanism whereby the setting of one measuring device can influence the reading of another instrument, however remote." Moreover, he concluded, "the signal involved must propagate instantaneously." Such long-distance correlations became known as "quantum entanglement."

Though renowned among physicists today, Bell's paper garnered no great fanfare when it appeared even though instantaneous signal transfer would violate the well-supported laws of Einstein's relativity, which holds that no signal or influence can travel faster than light. Among the physicists who did take notice was Nick Herbert. The subject began to occupy more and more of Herbert's attention, crowding out thoughts of his day job as an industrial physicist in the San Francisco Bay Area. At the time, Herbert was a core member of a quirky, informal discussion

### IN BRIEF

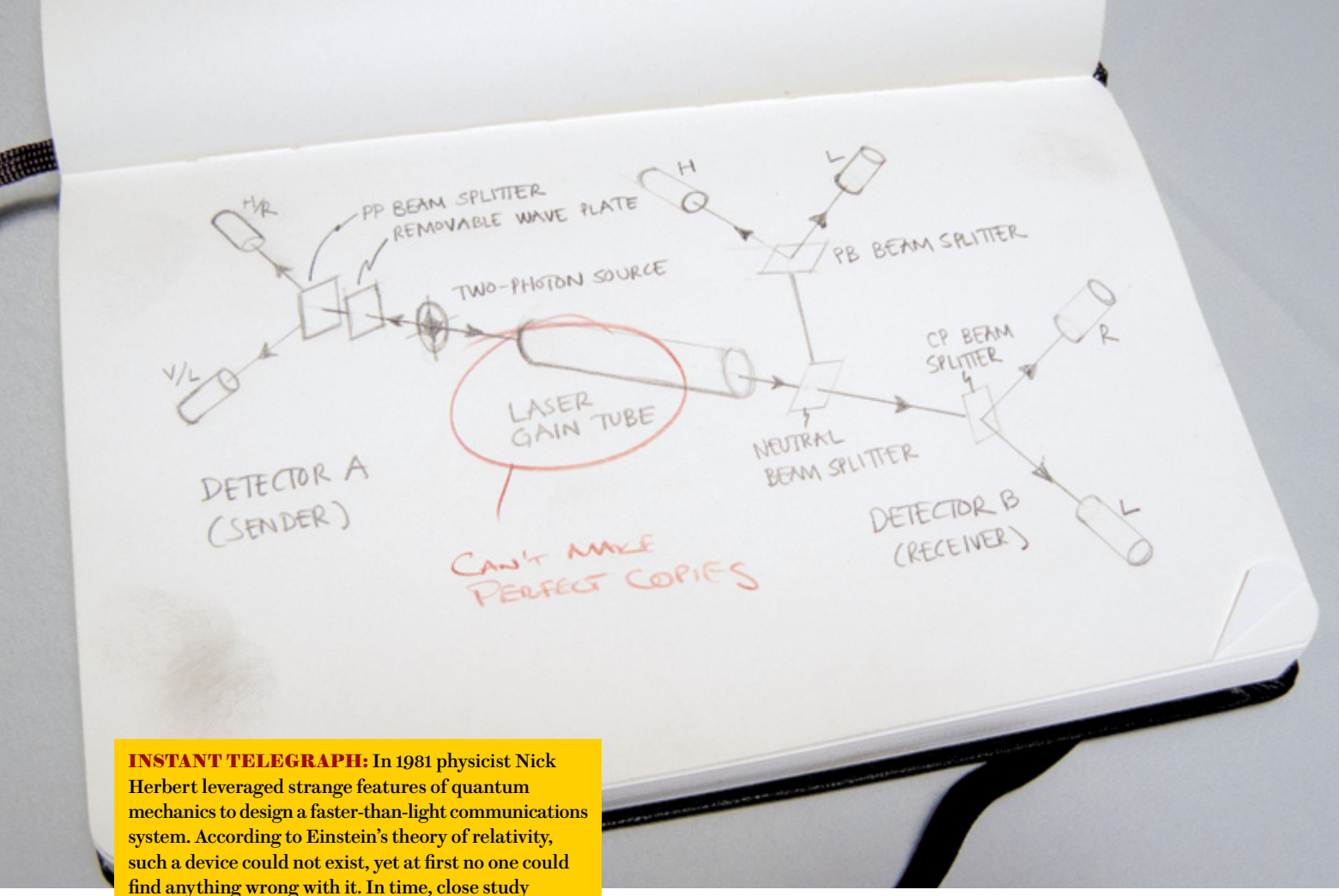
**Mistakes can push** scientific understanding forward. Errors that touch on deep features of the world can be more valuable in the long run than narrowly correct ideas.

**Famously important** scientific mistakes include Niels Bohr's atomic model, the theory of continental drift (in its original form) and the experiments of Enrico Fermi that led to nuclear fission.

**Two less well-known** errors also stand out: a vagabond physicist devised a faster-than-light telegraph in the 1980s. The hunt to uncover its flaws drove advances in quantum information theory.

**In the 1940s** Max Delbrück, the key founder of molecular biology, based his research on a number of incorrect and misleading assumptions. He would go on to win a Nobel Prize.

PRECEDING PAGES: PROP STYLING BY WENDY SCHELA; THIS PAGE: SOURCES: DONNA COVENEY (*Kaiser*); SAGE ROSS (*Creager*)




**INSTANT TELEGRAPH:** In 1981 physicist Nick Herbert leveraged strange features of quantum mechanics to design a faster-than-light communications system. According to Einstein's theory of relativity, such a device could not exist, yet at first no one could find anything wrong with it. In time, close study revealed Herbert's error: elementary particles can never be exactly copied in the way Herbert assumed. Physicists have exploited this insight to make crucial advances in quantum information science.

group called the Fundamental Fysiks Group. The participants met in Berkeley and mostly were young physicists who had earned their Ph.D.s at elite programs—Herbert did his doctoral work at Stanford University—only to fall victim to an unprecedented job crunch. In 1971, for example, more than 1,000 young physicists registered with the Placement Service of the American Institute of Physics, competing for just 53 jobs on offer.

Underemployed and with time on their hands, Herbert and his pals met weekly during the mid-1970s to brainstorm about deep puzzles of modern physics, topics that had received little attention in their formal physics training. They became mesmerized by Bell's theorem and quantum entanglement. Another group member, John Clauser, conducted the world's first experimental test of Bell's theorem and found the strange predictions about quantum entanglement to be spot-on. (In 2010 Clauser shared the prestigious Wolf Prize for his contributions.)

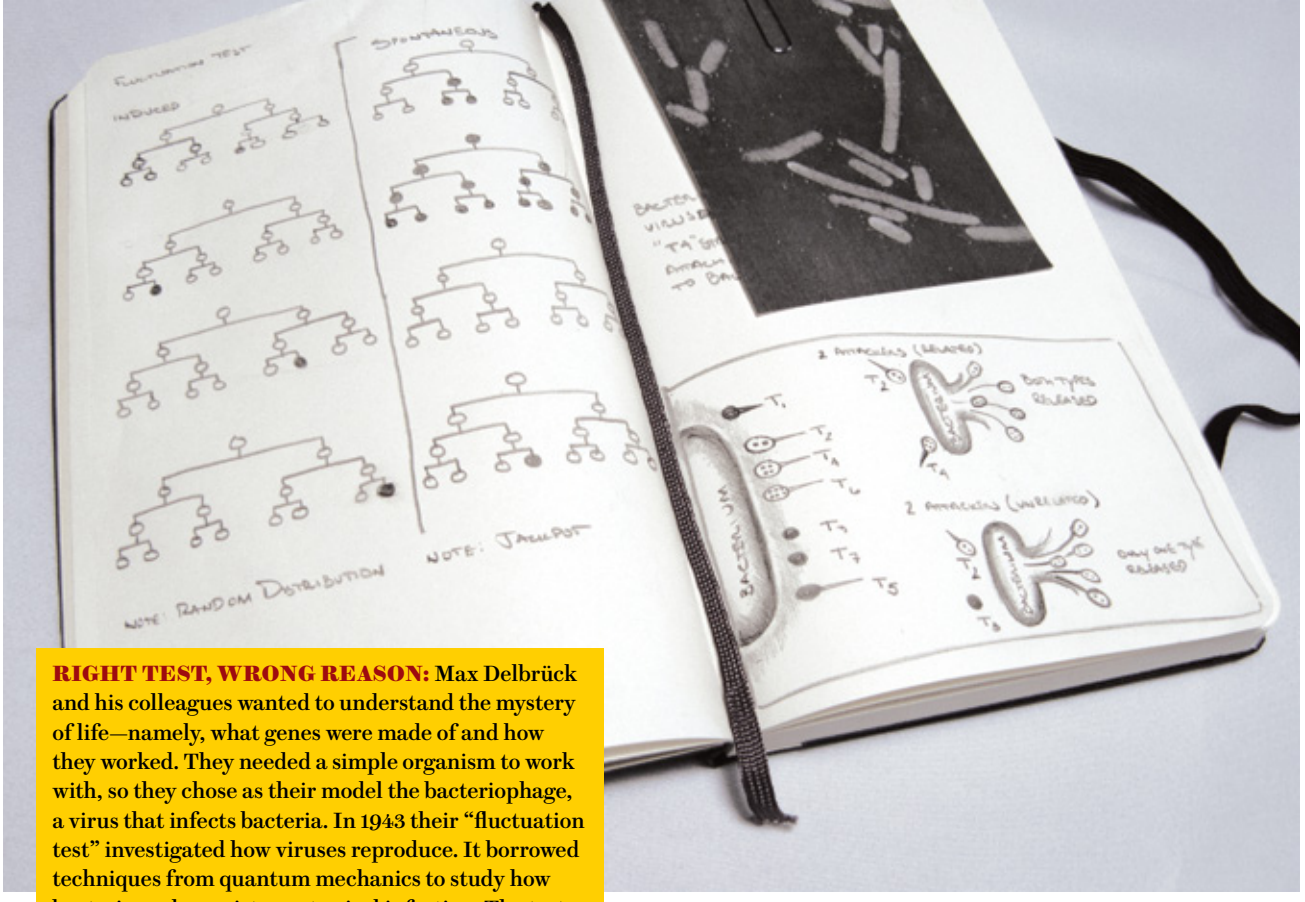
Meanwhile, all around them, the Bay Area was witnessing an explosion of interest in bizarre phenomena such as extrasensory perception and precognitive visions of the future. The *San Francisco Chronicle* and other mainstream newspapers ran stories about experiments in telepathy, while occult enthusiasts celebrated the arrival of a New Age. Herbert and his discussion-mates began to wonder whether Bell's theorem—which seemed to imply mysterious, instantaneous, long-distance connections between distant objects—might account for the latest crop of marvels.

