How Learning Preserves New Brain Cells

SCIENTIFIC AMERICAN

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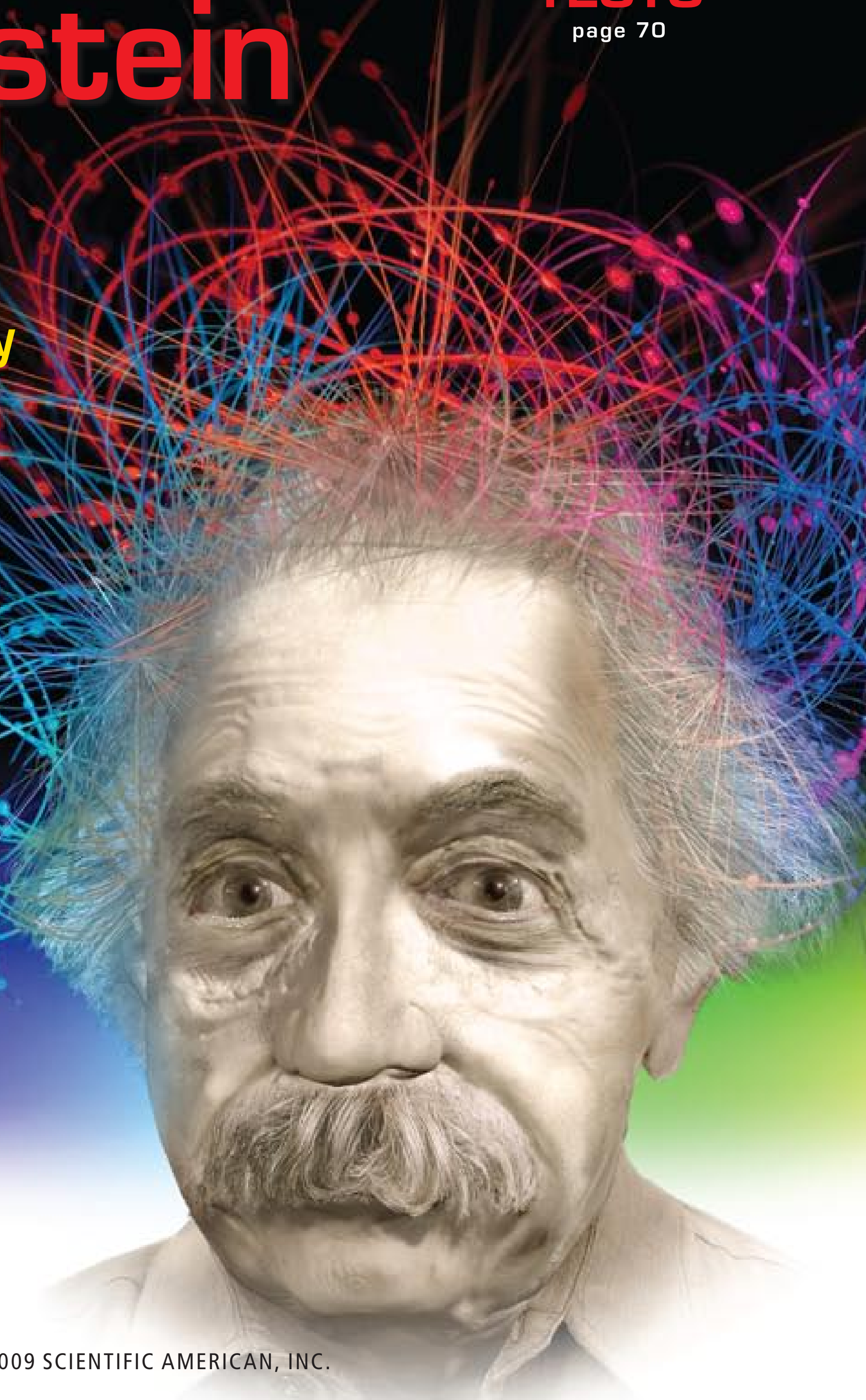
Detecting Secret
NUCLEAR TESTS

page 70

Was Einstein Wrong?

Quantum weirdness defies special relativity



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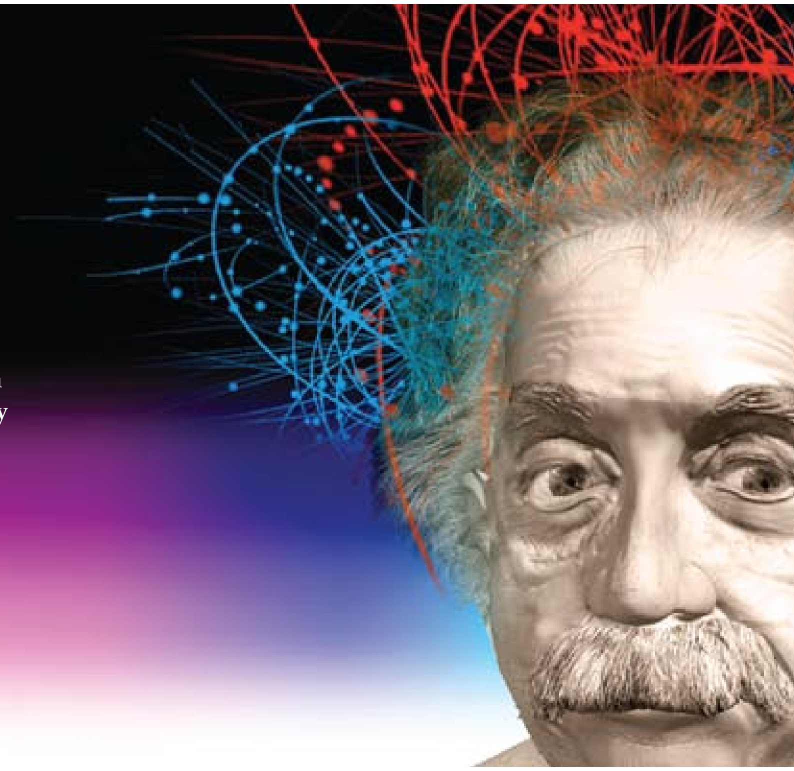
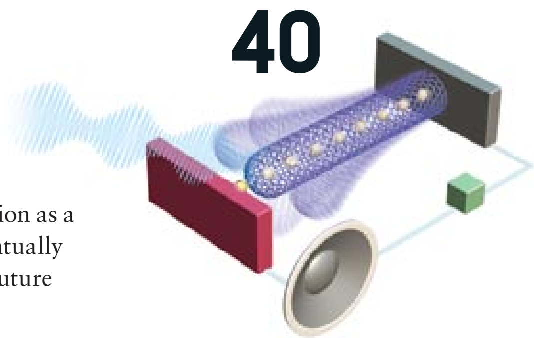
FEATURES

SCIENTIFIC AMERICAN March 2009 ▪ Volume 300 Number 3

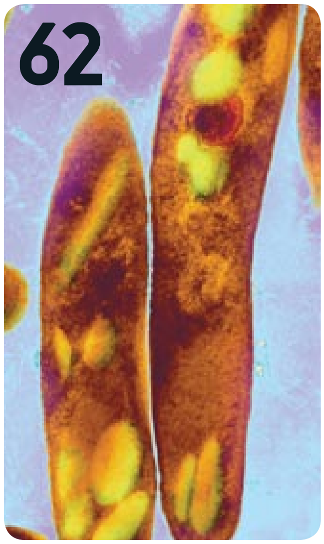




ON THE COVER

Einstein argued that quantum mechanics is fundamentally flawed by being at odds with his special theory of relativity, but it is his theory the conflict now challenges. Image by Jean-Francois Podevin.

MORE FEATURES



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COURTESY OF MICHAEL OLIVERI *http://michaeloliveri.com*

News

Did a Comet Hit Earth 12,000 Years Ago?

Nanodiamonds found across North America suggest that a climate change could have had a cosmic cause.

60-Second Psych Podcast

The Persistence of Racism

Even people who don't think of themselves as racist can be surprisingly tolerant of others' racial slurs.

Feature

Does Exercise Really Make You Healthier?

We examine five claims about the supposed benefits of weight lifting and aerobics to see which carry the most … weight.

In-Depth Report

The Science of Love

A close look at the scientific underpinnings of love—the most singularly human of emotions.

60-Second Science Podcast

Judging a Book by Its Genomes

DNA from the animal skins used to make ancient parchments can help pinpoint when and where some medieval manuscripts originated.

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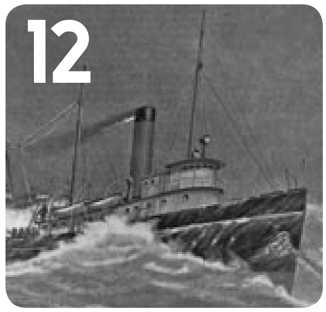
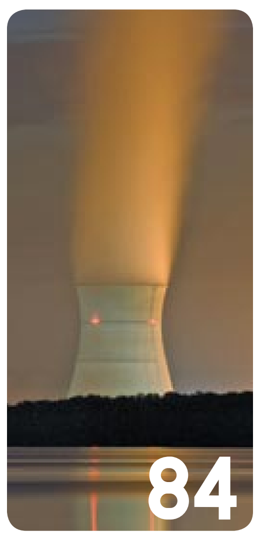
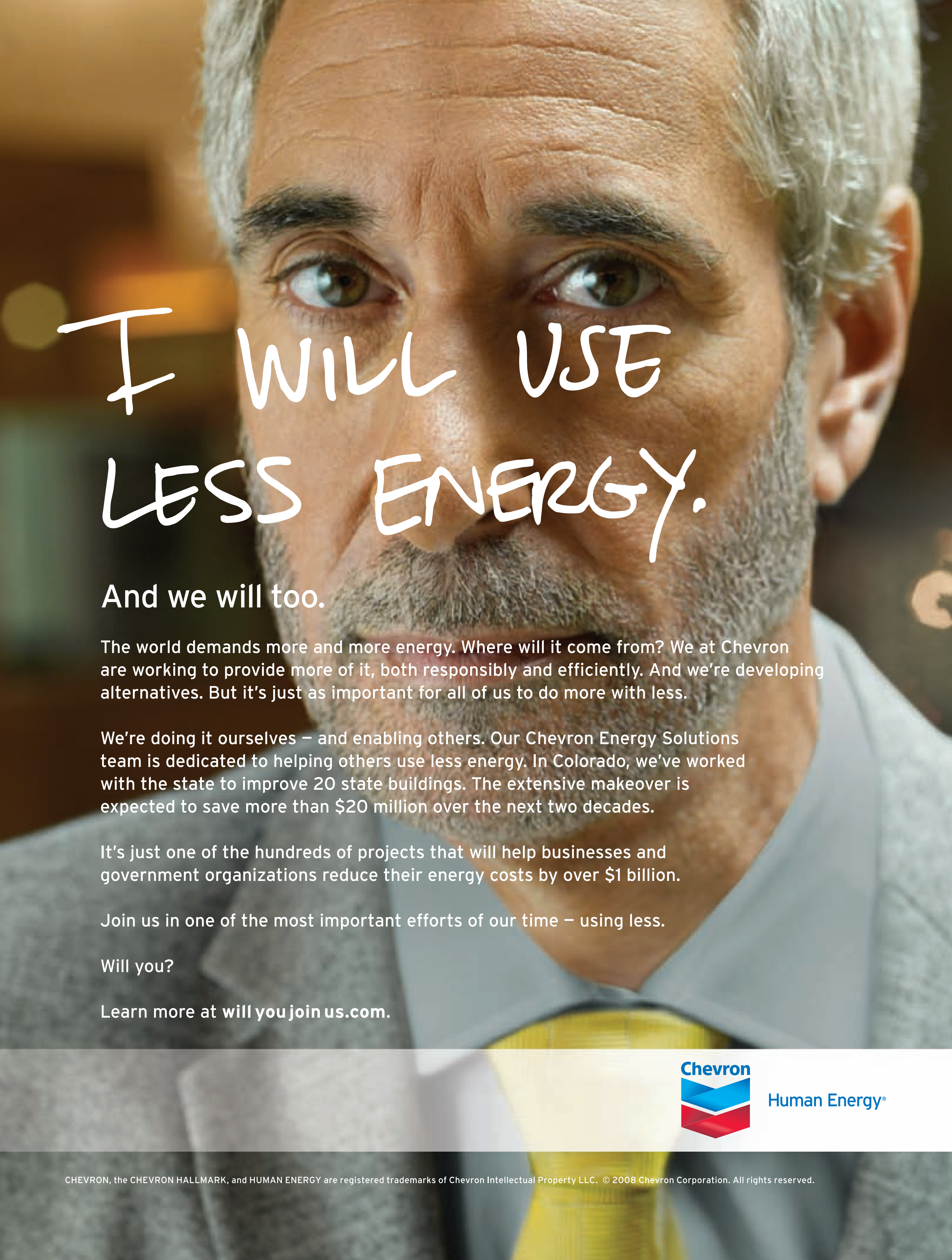
DEPARTMENTS



COURTESY OF MICHAEL C. SINGER




I WILL USE LESS ENERGY.
And we will too.
The world demands more and more energy. Where will it come from? We at Chevron are working to provide more of it, both responsibly and efficiently. And we're developing alternatives. But it's just as important for all of us to do more with less.
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The Unromantic Killer

Tuberculosis has never stopped being one of the world's most lethal infections

Most Americans have the luxury of knowing almost nothing about tuberculosis. Because it is typically not a fact of life for us or anyone we know—99 percent of its victims are the poor residing in developing countries—TB can sit comfortingly on the horizon of our awareness, perhaps colored by wisps of romanticized claptrap about John Keats and other consumptive poets whose presentiment of their looming mortality is imagined to have spiritually illuminated their genius.

TB is anything but romantic, however. It is a grindingly awful, painful, wretched affliction that preys on the weak and those already worst served by society. Roughly 5,000 more of them will die of it on the day you read this column.

This miserable state of affairs is at least an improvement over that of 1882, when TB more routinely killed one out of every seven people even in Europe and the Americas, particularly in the unhygienic, crowded cities packed by the rise of industrialism. On March 24 of that year the great microbiologist Robert Koch presented his isolation of the tuberculosis bacillus to his medical colleagues in Berlin. That date, which is commemorated annually as World TB Day, marked a turning point in humanity's struggle against the disease.

A turning point—but not a decisive victory. Because TB strikes those with weakened immune systems, it has joined forces in recent decades with HIV, the other modern infectious scourge, further complicating the management and treatment of both conditions. Moreover, TB is adept at evolving resistance to antibiotics. Health authorities have helplessly watched the emergence of both a multidrug-resistant strain that survives the two most powerful treatments and an extensively drug-resistant strain that shrugs off the second-line antibiotics as well.

The depleted state of medicine's arsenal against TB is all the more galling because it could and should have been avoided. TB became aggressively antibiotic-resistant because so many patients stopped taking their pills when they started to feel better—a failure of both human nature and the health care system. Economics, too, has abetted TB's survival: paltry financial incentives for serving the huge but poor market of its patients have historically dulled pharmaceutical industry interest. Fortunately, as Clifton E. Barry III and Maija S. Cheung describe in "New Tactics against Tuberculosis" (*page 62*), philanthropic and governmental grants are reinvigorating that research.

YOUNG TB VICTIM receives treatment in Thailand.

The most promising news in Barry and Cheung's article is that scientists are beginning to understand interactions between the TB bacillus and its human hosts at the molecular level. Not only do such studies directly suggest new drug targets for future antibiotics, but they can also help the investigators develop a virtual model of TB in the body that may point to entirely novel strategies for thwarting it. Simulation might reveal the so-called emergent properties (and potential vulnerabilities) of the microorganism that are not deducible from its biochemical components.

Koch's work with TB helped to establish the germ theory as a potent tool for protecting public health. Perhaps current efforts to combat TB will prove equally useful in pioneering better ways to contain the broader health threat of antibiotic resistance, too. ■

JOHN RENNIE
editor in chief

FLYNN LARSEN (*Rennie*); DAVID HOGSHOLT *Getty Images* (*boy*)

Among Our Contributors

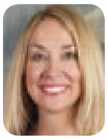
DAVID Z ALBERT is a professor of philosophy at Columbia University, but he also trained as a physicist and is a leading scholar on the interpretation of quantum mechanics.

CLIFTON E. BARRY III is chief of the tuberculosis research section at the National Institute of Allergy and Infectious Diseases and is involved in developing new chemotherapies for TB.

RIVKA GALCHEN has written stories and essays that have appeared in the *New Yorker* and other magazines and is author of the novel *Atmospheric Disturbances.*

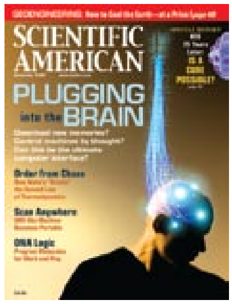
WON-YOUNG KIM is the principal investigator for the Lamont-Doherty Cooperative Seismographic Network, which monitors earthquakes in the northeastern U.S.

PAUL G. RICHARDS is a seismologist at the Lamont-Doherty Earth Observatory at Columbia University who has worked for more than two decades applying his expertise to nuclear arms control.



TRACEY J. SHORS is a professor of psychology at Rutgers University's Center for Collaborative Neuroscience who has long been fascinated by the neurobiology of learning.

Geoengineering ■ Brain Interface ■ Stage Theories



NOVEMBER 2008

"A technical fix to global warming would only encourage more carbon emissions."
—*Michael Ollinger* WASHINGTON, D.C.

■ Engineering Issues

"A Sunshade for Planet Earth," by Robert Kunzig, describes various geoengineering proposals to slow or reverse global warming. As an engineer, I appreciated the proposed technologies, but as an economist, I was appalled at what they would mean. First, it has been established that regulating a risky behavior only encourages more of that behavior. This tendency would mean that a technical fix to global warming would only encourage more carbon emissions. A related problem is that curbing emissions also lowers the current costs of dealing with the problem, making the development of other solutions less likely. Finally, big engineering fixes would require global support, yet there is a "free rider problem" in that many countries or coalitions will be unwilling to pay their share, and countries will have the incentive to cheat on the agreement. A neat engineering approach could lead to harsh economic and environmental conditions.

Michael Ollinger
Washington, D.C.

I find the fact that geoengineering solutions to global warming are now being given serious scientific consideration disturbing because there is no way to be certain that all the effects of these schemes can be accounted for. Many problems may be so indirectly caused as to be fundamentally unforeseeable yet so dangerous as to render the cure far more threatening than the disease. I am reminded of the scheme of introducing cane toads to Australia to combat pests: not only did the toads fail to control the pests, but they also became a major pest themselves. Action is needed against global warming, but geoengineering should be regarded as a last resort.

Jesse Hall
Ottawa

■ Cutting with Taxes

In "Overshadowing Difficulties" [Perspectives], the editors discuss the costs and potential dangers of geoengineering our way out of the global-warming crisis and conclude that we must focus on emissions reductions instead. But emissions reductions and increased use of renewable energy alone cannot avert the crisis. We must reduce the amount of carbon dioxide in the atmosphere, not simply the amount we are currently adding to it!

Any solution will require large-scale carbon removal from the atmosphere, and we must find a way to pay for that. Fortunately, there is a simple way: a carbon tax, which would simultaneously raise revenues for carbon removal and by increasing the cost of carbon-based fuels drive innovation in energy efficiency, emissions reduction and renewable energy.

Quinton Y. Zondervan
Cambridge, Mass.

■ Misreading Comprehension?

In discussing brain-machine interfaces, "Jacking into the Brain," by Gary Stix, refers to efforts to create a method to "download” information into the brain. This concept is based on a complete failure to understand what it means to comprehend something. Comprehension is not a passive information transfer; it involves the active construction of meaning: the contents to be learned have to be assimilated by the learner, reflected on, and linked to that person’s personal store of knowledge and experiences. Having the text of an F-15 aircraft manual in one’s brain would provide no advantage at all over reading it the old-fashioned way. There are several good ideas in this article that should not get mixed up with a truly bad one.

Walter Kintsch
Professor Emeritus
University of Colorado at Boulder

ROBERT LEEB *Laboratory of Brain-Computer Interfaces, Institute for Knowledge Discovery, Graz University of Technology*

TECHNOLOGY EXISTS to control prosthetics or a computer interface using brain waves. To achieve the reverse, inputting information into the brain, fundamental advances in understanding the way the brain functions would probably be necessary.

Narrative Link?

I agree with Michael Shermer’s main thesis in “Stage Fright” [Skeptic] that theories of predictable life stages in psychology (such as Elisabeth Kübler-Ross’s five stages of grief) are, for the most part, “toast.” But the column seems to equate stage theories in developmental psychology with stories (narrative accounts of one’s life thought to shape one’s identity) in narrative psychotherapy. As both a developmental psychologist and a narrative psychotherapist, I cannot find anything they have in common.

Stages are invariant across individuals; narratives are unique to each individual. Stages are sequential; narratives are not. Stages are presumed to be largely innate; narratives are defined as creations of personal interaction and cultural influences.

David L. Ransen
Nova Southeastern University

SHERMER REPLIES: *Stages in developmental psychology, particularly those linked to the physical development of the brain (such as the maturation of the prefrontal cortex) and body (such as the timed release of hormones), are different from the type of stages that appear to have no basis in biology that I am skeptical about, such as the stages of grief, personality and moral development. If there is a direct connection between a psychological state and a biological development, then the case can be made that there will be a chronological sequence to development that could be described in stages (although even here the labels given to the stages are subjective, and the timing can vary).*

But research by those who study grief shows unequivocally that stage sequence is quite variant across individuals, and I cited two sources for such research in my column: Russell P. Friedman and John W. James’s The Grief Recovery Handbook *(HarperCollins, 1998) and Robert A. Neimeyer’s* Meaning Reconstruction and the Experience of Loss *(American Psychological Association, 2001). I also recommend the introductory psychology textbook* Psychology, *by Carole Wade and Carol Tavris, published by Prentice Hall, which gives an excellent overview of the research.*

ERRATUM A source for the proton-related images on page 94 of “The Incredible Shrinking Scanner,” by Bernhard Blümich, went uncredited. It was chapter 2 of the textbook *All You Really Need to Know about MRI Physics,* by Moriel NessAiver, available at www.simplyphysics.com

CLARIFICATION “Dinner and a Show,” by Mark Fischetti [Working Knowledge], states that as water molecules absorb microwave energy they create friction that produces heat. Moving molecules do not *create* heat; they *are* heat.

Letters to the Editor

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Observing Evolution ▪ Seagoing Safety ▪ Anti–Bad Luck

Compiled by Daniel C. Schlenoff

MARCH 1959

VAN ALLEN BELTS—"Our planet is ringed by a region—to be exact, two regions—of high-energy radiation extending many thousands of miles into space. The discovery is of course troubling to astronauts; somehow the human body will have to be shielded from this radiation, even on a rapid transit through the region. But geophysicists, astrophysicists, solar astronomers and cosmic-ray physicists are enthralled by the fresh implications of these findings. The configuration of the region and the radiation it contains bespeak a major physical phenomenon involving cosmic rays and solar corpuscles in the vicinity of Earth. This enormous reservoir of charged particles plays a still-unexplained role as middleman in the interaction of Earth and sun which is reflected in magnetic storms, in the airglow and in the beautiful displays of the aurora. —James A. Van Allen"

DARWIN'S MISSING EVIDENCE—"Less than a century ago moths of certain species were characterized by their light coloration, which matched such backgrounds as light tree trunks and lichen-covered rocks, on which the moths passed the daylight hours sitting motionless. Today in many areas the same species are predominantly dark! Ever since the Industrial Revolution commenced in the latter half of the 18th century, large areas of the earth's surface have been contaminated by an insidious and largely unrecognized fallout of smoke particles. When the environment of a moth such as *Biston betularia* changes so that the moth cannot hide by day, the moth is ruthlessly eliminated by predators unless it mutates to a form that is better suited to its new environment. —H.B.D. Kettlewell"

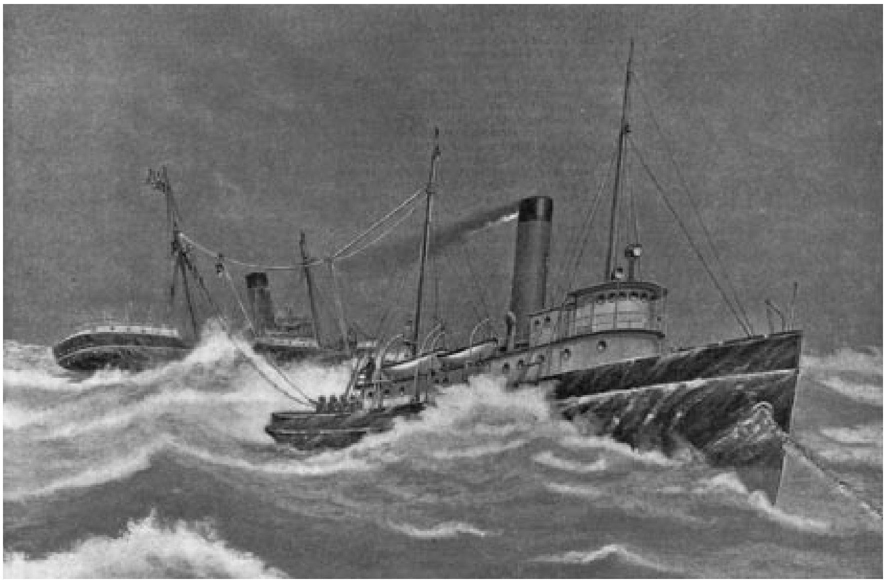
The entire article by Henry Bernard Davis Kettlewell is available at **www.SciAm.com/mar09**

MARCH 1909

RESCUE TUG—"The discovery of the mineral wealth of Alaska led immediately to a large development of the coastwise trade along the northwestern seaboard of the United States, and particularly in Puget Sound. After the 'Valencia' disaster, President Roosevelt appointed a commission to investigate the circumstance of the wreck and recommend some means whereby passengers might be saved under difficult conditions. The new life-saving vessel, the 'Snohomish,' is 152 feet in length over all. The most interesting and novel equipment is the special marine cableway—a breeches buoy apparatus, illustrated in use."

ANTI–BAD LUCK SOCIETY—"The only way to prove the position that superstition is nonsense is by a bold defiance. Some brave Frenchmen are trying to do this. A society has been formed at Bordeaux to put down the superstition of evil omens. As everybody knows, it is 'bad luck' to begin anything on a Friday, or to sit down at a table with thirteen, or to spill salt between yourself and a friend. The new society proposes to have regular dinners on Friday, to have thirteen guests, and spill salt around before commencing."

[NOTE: It appears that the society has not in fact survived.]



SAFETY AT SEA: The new rescue tug operated by the Revenue Cutter Service, 1909

MARCH 1859

GORILLA—"In Africa there is a tribe of huge monkeys known by the name of Gorillas. Their existence has been known to white men for some years, but none have ever been taken alive. They live in the lonely retired seclusions of the forests, and the males are capable of coping in fight with the lion. The skull of one is in the Boston Museum, sent thither by the Rev. Mr. Wilson, a missionary. Last year, the body of one was sent from Sierra Leone to Prof. Owen, packed in a cask of rum. The males have a horrible appearance; they attain to a stature of five feet, with wrists four times the size of a man's. Their strength is prodigious; one can wrench the head off of a man with his hands as easily as a person can husk an ear of corn."

SCIENTIFIC AMERICAN, VOL. C, NO. 10; MARCH 6, 1909


CLEAN COAL
FACILITY
ENTRANCE

Shuttle Postmortem ▪ Umami Mechanism ▪ Microswimmers ▪ Drugs from Goats

Edited by Philip Yam

Columbia's Last Moments

The final minutes of *Columbia,* which broke up on reentry on February 1, 2003, hold lessons for future vehicles [see "Rethinking the Shuttle"; SciAm, April 2003]. On December 30, 2008, NASA released its definitive report regarding the crew. Although the accident was not survivable by any means, the agency found several safety flaws.

FINAL FAREWELL: *Columbia*'s crew of seven did not stand a chance, even if all the safety measures had worked.

Relying on video analysis, recovered debris, medical findings and computer modeling, investigators conclude that the crew had about 40 seconds to recognize the situation and act before losing consciousness because of cabin depressurization. Shoulder restraints failed, allowing the crew's upper bodies to move as the cabin spun out of control. The pressure helmets did not conform to the astronauts' heads, like motorcycle helmets would, so they afforded little protection from impact. The report states that uncontrolled motions led to "injuries and lethal trauma."

For new spacecraft, the report recommends several changes, such as better restraints and parachutes that do not have to be activated by a conscious crew. More fundamentally, NASA needs to incorporate safety systems into the design from the get-go (pressure suits came about only after the *Challenger* accident in 1986). The sobering, 400-page report is available at www.nasa.gov/news/reports/index.html

Savory Sensation

The much debated fifth taste, umami, has slowly been building credibility since its discovery in 1908 by Japanese chemist Kikunae Ikeda; most scientists believed that it was a mix of the other four tastes [see "Magnifying Taste"; SciAm, August 2008]. But research in the past 10 years has uncovered details of how the receptor picks up glutamate, found in protein-heavy foods such as meat, fish and legumes, and delivers a savory sensation. A recent study reveals how the receptor, shaped like a Venus flytrap, snaps shut on glutamate and how two other molecules can act as umami enhancers by binding next to the receptor and keeping glutamate in it for longer. The study appears in the December 30, 2008, *Proceedings of the National Academy of Sciences USA*. *—Kate Wilcox*

MMM, umamilicious . . .

Four-Legged Pharmacies

A U.S. Food and Drug Administration advisory committee voted on January 9 to approve a drug made by genetically modified animals—in this case, transgenic goats from Framingham, Mass.–based GTC Biotherapeutics. The goats generate the human protein antithrombin, which inhibits clotting. Called ATryn, the drug was already approved in Europe in 2006 [see "The Land of Milk and Money"; SciAm, November 2005, and "Old MacDonald's Pharm"; SciAm, September 2006]. The company says that 150 transgenic goats could produce 100 kilograms of a protein drug a year for tens of millions of dollars. In comparison, a more conventional biotech system using vat-grown mammalian cells can run hundreds of millions in capital costs. Consumer advocates still voice caution, suggesting the FDA needs to ensure the goats do not enter the food supply. The agency was expected to give formal approval by early February. *—Charles Q. Choi*

GET YOUR GOAT: These genetically engineered ungulates produce a human anticlotting agent in their milk.

Spin to Swim

A goal in nanotechnology is a tiny engine that can power through blood vessels and microchip conduits, but fluid viscosity at this scale makes realizing such devices difficult [see "The Once and Future Nanomachine"; SciAm, September 2001]. A Spanish and British team has constructed tiny swimmers from beads made out of a plastic-magnetic material. The researchers used a short strand of DNA to connect a bead 2.8 microns wide with one (or more) that was a micron wide. A magnetic field can spin the beads, thereby moving them through narrow channels, the scientists report in the December 25, 2008, *Journal of Physical Chemistry B*.

NASA *Getty Images* (Columbia *crew*); EMILY HARRISON (*goats*); ARNOLD ZABERT *Getty Images* (*steak*)

SOCIOLOGY

Stick 'Em Up

Do economic recessions really lead to spikes in crime? BY MICHAEL MOYER

The robberies were a fitting end to a terrible year. On the Monday after Christmas, thieves in New York City held up five different banks in just over six hours, the near-final entries in the city's 444 bank robbery cases in 2008—a 54 percent increase over 2007. "It makes me think that the recession is making people go to extreme measures," one bystander told the *New York Times,* summing up the commonly held viewpoint that as the economy contracts, crime will swell to fill the void. And what a contraction we face: "People fear that we're headed for Armageddon," remarks David Kennedy, director of the Crime Prevention Center at the John Jay College of Criminal Justice.

But Kennedy and other researchers think that unemployment and financial desperation are not so inexorably linked to theft and murder. The factors that influence crime rates are far more varied and complex than any economic indicator.

MASKED INFLUENCE: **Standard economic indicators such as the unemployment rate may not be the best predictor of criminal activity. Unquantifiable outside forces play a strong role as well.**

MIKA Corbis

Take, for example, the Great Depression. In the years after the stock market crash of 1929, crime plummeted as well. "People sitting in their houses don't make great targets for crime," says Bruce Weinberg, an economist at Ohio State University. "People going out spending cash and hanging out in big crowds do." That was especially true in the Roaring Twenties, a time that also suffered from Prohibition and its attendant crime syndicates.

American cities have gone through two other major crime epidemics in the last century—one in the late 1960s into the early 1970s and another at the tail end of the 1980s into the early 1990s, when the nationwide murder rate hit an all-time high. The first happened at a boom time; the second struck during a recession. But in both cases, the primary underlying cause was a spike in the drug trade—heroin in the 1970s, crack cocaine in the 1990s.