Focusing on what Bell had described as instantaneous signals between quantum particles, Herbert wondered whether they could be tapped to send messages faster than light. He set to drawing up plans for what he called a "superluminal telegraph": a contraption that could harness a fundamental property of quantum theory to violate relativity and hence the laws of physics. After a few false starts, Herbert arrived at his "FLASH" scheme in January 1981. The acronym stood for "first laser-amplified superluminal hookup." It used an elaborate laser-based system to transmit a faster-than-light signal [*see illustration above*].

Herbert's scheme looked watertight. Several reviewers at the journal where he submitted his idea were convinced by his argument. "We have not been able to identify any fundamental flaws with the proposed experiment that reveal the origin of the paradox," reported two referees. Another referee, Asher Peres, took an even bolder step. He proclaimed in his brief report that Herbert's paper must be wrong—and hence it needed to be published. Because Peres himself could find no flaw, he argued that the error must be meaty, the kind that would prompt further advances.

Peres's unusual (even courageous) position was quickly borne out. Three groups of physicists subjected Herbert's paper to close scrutiny. GianCarlo Ghirardi and Tullio Weber in Italy, Wojciech Zurek and Bill Wootters in the U.S., and Dennis Dieks in the Netherlands all recognized that Herbert had made a subtle error

NOTEBOOK PHOTO/ILLUSTRATION BY STAFF




**RIGHT TEST, WRONG REASON:** Max Delbrück and his colleagues wanted to understand the mystery of life—namely, what genes were made of and how they worked. They needed a simple organism to work with, so they chose as their model the bacteriophage, a virus that infects bacteria. In 1943 their "fluctuation test" investigated how viruses reproduce. It borrowed techniques from quantum mechanics to study how bacteria evolve resistance to viral infection. The test became a landmark experiment—but for the study of bacteria, not viruses. Delbrück later complained that, in essence, other scientists were missing the point.

in his calculation of what the physicist who received the signal should see. Herbert had assumed that the laser amplifier in his contraption would be able to emit lots of light in the same state as the original light. In fact, the scientists realized, the laser could not make such copies of a single photon, but only random hash, like a photocopy machine that mixed together two different images to produce a hopeless blur.

In the process of unpacking Herbert's proposal, those three groups uncovered a fascinating, fundamental feature of quantum mechanics that no one had ever recognized. The FLASH system fails because of the "no-cloning theorem," which prohibits an unknown quantum state from being copied or cloned without disturbing the state. The theorem prevents would-be inventors from using quantum theory to build faster-than-light telegraphs, thus enabling quantum entanglement to coexist peacefully with Einstein's relativity. Event by event, the twin particles really do arrange themselves according to long-distance, instantaneous correlations, but those connections can never be used to send a message faster than light.

Very quickly a few other physicists realized that the no-cloning theorem offered more than just a response to Herbert's curious paper or the basis for an uneasy truce between entanglement and relativity. In 1984 Charles Bennett and Gilles Brassard built directly on the no-cloning theorem to design the very first protocol for "quantum encryption": a brand-new way to protect digital signals from potential eavesdroppers. As Bennett and Brassard realized, the fact that quantum mechanics forbids anyone from making copies of an unknown quantum state meant that partners could encode secret messages in entangled photons and pass them back and forth. If anyone tried to intercept a photon en route and make copies, they would immediately destroy the sought-after signal and announce their presence at the same time.

In recent years quantum encryption has moved to the forefront of a worldwide effort in quantum information science. Physicists such as Anton Zeilinger in Vienna and Nicholas Gisin in Geneva have conducted real-world demonstrations of quantum-encrypted bank transfers and electronic voting. Not a bad legacy for Herbert's intriguing—yet flawed—FLASH scheme.

### THE GENETIC PARADOX

OUR SECOND EXAMPLE of a mistaken scientist features the work of Max Delbrück, a professor at Vanderbilt University and, later, the California Institute of Technology. Delbrück, a former student of Bohr's, took from Bohr's famous 1932 lecture "Light and Life" the idea that understanding biological processes would turn up new paradoxes and that solving these paradoxes might lead to the discovery of new laws of physics. Delbrück recruited other scientists to the effort, helping create the field of molecular biology in the years following World War II.

One of the key questions being asked in the 1940s was "What is a gene"? In the mid-19th century the monk Gregor Mendel had proposed the existence of hereditary factors (later called genes), which possessed two distinctive properties. The first was the ability to duplicate themselves. The second was the ability to produce variations, or mutations, that were duplicated as faithfully as the original gene.

Yet in the 1940s no one knew what genes were made of or how they reproduced. As quantum physics pioneer Erwin

NOTEBOOK PHOTO/ILLUSTRATION BY STAFF

Schrödinger noted in his 1944 book *What Is Life?,* no ordinary physical system self-replicates. The seeming ability of genes to do so appeared to defy the second law of thermodynamics.

Delbrück was looking for the atomic gene—the indivisible physical system that was responsible for the mysteries of heredity. As a good physicist, Delbrück figured that the most fruitful approach would be to study life's smallest and simplest units: viruses. Specifically, he chose to study bacteriophages ("phages" for short)—viruses that infect bacteria. These were among the easiest viruses to isolate and the quickest to grow. Although like all viruses, phages reproduced only inside a host cell, Delbrück attempted to avoid what he saw as this unnecessary complexity. He, along with his colleague Emory Ellis, developed a growth method that allowed them to focus on the reproduction of the phages while ignoring the cellular complexities of the infected bacteria.

Delbrück was convinced that genes were made of protein. Understand how the protein parts of viruses reproduced, he thought, and you would understand genes. And the best way to study viral reproduction, he surmised, was to watch them reproduce.

But how could one actually capture viruses as they replicate, to understand the process? The reproduction time of different bacteriophages varied, and Delbrück and his collaborator Salvador Luria reasoned that if they infected the same bacteria with two strains of phage, one that reproduced more rapidly than the other, they should be able to catch replication intermediates of a slower-duplicating strain when the cells burst open.

The dual-infection experiment did not work as planned—Luria and Delbrück found that infection by one viral strain prevented infection by the other. At about the same time, Thomas Anderson of the University of Pennsylvania examined a sample of one of Delbrück and Luria's bacteriophage strains under an electron microscope. He discovered that the virus was far more complex than previously imagined—certainly it consisted of much more than a single atomic gene. It was a tadpole-shaped particle composed of both protein and nucleic acid, and it bound to the outside of bacteria to trigger an infection. The one-to-one correlation between viruses and genes that Delbrück had envisioned was beginning to unravel.

Still, Delbrück would not be dissuaded. In an effort to gain a better understanding of how some bacteria resisted phage infection, he and Luria devised what they called the fluctuation test. The test ended up revealing very little about viral replication, but its ingenious methodology showed that bacteria evolve according to Darwinian principles, with random mutations that occasionally confer survival advantages. It was a landmark in the study of bacterial genetics, opening up whole new fields of study. Delbrück and Luria (along with Alfred Hershey) would go on to win the 1969 Nobel Prize in Physiology or Medicine in part for this work.

The fluctuation test, however, did not advance the understanding of virus reproduction, to the evident frustration of Delbrück. In 1946 he even complained, in a public lecture, that the "explosive" possibilities for studying bacteria that he had created now threatened to displace his focus on viruses. Moreover, it was becoming clear that the phage used the cellular resources of the host *Escherichia coli* bacterium to reproduce itself. Contrary to Delbrück's initial presumption, the host could not be ignored after all.

Yet his instinct to focus on a simple system turned out to be very fruitful—even if bacteriophages proved far more complex than he anticipated. The phage blossomed into a model organism for a generation of biologists, even inspiring James Watson's quest for the structure of DNA. Delbrück chose his experimental subject well and devised groundbreaking methods to study it.

Delbrück abandoned phage research altogether in 1950s to focus on the biophysics of sensory perception, using an algae called *Phycomyces*. Although he was able to recruit some young physicists to work on this new model system, it was to prove far less fruitful than the phage. Yet he continued to be a lively critic of the phage experiments of others, and his tendency to misjudge key findings became legendary. Caltech molecular biologist Jean Weigle used to tell a story of encountering a young researcher who was dejected after Delbrück's reaction to his proposed experiment. Delbrück liked the idea, a sure sign that it was hopeless. For those on the right track, the highest praise one could expect from Delbrück was "I don't believe a word of it!"

## FAIR CREDIT

IN THESE EXAMPLES from physics and biology, smart scientists advanced mistaken ideas. No ordinary mistakes, they spurred major developments in different areas of fundamental science. In rapid order, those scientific insights helped to spawn multibillion-dollar research programs and to seed industries that even today are feverishly remaking the world in which we live.

In one important way, however, Herbert's and Delbrück's mistakes spawned rather different legacies. Delbrück (rightly) enjoyed a tremendously successful scientific career. He valued unconventional approaches and subjected even the best science to critical scrutiny; his status was high enough to afford heterodoxy. Herbert, on the other hand, struggled to make ends meet, even spending time on public assistance—hardly the most productive way to encourage a thinker whose work helped to clarify deep insights in quantum theory and launch a technological revolution.

This tremendous divergence in professional trajectories suggests the need for some new accounting scheme by which we apportion credit in the sciences. Those who evaluate the contributions of scientists will never achieve the clarity enjoyed by sports statisticians—endlessly tracking strikeouts or assists—in part because the significance of scientific mistakes will change over time as investigators wrestle with their implications. Nevertheless, it is worth pondering how best to acknowledge—and encourage—the kinds of creative leaps that fall short yet push the game forward.

After all, anyone can make mistakes. Indeed, the sheer volume of today's scientific publications suggests that most of us are probably wrong most of the time. Yet some errors can serve a generative role in research. While striving to be correct, let us pause to admire the great art of being productively wrong. SA


MORE TO EXPLORE

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**SCIENTIFIC AMERICAN ONLINE**

How Nick Herbert's faster-than-light telegraph was supposed to work: ScientificAmerican.com/jun2012/mistakes

SOCIOBIOLOGY

# Life Is a Shell Game

## Like people, hermit crabs and other animals trade up by treasuring what others leave behind

*By Ivan Chase*

ONE EARLY MORNING IN JUNE OF 1986, I waded into a shallow tide pool on Long Island, squatted on a plastic milk crate and dropped an empty snail shell into the water. In a few minutes a small hermit crab skittered toward the shell, probed the opening with its claws to measure the size of the interior space and rotated the spiral casing several times to look for holes. Almost quicker than I could follow, the crab pulled itself out of its old refuge and thrust its vulnerable abdomen into the snail shell I had dropped. Satisfied with the exchange, the animal strolled away, leaving its previous, smaller shell behind. A few minutes later another hermit crab discovered the first one's discarded dwelling and, after the same inspection ritual, scuttled away with its newfound lodging. About 10 minutes later a third crab found the second's old home and claimed its prize, abandoning a small shell with a large hole.



*Photographs by Adam Voorhes*

**Ivan Chase** is an emeritus professor at Stony Brook University, where he directs the Laboratory for the Study of Social Organization. Chase studies dominance hierarchies and distribution of scarce resources, among other subjects in sociology, ecology and evolution. He is also an avid sea kayaker.

It may seem strange, but this was one of the happiest moments in my life as a researcher. For nearly 10 years I had been wondering whether hermit crabs take up residence in one another's vacated shells. I finally had my confirmation. I was the first person to observe an animal making use of what sociologists and economists call a "vacancy chain"—an organized method of exchanging resources in which every individual benefits by claiming a more desirable possession abandoned by another individual. Even though hermit crabs have relatively simple brains and nervous systems, they have evolved sophisticated social behaviors to make the most of vacancy chains.

In all likelihood, researchers will soon discover the same thing about other animals; already preliminary evidence hints that in addition to hermit crabs, limpets, lobsters, fishes, octopuses and woodpeckers also take turns upgrading their homes. Studying these animals may help us recognize and improve vacancy chains in our own communities, providing new insights for problems such as Manhattan apartment shortages and drug crime. The fact that hermit crabs and other critters depend on vacancy chains is also changing the way sociologists think about economic strategies. Some tactics, it seems, do not require human-level intelligence or altruism—they are far more universal.

## CRABS IN QUEUE

FROM JUNE TO SEPTEMBER 1986, as well as the next summer, I brought groups of students to West Meadow Beach on Long Island to observe vacancy chains in *Pagurus longicarpus*—a hermit crab common to the East Coast. I wanted to discover basic facts about the chains, such as how many crabs acquired new shells in the average sequence and whether the availability of bigger shells created longer chains. After a morning's observations, we drove to my laboratory and immersed the crustaceans in warm water so that they would relax and we could remove them from their shells without hurting them. We weighed and measured the crabs and their shells to determine their sizes at various positions in the chains. When we had what we needed, we put each crab into a tank filled with cool water and a large selection of empty shells. When the animals had chosen a shell, we returned them to the beach and set them free.

We found that the crabs usually traded up to bigger shells and that the chains we initiated with large shells were indeed longer—allowing more crabs to get new shells—than the chains we started with small shells. Between two and three crustaceans upgraded to a new home in the chains we started—2.5 on average. Some people are disappointed to hear this number. They expect it to be larger—something on the order of 10 or even 50 crabs benefiting in each chain. I tell them that this number is large if you look at it in the right way. Usually when we think about competition, we presume that one individual or group is successful and that the other competitors are not. But in a vacancy chain, even a short one, more than one individual obtains a new possession. If only two hermit crabs acquired new shells, that figure would still be twice the number of individuals obtaining a resource compared with more typical competition.

After our studies, other researchers reported vacancy chains in various species of hermit crabs, including Caribbean land hermit crabs, which are sometimes sold as pets. One of the strangest examples involves a predatory snail that attacks other kinds of snails, including some whose shells hermit crabs particularly like. As the predatory snail grasps the prey snail, drills a hole in its shell with a rasplike tongue and injects digestive enzymes, nearby hermit crabs gather around, following the scent of chemicals released by the injured snail. When the predatory snail finally pulls its prey from its protective casing—a process that can take as long as an hour—the nearest crab dives into the now empty shell. In turn, another crab immediately snatches the first crab's old shell, and so on. Instead of following the careful inspection rituals that we observed on Long Island, crabs at the scene of a mollusk murder make split-second decisions—choosing new homes based on vision alone. Everyone in the vacancy chain benefits, but the immediacy of the competition speeds everything up.

Recently researchers have made further surprising discoveries about vacancy chains in hermit crabs. It turns out that crabs use at least two kinds of chains: synchronous and asynchronous. In the asynchronous type (the kind we observed), usually one crab at a time comes across a vacant shell. But in synchronous chains, the animals queue up by size in descending order behind a crab examining a vacant shell. When the first crab in line settles on a new shell, the crab behind him takes his shell, and so on, within seconds. Such well-orchestrated behaviors suggest sophisticated social cognition, especially for an animal with a relatively small and simple brain.

Few published studies focus on vacancy chains in animals besides hermit crabs, but preliminary observations suggest that the strategy has evolved in many different species. Like hermit crabs, several species of octopuses and cichlid fish live in and defend empty snail shells. Limpets hunker down in the recesses of rocks, and clown fish snuggle up to sea anemones. Maine and southern spiny lobsters occupy small caves in rock or coral. And the red-cockaded woodpecker carves nest hollows out of the trunks of pine trees. As many of these creatures grow larger and older, they seek better-suited shelters, creating vacancies for other animals. People do exactly the same thing.

## WHAT PEOPLE DO

THE FIRST STUDIES of vacancy chains in people took place in the 1960s in Manhattan, only 60 miles from the beach where I watched hermit crabs exchange shells. The late Frank Kristof, then head of planning and research for the New York City Housing and Redevelopment Board, realized that the construction of new

### IN BRIEF

**Sociologists and economists** use the term "vacancy chain" to describe a sequential exchange of resources that benefits every individual in the sequence.
**In recent decades** scientists have gathered evidence that hermit crabs—and possibly other animals—use vacancy chains, too.
**Studying how** these animals behave may help us improve how we distribute resources—such as apartments, cars and jobs—among ourselves.

apartments created chain reactions that enabled families to move from smaller, substandard apartments to larger, more adequate ones. Kristof found that about 2.4 families moved to better apartments for each newly constructed housing unit. Following Kristof's work, other researchers described real estate vacancy chains in the U.S. and abroad. One of the most comprehensive of these studies, examining the national housing market, discovered that the average chain helped about 3.5 families to move.

**Some social patterns are so fundamental that we share them even with primitive creatures.**

But Kristof was not the only one interested in vacancy chains in the 1960s. Harrison White, a professor of sociology then at Harvard University who coined the term "vacancy chain," independently discovered such sequences within religious groups—specifically, Methodist, Presbyterian and Episcopal congregations. He found that the retirement or death of a preacher, the opening of a new church or a pastor's decision to switch careers all created vacancy chains.

After White's work, sociologists and economists investigated vacancy chains among a variety of professions: football coaches, state police, officers in the armed forces and syndicates selling illegal drugs. White and other researchers found that typically about 2.5 to 3.5 people moved to new and usually better-paying jobs in the chains. That domino effect was not always a good thing, though. Research into drug sales revealed that when the police arrest high-ranking drug dealers, they unwittingly create long vacancy chains that allow many people to advance within the illicit organization.

Vacancy chains are probably at work when people purchase some types of major consumer goods as well, particularly cars. I know of no recent published studies on this subject, but some early work points in that direction. In 1941 business scholar Theodore H. Smith carried out a massive study of the new and used car market in the U.S. Although he did not actually use the term "vacancy chain," he concluded that such exchanges are crucial for the automobile industry. In the early 20th century car dealers realized that to sell new cars more easily, they would have to take the old vehicles of the new car buyers in trade and then sell those old cars to yet other buyers, and so on. Using Smith's data, I estimate that about three people got cars in the average chain in his era.

Why do vacancy chains tend to benefit about three individuals or groups, both in different species of hermit crabs and in humans? My guess is that some as yet undiscovered correspondence between the demography of humans and hermit crabs explains the effect—their birth and death rates, perhaps, or the rates at which new resource units are produced and used. But these are hunches. What is clear, however, is that vacancy chains in both animals and people cannot happen with any old kind of resource—they are made possible by resources that share a distinct set of properties.

## PRINCIPLES EMERGE

WHITE DEFINED these properties. First, such resources are coveted and relatively hard to get; jobs, cars and houses are not lying around unoccupied in large numbers, waiting to be freely taken. Second, they are the kind of thing that can be occupied or owned by only one individual or family group at a time, and these "resource units" get left behind when a new one is obtained. Finally, and most important, a resource unit cannot be taken unless it is vacant. White was thinking about people, but the same features characterize hermit crab chains. Shells are relatively scarce; only one crab at a time occupies a shell. Nearly all adult crabs have shells to leave behind when they get another, and crabs must wait for shells to become vacant before they move in.

Focusing on resources themselves turns the typical way of looking at their distribution on its head. Economists and sociologists usually think about who gets what and whether the distribution of valuable items is fair. We wonder, for example, how important intelligence, ethnicity, education or socioeconomic status is for getting jobs or homes. These questions are significant in their own right. But they sometimes prevent us from discovering other processes that influence how resources get distributed, and they can obscure commonalities across species.