Even though these "outside shocks to the system," as Kennedy calls them, play a strong role in determining crime rates, recent research has teased out some links between the overall economy and crime. When Weinberg and his collaborators Eric D. Gould of Hebrew University and David Mustard of the University of Georgia examined young males with no more than a high school education—the demographic group that commits the most crime—they found that average wages and unemployment rates were directly linked to the incidence of property crimes. (Here property crimes refer to felonies such as burglary, auto theft and robbery, the last of which is ordinarily classified as a violent crime because of the implied use or threat of force.) Hard times also lead to more domestic abuse.

Murder rates have never linked very well to the unemployment rate or other standard economic indicators, but Rick Rosenfeld, a criminologist at the University of Missouri–St. Louis, thinks that is because those statistics do not tell the full story. "When we're trying to understand criminal behavior, we're trying to understand the behavior of people," he says, "so it's preferable to use subjective indicators as well as objective indicators." He and Robert Fornango of Arizona State University traced murder rates against the Consumer Sentiment Index—a survey of how people view their current financial situation and how hopeful they are about the future. They found that lower index scores strongly correlate with higher murder rates.

"I don't think that newly unemployed people become criminals," Rosenfeld notes, but "marginal consumers—the shopper who goes to discount stores—many of those consumers turn to street markets during an economic downturn. These are often markets for used goods, but some are stolen goods. As demand increases, incentives for criminals to commit crimes expand." And on the black market, any dispute between buyer and seller that would ordinarily be handled by the Better Business Bureau might now be settled with violence. The Consumer Sentiment Index reached a 28-year low last November.

Could this signal a coming jump in the murder rate? Not necessarily, criminologists say. Another outside force has appeared, this one in the form of modern crime deterrent tactics. Many police departments now maintain frequently updated maps of high-crime areas to more effectively deploy foot patrols—"putting cops on the dots," as William Bratton, chief of the Los Angeles Police Department who pioneered the technique in New York City in the early 1990s, likes to say. Police departments have also begun to interact directly with known criminal groups, placing them on notice that violence by any member of the group will result in a harsh crackdown on all. The technique leads to more self-policing within the group and resulted in the "Boston Miracle" of the 1990s. It has since been expanded to hundreds of municipalities around the country.

In addition, a recent study showed that a direct economic stimulus can act as a salve. Communities in the 1930s that spent more on public works programs had lower crime rates than other communities, an auspicious portent for the current federal government's stimulus package. "Can we prevent this stuff entirely?" Kennedy asks. "No, we can't. But medicine used to be a thing where, when an epidemic swept through, you put on a mask and hoped. Now you get a flu shot, and it helps."

HOOLIGANISM

Taming the Madness of Crowds

It is called "football crowd disorder" in the academic literature. On the street, it's known simply as hooliganism. The melees at international soccer matches are infamous for the intensity of violence. Among the worst was the rioting that killed 39 fans at Belgium's Heysel Stadium during a 1985 match between English and Italian clubs. To keep public order, many countries flood big games with police in full riot gear. But the hard-line display of uniforms, helmets and batons often has the opposite effect, acting as a spark that incites disturbances.

Social scientists who study hooligan chaos think they have found a better way to keep the peace. Last year Clifford Stott of the University of Liverpool in England and his colleagues published in *Psychology, Public Policy, and Law* a paper that relates a giant experiment at the Euro2004 championship finals. There Portuguese security adopted the researchers' recommendation to institute low-profile, non-aggressive tactics—the most visible of which was to leave the riot gear behind for police officers closest to fans. "We had a working hypothesis that predicted what would happen, but we had never had an entire European nation implement a style of policing based on our predictions," Stott says.

The Portuguese deployed on average seven police near every 100 fans during high-risk matches as compared with one officer for every two fans at Euro2000 in the Netherlands and Belgium. One English fan among the 150,000 at Euro2004 was arrested for violent offenses as against nearly 1,000 of the English contingent at Euro2000. (Stott's team tracked the English spectators closely because fans of that nation are so intimately associated with soccer hooliganism.)

The laissez-faire style, the team contends, did not alienate fans in the same way that legions of police in riot gear do. Shows of force, it seems, tend to antagonize crowds, especially if police display favoritism, as in the case of a 2001 match in Rome when the officers stood by while Italian fanatics pelted Manchester United aficionados with full plastic bottles.

Stott and his colleagues are now involved in a European Union–sponsored project to implement these policing methods in almost all member countries. If they are successful, European fans would feel the sting only of their team's loss, rather than that of tear gas.

—*Gary Stix*

LIVERPOOL FANS back their team at a 2007 home match.

BEN RADFORD *Corbis*

PUBLIC HEALTH

Bug for a Bug for a Bug

Life-shortening bacterium could beat mosquito-borne disease BY BIANCA NOGRADY

Even in the teeming and varied world of bacteria, *Wolbachia* is something of a standout. Within its insect host, the bacterium acts as a gender-bending, egg-killing, DNA-hijacking parasite that is passed down from one generation to the next via the female to her eggs. Hosted by at least one fifth of all insect species, it is possibly the most prolific parasite on earth. But now *Wolbachia* itself is being hijacked, to help humans gain the upper hand in the long-running war against mosquito-borne diseases.

In particular, a team at the University of Queensland in Australia and Central China Normal University in Wuhan zeroed in on a *Wolbachia* strain that halves the life span of its natural, fruit-fly host. The scientists have successfully introduced it into an entirely new host: *Aedes aegypti,* the mosquito that spreads the virus that causes dengue fever, which produces severe, flulike symptoms and rash—and, in its more dangerous hemorrhagic form, can be fatal in about 5 percent of cases.

Wolbachia's life-shortening effect does not appear to inconvenience *A. aegypti*'s reproduction. In fact, it confers an advantage to infected females by killing the eggs of uninfected females fertilized by an infected male. But the bacterium could be disastrous for the dengue virus, which has a long incubation period: it takes up to two weeks to invade the mosquito, replicate, get into the mosquito's salivary glands and then spread to a new host, explains Scott O'Neill, an entomologist at the University of Queensland.

If infected with the life-shortening *Wolbachia* strain, the mosquito may not live long enough for its dengue passenger to incubate and move on. Given that newly hatched female mosquitoes usually wait two days before they have their first blood meal and potentially take the dengue virus onboard, the 21- to 27-day life span of a *Wolbachia*-harboring mosquito therefore offers only a narrow time frame for dengue to incubate and spread.

Researchers have also found another surprising side effect. Infected mosquitoes attempted to bite human volunteers more frequently but could not draw any blood. On closer inspection, the team discovered that the mosquitoes' proboscises had become "bendy" and could not penetrate the skin.

BITING BACK: **With a bacterium-shortened life span, mosquitoes may not live long enough to spread deadly illnesses.**

SINCLAIR STAMMERS *Photo Researchers, Inc.*

It was an unexpected windfall, O'Neill remarks, as a mosquito that cannot bite cannot transmit dengue—or any other disease. "We're talking about shortening life by 50 percent, but they're already dead if they can't stick their stylet into somebody's arm," he says.

The research has attracted considerable interest, particularly in far-north Queensland, which is in the grip of a major dengue outbreak. Current methods of dengue control focus on eliminating the mosquito's favorite breeding sites in containers of water, explains Scott Ritchie, a medical entomologist at Queensland Health, the state's health department, and the University of Queensland. But it is no easy task.

"It's very labor intensive, as guys have to go house to house and try to get rid of containers that are holding water, and in a lot of areas those containers are holding potable water that people need," Ritchie says. Although this tactic is reasonably successful in urban Australia, it would be far less practical, or safe, in the densely populated shantytowns of Brazil's Rio de Janeiro, for example. In which case, a biological control such as *Wolbachia* that spreads naturally starts to look pretty enticing.

Wolbachia appears even more attractive considering its potential application in controlling other insect-borne diseases, such as malaria and the tsetse fly's sleeping sickness. Filariasis might be an especially good target because the parasitic worms that cause the illness incubate "for a long period," says Ramakrishna U. Rao, a molecular parasitologist at the Washington University School of Medicine in St. Louis. Rao notes, however, that the success occurred in the laboratory, "so what happens if you actually introduce [*Wolbachia*-infected mosquitoes] into the field?"

O'Neill and his colleagues are setting up such field trials, bringing wild, uninfected mosquitoes into outdoor cages of infected individuals, to see if the *Wolbachia* strain will take over under natural conditions. (Thankfully this strain does not show the gender-altering effects of other *Wolbachia* varieties, such as the one that infects wood lice; otherwise it might reduce the fitness of the infected population.) Researchers hope the *Wolbachia*-harboring mosquitoes will gradually come to dominate—and along the way get rid of the mosquitoes' other, less human-friendly passengers.

Bianca Nogrady is a science and medical writer based near Sydney, Australia.

ENERGY

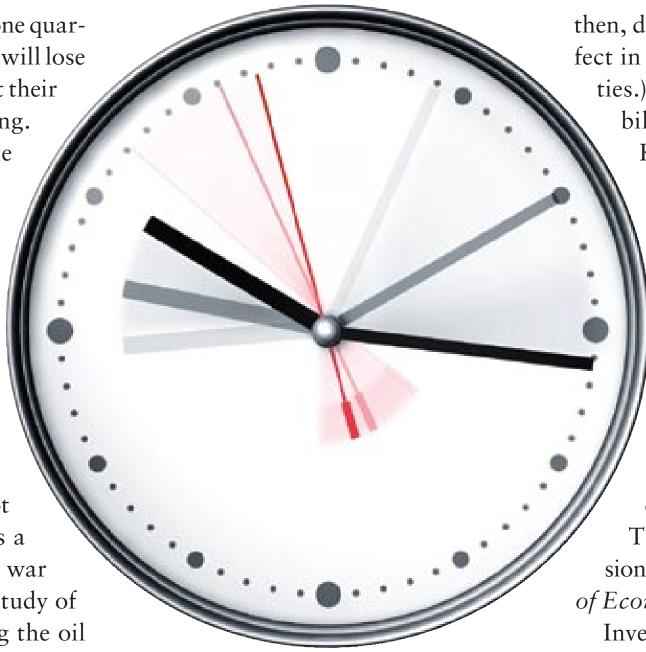
Spring Forward or Not?

Doubts on whether daylight saving time really conserves energy BY CHARLES Q. CHOI

Starting this month, roughly one quarter of the world's population will lose sleep and gain sunlight as they set their clocks ahead for daylight saving. People may think that with the time shift, they are conserving electricity otherwise spent on lighting. But recent studies have cast doubt on the energy argument—some research has even found that it ultimately leads to greater power use.

Benjamin Franklin is credited with conceiving the idea of daylight saving in 1784 to conserve candles, but the U.S. did not institute it until World War I as a way to preserve resources for the war effort. The first comprehensive study of its effectiveness occurred during the oil crisis of the 1970s, when the U.S. Department of Transportation found that daylight saving trimmed national electricity usage by roughly 1 percent compared with standard time.

Scant research had been done since, during which time U.S. electricity usage patterns have changed as air conditioning and household electronics have become more pervasive, observes economist Matthew Kotchen of the University of California, Santa Barbara. But lately, changes to daylight saving policies on state and federal levels have presented investigators new chances to explore the before-and-after impacts of the clock shift.



HOUR IN ADVANCE: Daylight saving time, which falls on March 8 in the U.S. this year, may not actually save any energy.

In 2006 Indiana instituted daylight saving statewide for the first time. (Before then, daylight time confusingly was in effect in just a handful of Indiana's counties.) Examining electricity usage and billing since the statewide change, Kotchen and his colleague Laura Grant unexpectedly found that daylight time led to a 1 percent overall rise in residential electricity use, costing the state an extra $9 million. Although daylight time reduces demand for household lighting, the researchers suggest that it increased demand for cooling on summer evenings and heating in early spring and late fall mornings. They hope to publish their conclusions this year in the *Quarterly Journal of Economics*.

Investigators got another opportunity in 2007, when daylight time nationwide began three weeks earlier, on the second Sunday in March, and ended one week later in the fall. California Energy Commission resource economist Adrienne Kandel and her colleagues discovered that extending daylight time had little to no effect on energy use in the state. The observed drop in energy use of 0.2 percent fell within the statistical margin of error of 1.5 percent.

Not all recent analyses suggest that

Moving the Hands Is Bad for the Heart

Springing forward may both end and save lives. Researchers at the Karolinska Institute in Stockholm and their colleagues looked at myocardial infarction rates in Sweden since 1987 and found that the number of heart attacks rose about 5 percent during the first week of daylight saving time (called summer time in Europe). In the October 30, 2008, *New England Journal of Medicine,* they suggest that this rise may result from the disruption of sleep patterns and biological rhythms.

On the other hand, the clock shift could help prevent traffic accidents by enabling more people to drive home in sunlight. By analyzing 28 years of U.S. automobile crash data, RAND Corporation economists and their colleagues suggest that a 1986 change in federal daylight saving time law—which moved the start of daylight time from the last Sunday in April to the first—produced an 8 to 11 percent drop in crashes involving pedestrians and a 6 to 10 percent dip in crashes for vehicular occupants. They reported the findings in a 2007 *B.E. Journal of Economic Analysis & Policy* study. —*C.Q.C.*

HEART UNHEALTHY: Losing an hour of sleep leads to a spike in cardiac problems.

HAAG + KROPP GBR *Getty Images* (clock); JANIE AIREY *Getty Images* (defibrillator) daylight saving is counterproductive. Instead of studying the impact daylight saving changes had on just one state, senior analyst Jeff Dowd and his colleagues at the U.S. Department of Energy investigated what effect it might have on national energy consumption, looking at 67 electric utilities across the country.

In their October 2008 report to Congress, they conclude that the four-week extension of daylight time saved about 0.5 percent of the nation's electricity per day, or 1.3 trillion watt-hours in total. That amount could power 100,000 households for a year. The study did not just look at residential electricity use but commercial use as well, Dowd says.

The disparities between regional and national results could reflect climate differences between states. "The effect we saw could be even worse in Florida, where air conditioning is used heavily," Kotchen suggests.

If time shifting turns out to be an energy waster, should the sun set on daylight saving? Certainly that would please farmers, who have long opposed it for how it disrupts their schedules. The chances, though, appear nil. "I'm skeptical we could change daylight saving time on a national level, because we've become accustomed to it," Kotchen says, adding that "we might want to consider it for other costs or benefits it could have." Retailers, especially those involved with sports and recreation, have historically argued hardest for extending daylight time. Representatives of the golf industry, for instance, told Congress in 1986 that an extra month of daylight saving was worth up to $400 million annually in extra sales and fees.

So instead of worrying about cranking up the air conditioner at home, think about what more you can do outdoors when the sun is out. Softball, anyone?

Charles Q. Choi is a frequent contributor based in New York City.

META-PHYSICS

Impossible Inferences

A mathematical theory of knowledge's limits takes shape BY GRAHAM P. COLLINS

Deep in the deluge of knowledge that poured forth from science in the 20th century were found ironclad limits on what we can know. Werner Heisenberg discovered that improved precision regarding, say, an object's position inevitably degraded the level of certainty of its momentum. Kurt Gödel showed that within any formal mathematical system advanced enough to be useful, it is impossible to use the system to prove every true statement that it contains. And Alan Turing demonstrated that one cannot, in general, determine if a computer algorithm is going to halt.

David H. Wolpert, a physics-trained computer scientist at the NASA Ames Research Center, has chimed in with his version of a knowledge limit. Because of it, he concludes, the universe lies beyond the grasp of any intellect, no matter how powerful, that could exist within the universe. Specifically, during the past two years, he has been refining a proof that no matter what laws of physics govern a universe, there are inevitably facts about the universe that its inhabitants cannot learn by experiment or predict with a computation. Philippe M. Binder, a physicist at the University of Hawaii at Hilo, suggests that the theory implies researchers seeking unified laws cannot hope for anything better than a "theory of almost everything."

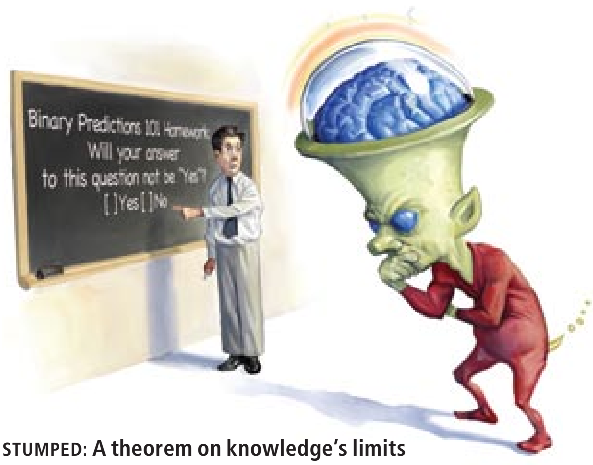
Wolpert's work is an effort to create a formal rigorous description of processes such as measuring a quantity, observing a phenomenon, predicting a system's future state or remembering past information—a description that is general enough to be independent of the laws of physics. He observes that all those processes share a common basic structure: something must be configured (whether it be an experimental apparatus or a computer to run a simulation); a question about the universe must be specified; and an answer (right or wrong) must be supplied. He models that general structure by defining a class of mathematical entities that he calls inference devices.