Because the type of resource defines vacancy chains in both people and animals—not the kind of individuals participating in the chains—studying hermit crabs might clarify how best to maximize resource redistribution in human populations. Researchers could, for example, give a group of hermit crabs shells of different sizes and conditions, vary their birth rates, death rates and "retirement ages" by adding and removing crabs, and generally manage them and their shells to determine what situations result in the most individuals or groups moving up in the world most quickly. After all, we can ethically manipulate groups of hermit crabs in ways we cannot apply to people. We humans already rely on various small creatures to understand ourselves—we study fruit flies to learn about our genetics, rats and mice to investigate some of our diseases, and sea slugs to pin down the molecular basis of learning and memory. Experiments with hermit crabs could now become among the first to model human social systems with simpler animals.

Not long ago I returned for inspiration to the beach where I first began my observations. I walked down to the tide pool and watched the hermit crabs slowly crawling along the sand below the water. I looked at them with what I can only call gratitude. What began as a fun pursuit to satisfy my curiosity ultimately revealed insights and connections that I could never have anticipated that first day on Long Island. Most of all, I have been delighted to learn that some patterns of our social life are so fundamental that we share them even with rather primitive creatures. SA

### MORE TO EXPLORE


**Vacancy Chains.** Ivan D. Chase in *Annual Review of Sociology*, Vol. 17, pages 133–154; 1991.

**Forging the Vacancy Chain: Law Enforcement Efforts and Mobility in Criminal Economies.** H. R. Friman in *Crime, Law & Social Change*, Vol. 41, pages 53–77; 2004.

**Social Context of Shell Acquisition in *Coenobita clypeatus* Hermit Crabs.** R. D. Rotjan, J. R. Chabot and S. M. Lewis in *Behavioral Ecology*, Vol. 21, No. 3, pages 639–646; 2010.


**SCIENTIFIC AMERICAN ONLINE**

To watch a video of hermit crabs exchanging shells, visit ScientificAmerican.com/jun2012/vacancy

VIROLOGY

# Resistance Fighter

## Thumbi Ndung'u has moved from Africa to Massachusetts and back in a quest to halt the AIDS epidemic

*Interview by Brendan Borrell*

**IN BRIEF**

WHO
**THUMBI NDUNG'U**

VOCATION | AVOCATION
**Scientific director, HIV Pathogenesis Program**

WHERE
**University of KwaZulu-Natal Durban, South Africa**

RESEARCH FOCUS
**New approaches to developing an HIV vaccine.**

BIG PICTURE
**Certain proteins may reveal vulnerabilities in the virus that can be exploited by a vaccine or treatment.**

THE UNLIKELY PATH THAT THUMBI NDUNG'U FOLLOWED TO BECOME A WORLD-class AIDS researcher began in a rural highland village in Kenya. Ndung'u grew up with five brothers and five sisters in a house with no running water or electricity. He picked coffee beans and milked the family cows when he wasn't at school. By Kenyan standards, he was middle class, and his father was a hardworking teacher at a neighborhood school. It would take a series of lucky breaks for this gifted scientist to wend his way to the Ph.D. program at Harvard University, becoming the first scientist to clone HIV subtype C—the most prevalent strain of HIV in Africa and one long ignored by Western scientists.

This year Ndung'u, 43, was awarded the Howard Hughes Medical Institute's International Early Career Scientist award, which gives him five years of funding to pursue his work on genes in the immune system that help to fight AIDS and may lead to a vaccine. He heads the HIV Pathogenesis Program at the University of KwaZulu-Natal, located in a corner of South Africa where HIV prevalence hovers at 39.5 percent, placing it among the hardest-hit populations in the world. With a broad smile and unshakable optimism, he mentors up-and-coming African scientists, whose thank-you notes line his modest office, which has just enough room to squeeze in a second chair.

SCIENTIFIC AMERICAN recently spoke with Ndung'u to understand the state of AIDS research in Africa and how the course of his life has shaped his scientific mission. Excerpts follow.


*Photographs by Jodi Bieber*

***Scientific American: While you were growing up in rural Kenya in the 1980s, do you remember the first time you heard about someone with HIV/AIDS?***

NDUNG'U: I do remember particular people I knew had AIDS, although it was one of those things you never mentioned openly. But you heard rumors, and more often than not they did have it. There was such stigma and such fear of the disease. The suffering was horrendous because there were no antiretroviral drugs.

***So was this at the back of your mind as you developed an interest in science?***

I just developed an interest in science and mathematics from a young age because I was good at them and my father encouraged it. He was an English teacher at a neighborhood school. He always brought the newspaper home, and I read it religiously. I was very much aware of the greater world, even though I came from a small village.

I decided to get a degree in veterinary medicine. One of my lecturers from school introduced me to a professor at the University of Nairobi doing vaccine research on schistosomiasis, a parasitic disease that is common in developing countries. That experience fascinated me and set me on the path toward my Ph.D.

***You didn't just get your Ph.D. anywhere, of course. You studied at Harvard. How did that happen?***

I was also very lucky because when I got that position studying schistosomiasis, the [U.S. Agency for International Development] provided a six-month training at the Harvard School of Public Health to learn some techniques for making monoclonal antibodies. My mentors encouraged me to pursue a career in science. Later, I enrolled for a Ph.D. and was fortunate to receive a full scholarship.

***Was that the first time you made a visit to the U.S.?***

That was my first time out of Kenya! When I arrived in Boston, someone was supposed to be waiting for me at the airport, but for whatever reason they didn't show up. So I took a cab on my own. I just showed up at the door of the Harvard School of Public Health. I still remember I was hungry that particular afternoon, and the first thing I did was to look for a place where I could get a cup of coffee. I ended up at a Dunkin' Donuts.

***Did you feel you had a lot to learn in terms of the U.S. culture and Harvard culture?***

It was overwhelming. I had never been to a proper research laboratory before. The resources in Nairobi were really at a minimum. It was very difficult to get reagents. And there is not a critical mass of scientists, so that most of the time you are working on your own or with two people.

To find myself in a place where there were books everywhere and reagents and bottles and the things we find typical in a well-functioning lab in the U.S. was incredible—really astounding to me. I had quite a lot to learn. I had never seen a flow cytometer, which I could use to count cells. Luckily, there were some very good people at the lab that I went to, and they helped me settle down quickly. They soon started encouraging me to apply to the Ph.D. program, which I did in 1995.

***How did you make the decision to return to Africa?***

I had a very tough time after my Ph.D. deciding what I wanted to do. Deep down in my heart, I always wanted to go back, but at the same time I had doubts as to whether I could succeed. I knew many people who had gone back and not had a positive experience. They went back but didn't get the necessary support they needed to run a lab.

But my Ph.D. supervisor, Max Essex, helped to establish a lab in Botswana and suggested I should work there. It allowed me access to the resources that an institution like Harvard has, but at the same time it gave me an opportunity to work directly in Africa, where I wanted to make a difference. So it was an offer that I couldn't refuse.

***Much of your work has focused on the progression of HIV into full-blown AIDS. Can you explain that process?***

AIDS is the immune deficiency syndrome caused by HIV. When you get infected with HIV, it doesn't mean that you have AIDS. In fact, the hallmark of HIV infection is that it takes many years before the disease develops. So you can be infected for 10 years and not show any symptoms. What happens with HIV infection is that, slowly, the virus starts destroying the immune system, and then you start to get opportunistic infections that somebody with a normal immune system would normally not get. That's when we say that you have AIDS. My research focuses on why the disease course varies so much in infected people.

***Some people take one year to develop AIDS; others may take 20 years. What accounts for those differences?***

What happens is that you start to have a progressive loss of the main cells of the immune system, called CD4 cells. The types of opportunistic infections you get differ from one person to the next based on where they are located. For example, we know that pneumocystis pneumonia, a typical indication of AIDS in the West, is not as common in African countries, perhaps because the environment is just different. Here in Africa the most common opportunistic infection is tuberculosis. Most important, we have evidence that genetic factors, the immune response and the nature of the virus itself combine to determine the outcome of infection.

***Some people are also naturally resistant to catching these opportunistic infections.***

That's right. We have collaborations with four hospitals to try and understand which of those genetic, immunological and biological factors might be responsible for these differences we see in disease progression. Some people who have HIV don't have AIDS or detectable virus, and

their CD4 counts are completely normal. We know they are infected because they make antibodies to HIV. You can take cells from their blood and grow the virus in vitro, but in their body the virus is kept in check, probably by a potent immune system. That is what we are trying to understand.

**IN NDUNG'U'S LAB,** researchers study blood samples for vulnerabilities in HIV that may someday lead to a vaccine.

***You've found some particular immune proteins that play an important role.***

Yes, the human leukocyte antigen proteins, or HLAs. They are like flags. They attach to virus proteins to alert the disease-fighting cells of the immune system of the presence of the virus. Then those immune cells will home in on human cells infected with the virus and kill them. These HLA proteins are the most diverse proteins of the body, and people in different populations have different types of these HLA molecules. Many studies, including our own, have shown that the type of HLA proteins a person has is the most important genetic determinant of who are HIV controllers and who are fast progressors. People with certain protective alleles [variants] have a viral load generally three times or more lower than that of others in the population.

***How do these proteins do that?***

It's really about how those proteins influence our immune response and what HIV does in response to them. HIV evolves to escape recognition by these particular HLA proteins, but the virus becomes crippled by those changes. It's no longer able to replicate as efficiently as it did before. We may be able to make a vaccine that targets those vulnerable regions of the virus.

***What would be the next step in terms of developing an AIDS vaccine strategy?***

Identifying those vulnerable regions of the virus using the assay we have in the laboratory. Then we can identify which other segments of the virus are vulnerable, and we can try to see whether we can use them in a vaccine construct that would cripple the virus. Obviously there might be other mechanisms of viral control. And we and others continue to investigate whether we can complement those mechanisms. By combining those kinds of strategies, we hope to come up with an effective vaccine construct.

***Are there any other ways we can control the spread of HIV?***

Yes. We know there are some people who can resist HIV infection. A good example is the CCR5-delta 32 mutation, which prevents HIV from entering cells and enables people to resist infection completely. We also know from studies in Nairobi and South Africa that some individuals may have other mechanisms of resistance. We hope it might be related to some human genes that HIV needs to replicate itself. HIV requires human proteins to complete its life cycle, but if those proteins are different, they may affect HIV replication. We have ongoing work on that aspect.

***In addition to the possibility of a vaccine, antiretroviral therapy and protease inhibitors have already made HIV quite manageable in the West. How widespread are they in Africa today?***

Antiretroviral drugs are available here in South Africa. In most cases, they are even available for free from the government. Certainly the situation differs from place to place, and we still do not have everybody in treatment who should be. And it tends to vary, depending on the political will within certain countries and their health care capabilities.

***Right. Former South African president Thabo Mbeki was an AIDS denialist. How did his views affect the country's effort to rein in AIDS?***

It's a very tragic story, and South Africa's lack of response to the epidemic did slow down efforts to fight HIV/AIDS. The government then was not as committed as it is right now. It undoubtedly set South Africa back in the battle against the disease. Those who were in the forefront of that denial were very influential people, and so there were quite a lot of misconceptions.

But things now are much better. There is much more cooperation among the government, NGOs [nongovernmental organizations] and others involved in the fight against AIDS.

***When you go back to your village in Kenya, are you a bit of a celebrity?***

I'm not so sure that I'm a celebrity exactly, but they are very, very proud of me. I'm also very grateful to my family and my community for their support over the years.

***Brendan Borrell*** *is based in New York City and frequently writes about science and the environment for* Scientific American *and* Nature.

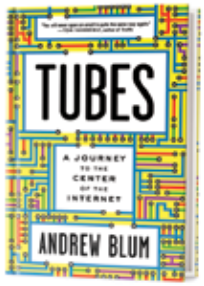
MORE TO EXPLORE

**AIDS in Africa.** Edited by Max Essex, Souleymane Mboup, Phyllis J. Kanki, Richard G. Marlink and Sheila D. Tlou. Kluwer Academic Publishers, 2002.

**SCIENTIFIC AMERICAN ONLINE**

Read about the most exciting moment of Ndung'u's career at ScientificAmerican.com/jun2012/vulnerable-hiv

**BOOKS**




## Tubes: A Journey to the Center of the Internet

by Andrew Blum. Ecco, 2012 ($26.99)

**In 2006** Alaskan senator Ted Stevens described the Internet as a "series of tubes," a quip that earned the octogenarian widespread mockery. But as Blum notes in his charming look at the physical infrastructure that underlies the Web, Stevens wasn't all that wrong. Bits sail through a worldwide network of fiber-optic cables and come together in junctions where Internet providers connect their pipes to the networks of others. Blum's transcontinental journey exposes some of the important issues confronting the Internet, such as the occasional disconnect between the interests of the corporations who control the physical pipes and the good of the network as a whole. "If you believe the Internet is magic," he writes, "then it's hard to grasp its physical reality." I'd turn this around: only by understanding the physical richness of the Internet can we truly grok the thorny forces that are shaping its growth. —*Michael Moyer*


## Darwin's Ghosts: The Secret History of Evolution

by Rebecca Stott. Spiegel & Grau, 2012 ($27)

**Stott grew up** in a household in Brighton, England, that was so strictly creationist that her grandfather cut Charles Darwin's entry out of the family's *Encyclopedia Britannica*. Here Stott pours what remains of her pent-up fascination with Darwin into a beautifully written narrative about his intellectual predecessors. These include Leonardo da Vinci, who understood that shells found in the mountains of Italy meant that the earth was far older than the church would let on, and Aristotle, who understood that gradual change was at the heart of nature.




## Prize Fight: The Race and the Rivalry to Be the First in Science

by Morton Meyers. Palgrave Macmillan, 2012 ($27)

**In a series** of case studies, Meyers analyzes how credit has been doled out in major

scientific discoveries, including the creation of MRI and the development of streptomycin, the first antibiotic against tuberculosis. Readers come away with an enhanced understanding of the conflicting impulses that drive scientists and of the historical context behind present-day research scandals.

## ALSO NOTABLE

### BOOKS

**Rainy Brain, Sunny Brain: How to Retrain Your Brain to Overcome Pessimism and Achieve a More Positive Outlook,** by Elaine Fox. Basic Books, 2012 ($26.99)

**Volcano: Nature and Culture,** by James Hamilton, and **Waterfall: Nature and Culture,** by Brian J. Hudson. Both are part of a new Earth series. Reaktion Books, 2012 ($24.95 each)

**From Here to Infinity: A Vision for the Future of Science,** by Martin Rees. W. W. Norton, 2012 ($23.95)

**The Beach Book: Science of the Shore,** by Carl H. Hobbs. Columbia University Press, 2012 ($60)

### EVENT

**World Science Festival.** Held May 30–June 3 in New York City and streamed live at **worldsciencefestival.com**

NICHOLAS AND SHERRY LU ALDRIDGE *Minden Pictures*

SAVED: British heathland


## Wild Hope: On the Front Lines of Conservation Success

by Andrew Balmford. University of Chicago Press, 2012 ($26)

**Tired of leaving** policy makers and the general public with "a dismal choice between despair and denial," Balmford traveled to six continents to track down environmental success stories. Among them: how villagers in Assam, India, helped to bring back rhinos and how British foresters helped to save heath. Balmford, a conservation scientist, does not gloss over the damage humans have inflicted but reminds us that conservation can pay off. As he says in one tongue-in-cheek passage: we may have halved the populations of wild species since the industrial revolution, but half those species remain. In other words, the glass is half full.

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


# The Science of Righteousness

## Evolution helps to explain why parties are so tribal and politics so divisive

**Which of these** two narratives most closely matches your political perspective?

*Once upon a time people lived in societies that were unequal and oppressive, where the rich got richer and the poor got exploited. Chattel slavery, child labor, economic inequality, racism, sexism and discriminations of all types abounded until the liberal tradition of fairness, justice, care and equality brought about a free and fair society. And now conservatives want to turn back the clock in the name of greed and God.*

*Once upon a time people lived in societies that embraced values and tradition, where people took personal responsibility, worked hard, enjoyed the fruits of their labor and through charity helped those in need. Marriage, family, faith, honor, loyalty, sanctity, and respect for authority and the rule of law brought about a free and fair society. But then liberals came along and destroyed everything in the name of "progress" and utopian social engineering.*

Although we may quibble over the details, political science research shows that the great majority of people fall on a left-right spectrum with these two grand narratives as bookends. And the story we tell about ourselves reflects the ancient tradition of "once upon a time things were bad, and now they're good thanks to our party" or "once upon a time things were good, but now they're bad thanks to the other party." So consistent are we in our beliefs that if you hew to the first narrative, I predict you read the *New York Times,* listen to progressive talk radio, watch CNN, are pro-choice and anti-gun, adhere to separation of church and state, are in favor of universal health care, and vote for measures to redistribute wealth and tax the rich. If you lean toward the second narrative, I predict you read the *Wall Street Journal,* listen to conservative talk radio, watch Fox News, are pro-life and anti–gun control, believe America is a Christian nation that should not ban religious expressions in the public sphere, are against universal health care, and vote against measures to redistribute wealth and tax the rich.

Why are we so predictable and tribal in our politics? In his remarkably enlightening book, *The Righteous Mind: Why Good People Are Divided by Politics and Religion* (Pantheon, 2012), University of Virginia psychologist Jonathan Haidt argues that to both liberals and conservatives, members of the other party are not just wrong; they are righteously wrong—morally suspect and even dangerous. "Our righteous minds made it possible for human beings," Haidt argues, "to produce large cooperative groups, tribes, and nations without the glue of kinship. But at the same time, our righteous minds guarantee that our cooperative groups will always be cursed by moralistic strife." Thus, he shows, morality binds us together into cohesive groups but blinds us to the ideas and motives of those in other groups.

The evolutionary Rubicon that our species crossed hundreds of thousands of years ago that led to the moral hive mind was a result of "shared intentionality," which is "the ability to share mental representations of tasks that two or more of [our ancestors] were pursuing together. For example, while foraging, one person pulls down a branch while the other plucks the fruit, and they both share the meal." Chimps tend not to display this behavior, Haidt says, but "when early humans began to share intentions, their ability to hunt, gather, raise children, and raid their neighbors increased exponentially. Everyone on the team now had a mental representation of the task, knew that his or her partners shared the same representation, knew when a partner had acted in a way that impeded success or that hogged the spoils, and reacted negatively to such violations." Examples of modern political violations include Democrat John Kerry being accused of being a "flip-flopper" for changing his mind and Republican Mitt Romney declaring himself "severely conservative" when it was suggested he was wishy-washy in his party affiliation.

Our dual moral nature leads Haidt to conclude that we need both liberals and conservatives in competition to reach a livable middle ground. As philosopher John Stuart Mill noted a century and a half ago: "A party of order or stability, and a party of progress or reform, are both necessary elements of a healthy state of political life." SA

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*Illustration by Brian Cairns*


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The ongoing search for fundamental farces

**Steve Mirsky** has been writing the Anti Gravity column since a typical tectonic plate was about 33 inches from its current location. He also hosts the *Scientific American* podcast Science Talk.


# Freaks and Tweaks

## When it comes to athletic performance, it's not how you start—it's how you Finnish

**The London Olympic Games** and the Tour de France are on the horizon in Europe. Here in North America, the baseball season is under way, with football soon to follow. All of which means that around the world, in gleaming state-of-the-art facilities and dingy state-of-the-meth-lab basements, chemists are hard at work making molecules for athletes to swallow, snort, apply and inject into one another's butts.

Almost all sports fans decry the use of performance-enhancing drugs. It's cheating. It gives the user attributes he or she did not rightfully earn. It just feels wrong to most fans. It feels wrong to me. But I have a question that almost inevitably leads to heated arguments—which leads me to suspect that we're dealing with deep emotional issues as much as intellectual analysis.