The inference devices act on a set of possible universes. For instance, our universe, meaning the entire world line of our universe over all time and space, could be a member of the set of all possible such universes permitted by the same rules that govern ours. Nothing needs to be specified about those rules in Wolpert's analysis. All that matters is that the various possible inference devices supply answers to questions in each universe. In a universe similar to ours, an inference device may involve a set of digital scales that you will stand on at noon tomorrow and the question relate to your mass at that time. People may also be inference devices or parts of one.

Wolpert proves that in any such system of universes, quantities exist that cannot be ascertained by any inference device inside the system. Thus, the "demon" hypothesized by Pierre-Simon Laplace in the early 1800s (give the demon the exact positions and velocities of every particle in the universe, and it will compute the future state of the universe) is stymied if the demon must be a part of the universe.

Researchers have proved results about the incomputability of specific physical systems before. Wolpert points out that his result is far more general, in that it makes virtually no assumptions about the laws of physics and it requires no limits on the computational power of the inference device other than it must exist within the universe in question. In addition, the result applies not only to predictions of a physical system's future state but also to observations of a present state and examining a record of a past state.

The theorem's proof, similar to the results of Gödel's incompleteness theorem and Turing's halting problem, relies on a variant of the liar's paradox—ask Laplace's demon to predict the following yes/no fact about the future state of the universe: "Will the universe not be one in which your answer to this question is yes?" For the demon, seeking a true yes/no answer is like trying to determine the truth of "This statement is false." Knowing the exact current state of the entire universe, knowing all the laws governing the universe and having unlimited computing power is no help to the demon in saying truthfully what its answer will be.



STUMPED: **A theorem on knowledge's limits echoes the struggle by Laplace's brainy demon.**

MATT COLLINS

In a sense, however, the existence of such a paradox is not exactly earth-shattering. As Scott Aaronson, a computer scientist at the Massachusetts Institute of Technology, puts it: "That your predictions about the universe are fundamentally constrained by you yourself being part of the universe you're predicting, always seemed pretty obvious to me—and I doubt Laplace himself would say otherwise if we could ask him." Aaronson does allow, though, that it is "often a useful exercise to spell out all the assumptions behind an idea, recast everything in formal notation and think through the implications in detail," as Wolpert has done. After all, the devil, or demon, is in the details.

NANOTECH

Grinding Out Graphene

Mass production of carbon nanosheets for electronics inches closer BY STEVEN ASHLEY

Silicon has transformed the digital world, but researchers are still eager to find substances that will make integrated circuits smaller, faster and cheaper. High on the list is graphene—planar sheets of honeycomb carbon rings just one atom thick. This nanomaterial sports a range of properties—including ultrastrength, transparency (because of its thinness) and blisteringly fast electron conductivity—that make it promising for flexible displays and superspeedy electronics. Isolated only four years ago, graphene already appears in prototype transistors, memories and other devices.

But to go from lab benches to store shelves, engineers need to devise methods to make industrial quantities of large, uniform sheets of pure, single-ply graphene. Researchers are pursuing several processing routes, but which approach will succeed remains unclear. "We've seen claims by groups that say that they can coat whole silicon wafers with monolayer sheets of graphene cheaply," reports James M. Tour, a chemist at Rice University. "But so far no one has publicly demonstrated it."

Making small amounts is surprisingly easy, states graphene's discoverer, Andre K. Geim of the University of Manchester in England. In fact, "you produce a bit of graphene every time you drag a pencil point across paper," he notes—the pencil's graphite is actually a stack of graphene layers. The initial graphene-making methods worked similarly to pencil writing: researchers would abrade some graphite and then search the debris with a microscope for suitable samples or separate individual flakes with sticky tape.

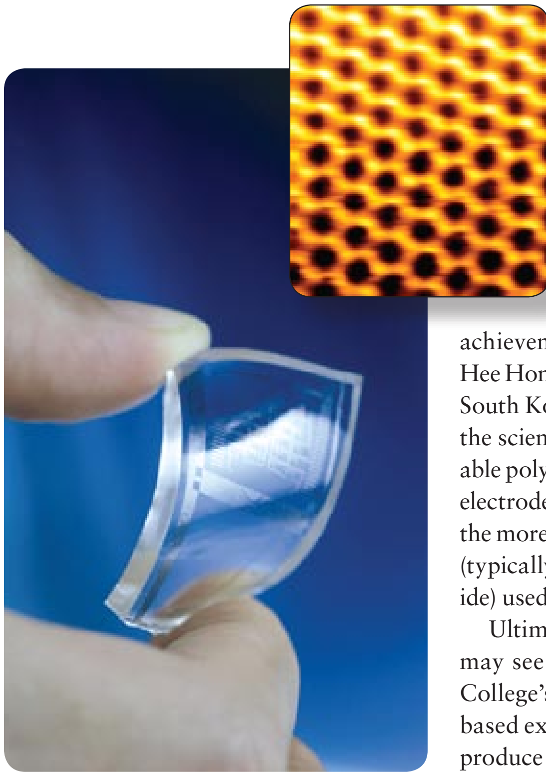
Although most scientists consider such mechanical "exfoliation" techniques to be suited only for making tiny amounts, Geim does not necessarily agree: "Recently the procedure was scaled up to produce as much graphene as you want." He uses ultrasound to break up graphite into individual layers that are dispersed in a liquid. The suspension can then be dried out on a surface, which leaves a film of overlapping pieces of graphene crystals. Whether these sheets of multiple crystals can work well enough for many applications is uncertain, however, because edge boundaries of individual flakes tend to impede the rapid flow of electrons.

Bigger samples might come from chemical exfoliation. Last May collaborators James P. Hamilton of the University of Wisconsin–Platteville and Jonathan N. Coleman of Trinity College Dublin in Ireland showed that graphene dissolves in certain organic solvents. "You place graphite in a bucket, dump in organic liquids that dissolve it," Hamilton says, "then you remove the solvent and out comes this gray stuff that's pure graphene." Hamilton's start-up company, Graphene Solutions, hopes to convert that graphene into uniform, single-crystal sheets and, ultimately, to commercialize the process.

Other chemical exfoliation techniques are possible. Rod Ruoff, now at the University of Texas at Austin, and his former colleagues at Northwestern University have shown that adding acid to graphite in water can yield graphite oxide that can be separated into individual pieces. Suspended in liquid, the flakes are then deposited onto a substrate to form a film. The addition of other chemicals or heat can drive off the oxygen groups, yielding graphene.

One such oxygen-removing agent is rocket fuel, scientists from Rutgers University found—specifically, vapors of hydrazine, a highly reactive and toxic compound. Last year Yang Yang and Richard B. Kaner of the University of California, Los Angeles, simplified the Rutgers approach by using liquid hydrazine. "We then deposit the pieces onto silicon wafers or other, more flexible substrates," Yang says. The results are single-layer films composed of many platelets. The pair are now trying to improve the quality of the sheets, as well as find a safer alternative to hydrazine.

Researchers at the Massachusetts Institute of Technology and elsewhere are looking to make graphene using chemical vapor deposition (CVD), an established process that could be readily integrated into microchip fabrication. In CVD, volatile chemicals react and deposit themselves on a substrate as a thin coating. The M.I.T. process employs a simple, tube-shaped furnace containing nickel substrates, electrical engineer Jing Kong says. "At one end, we flow in hydrocarbon gas, which decomposes in the heat," she explains. Carbon atoms then fall onto the nickel surface, which acts as a catalyst to help form the graphene films. The quality of the graphene, though, depends on the substrate—whether it consists of many nickel crystals or only one, Kong explains. Unfortunately, single-crystal nickel, the most desirable, is costly.



FLEX TIME: **Transparent electrode is made from a sheet of carbon rings called graphene (*inset*) stamped on a clear polymer.**

COURTESY OF UNIVERSITY OF AUGSBURG (*graphene*); COURTESY OF JI HYE HONG *Published online in* Nature, *January 14, 2009 (fingers holding polymer)*

Graphene from CVD has led to one of the biggest achievements yet. A group led by Byung Hee Hong of Sungkyunkwan University in South Korea made high-quality films that the scientists stamped onto a clear, bendable polymer. The result was a transparent electrode. Improved versions could replace the more expensive transparent electrodes (typically made from indium titanium oxide) used in displays.

Ultimately, the graphene-making game may see more than one winner. Trinity College's Coleman says that the solution-based exfoliation methods, which to date produce graphene up to several tens of microns wide, are probably best suited for "middle-size industrial quantities, whereas the Intels of the world will likely be more interested in growing huge areas of graphene using CVD-type processes," which so far can make samples up to a few square centimeters. But perhaps best of all, none of the approaches seem to face insurmountable hurdles. As Rice's Tour puts it: "I'll bet that the problems will be solved within a year or two."

PLANETARY SCIENCE

More Mysterious Methane

Localized burps add intrigue to the question of Martian life BY JOHN MATSON

The presence of methane on Mars, first discovered a few years ago, has piqued the curiosity of researchers, who wonder if the gas results from geologic activity or, more intriguingly, from living organisms, as is largely the case on Earth. Though by no means settling the issue, new detections of methane at least point in the direction of further study.

Using ground-based telescopes, Michael J. Mumma of the NASA Goddard Space Flight Center and his colleagues monitored about 90 percent of the Red Planet's surface for three Martian years (equal to seven Earth years). They detected large methane belches during the summer of 2003 and located the areas of those emissions.

Mumma is careful not to overstate the significance of his study, published online January 15 by *Science*. Although the methane could have come from the activity of microbes living below the permafrost, an equally plausible explanation is that it came from reactions between minerals and water trapped in rocky layers underneath. The methane could also be a relic of past processes, somehow sequestered and then released. Still, by knowing that Mars's methane comes from discrete areas, scientists can look for new sources and target the regions for future lander missions.

ECOLOGY

Crawling to Oblivion

Invasive earthworms denude Great Lakes forests BY MICHAEL TENNESEN

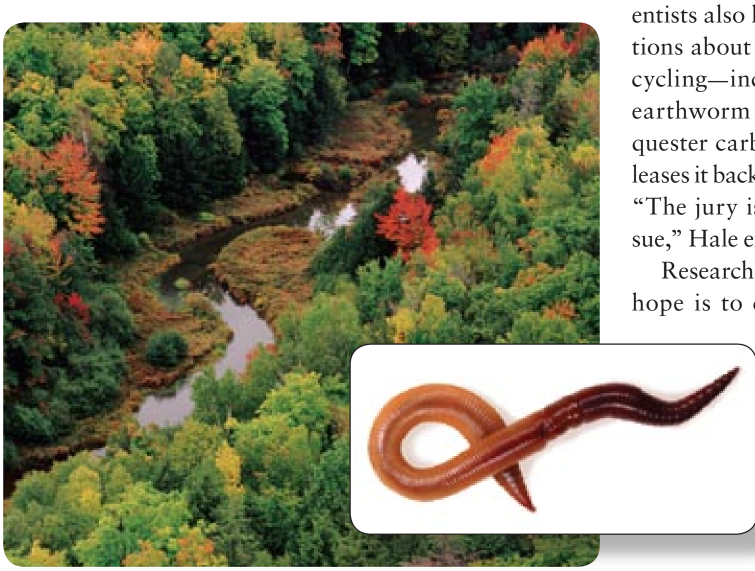
Cindy Hale, an ecologist at the University of Minnesota, answers e-mails from a lot of distraught citizens of the Great Lakes region. The residents, it seems, have introduced certain earthworms into their gardens, she says, "and now they've got that 'nothing grows here syndrome.'"

Long considered a gardener's friend, earthworms can loosen and aerate the soil. But the story is different in the Great Lakes region. The last Ice Age wiped out native earthworms 10,000 years ago, and ever since the Northeast forest has evolved without the crawlers, Hale says. But now earthworms are back, a product of fishers who toss their worms into the forest, of off-road vehicles and lumber trucks that carry them in the treads of their tires, and of people who bring in mulch—and any worms that might be in it—from other areas.

As invasive creatures, the earthworms wreak the most havoc with hardwood forests, such as those consisting of maple, basswood, red oak, poplar or birch species. (Conifer-dominated forests seem to experience less dramatic impacts.) According to Peter Groffman, a microbial ecologist at the Cary Institute of Ecosystem Studies in Millbrook, N.Y., northern hardwood forests have relied on thick layers of leaf litter that serve as a rooting medium. The earthworms, Groffman reports, "come into an area with a thick organic mat, and two to five years later that layer is gone."

As a result, some northern hardwood forests that once had a lush understory now have but a single species of native herb and virtually no tree seedlings. Evidently, earthworms change the forest soils from a fungal to a bacterial-dominated system, which speeds up the conversion of leaf detritus to mineral compounds and thereby potentially robs plants of organic nutrients.

Not all foreign earthworms are destructive. Of the 5,000 species around the globe, only about 16 of the European and Asian varieties do the real damage. One of them is the night crawler (*Lumbricus terrestris*), a popular fish bait that can measure up to 15 to 20 centimeters (six to eight inches). Another is the Alabama jumper (*Amynthas agrestis*)—also known as the snake worm or crazy worm—an aggressive Asian worm that lives at high densities and can literally jump off the ground or out of a bait can, according to fishing lore. A voracious eater, it does the most harm to the soil.



HARDWOOD FORESTS near the Great Lakes are being damaged by introduced earthworms such as the night crawler (*inset*). The worms eat the leaf litter, which acts as a rooting medium.

The presence of the earthworms affects more than just the plants. John Maerz, a wildlife ecologist at the University of Georgia, says that adult salamanders that consume these earthworms are more successful at reproduction but that earthworms are too big for juvenile salamanders to eat, which leads to a net loss in salamander numbers. The amphibians themselves, Maerz notes, are an important prey species for "snakes, small mammals, turkeys and a host of forest creatures."

Once established, earthworms are impossible to remove from the environment, Hale says. Concerned about their impact, the U.S. Department of Agriculture recently awarded Hale and her fellow biologists a three-year, $397,500 grant to study the ecology of the earthworm invasions in cold-temperate hardwood forests. The scientists also hope to answer questions about nutrient and carbon cycling—including whether the earthworm activity helps to sequester carbon in the soil or releases it back into the atmosphere. "The jury is still out on this issue," Hale explains.

Researchers agree that the best hope is to contain the worms, which spread only five to 10 meters a year on their own. That may mean new regulations governing off-road vehicles, bait disposal by anglers, or equipment hygiene and use in the logging industry. Hale would like to control community mulch piles as well: "I remember when I first heard about them, I thought, what a great idea, but think about it. You take leaves, weed seeds and earthworms from all over, bring them in, mix them up and then disperse them back out. That's a horrible idea."

Michael Tennesen, based near Los Angeles, described how forest sounds could reveal ecological health in the October 2008 issue.

LARRY MICHAEL *Minden Pictures* (*trees*); KIM TAYLOR *Minden Pictures* (*worm*)

SPACE

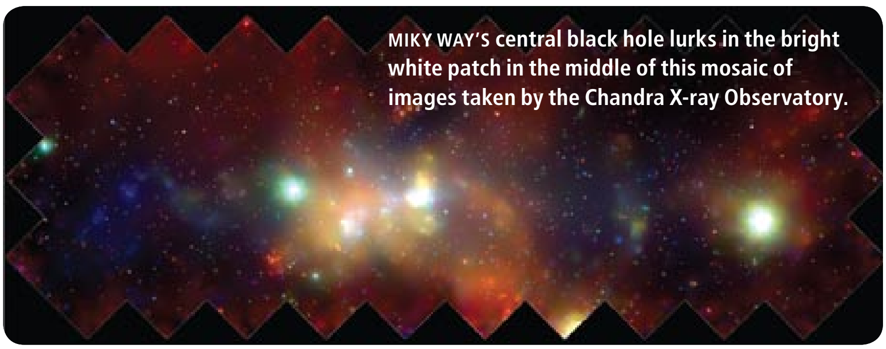
Silkworms: What the Astronauts Eat?

Interplanetary travel probably means that astronauts will need to carry ecosystems along to supply food and oxygen. Past studies of potential space food have considered poultry, fish and even snails, newts and sea urchin larvae, but they all have downsides. Chickens, for instance, require a lot of food and space, and aquatic life is sensitive to water conditions that may be hard to maintain.