My question is: Why is it not questionable for a Boston Red Sox team doctor to have surgically and temporarily stabilized Curt Schilling's peroneus brevis tendon by suturing it into deep connective tissue before Game 6 of the 2004 American League Championship Series against the New York Yankees? (The jerry-rigged nature of what is now called the "Schilling tendon procedure" begat the Beantown-blessed bloody sock.)

Okay, the question is usually worded more like this: "Sure, steroids are cheating, but why was it legal for them to sew Curt Schilling's ankle together for a few hours just so he could pitch?" If I, a Yankees fan, put the question to a Red Sox fan, I quickly add, over my shoulder, "Stop chasing me with that fireplace poker, I'm not saying it wasn't okay, I just wanna know why it was."

Barry Bonds, who allegedly used so many steroids that other hitters looking to beef up could just lick him, probably ruined his chances for admission to the National Baseball Hall of Fame. Schilling's bloody sock is already on display there.

Pitcher Mordecai Brown mangled his hand in a piece of farming equipment, which earned him the nickname "Three-Finger" but made his curveball better. Pitcher Antonio Alfonseca's hereditary polydactyly gave him six fingers per hand. Do we need a five-finger rule?

Furthermore, why is "Tommy John surgery" okeydoke? When I was a boy, when a pitcher's arm fell off, he just pitched with his other arm. Sorry, I slipped into caricature-old-man mode for a second there. Let me try again.

When I was a kid, if a pitcher suffered damage to the ulnar collateral ligament of his elbow, he either kept trying to pitch through the pain, or he retired. But in 1974 orthopedic surgeon Frank Jobe replaced pitcher Tommy John's ligament with a tendon from John's arm. And John pitched in the major leagues until 1989. So many pitchers have performed so well after Tommy John surgery, some young pitchers have considered having it done electively.

The usual answer I get is that surgical procedures merely allow the athlete to return to his or her previous, natural condition. They do not enhance anybody's performance. Which seems reasonable—until I wonder whether it was natural for some athletes to break down under the stress when other athletes stay whole.

Speaking of what's natural, let's talk about my all-time favorite Olympic athlete, seven-time cross-country skiing medalist Eero Mäntyranta. Because Mäntyranta, who competed for Finland in the 1960s, was straight out of Xavier's School for Gifted Youngsters.

Mäntyranta has a genetic condition that can bring about fantastic increases in red blood cells, hemoglobin and oxygen-carrying capacity. Which is a pretty terrific thing for an endurance athlete to have. (Much, much better than an extra finger on each hand.)

Actually it's blood doping, but natural. Well, it's natural if a mutation is natural. And although most world-class athletes probably won't have a single major Mäntyranta-like mutation, I would bet they have a constellation of uncommon, performance-enhancing genetic constructs. So if users of performance-enhancing drugs are disqualified, should holders of performance-enhancing mutations be barred, too? Stop levitating the poker, Magneto, I'm just asking. SA

**SCIENTIFIC AMERICAN ONLINE**
Comment on this article at ScientificAmerican.com/jun2012



*Illustration by Matt Collins*

SCIENTIFIC AMERICAN Travel

# BRIGHT HORIZONS 15

**OCTOBER 25 – NOVEMBER 5, 2012 ✷ E. MEDITERRANEAN ✷ www.InsightCruises.com/sciam15**

**BEEN THERE, DONE THAT? ITALY, TURKEY, ISRAEL, AND GREECE** have drawn explorers over the span of 5,000 years. Bright Horizons is heading in to experience the region through new eyes, new data, and new discoveries as classical cultures and cutting-edge science converge in the Eastern Mediterranean. Share in the new thinking required by a changing world on **Bright Horizons 15** aboard the Costa Mediterranea, roundtrip Genoa, Italy, October 25–November 5, 2012.

Face the challenges posed by conservation planning and wildfire management, guided by Dr. Yohay Carmel. Dive into discoveries in astro-particle physics with Dr. David Lunney. Glimpse the neuroscience behind sensory perception and visual illusions with Dr. Stephen Macnik and Dr. Susana Martinez-Conde. Focus on developments in the nature and maintenance of memory with Dr. Jeanette Norden. Take in evolving thought on humankind's emigration from Africa with Professor Chris Stringer.

Discover the possibilities in environmental and neuroscience, particle physics, and anthropology. Visit archaeological sites and imagine the finds to come. Soak in the Mediterranean lifestyle. Savor the cuisine of Genoa. If you're game for field trips, we've designed behind-the-scenes experiences to extend your fun, from the European Organization for Nuclear Research, known as CERN, in Geneva to fascinating Herodium in Palestine. Send your questions to concierge@insightcruises.com or call 650-787-5665. Please join us!

Cruise prices range from $1,299 for an Interior Stateroom to $4,499 for a Grand Suite, per person. (Cruise pricing is subject to change.) For those attending our Educational Program as well, there is a $1,475 fee. Government taxes, port fees, and Insight Cruises' service charge are $299 per person. Gratuities are $11 per person per day. **For more info please call 650-787-5665 or email us at concierge@insightcruises.com.**




## NUCLEAR ASTROPHYSICS

**Speaker: David Lunney, Ph.D.**

### A Hitchhiker's Guide to the Universe

An introduction to the formation and composition of the visible universe, emphasizing the synthesis of Earth's chemical elements in the stars. Discover the key reactions, the evolutionary process of nuclear systems, and the forces that shape ongoing debates in nuclear astrophysics.

### Nuclear Cooking Class

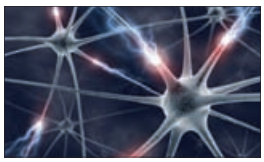
Get cooking with a discussion of the physics behind element formation by fusion and capture reactions. Dr. Lunney will highlight the need to weigh ingredient atoms to precisely determine mass. Take a seat in a precise corner of the physics kitchen and feast on the latest on nucleosynthesis.

### Weighing Single Atoms

The most precise balance known to man is an electromagnetic trap in which ionized atoms are made to dance, revealing their mass. We'll look at the basics of atomic mass measurement. Learn about current techniques of mass measurement, how these methods compare, and the diverse programs worldwide that use them. Glimpse the shape of the future of precision measurement.

### Panning the Seafloor for Plutonium: Attack of the Deathstar

Long, long ago, not so far away, did an exploding supernova bathe our planet with its stellar innards? Explore the research, theories, and phenomena that suggest the role of a local supernova in the creation of the sun and its planetary system.



## NEUROSCIENCE MEMORY

**Speaker: Jeanette Norden, Ph.D.**

### How the Brain Works

Get the lay of the land in this introductory neuroscience session showing how the brain is divided into functional systems. A special emphasis will be on limbic and reticular systems, which underlie learning and memory, executive function, arousal, attention, and consciousness.

### Memory and All That Jazz

Memory is among the most precious of human abilities. Find out what neuroscience has revealed about how we learn and remember. Pinpoint how different areas of the brain encode different types of information—from the phone number we need to remember for only a moment to the childhood memories we retain for a lifetime.

### Losing your Memory

When we lose our memories, we lose a critical part of ourselves and our lives. Dr. Norden will introduce the many clinical conditions that can affect different types of learning and memory.

### Use it or Lose it!

While memory can be lost under a wide variety of clinical conditions, most memory loss during aging is not due to strokes or neurodegenerative disease, but to lifestyle. Building evidence suggests that aging need not lead to significant memory loss. Find out how to keep your brain healthy as you age.

## COGNITIVE NEUROSCIENCE

**Speakers: Stephen Macknik, Ph.D. and Susana Martinez-Conde, Ph.D.**

### How the Brain Constructs the World We See

All understanding of life experiences is derived from brain processes, not necessarily the result of actual events. Neuroscientists are researching the cerebral processes underlying perception to understand our experience of the universe. Discover how the brain constructs, not reconstructs, the world we see.

## 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

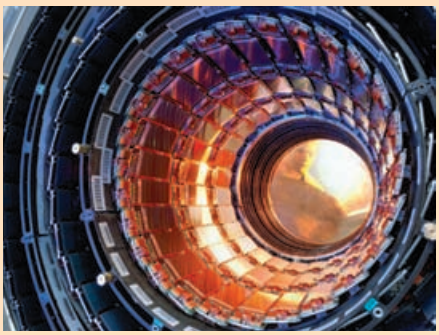
Our close relatives, the Neanderthals, evolved in parallel with *Homo sapiens.* Often depicted as bestial ape-men, in reality they walked upright as well as we do, and their brains were as large as ours. So how much like us were they? What was their fate? Track the evolution of the Neanderthals in light 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™ 17

**APRIL 11TH – 25TH, 2013 ✷ ASIA ✷ www.InsightCruises.com/sciam17**

GET THE BIG PICTURE ON ASTRONOMY, GENOMICS, AND MIND-boggling East Asia with Scientific American on Bright Horizons 17. Go deep into cutting edge science while absorbing experiential knowledge of the dynamism and duality of a region on the move. Join us on the Celebrity Millennium April 11–25, 2013 from Hong Kong to Shanghai, visiting ports in China, Taiwan, Japan, and Korea.

Look into the big picture of geospatial imaging with Dr. Murray Felsher. Peer into the past and future of telescopic space exploration with Dr. Stephen Maran. Hear a forecast on genomic technologies, next generation science and medicine with Professor John Mattick. Map the potential research directions whole-genome sequences facilitate with Dr. Mohamed Noor. Update your knowledge of galaxy evolution with Dr. Elaine Sadler.

The peoples and cultures of Asia have drawn curious travelers and admirers for ages. Enjoy the beauty, ponder the issues, absorb the energy, trace the history, and observe the traditions while Bright Horizons takes care of the details. We've created pre-, mid-, and post-cruise optional excursions to enrich your adventure.

Gain new perspectives and expand your horizons on Bright Horizons 17. If you've dreamed of the Hong Kong skyline, the bustle of Japan's cities, and the ancient culture of China, this is the time to see it in comfort, with ease. If you've wondered what's next in astronomy and evolutionary biology, Bright Horizons' experts are ready with facts and concepts. Please join us!

Cruise prices start at $1,299, per person, based on double occupancy. For those attending our seminars, there is a $1,575 fee. Port charges are $345. Government taxes and fees total $195 per person. Gratuities are approximately $195 per person. Program subject to change. For more info please call 650-787-5665 or email us at **Concierge@InsightCruises.com**


## MOLECULAR BIOLOGY

**Speaker: John Mattick, Ph.D.**

### The History of Molecular Biology and the New Age of Medicine

The 20th century was dominated by nuclear physics, organic chemistry, electronics and computing. It also saw the birth of molecular biology, which came of age with the 2001 sequencing of the human genome, at a cost of $3 million. Today we can sequence a human genome for just $3,000, and the price is dropping quickly. Come hear about the events leading up to the founding of molecular biology and the human genome project and how genomics is set to revolutionize society, medicine, and your health future.

### The Programming of Human Development

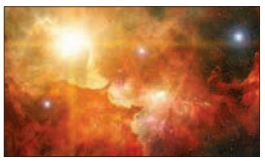
The human genome is a marvel. It is a zip file containing 3 billion letters (equivalent to 6 gigabytes) that programs the development of an organism with 100 trillion cells arranged into a myriad of muscles, bones, and organs. Less than 2% of the human genome encodes proteins, with most of the rest thought to be junk because it does not fit the conventional concept of a gene. Find out how molecular biology now understands the structure of human genetic programming.

### The Evolution and Molecular Basis of Human Cognition

Life has existed on Earth for around 4 billion years, mostly in microbial form. It was not until the last billion years that developmentally complex organisms began to evolve, culminating 500 million years ago in the so-called 'Cambrian explosion,' when ancestors of all animal phyla appeared. While plants and animals diversified, information processing capacity evolved which ultimately led to the rise of human intelligence and cognition. Come hear about the developments which led to the evolution of intelligence in the primates.

### Epigenetic Inheritance

For decades it has been an article of faith in evolutionary biology that mutation is random and that sperm and ova are immune from environmental influence. However, recent evidence suggests that the processes that control our development can be influenced by experience and that experience can be transmitted between generations. Learn how we may be the product of both our ancestors' genes and their experiences, and how the new field of 'epigenetics' is influencing ideas of health and health policy.



## COSMOLOGY

**Speaker: Elaine Sadler, Ph.D.**

### The Lives of Galaxies

How did galaxies like our own Milky Way begin? Why do galaxies look the way they do, and how do they change over cosmic time? Learn the latest ideas and findings on both nearby and distant galaxies as well as how our understanding of galaxies as 'cosmic ecosystems' has progressed rapidly in recent years.

### Secrets of the Invisible Universe

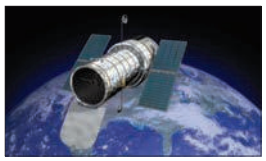
Modern telescopes allow us to study the universe at radio, X-ray and gamma-ray wavelengths which are invisible to the human eye. They reveal an energetic and sometimes violent universe populated by supermassive black holes, exploding stars and other exotic cosmic phenomena. Come discover some of the many secrets of the invisible universe.

### Astronomy in Australia

Astronomy is seen as a flagship of Australian science. Find out why in a short history of Australian astronomy from the Dreamtime to the present day. You'll learn about some of the main astronomical observatories and instruments in Australia, including those currently under construction as pathfinders for the international Square Kilometre Array (SKA) radio telescope.

### Serendipity and Discovery in Modern Astronomy

All scientists hope to make discoveries which change our view of the world, and the past 100 years have seen immense shifts in our understanding of the Universe we live in. So how is progress really made? We will discuss some Nobel-prizewinning discoveries, the search for exoplanets, the role of serendipity in astronomical discovery, the contributions of amateur astronomers and the rise of 'citizen science'.



## PLANETARY SCIENCE

**Speaker: Stephen P. Maran, Ph.D.**

### Galileo To Hubble and Beyond

How do Galileo's mind-blowing first telescopic discoveries contrast with current knowledge of the same celestial phenomena, examined with 21st century telescopes and space probes? Both Galileo and Hubble Space Telescope focus on centers of revolution, moons, planets, and rings, and galaxies. Find out how 17th and 21st century optical astronomy compare and relate.

### Mystery Forces in the Solar System

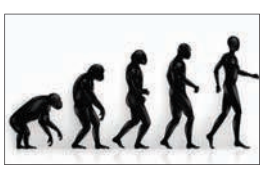
Astronomers have investigated puzzles and discrepancies noted in the paths of moving bodies, and discovered previously unknown celestial objects and astrophysical phenomena. While each mystery solved is just a footnote in space discovery, together they demonstrate the unforeseen benefits of scientific exploration. Get the details with Stephen Maran.

### Through Time and Space with the Hubble Space Telescope

What is the significance of the Hubble Space Telescope? Join Dr. Maran for a look at the whats and hows, highs and lows of the Hubble Space Telescope. The epic story spans vision, disaster, innovation, and outstanding discovery, much of which was unforeseen when the Hubble project began. Listen in on missions accomplished and new beginnings afoot.

### Exoplanets and Life in Space

My, how things have changed! For years astronomers largely denied the existence of exoplanets. Now astronomers find planets wherever they look. Explore the stunning contributions of NASA's planet-hunting Kepler mission to the search for exoplanets and Goldilocks zones where life could exist. Join the discussion about the possibilities and implications.



## EVOLUTION

**Speaker: Mohamed Noor, Ph.D.**

### What is "Evolution" Anyway and Why Should I Care?

The mere word "evolution" conjures images in the public ranging from movie dinosaurs to something vaguely half-human-half-gorilla. What does the word "evolution" actually mean in the biological sciences, what is the evidence that it is "true", and why should the general public know and care? Evolution affects your everyday life, from your health to your livelihood, and this class will help you learn why!

### Sexual Selection — Trials and Tribulations of Picking a Mate

Darwin recognized the importance of "sexual selection" in causing elaborate displays and differences between species. Recent work, however, shows that adaptations to get more matings or offspring sometimes causes harm to the other sex, and results in "arms races" between males and females. Come hear and see some interesting case studies on the trials and tribulations of picking (or resisting) a mate.

### Molecular Adaptation

While we know some traits are "adaptive," like giraffe's necks or "bad" like genetic diseases, what is the genetic basis of these traits and what evolutionary forces affect them? With the growth of genetic mapping and the emergence of extensive genome sequencing, we have far more case studies of "molecular adaptation" than ever in the past. We will explore classic and recent advances in the study of molecular adaptation.

### The Wonder of Recombination

Geneticists often describe "mutations" as the ultimate source of all genetic variation. However, genetic recombination is fundamentally important in all realms of genetics and evolution— ranging from the evolution of sex to the formation of new species to generating variation on which natural selection can act. Come learn some of the evolutionary wonder associated with this basic genetic process.

## GEOSPATIAL IMAGING

**Speaker: Murray Felsher, Ph.D.**

### Observing a Changing World

Geospatial imaging uses an array of remote sensing technologies to image the Earth from Space. Gain a basic understanding of how sensor technology now aboard earth-orbiting spacecraft provides data and information about planet Earth. Join Dr. Felsher in a program which will test your assumptions, expand your horizons, and pique your curiosity.

Topics include:

- Natural disaster monitoring, assessment, and mitigation: flood plain inundation, tsunami, earthquakes, and volcanic eruptions
- Renewable and non-renewable resource mapping: crop identification and yield, precision agriculture, and petroleum and mineral exploration
- Environmental applications: desertification and deforestation and oil spills
- Science applications: meteorology, oceanography, and hydrology
- Policy and political considerations: land use planning, coastal zone management
- Homeland defense and security implications
- "The View From Space: Planet Earth as an Artist's Palette", a look at terrestrial images from an aesthetic perspective

# SCIENTIFIC AMERICAN Travel HIGHLIGHTS

## GUILIN, HONG KONG, AND MACAU

**Pre-Cruise: April 8–12** — While locals assert that Guilin's mountain and water scenery is "best under heaven" any visitor can agree that the region's otherworldly beauty is among the most picturesque anywhere. Soak in Guilin's vistas, then contrast it with the bustle and urban delights of Hong Kong, China's longtime interface with the Western world.

Trip Includes: • Visits to Guilin Village, Barrier Gate, A-Ma Temple, and St. Paul's Cathedral • 3 nights accommodation in outstanding hotels (Shangri-la Hotel in Guilin, Ritz Carlton Hotel in Hong Kong) • Services of a Western bilingual China Host and local tour guides • All land transportation (as listed on the itinerary) • Entrance fees to all tourist sites (as listed on the itinerary)

## BEIJING

**Mid-Cruise: April 20–22**—Simply put, Imperial Tours has made a connoisseur's visit to Beijing possible. Extraordinary access to behind the scenes, extraordinary experiences, and extraordinary memories await you.

Trip Includes: • Visits to the Great Wall, Tian'anmen Square, the Forbidden Palace, and the Summer Palace • 2 nights accommodation in an outstanding five star hotel (China World Summit Wing) • Services of a Western bilingual China Host and local tour guides • All land transportation (as listed on the itinerary) • Entrance fees to all tourist sites (as listed on the itinerary)

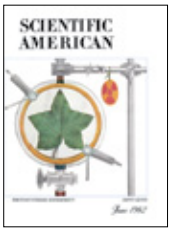
## SHANGHAI & XI'AN

**Post-Cruise: April 25–28** — Tap into 2,300 years of China's vitality, continuity, and beauty. From Shanghai's dynamism to Xi'an's Silk Road heritage and incomparable terra cotta warriors, you'll sense China's rich, complex history.

Trip Includes: • Visits to Yu Garden, Terracotta Warriors, and the Great Mosque in Xi'an • 3 nights accommodation in outstanding five star hotels (Peninsula Hotel Shanghai and Hilton Xi'an) • Services of a Western bilingual China Host and local tour guides • All land transportation (as listed on the itinerary) • Entrance fees to all tourist sites (as listed on the itinerary)

# 50, 100 & 150 Years Ago compiled by Daniel C. Schlenoff

Innovation and discovery as chronicled in *Scientific American*




## June 1962

### From Babbage to Google

"The possibility of applying machines of the digital-computer type to the twin problems of mechanical translation and information retrieval has spurred an increasing number of workers to reexamine language. If we could perfect a translating machine, a great stride would have been made toward removing language barriers. If we could perfect an information-retrieval machine, the wisdom accumulated in the libraries of the world would be more readily available."