SNACK ON THIS: Silkworms might make for nutritious and practical space food.

Scientists at Beihang University in Beijing suggest recruiting silkworms, which are already eaten in parts of China. These insects breed quickly, require little space, food or water, and produce only minute amounts of excrement, which could serve as fertilizer for onboard plants. Silkworm pupae, which are mostly edible protein, contain twice as much essential amino acids as pork and four times as much as eggs and milk. The scientists, whose conclusions were published online December 24, 2008, by *Advances in Space Research,* also point out that chemical processes could even make the silk digestible. Move over, Tang. *—Charles Q. Choi*

ASTRONOMY



MIKY WAY'S central black hole lurks in the bright white patch in the middle of this mosaic of images taken by the Chandra X-ray Observatory.

Galactic Chicken and Egg

Galaxies and the giant black holes at their hubs fit together as if they were made for one another. Did the holes come first and guide the formation of their galaxies, did the galaxies come first and build up holes, or did some common factor sculpt both? At the American Astronomical Society meeting in January, Christopher Carilli of the National Radio Astronomy Observatory and his colleagues argued that the holes came first. They found that galaxies in the early universe were 30 times more massive than their black holes, whereas present-day galaxies are 1,000 times heavier. "Black holes came first and somehow—we don't know how—grew the galaxy around them," Carilli said. Other astronomers were skeptical, wondering whether the ancient galaxies seem undersized merely because of a statistical selection effect. Even if true, the study does not explain how a black hole can nurture a galaxy; if anything, it should tear it apart. *—George Musser*

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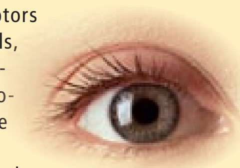
In Brief

PROTEIN FOR SIGHT

A protein called histone deacetylase 4 (HDAC4), which regulates bone and muscle development, also promotes healthy vision, according to Harvard Medical School researchers. Reducing levels of this protein in the eyes of lab mice led to the death of retinal cells—specifically, rod photoreceptors and bipolar cells, which relay signals from photoreceptors to the optic nerve. Boosting its levels decreased naturally occurring death among the bipolar cells and prolonged the lives of photoreceptors in mice with diseased eyes. See more in the January 9 *Science.* *—Charles Q. Choi*



REPULSIVE FLUCTUATIONS

Physicists have detected a novel effect resulting from the quantum fluctuations that percolate through empty space—specifically, the repulsive form of the Casimir force, which ordinarily pulls two closely spaced, metal plates ever so slightly together. The repulsive version can come about when the surfaces consist of materials that have different electrical properties—in the case of the experiment, silica and gold. As predicted, quantum fluctuations drove the materials apart. Further study of the effect, which is seen only on the nanometer scale, could benefit engineers making tiny mechanical devices. *—John Matson*

TOP 25 SOFTWARE ERRORS

Software engineers continue to make the same security blunders, warns a report from the SANS (SysAdmin, Audit, Network, Security) Institute, a cooperative research and education organization in Bethesda, Md. Their list of the top 25 most dangerous errors includes "cleartext transmissions," in which sensitive data are sent unencrypted, and "improper input validation," in which the software fails to recognize and reject phony input (such as 20-digit credit-card numbers) that can be used to bring down a Web site. A handful of these mistakes led to more than 1.5 million Web site security breaches last year, according to the January 12 report. *—Larry Greenemeier*

STEPHEN DALTON *Minden Pictures (silkworm);* COURTESY OF NASA AND D. WANG ET AL. *University of Massachusetts (Milky Way);* STEVE DUNWELL *Getty Images (eye)*

Data Points

Energizing Earth

Existing technology can derive enough energy from renewable sources to meet the world's needs several times over, according to a Worldwatch Institute report released in January. (For an assessment of the practical aspects, see "The Power of Renewables," by Matthew L. Wald, on page 56.) The report also summarizes the fourth assessment of the Intergovernmental Panel on Climate Change and the policies needed to survive a warmer world.

Trillions of kilowatt-hours of global energy used annually: 132.5

Years this amount would power a U.S. home: 13 billion

Trillions of kilowatt-hours of energy that can, in principle, be harvested with current technology:

Solar: 444

Wind: 167

Geothermal: 139

Biomass: 69

Percent of global energy used:

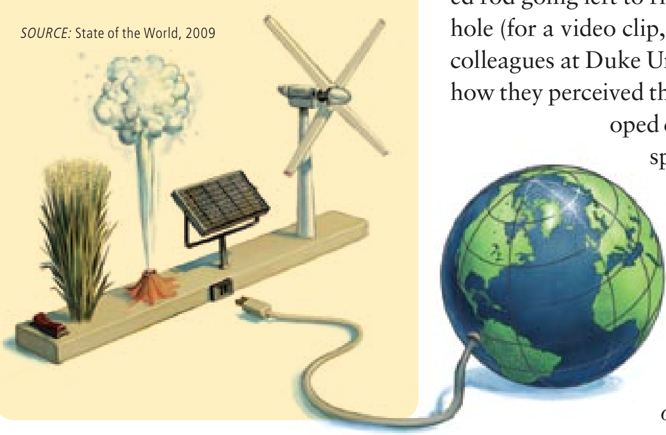
By buildings: 40

For electricity generation: 41

Percent of global energy generated from renewable sources, including hydropower: 20

Fraction of energy wasted as heat during electricity generation: 2/3

SOURCE: State of the World, 2009



EXTINCTIONS

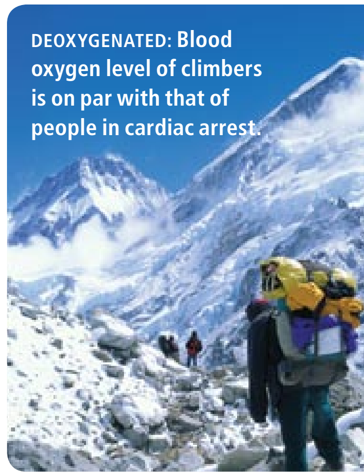
Cometary Wipeout of Mammals

Roughly 12,900 years ago a global-cooling anomaly contributed to the extinction of 35 mammal species, including the mammoth. In some areas, average temperatures may have dropped as much as 15 degrees Celsius (27 degrees Fahrenheit). New evidence, in the form of diamonds several nanometers wide, supports a theory proposed last year that a comet collision or a similar explosive event threw up debris and caused the cooling.

Nanodiamonds occur only in sediment exposed to high temperatures and pressures, such as that produced by a cometary impact. Researchers uncovered them in six sites in North America: Murray Springs, Ariz.; Bull Creek, Okla.; Gainey, Mich.; Topper, S.C.; Lake Hind, Manitoba; and Chobot, Alberta. Preliminary searches in Europe, Asia and South America have also turned up similar finds in sediments of the same age, showing that the event had global reach. But it was definitely not as large as the one that wiped out the dinosaurs 65 million years ago. The study landed in the January 2 *Science*. —*David Biello*

PHYSIOLOGY

Mountain Thin Air



DEOXYGENATED: Blood oxygen level of climbers is on par with that of people in cardiac arrest.

Climbers summiting Mount Everest have as little oxygen in their bloodstream as residents of coastal areas who are in cardiac arrest—or who are even dead. Four physicians from University College London trekked up Everest and drew their own blood for analysis. They found that because of the altitude, they had about a quarter less oxygen in their blood than is normal for people at sea level. The analysis also confirmed other effects of being at high altitudes, such as the increase in hemoglobin to ferry as much oxygen as possible. Besides helping climbers, the findings, in the January 8 *New England Journal of Medicine*, could lead to better treatments for oxygen-deprived heart and lung patients on the ground. —*Jordan Lite*

PERCEPTION

Explaining the Aperture Illusion

Looking through a peephole can change the direction an object appears to move—a tilted rod going left to right seems to move downward at an angle when viewed through a hole (for a video clip, go to www.SciAm.com/mar2009/aperture). Dale Purves and his colleagues at Duke University think they know why. They asked volunteers to describe how they perceived the motion of moving lines seen through apertures. They also developed computer simulations of a virtual rod moving in three-dimensional space in which information regarding its direction was stripped out (via projection onto a two-dimensional surface). How the volunteers saw the movement nearly perfectly matched those generated by the flattened-out simulation, suggesting that images formed on our basically two-dimensional retinas do not convey aspects of three-dimensional motion. Hence, our perceptions of the directions of moving objects are mental constructs based on past experience. Scrutinize the analysis in the January 6 *Proceedings of the National Academy of Sciences USA*. —*Charles Q. Choi*

AXIOM PHOTOGRAPHIC AGENCY *Getty Images (Mount Everest)*; ILLUSTRATION BY MATT COLLINS

How can we squeeze more food from a RAINDROP?

Farming feeds the world, but it depends on vital natural resources. Just consider this: irrigation for agriculture consumes 2/3 of the world's fresh water.

Experts have concluded that agricultural output will need to double by 2050 to feed a growing world. We'll need to get more from each drop of irrigated water.

We'll also need to do more with the solution nature already provides: rain. The challenge for farmers is squeezing the most out of unpredictable rainfall. That requires putting the latest science-based tools in farmers' hands, including advanced hybrid and biotech seeds. Our goal is to develop seeds that significantly increase crop yields and can help farmers use 1/3 less water per unit produced.

Producing more. Conserving more. Improving farmers' lives. That's sustainable agriculture. And that's what Monsanto seeds are all about.

Non-irrigated agriculture produces 60% of the world's food. It will need to do more.

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SciAm Perspectives

Acceptable Risks for Arms Control

The U.S. should ratify the Comprehensive Nuclear-Test-Ban Treaty as soon as possible

BY THE EDITORS

Among the many sea changes in policy President Barack Obama is bringing to Washington is his support for the Comprehensive Nuclear-Test-Ban Treaty (CTBT). Ever since the U.S. Senate rejected the CTBT in 1999, the treaty has languished in parliamentary purgatory. Yet during last fall's presidential campaign, Obama told the journal *Arms Control Today,* "As president, I will reach out to the Senate to secure the ratification of the CTBT at the earliest practical date." We urge the president to make good on his promise.

The CTBT would prohibit the U.S. and every other signatory from conducting test explosions, no matter how small, of nuclear weapons underground, in space or anywhere else. If ratified, the ban would affect existing stockpiles as well as any future weapons. We addressed the issues of managing an aging stockpile without testing in 2007 [see "A Need for New Warheads?"; Scientific American, November]. In brief, the weapons scientists interviewed by staff editor David Biello concurred with the conclusion of a 2002 report by a committee of the National Academy of Sciences (NAS): that the ongoing stockpile stewardship program can maintain and verify the reliability of U.S. nuclear weapons without explosive testing. Indeed, the National Nuclear Security Administration recently announced that an eight-year program to refurbish B61 nuclear bombs and ensure their reliability was completed without explosive testing a year ahead of schedule. As for future nuclear weapons, since their capability and reliability could not be tested, parties to the treaty would be unlikely to risk deploying them in their own military arsenals.

MATT COLLINS

But wouldn't a ratified treaty that goes into force leave the U.S. and other countries that abided by it vulnerable to cheaters that clandestinely develop and test their nuclear capabilities? Isn't that reason to enough to reject the treaty? The answer may seem counterintuitive, but the CTBT would make the world a safer, more secure place *for the U.S.* than a world without the treaty.

An essential element of the CTBT is a monitoring system intended to support compliance and deter cheating by ensuring that cheaters are unmasked [see "Monitoring for Nuclear Explosions," by Paul G. Richards and Won-Young Kim, on page 70]. Of course, no policing system is perfect. But the NAS report concluded that once the planned International Monitoring System of the CTBT is fully operational (it is about two-thirds complete today), no underground test with an explosive yield of more than one kiloton could "be confidently hidden." Moreover, even if a test smaller than a kiloton were somehow concealed, it would do little to harm the strategic interests of the U.S. Because of their prior experience with nuclear testing, Russia and China could learn the most from a low-yield test—but the NAS report concludes that such a test could only marginally increase the great threat they already pose. New, aspiring nuclear powers would be less likely to derive technical benefits from a test small enough to hide, and they would be far less skilled at keeping it hidden.

Still, successful cheating could be harmful to U.S. interests. But compared with what? The only realistic alternative to living with the risk that parties to the CTBT will cheat at a low, undetectable yield is living in a world without the treaty—the world we inhabit today. In that world, India, Pakistan and North Korea can test at whatever explosive yield they like, as they have done. Iran's nuclear ambitions deeply threaten the stability of the Middle East, but with the CTBT in force an Iranian nuclear explosion would risk even greater international condemnation than it does today. And testing begets testing: the anxiety among the nonnuclear neighbors of a testing state makes the pressure for the neighbors to "go nuclear" almost irresistible. Such proliferation is far more dangerous to the U.S.—not to mention the countries directly involved—than the worst-case risk of putting the CTBT in force.

The NAS draws the same conclusion in its 2002 report. Yet there is some hope that the reasoning from enlightened self-interest that leads to its conclusion will finally get the high-level hearing it deserves in Washington. The chair of the committee and lead author of the NAS report was John P. Holdren, now Obama's choice to become the presidential science adviser. ■

Sustainable Developments

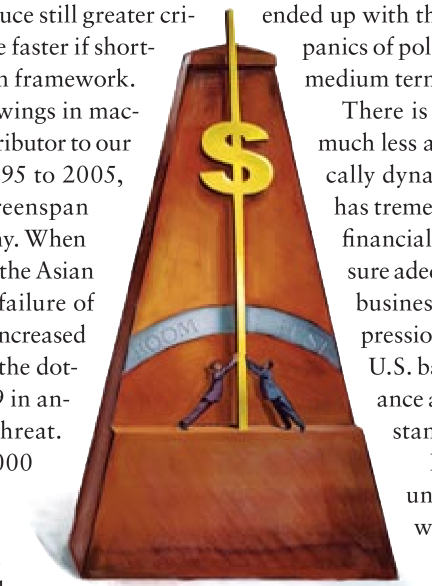
The Need for Stable Policies

An exaggerated swing toward economic stimulus will only delay the return of sustainable prosperity

BY JEFFREY D. SACHS

The U.S. political-economic system gives evidence of a phenomenon known as "instrument instability." Policy makers at the Federal Reserve and the White House are attempting to use highly imperfect monetary and fiscal policies to stabilize the national economy. The result, however, has been ever more desperate swings in economic policies in the attempt to prevent recessions that cannot be fully eliminated.

President Barack Obama's economic team is now calling for an unprecedented stimulus of large budget deficits and zero-interest rates to counteract the recession. These policies may work in the short term, but they threaten to produce still greater crises within a few years. Our recovery will be faster if short-term policies are put within a medium-term framework.



There is little doubt that unduly large swings in macroeconomic policies have been a major contributor to our current crisis. During the decade from 1995 to 2005, then Federal Reserve chairman Alan Greenspan overreacted to several shocks to the economy. When financial turbulence hit in 1997 and 1998—the Asian crisis, the Russian ruble collapse and the failure of Long-Term Capital Management—the Fed increased liquidity and accidentally helped to set off the dot-com bubble. The Fed eased further in 1999 in anticipation of the illusory Y2K computer threat. When it subsequently tightened credit in 2000 and the dot-com bubble burst, the Fed quickly turned around and lowered interest rates again. The liquidity expansion was greatly amplified following 9/11, when the Fed cut interest rates sharply (eventually to a low of 1 percent in June 2003) and thereby helped to set off the housing bubble, which has now collapsed.

We need to avoid destabilizing, short-term swings in policy. Massive deficits and zero-interest rates might temporarily perk up spending but at the risk of a collapsing currency, loss of confidence in the government, and growing anxieties about the government's ability to pay its debts. That outcome could frustrate rather than speed the recovery of private consumption and investment. Although deficit spending in a recession makes sense, the deficits should remain limited (less than 5 percent of GNP), and our interest rates should be kept far enough above zero to avoid wild future swings.

We should also avoid further gutting the government's revenues with more tax cuts. Tax revenues are already too low to cover the government's bills, especially when we take into account the unmet and growing needs for outlays on health, education, state and local government, clean energy, and infrastructure. We will in fact need a trajectory of rising tax revenues to balance the budget within a few years.

Most important, we should stop panicking. One of the reasons we got into this mess was the Fed's exaggerated fear in 2002 and 2003 that the U.S. was following Japan into a decade of stagnation caused by deflation (falling prices). To avoid a deflation, the Fed created a bubble. Now the bubble has burst, and we have ended up with the deflation we feared! Panics end badly, even panics of policy; more moderate policies will be safer in the medium term.

There is little reason to fear a decade of stagnation, much less a depression. The U.S. economy is technologically dynamic and highly flexible. The world economy has tremendous growth potential if we do not end up in financial and trade conflict and if the central banks ensure adequate liquidity to avoid panicky runs on banks, businesses and sovereign borrowers. The Great Depression itself resulted from a horrendous run on the U.S. banking system in an era without deposit insurance and when the Fed and Congress did not understand the critical role of a lender of last resort.

In short, although the sharp downturn will unavoidably last another year or even two, we will not need zero-interest rates and megadeficits to avoid a depression or even to bring about a recovery. In fact, the long-term, sustainable recovery will be accelerated by a policy framework in which the budget credibly returns to near balance over several years, the government meets its critical responsibilities in social services, infrastructure and regulation, and the Fed avoids dangerous swings in interest rates that actually contribute to the booms and busts we seek to avoid. ■

Jeffrey D. Sachs is director of the Earth Institute at Columbia University (www.earth.columbia.edu).

SCI AM An extended version of this essay is available at **www.SciAm.com/mar2009**

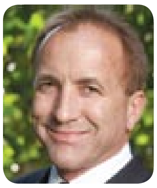
PHOTOGRAPH BY BRUCE GILBERT/EARTH INSTITUTE; ILLUSTRATION BY MATT COLLINS

Skeptic

The Art of the Con

How we can avoid falling prey to con men such as Bernard Madoff

BY MICHAEL SHERMER



On a Los Angeles street corner in 2000, I was the "inside man" in a classic con game called the pigeon drop. A magician named Dan Harlan orchestrated it for a television series I cohosted called *Exploring the Unknown* (type "Shermer, con games" into Google). Our pigeon was a man from whom I asked directions to the local hospital while Dan (the "outside man") moved in and appeared to find a wallet full of cash on the ground. After it was established that the wallet belonged to neither of us and appeared to have about $3,000 in it, Dan announced that we should split the money three ways.

I objected on moral grounds, insisting that we ask around first, which Dan agreed to do only after I put the cash in an envelope and secretly switched it for an envelope with magazine pages stuffed in it. Before he left on his moral crusade, however, Dan insisted that we each give him some collateral ("How do I know you two won't just take off with the money while I'm gone?"). I enthusiastically offered $50 and suggested that the pigeon do the same. He hesitated, so I handed him the sealed envelope full of what he believed was the cash (but was actually magazine pages), which he then tucked safely into his pocket as he willingly handed over to Dan his entire wallet, credit cards and ID. A few minutes after Dan left, I acted agitated and took off in search of him, leaving the pigeon standing on the street corner with a phony envelope and no wallet!

After admitting my anxiety about performing the con (I didn't believe I could pull it off) and confessing a little thrill at having scored the goods, I asked Dan to explain why such scams work. "We are that way as the human animal," he reflected. "We have a conscience, but we also want to go for the kill." Indeed, even after we told our pigeon that he had been set up, he still believed he had the three grand in his pocket!

Greed and the belief that the payoff is real also led high-rolling investors to fuel Wall Street financier Bernard Madoff's record-breaking $50-billion Ponzi scheme in which he kept the money and paid an 8 to 14 percent annual annuity with cash from new investors. As long as more money comes in than goes out, such scams can continue, which this one did until the 2008 market meltdown, when more investors wanted out than wanted in. But there were other factors at work as well, as explained by the University of Colorado at Boulder psychiatry professor Stephen Greenspan in his new book *The Annals of Gullibility* (Praeger, 2008), which, with supreme irony, he wrote before he lost more than half his retirement investments in Madoff's company! "The basic mechanism explaining the success of Ponzi schemes is the tendency of humans to model their actions, especially when dealing with matters they don't fully understand, on the behavior of other humans," Greenspan notes.

The effect is particularly powerful within an ethnic or religious community, as in 1920, when the eponymous Charles Ponzi promised a 40 percent return on his fellow immigrant Italian investors' money through the buying and selling of postal reply coupons (the profit was supposedly in the exchange rate differences between countries). Similarly, Madoff targeted fellow wealthy Jewish investors and philanthropists, and that insider's trust was reinforced by the reliable payout of moderate dividends (so as not to attract attention) to his selective client list, to the point that Greenspan said he would have felt foolish had he not grabbed the investment opportunity.

The evolutionary arms race between deception and deception detection has left us with a legacy of looking for signals to trust or distrust others. The system works reasonably well in simple social situations with many opportunities for interaction, such as those of our hunter-gatherer ancestors. But in the modern world of distance, anonymity and especially complicated investment tools (such as hedge funds) that not one in a thousand really understands, detecting deceptive signals is no easy feat. So as Dan reminded me, "If it sounds too good to be true, it is." ■

Michael Shermer is publisher of Skeptic *(www.skeptic.com) and author of* The Mind of the Market.

PHOTOGRAPH BY BRAD SWONETZ; ILLUSTRATION BY MATT COLLINS

Anti Gravity

Playing by Ear

Carrying a big stick may force friends to speak loudly

BY STEVE MIRSKY

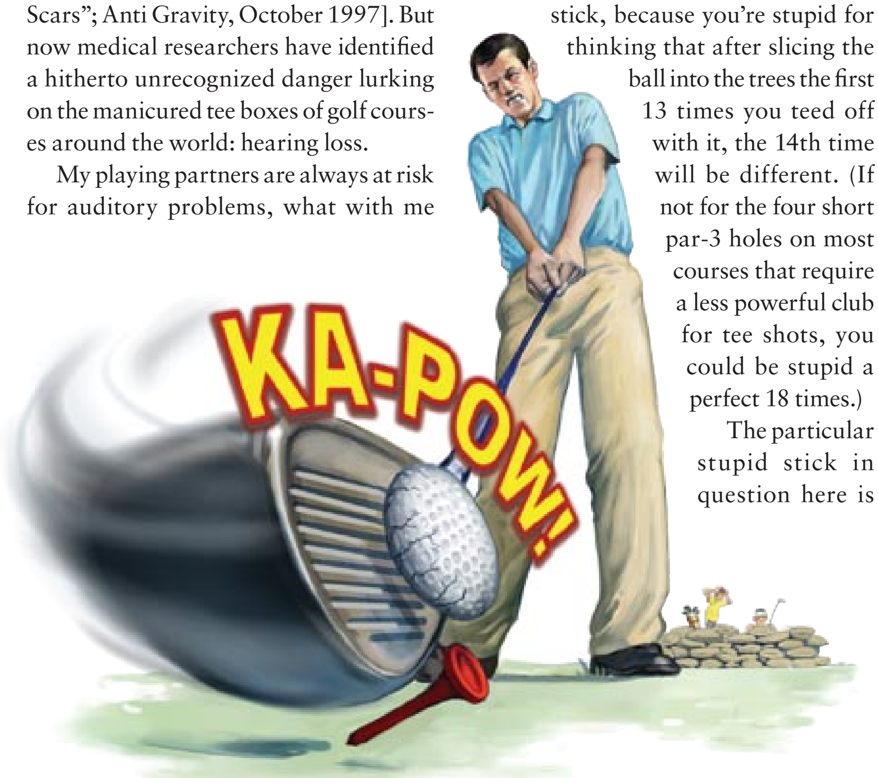
Golf is a game fraught with peril. The torque generated when swinging a golf club can torture the lower back. The repetitive stress involved in smacking the ball may induce the tendonitis known as medial epicondylitis, or golfer's elbow. The beers imbibed on the course might lead to comic yet hazardous tumbles from the golf cart.

Some 11 years ago I noted in this space that bad golfers face additional hazards, ahem. Because their errant tee shots force them to wander into high grass or forest, duffers are more likely to get the tick-borne disease ehrlichiosis—fever, chills and the shakes are particularly problematic while putting [see "He Shoots, He Scars"; Anti Gravity, October 1997]. But now medical researchers have identified a hitherto unrecognized danger lurking on the manicured tee boxes of golf courses around the world: hearing loss.

My playing partners are always at risk for auditory problems, what with me screaming "Fore!" (and other four-letter words) at the top of my lungs so often and so close to them. But the recently revealed hearing issues are related to a technological advance now commonly employed by avid amateurs everywhere—the humongous driver, the head of which looks like it should be tested for steroids. When that monster club smashes the ball, the sound produced is "like a gun going off." That's what one golfer said about his gigantic driver, anyway. The constant ka-blam degraded his hearing and led to bouts of tinnitus (the high-pitched whining that sounds like it's caused by the insects in the woods with you as you search for your ball but isn't). Research on the hard-of-hearing hacker appears in the December 17, 2008, *British Medical Journal*.

The driver is also known as the stupid stick, because you're stupid for thinking that after slicing the ball into the trees the first 13 times you teed off with it, the 14th time will be different. (If not for the four short par-3 holes on most courses that require a less powerful club for tee shots, you could be stupid a perfect 18 times.)

The particular stupid stick in question here is



PHOTOGRAPH BY FLYNN LARSEN; ILLUSTRATION BY MATT COLLINS the King Cobra LD thin-faced titanium driver. A typical driver 30 years ago had a thick stainless-steel face on a head about the size of Fred Funk's fist. The King Cobra has a head about the size of Padraig Harrington's head. (Or possibly Mark Calcavecchia's cranium, Greg Norman's noggin or even John Daly's dome.)

The study's authors searched the Internet for corroborating anecdotal reports about the driver's sound and found comments such as "Drives my mates crazy with that distinctive loud BANG sound" and "Not so much a ting but a sonic boom which resonates across the course!" Indeed, about 112 decibels sprang forth from the King Cobra LD in tests cited in the *BMJ* report. (A club called the Ping G10 topped 120 decibels, if you're really looking to rattle the clubhouse windows.)

The Cobra is in fact such a terrific driver that it is not even legal for use in competition sanctioned by the U.S. Golf Association. Official rules put an upper limit on the coefficient of restitution (COR), which is not a measure of how much money you owe your buddy after betting a Nassau with an automatic press (IOU). Wikipedia helpfully explains the science and cultural importance of COR: "The ratio of velocities before and after an impact.... The coefficient of restitution entered the common vocabulary, among golfers at least, when golf club manufacturers began making thin-faced drivers with a so-called 'trampoline effect' that creates drives of a greater distance as a result of an extra bounce off the clubface."

The CORs of the King Cobra and other nonsanctioned drivers are so high the clubs should come with a label warning "not to be used by small children as an actual trampoline." Anyway, the excessive COR helps to create the explosive noise. Which, to some golfers, is its own reward. One Cobra owner's Internet comment was, "I don't mind the loud BANG as it sounds like the ball goes a really long way." It sounds long. Hey, it's not called the stupid stick for nothing. ■

A Quantum Threat

Entanglement, like many quantum effects, violates some of our deepest intuitions about the world. It may also undermine Einstein's special theory of relativity

By David Z Albert and Rivka Galchen

JEAN-FRANCOIS PODEVIN

Our intuition, going back forever, is that to move, say, a rock, one has to touch that rock, or touch a stick that touches the rock, or give an order that travels via vibrations through the air to the ear of a man with a stick that can then push the rock—or some such sequence. This intuition, more generally, is that things can only directly affect other things that are right next to them. If A affects B *without* being right next to it, then the effect in question must be *in*direct—the effect in question must be something that gets transmitted by means of a chain of events in which each event brings about the next one directly, in a manner that smoothly spans the distance from A to B. Every time we think we can come up with an exception to this intuition—say, flipping a switch that turns on city street lights (but then we realize that this happens through wires) or listening to a BBC radio broadcast (but then we realize that radio waves propagate through the air)—it turns out that we have not, in fact, thought of an exception. Not, that is, in our everyday experience of the world.

We term this intuition "locality."

Quantum mechanics has upended many an intuition, but none deeper than this one. And this particular upending carries with it a threat, as yet unresolved, to special relativity—a foundation stone of our 21st-century physics.

KEY CONCEPTS

- In the universe as we experience it, we can directly affect only objects we can touch; thus, the world seems local.
- Quantum mechanics, however, embraces action at a distance with a property called entanglement, in which two particles behave synchronously with no intermediary; it is nonlocal.
- This nonlocal effect is not merely counterintuitive: it presents a serious problem to Einstein's special theory of relativity, thus shaking the foundations of physics.

—The Editors

The Thing from Outer Space

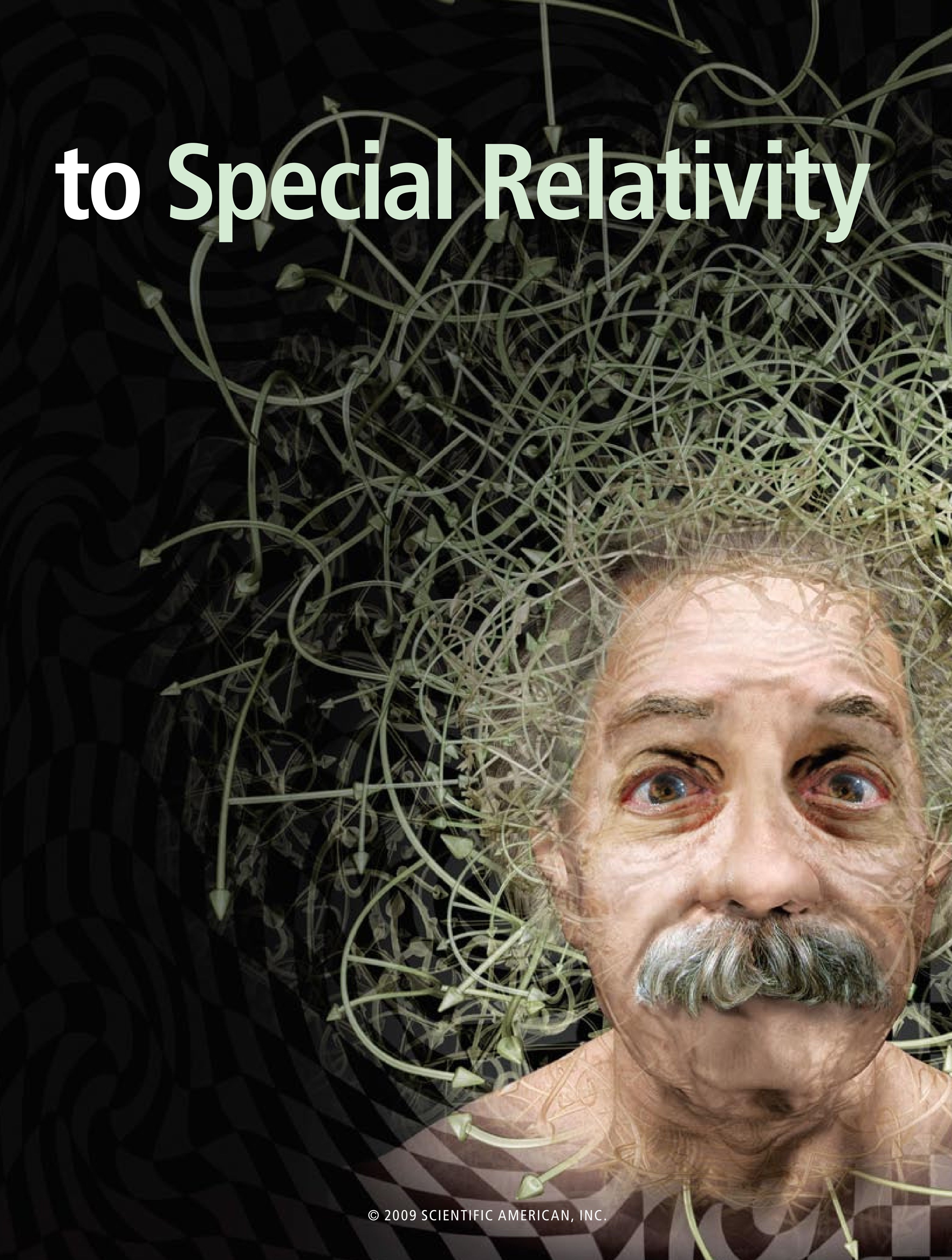
Let's back up a bit. Prior to the advent of quantum mechanics, and indeed back to the very beginnings of scientific investigations of nature, scholars believed that a complete description of the physical world could in principle be had by describing, one by one, each of the world's smallest and most elementary physical constituents. The full story of the world could be expressed as the sum of the constituents' stories.

Quantum mechanics violates this belief.