### Magnet Leap

"Superconducting magnets are particularly intriguing in the field of power generation, both for magnetohydrodynamic devices and for controlled nuclear fusion. This latter application is one of the most interesting and potentially the most important. There are many problems that must be solved before fusion power becomes a practical reality. One is the confinement of hot ionized gases, or plasmas, in some sort of container. Because the plasmas will be at temperatures in the range of 100 million degrees centigrade, no material substance can be used to contain them. They can, however, be confined by the force of a magnetic field. Current thinking involves the use of superconductors to provide the magnetic field."

**INDUSTRIAL CHEMIST** hard at work, trying to figure out how to turn waste into profit, 1912

## June 1912

### Hydraulic Shock Absorber

"The latest 'impossibility' which George Westinghouse has made a success is the air-spring for automobiles. One day some men from up-state New York brought him a contrivance which they had designed and tried. They frankly said it was imperfect, and asked him for advice. The man who had done so much with compressed air for train-brakes would surely know, if any one could know, how to seal the air in cylinders which might be substituted for motor-car springs. Mr. Westinghouse bought the control of the invention and then set about perfecting it. He sealed the air with oil, and invented and inserted a little automatic pump to keep the oil in the proper places. Not many months since he placed it on the market in readiness for the season of 1912."

*For a look at the cutting edge of motorcars and trucks in 1912, see the slide show at www.ScientificAmerican.com/jun2012/automobile*

### Transformation of Waste

"The most fantastic tale that ever appeared in the Arabian Nights is no more astonishing than the feats performed with waste material by the German industrial chemist [*see illustration*]. To the German a dump heap is a kind of gold mine. He demonstrated the truth of Lord Palmerston's saying: 'Dirt is merely matter in the wrong place.' It was the German, for example, who taught us how to use the by-products of the blast furnace. One interesting example of German industrial thrift is the briquetting of enormous quantities of flue dust produced in the iron foundry, which generally contains considerable coke and iron ore."

SCIENTIFIC AMERICAN, VOL. CVI, NO. 24, JUNE 15, 1912

## June 1862

### Difference Engine

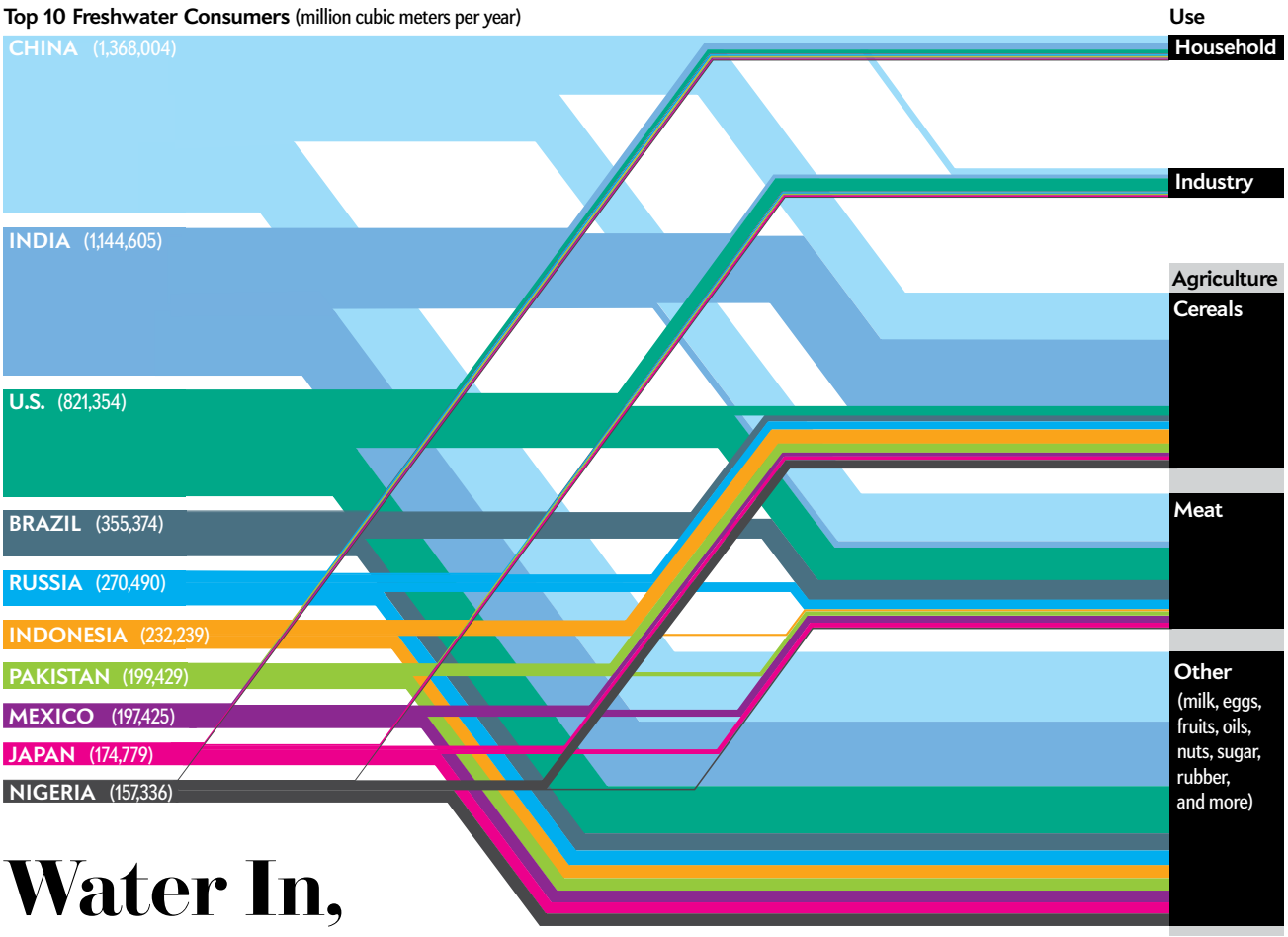
"At the London Exhibition, another curious instrument is Mr. Babbage's great calculating machine, which will work quadrations and calculate logarithms up to seven places of figures. It was the account of this invention written by the late Lady Lovelace—Lord Byron's daughter—that led the Messrs. Scheutz, of Stockholm, to improve upon it. This improvement was at once bought up precisely by the English government, but it is not now shown at the exhibition, as it is very busy at Somerset House night and day working out annuity and other tables for the Registrar General."

### Sea of Meat

"A shoal of whales ran ashore lately at Whiteness, Isle of Shetland, and getting into shallow water, immense numbers—four hundred, it is said—were captured by the islanders. They were attacked both by sea and land; almost the entire shoal was captured. People came from miles around, and a number of riflemen hurried to the spot to enjoy the novel sport of whale shooting."

### Pepper for Soldiers

"A gentleman who saw and conversed with several of the wounded soldiers who arrived from Newbern a few days since says that they told him that pepper would be one of the most acceptable and best things that could be sent by friends to the soldiers. Pies and rich cakes are so injurious that many Generals forbid their being eaten, but pepper is an excellent preventative of diarrhoea, which is prostrating large numbers in the warmer climate. It is put up in tin boxes holding a quarter or half pound each; the soldiers punch holes in one end and thus make pepper castors."




# Water In, Water Out

## Much of the life-sustaining resource is traded across national borders

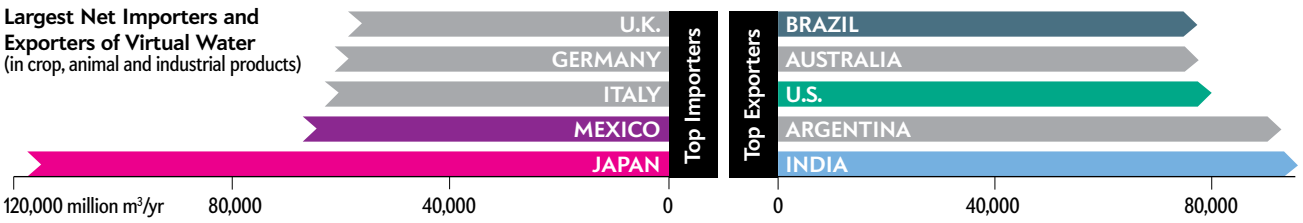
**A vast amount of water** is used to produce the food and products that nations consume (*above*). Large population is the greatest factor, but inefficient agriculture or dependence on water-intensive cuisine can exacerbate demand; meat consumption accounts for 30 percent of the U.S. water footprint.

Certain countries, such as India and the U.S., also export significant quantities of water in the form of food and products (*below, right*), despite their own robust consumption. Populous nations that have little land (Japan) or little water (Mexico) are huge net importers (*below, left*).

Those insights come from engineers Arjen Y. Hoekstra and Mesfin M. Mekonnen of the University of Twente in the Netherlands. Over the long term, net exporters may want to alter trade policies to avoid creating their own water shortages or raise prices to reflect the cost of increasingly scarce water resources. Inefficient water nations might improve agricultural practices. And net importers might lower exports to save water for domestic use.

*—Mark Fischetti*

**SCIENTIFIC AMERICAN ONLINE**
Details about how water footprints were calculated can be found at ScientificAmerican.com/jun2012/graphic-science




SOURCE: "THE WATER FOOTPRINT OF HUMANITY," BY ARJEN Y. HOEKSTRA AND MESFIN M. MEKONNEN, IN *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA*. PUBLISHED ONLINE FEBRUARY 13, 2012



*Graphics by Jen Christiansen*

SIEMENS



# School buildings that make a lasting impression.

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At 8:00 a.m. every day, the first period bell rings across a Tennessee school district. As desks fill up and notebooks open, the classrooms look nothing out of the ordinary. But here, teachers and textbooks aren't the only things that will make an impact on the lives of students far into the future.

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