Real, measurable, physical features of collections of particles can, in a perfectly concrete way, exceed or elude or have nothing to do with the sum of the features of the individual particles. For example, according to quantum mechanics one can arrange a pair of particles so that they are precisely two feet apart and yet neither particle on its own has a definite position. Furthermore, the standard approach to understanding quantum physics, the so-called Copenhagen interpretation—proclaimed by the great Danish physicist Niels Bohr early last century and handed down from professor to student for generations—insists that it is not that we do not know the facts about the individual particles' exact locations; it is that there simply *aren't* any such facts. To ask after the position of a single particle would be as meaningless as, say, asking after the marital status of the number five. The problem is not epistemological (about what we know) but ontological (about what is).

Physicists say that particles related in this fashion are quantum mechanically entangled with one another. The entangled property need not be location: Two particles might spin in opposite ways, yet with neither one definitely spinning clockwise. Or exactly one of the particles might be excited, but neither is definitely the excited one. Entanglement may connect particles irrespective of where they are, what they are and

to Special Relativity



[BASICS]

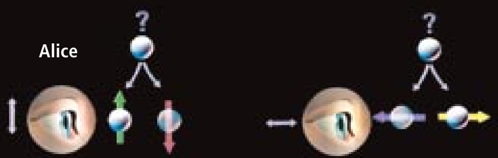
The EPR Thought Experiment

Albert Einstein, Boris Podolsky and Nathan Rosen ("EPR") pointed out that quantum entanglement of two particles produces inexplicable results if two people who are far apart (*here Alice and Buzz*) each examine one of the particles.

Quantum spins

Electrons have a property called spin, represented here by arrows that may point in any direction. When Alice measures an electron's spin (*below*), she chooses an axis. Measuring along a vertical axis, she will find the electron in either the up or the down state, with some probability for each. Using an east-west axis, she will find east or west spin.

Measurements

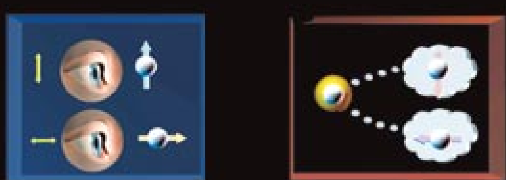


Two particles may be entangled so that they have their spins pointing in opposite directions, even though neither has a definite direction of its own. Suppose that Alice and Buzz share such a pair and that Alice finds hers to have spin up (*below*). No matter how far away Buzz and his particle are from Alice, if he measures his particle along the vertical axis he will definitely see that his particle has spin down, the opposite of Alice's.

Entangled spins

EPR argued that because Buzz can be 100 percent certain of measuring spin down, the spin of his particle must already be down, even prior to his measuring it. But Alice could equally well have measured along east-west and obtained, say, east spin, implying that Buzz's particle already has a west spin.

EPR argument



Because no quantum state permits Buzz's particle to be certainly spin down *and* certainly spin west, EPR concluded that quantum mechanics must be an incomplete theory.

what forces they may exert on one another—in principle, they could perfectly well be an electron and a neutron on opposite sides of the galaxy. Thus, entanglement makes for a kind of intimacy amid matter previously undreamt of.

Entanglement lies behind the new and exceedingly promising fields of quantum computation and quantum cryptography, which could provide the ability to solve certain problems that are beyond the practical range of an ordinary computer and the ability to communicate with guaranteed security from eavesdropping [see "Quantum Computing with Ions," by Christopher R. Monroe and David J. Wineland; Scientific American, August 2008].

But entanglement also appears to entail the deeply spooky and radically counterintuitive phenomenon called nonlocality—the possibility of physically affecting something without touching it or touching any series of entities reaching from here to there. Nonlocality implies that a fist in Des Moines can break a nose in Dallas without affecting any other physical thing (not a molecule of air, not an electron in a wire, not a twinkle of light) anywhere in the heartland.

The greatest worry about nonlocality, aside from its overwhelming intrinsic strangeness, has been that it intimates a profound threat to special relativity as we know it. In the past few years this old worry—finally allowed inside the house of serious thinking about physics—has become the centerpiece of debates that may finally dismantle, distort, reimagine, solidify or seed decay into the very foundations of physics.

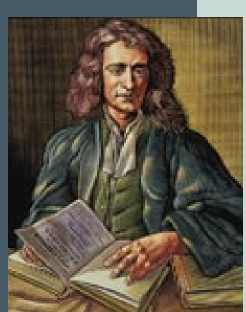
Radical Revisions of Reality

Albert Einstein had any number of worries about quantum mechanics. The overquoted concern about its chanciness ("God does not play dice") was just one. But the only objection he formally articulated, the only one he bothered to write a paper on, concerned the oddity of quantum-

NONLOCALITY THROUGH THE CENTURIES

Changing Views of "Reality"

Our intuition is that the world is local: we can move a rock only by touching it directly, or by touching a stick that touches it, or by creating some unbroken chain of such direct, local connections. Yet since the beginnings of modern science in the 1600s, apparent nonlocalities have been challenging scientists.



1687: Isaac Newton's law of universal gravitation, the first modern scientific description of gravity, involves "action at a distance." Newton is sure there must be an account of gravity without this nonlocality and even tries an unsuccessful theory in which tiny invisible, jiggling particles fill all of seemingly empty space.

1785: Charles Coulomb introduces the inverse-square law for electrostatic forces, analogous to Newton's inverse-square law for gravity. Electric effects seem to involve action at a distance.

B. SANERSON *Photo Researchers, Inc.* (*Newton*); THE GRANGER COLLECTION (*Coulomb apparatus*); ALFRED T. KAMAJIAN (*illustrations*) mechanical entanglement. This objection lies at the heart of what is now known as the EPR argument, named after its three authors, Einstein and his colleagues Boris Podolsky and Nathan Rosen [*see box on opposite page*]. In their 1935 paper "Can Quantum-Mechanical Description of Physical Reality Be Considered Complete?", they answer their own question with a tightly reasoned "no."

Their argument made pivotal use of one particular instruction in the quantum-mechanical recipe, or mathematical algorithm, for predicting the outcomes of experiments. Suppose that we measure the position of a particle that is quantum mechanically entangled with a second particle so that neither individually has a precise position, as we mentioned above. Naturally, when we learn the outcome of the measurement, we change our description of the first particle because we now know where it was for a moment. But the algorithm also instructs us to alter our description of the second particle—and to alter it instantaneously, no matter how far away it may be or what may lie between the two particles.

Entanglement was an uncontroversial fact of the picture of the world that quantum mechanics presented to physicists, but it was a fact whose implications no one prior to Einstein had thought much about. He saw in entanglement something not merely strange but dubious. It struck him as spooky. It seemed, in particular, nonlocal.

Nobody at that time was ready to entertain the possibility that there were genuine physical nonlocalities in the world—not Einstein, not Bohr, not anybody. Einstein, Podolsky and Rosen took it for granted in their paper that the apparent nonlocality of quantum mechanics must be apparent only, that it must be some kind of mathematical anomaly or notational infelicity or, at any rate, that it must be a disposable artifact of the algorithm—surely one could cook up quantum mechanics's predictions for experiments without needing any nonlocal steps.

And in their paper they presented an argument to the effect that if (as everybody supposed) no genuine physical nonlocality exists in the world and if the experimental predictions of quantum mechanics are correct, then quantum mechanics must leave aspects of the world out of its account. There must be parts of the world's story that it fails to mention.

Bohr responded to the EPR paper practically overnight. His feverishly composed letter of refutation engaged none of the paper's concrete scientific arguments but instead took issue—in an opaque and sometimes downright oracular fashion—with its use of the word "reality" and its definition of "elements of physical reality." He talked at length about the distinction between subject and object, about the conditions under which it makes sense to ask questions and about the nature of human language. What science needed, according to Bohr, was a "radical revision of our attitude as regards physical reality."

Bohr did go out of his way to agree with the EPR paper on one point: that of course there can be no question of a genuine physical nonlocality. The apparent nonlocality, he argued, was just one more reason why we must abandon the quaint and outdated aspiration, so manifest in the EPR paper, of being able to read from the equations of quantum mechanics a realistic picture of the world—a picture of what actually exists before us from moment to moment. Bohr insisted, in effect, that not only do we see the world through a glass darkly but that this shadowy and indefinite view is as real as anything gets.

Bohr's was a curiously philosophical response to an explicitly scientific concern. More curious still was the enshrinement of Bohr's response as the official gospel of theoretical physics. To spend any more time on these matters became, thereafter, apostasy. The physics community thus turned away from its old aspirations to uncover what the

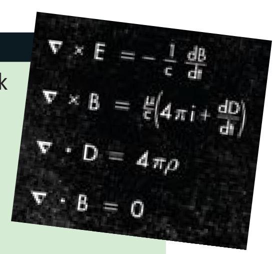
[THE AUTHORS]

David Z Albert and **Rivka Galchen** both teach at Columbia University, one on how physics tells the story of the world, the other on how to write stories. Albert is Frederick E. Woodbridge Professor of Philosophy at Columbia and author of *Quantum Mechanics and Experience* and *Time and Chance.* Galchen is adjunct assistant professor in the writing division of Columbia's School of Arts. Her often science-steeped stories and essays have appeared in the *New Yorker,* the *New York Times* and the *Believer.* Her first novel, *Atmospheric Disturbances,* was published by Farrar, Straus, and Giroux last May.

1831: Michael Faraday introduces the idea of magnetic lines of force. Physicists at this time use a notation involving electric and magnetic fields that fill space. The forces on a particle become, at least formally, a local action of the fields on them. But these fields are viewed as convenient calculational tools, not as things that are real.

1849: Hippolyte Fizeau and Jean-Bernard Foucault measure the speed of light to be 186,000 miles per second, or 298,000 kilometers per second, but no one knows what light really is.

1865: James Clerk Maxwell's equations reveal that electromagnetic fields have a rich dynamical life of their own, pushing and pulling each other, and crossing empty space at 298,000 km/s. Electromagnetism is local and light is an electromagnetic wave!



CORDELIA MOLLOY *Photo Researchers, Inc.* (*Faraday's magnetic repulsion*); LAWRENCE MANNING *Corbis* (*Fizeau and Foucault's speed of light*); SPL/PHOTO RESEARCHERS, INC. (*Maxwell's equations*); COURTESY OF DAVID Z ALBERT (*Albert*); COURTESY OF KEN GOEBEL (*Galchen*)

[THEORY MEETS REALITY]

Bell's Theorem and the Physical World

The nonlocality of our physical world follows from a combination of a theorem proved by John S. Bell in 1964 and experimental results obtained since the early 1980s. His theorem builds on the puzzle about entangled particles pointed out by Einstein, Podolsky and Rosen in 1935 [*see box on page 34*]. The EPR argument assumes that nature is local so that in particular a measurement (by, say, Alice) on one particle of a widely separated entangled pair cannot instantaneously alter the physical state of the faraway partner particle (which, say, Buzz can measure). They conclude that Buzz's particle must already have determinate values for spins in every direction. Thus, quantum mechanics must be incomplete because it does not determine those values except to guarantee they will be consistent with whatever result Alice gets when she measures her particle.

Bell asked: supposing that Alice's and Buzz's entangled particles have determinate values, can such particles reproduce the results predicted by quantum mechanics for all the ways that Alice and Buzz might measure their particles? Recall that for particles with entangled spins, Alice and Buzz must each choose an axis to measure the spin along. Bell proved mathematically that if Alice and Buzz chose to measure along axes at angles such as 45 and 90 degrees from each other, their measurements from numerous runs of the experiment would produce a statistical distribution of results that disagreed with that predicted by quantum mechanics—no matter what distribution of determinate values the particles had.

Researchers carried out experiments using entangled photons instead of electrons (which alters the angles to use but makes the experiment technically much less difficult) and found results that conformed with quantum mechanics's predictions. And so by Bell's theorem there must not *be* any determinate values carried by those photons. And because that contradicts EPR's conclusion, the assumption that nature is local is also wrong. And so the universe we live in cannot be local. ***—D.Z.A. and R.G.***

world is really like and for a long time thereafter it relegated metaphysical questions to the literature of fantasy.

Even today this crucial part of Einstein's legacy remains very much obscured. The best-selling 2007 Walter Isaacson biography of Einstein simply assures the reader that Einstein's criticism of quantum mechanics has since been resolved. And this is not true.

Return of the Repressed

The first serious scientific engagement with the EPR argument came (after 30 years of more or less complete neglect) in a famous 1964 paper by the extraordinary Irish physicist John S. Bell. From Bell's work it emerged that Bohr was wrong that nothing was wrong with his understanding of quantum mechanics and that Einstein was wrong about *what* was wrong with Bohr's understanding. To take in what was actually wrong involves abandoning the idea of locality.

The crucial question is whether the nonlocalities that at least appear to be present in the quantum-mechanical algorithm are merely apparent or something more. Bell seems to have been the first person to ask himself precisely what that question means. What could make genuine physical nonlocalities distinct from merely apparent ones? He reasoned that if any manifestly and completely local algorithm existed that made the same predictions for the outcomes of experiments as the quantum-mechanical algorithm does, then Einstein and Bohr would have been right to dismiss the nonlocalities in quantum mechanics as merely an artifact of that particular formalism. Conversely, if no algorithm could avoid nonlocalities, then they must be genuine physical phenomena. Bell then analyzed a specific entanglement scenario and concluded that no such local algorithm was mathematically possible.

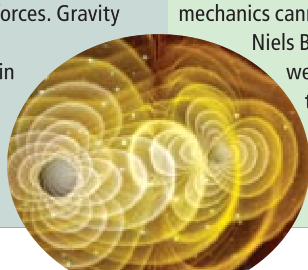
And so the actual physical world is nonlocal. Period.

This conclusion turns everything upside down. Einstein, Bohr and everyone else had always taken it for granted that any genuine incompatibility between quantum mechanics and the principle of locality would be bad news for quantum mechanics. But Bell had now shown that locality was incompatible not merely with the abstract theoretical apparatus of quantum mechanics but with certain of its empirical predictions as well. Experimenters—in particular work by Alain Aspect of the Institute of Optics in Palaiseau, France, and his co-workers in 1981 and later—have left no doubt that those predictions are indeed correct. The bad news, then, was not for

[NONLOCALITY THROUGH THE CENTURIES]

1905: Einstein's special theory of relativity reconciles Maxwell's equations with the principle that observers moving at a constant relative velocity should see identical laws of physics. But it destroys the possibility of distant events being simultaneous in any absolute sense.

1915: In Einstein's general theory of relativity, the curvature of spacetime plays the role that electromagnetic fields play for electromagnetic forces. Gravity is local: if a mass is jiggled, ripples in the curvature travel out at the speed of light.



1935: Einstein, Boris Podolsky and Nathan Rosen argue that because quantum-mechanical calculations involve nonlocal steps, quantum mechanics cannot be the full story. Niels Bohr (*far right*) insists we must accept quantum mechanics and instead give up old notions of "reality."

HULTON-DEUTSCH (*Einstein*); C. HENZE/NASA (*curvature of spacetime*); PAUL EHRENFEST, COURTESY OF EMILIO SEGRÈ VISUAL ARCHIVES, EHRENFEST COLLECTION (*Einstein and Bohrs*) quantum mechanics but for the principle of locality—and thus, presumably, for special relativity, because it at least appears to rely on a presumption of locality [*see box on next page*].

Metaphysical Mystery Tour

The main reaction to Bell's work—one that persists in many quarters even today—was still more obfuscation. Bell had shown that any theory capable of reproducing the empirical predictions of quantum mechanics for entangled pairs of particles—including quantum mechanics itself—had to be genuinely physically nonlocal.

This message has been virtually ignored. Instead almost everyone says that what Bell showed is that any attempt at replacing the orthodox quantum-mechanical picture of the world with something more in tune with our classical metaphysical expectations—any so-called hidden-variable, deterministic or philosophically realist theory—would have to be nonlocal if it could reproduce the quantum-mechanical predictions for EPR systems [*for a couple of proposed escape clauses from Bell's conclusion, see box at right*]. People were at least reading Bell's work but as if through a convex looking glass.

Only a very small minority of physicists managed to avoid this particular misunderstanding and grasp that Bell's proof and Aspect's experiments meant the world itself had been discovered to be nonlocal, but even they almost universally believed that the nonlocality in question here posed no particular threat to special relativity.

This belief arises out of the idea that special relativity is inextricably bound up with the impossibility of transmitting messages faster than the speed of light. After all, if special relativity is true, one can argue that no material carrier of a message can be accelerated from rest to speeds greater than that of light. And one can argue that a message transmitted faster than light would, according to some clocks, be a message that arrived before it was sent, potentially unleashing all the paradoxes of time travel.

As long ago as 1932 the brilliant Hungarian mathematician John von Neumann proved that the nonlocality of quantum mechanics cannot ever be parlayed into a mechanism to transmit messages instantaneously. For many decades, virtually the entire theoretical physics community regarded von Neumann's proof as an assurance that quantum-mechanical nonlocality and special relativity can perfectly peacefully coexist.

Varieties of Nonlocal Experience

It took yet another 30 years after the publication of Bell's paper for physicists to finally look these issues squarely in the face. The first clear, sustained, logically flawless and uncompromisingly frank discussion of quantum nonlocality and relativity appeared in 1994, in a book with precisely that title by Tim Maudlin of Rutgers University. His work highlighted how the compatibility of nonlocality and special relativity was a much more subtle question than the traditional platitudes based on instantaneous messages would have us believe.

Maudlin's work occurred against the backdrop of a new and profound shift in the intellectual environment. From the early 1980s onward, the grip of Bohr's conviction—that there could be no old-fashioned, philosophically realistic account of the subatomic world—was everywhere palpably beginning to weaken. By then a number of promising concrete scientific proposals seemed to provide a good account of that kind, at least in the approximation that neglects the effects of special relativity. These proposals included the Bohmian mechanics of David Bohm in England (developed in the early 1950s and an inspiration for Bell's work but otherwise largely ignored) and the GRW model of GianCarlo Ghirardi, Alberto Rimini and Tullio Weber in Italy [see "Bohm's Alternative to Quantum Mechanics," by David

OTHER WAYS OUT

Some physicists argue that John S. Bell's mathematical proof of the nonlocality of the quantum-mechanical world has some escape clauses.

MANY WORLDS

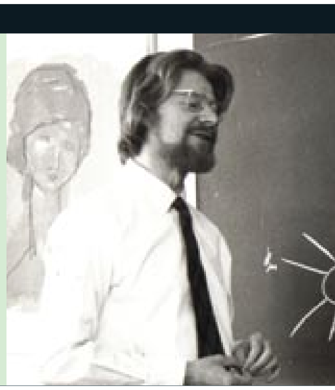
Bell innocently assumes that quantum experiments have unique outcomes. The many-worlds interpretation, however, asserts that quantum measurements in effect split the universe into branches where all the different outcomes occur in parallel [see "The Many Worlds of Hugh Everett," by Peter Byrne; SCIENTIFIC AMERICAN, December 2007]. So your universe can be "local" if copies of you inhabit myriad unseen parallel universes. This approach, however, is beset by many difficult problems.

REALISM?

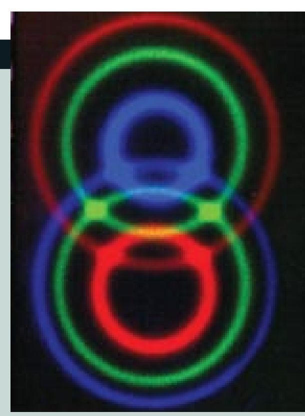
Many believe that because Bell starts by assuming the world conforms to what is called local realism, he therefore proved that *either* locality or realism is violated. Thus, the world could be local if it violates "realism." But this idea overlooks—or misunderstands—that the original "EPR" argument of Albert Einstein, Boris Podolsky and Nathan Rosen rules out the possibility of quantum locality without the realism Bell uses.

— D.Z.A. and R.G.

1964: John S. Bell (*right*) extends the "EPR" reasoning to cases in which spins are measured along nonparallel axes and shows that no local theory can possibly reproduce all of quantum mechanics's predictions for experimental results. The predictions of any local theory must always satisfy mathematical relations known as Bell's inequalities.



1981–present: Experiments using entangled states of light (*right*), in particular by Alain Aspect and his co-workers, verify that the world follows the predictions of quantum mechanics even in those situations in which quantum mechanics violates Bell's inequalities. The world is nonlocal after all.



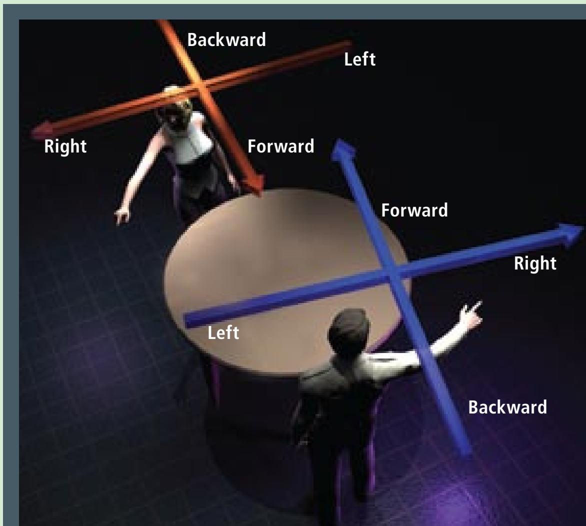
CERN, COURTESY OF AIP EMILIO SEGRÈ VISUAL ARCHIVES (*Bell*); PAUL KWIAT AND MICHAEL RECK *University of Vienna (entanglement)*

[THE PROBLEM]

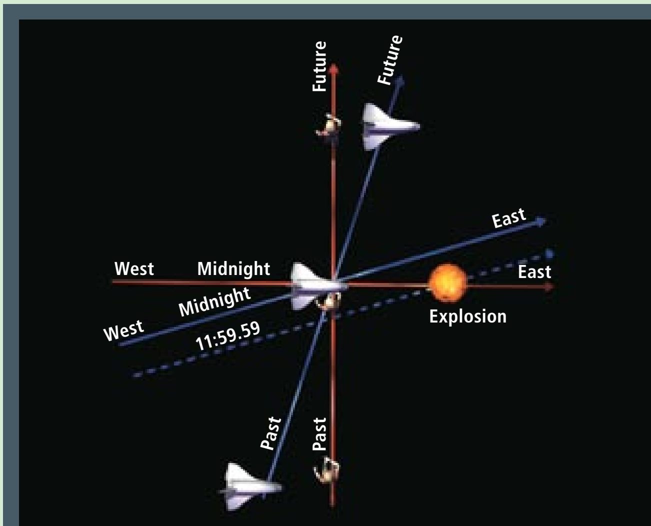
Why Special Relativity Dislikes Nonlocality

The special theory of relativity reveals an essential geometric relation between space and time that had never previously been imagined. The relation makes the concept of "instantaneous action at a distance" not merely strange but downright unintelligible.

Here, Alice and Buzz cannot agree about which distant events are simultaneous, nor can they agree about a theory involving action at a distance, such as one in which Alice causes the distant explosion "instantaneously" by pressing a button at midnight.



Alice and Buzz, who are standing at different places around a table, disagree about the spatial directions "right," "left," "forward" and "backward." Special relativity shows that people in relative motion disagree about time as well as space.



Alice's space and time axes (*red*) are centered on where she stands at precisely midnight. Buzz flies over Alice, heading east at nearly the speed of light. His motion tilts his space and time axes (*blue*) relative to Alice's. The duo disagree about when a bomb exploded several kilometers away: Alice insists it happened at midnight, but Buzz says it happened a second earlier (*blue dashed line*).

Z Albert; Scientific American, May 1994]. The old aspirations of physics to be a guide to metaphysics, to tell us literally and straightforwardly how the world actually is—aspirations that had lain dormant and neglected for more than 50 years—began, slowly, to reawaken.

Maudlin's book focused on three important points. First, the special theory of relativity is a claim about the geometric structure of space and time. The impossibility of transmitting mass or energy or information or causal influences faster than light—none of these requirements are even remotely, in and of themselves, sufficient to guarantee that the theory's claim about geometry is correct. Thus, von Neumann's proof about message transmission, in and of itself, offers us no assurance that quantum-mechanical nonlocality and special relativity can peacefully coexist.

Second, the truth of special relativity is (as a matter of fact) perfectly compatible with an enormous variety of hypothetical mechanisms for faster-than-light transmission of mass and energy and information and causal influence. In the 1960s, for example, Gerald Feinberg of Columbia published an internally consistent and fully relativistic theory of a hypothetical species of particle—tachyons—for which it is physically impossible ever to travel *slower* than light. Maudlin invented other examples.

Thus, the mere existence of a nonlocality in quantum mechanics, in and of itself, does not mean that quantum mechanics cannot coexist with special relativity. So perhaps there is hope.

As Maudlin emphasized in his third point, however, the particular variety of action at a distance that we encounter in quantum mechanics is an entirely different animal from the kind exemplified by Feinberg's tachyons or Maudlin's other examples. What is uncanny about the way that quantum-mechanical particles can nonlocally influence one another is that it does not depend on the particles' spatial arrangements or their intrinsic physical characteristics—as all the relativistic influences alluded to in the preceding paragraphs do—but only on whether or not the particles in question are quantum mechanically entangled with one another.

The kind of nonlocality one encounters in quantum mechanics seems to call for an absolute simultaneity, which would pose a very real and ominous threat to special relativity.

That's the rub.

➥ ON THE WEB

For a narrative on nonlocality from Newton to Maxwell by Rivka Galchen and David Z Albert, go to **www.SciAm.com/mar2009**

ALFRED T. KAMAJIAN

Hope for Special Relativity?

Two new results—pulling in curiously different directions—have emerged from this discussion in just the past few years. The first suggests a way that quantum-mechanical nonlocality could be compatible with special relativity; the other reveals a new blow that the combination of quantum mechanics and special relativity strikes against our deepest intuitions of the world.

The first result appeared in an astonishing 2006 paper by Roderich Tumulka, a young German mathematician now at Rutgers. Tumulka showed how all the empirical predictions of quantum mechanics for entangled pairs of particles could be reproduced by a clever modification of the GRW theory (recall that this theory proposes a philosophically realist way to get the predictions of quantum mechanics under many circumstances). The modification is nonlocal, and yet it is fully compatible with the spacetime geometry of special relativity.

This work is still very much in its infancy. No one has yet been able to write down a satisfactory version of Tumulka's theory that can be applied to particles that attract or repel one another. Moreover, his theory introduces a new variety of nonlocality into the laws of nature—a nonlocality not merely in space but in time! To use his theory to determine the probabilities of what happens next, one must plug in not only the world's current complete physical state (as is customary in a physical theory) but also certain facts about the past. That feature and some others are worrying, but Tumulka has certainly taken away some of the grounds for Maudlin's fear that quantum-mechanical nonlocality cannot be made to peacefully coexist with special relativity.

The other recent result, discovered by one of us (Albert), showed that combining quantum mechanics and special relativity requires that we give up another of our primordial convictions. We believe that everything there is to say about the world can in principle be put into the form of a narrative, or story. Or, in more precise and technical terms: everything there is to say can be packed into an infinite set of propositions of the form "at *t*1 *this* is the exact physical condition of the world" and "at *t*2 *that* is the exact physical condition of the world," and so on. But the phenomenon of quantum-mechanical entanglement and the spacetime geometry of special relativity—taken together—imply that the physical history of the world is infinitely too rich for that.

The trouble is that special relativity tends to mix up space and time in a way that transforms quantum-mechanical entanglement among distinct physical systems into something along the lines of an entanglement among physical situations at different times—something that in a perfectly concrete way exceeds or eludes or has nothing to do with any sum of situations at distinct temporal instants.

That result, like most theoretical results in quantum mechanics, involves manipulating and analyzing a mathematical entity called a wave function, a concept Erwin Schrödinger introduced eight decades ago to define quantum states. It is from wave functions that physicists infer the possibility (indeed, the necessity) of entanglement, of particles having indefinite positions, and so forth. And it is the wave function that lies at the heart of puzzles about the nonlocal effects of quantum mechanics.

But what *is* it, exactly? Investigators of the foundations of physics are now vigorously debating that question. Is the wave function a concrete physical object, or is it something like a law of motion or an internal property of particles or a relation among spatial points? Or is it merely our current information about the particles? Or *what?*

Quantum-mechanical wave functions cannot be represented mathematically in anything smaller than a mind-bogglingly high-dimensional space called a configuration space. If, as some argue, wave functions need to be thought of as concrete physical objects, then we need to take seriously the idea that the world's history plays itself out not in the three-dimensional space of our everyday experience or the four-dimensional spacetime of special relativity but rather this gigantic and unfamiliar configuration space, out of which the illusion of three-dimensionality somehow emerges. Our three-dimensional idea of locality would need to be understood as emergent as well. The nonlocality of quantum physics might be our window into this deeper level of reality.

The status of special relativity, just more than a century after it was presented to the world, is suddenly a radically open and rapidly developing question. This situation has come about because physicists and philosophers have finally followed through on the loose ends of Einstein's long-neglected argument with quantum mechanics—an irony-laden further proof of Einstein's genius. The diminished guru may very well have been wrong just where we thought he was right and right just where we thought he was wrong. We may, in fact, see the universe through a glass not quite so darkly as has too long been insisted. ■

➥ MORE TO EXPLORE

Quantum Theory and Measurement. Edited by John Archibald Wheeler and Wojciech Hubert Zurek. Princeton University Press, 1983. (Includes the original "EPR" paper and Niels Bohr's response.)

Quantum Mechanics and Experience. David Z Albert. Harvard University Press, 1992.

The Shaky Game: Einstein, Realism, and the Quantum Theory. Second edition. Arthur Fine. University of Chicago Press, 1996.

Quantum Non-Locality and Relativity: Metaphysical Intimations of Modern Physics. Second edition. Tim Maudlin. Wiley-Blackwell, 2002.

Speakable and Unspeakable in Quantum Mechanics: Collected Papers on Quantum Philosophy. Second edition. J. S. Bell. Cambridge University Press, 2004.

THE WORLD'S SMALLEST Radio

BY ED REGIS

A single carbon nanotube can function as a radio that detects and plays songs

KEY CONCEPTS

- Nanotechnology has demonstrated more hyperbole than substance for many years—and the "nano" label has been applied to items ranging from motor oil to lipstick.
- One of the first true nanoscale machines is a radio that can play songs such as Eric Clapton's "Layla" and the theme from *Star Wars.*
- A single nanotube in this device performs the function of multiple components in larger radios. The nanoapparatus may ultimately find uses in drug delivery devices, prosthetics or explosives detectors.

—The Editors

Nanotechnology is arguably one of the most overhyped "next big things" in the recent history of applied science. According to its most radical advocates, nanotechnology is a molecular manufacturing system that will allow us to fabricate objects of practically any arbitrary complexity by mechanically joining molecule to molecule, one after another, until the final, atomically correct product emerges before our eyes.

The reality has been somewhat different: today the word "nano" has been diluted to the point that it applies to essentially anything small, even down to the "nanoparticles" in commodities as diverse as motor oil, sunscreen, lipstick and ski wax. Who, then, would have expected that one of the first truly functional nanoscale devices—one that would have a measurable effect on the larger, macroscale world—would prove to be … a radio? But the nanotube radio, invented in 2007 by physicist Alex Zettl and his colleagues at the University of California, Berkeley, performs a set of amazing feats: a single carbon nanotube tunes in a broadcast signal, amplifies it, converts it to an audio signal and then sends it to an external speaker in a form that the human ear can readily recognize. If you have any doubts about this assertion, just visit www.SciAm.com/nanoradio and listen to the song "Layla."

The nanotube radio, its fabricators say, could be the basis for a range of revolutionary applications: hearing aids, cell phones and iPods small enough to fit completely within the ear canal. The nanoradio "would easily fit inside a living cell," Zettl says. "One can envision interfaces to brain or muscle functions or radio-controlled devices moving through the bloodstream."

The Call of the Nanotube

Zettl, who directs 30 investigators engaged in creating molecular-scale devices, decided to make nanotubes a focus of his work because they are remarkable structures. The question of who first discovered them is controversial, but Japanese physicist Sumio Iijima is generally credited with having put them on the scientific map, when in 1991 he announced finding "needlelike tubes" of carbon on the tip of a graphite electrode that emitted an arc, a luminous discharge of electricity.

Those nanotubes had some surprising properties. They came in a large variety of sizes and shapes: they were single-walled, double-walled and multiwalled. Some were straight, some were bent and some even looped back on themselves in toroidal configurations. Common to them all was their exceptional tensile strength, the resistance to being pulled apart along their length without breaking. The reason for this unusual property, Zettl says, is that "the force that holds the carbon atoms together in the carbon nanotube is the strongest bond in nature." Nanotubes are also excellent conductors of electricity, far better than copper, silver or even superconductors. "It's because the electrons don't hit anything," he explains. "The tube is such a perfect structure."

Zettl got the idea for a nanoradio when he decided he wanted to create tiny sensing devices that could communicate with one another and broadcast their observations wirelessly. "They were to do monitoring of environmental conditions," he says. They would be distributed in the field near some factory or refinery and would radio their results back to some collecting point. Anyone could then go to Google "and click on the air quality of a city and see it in real time."

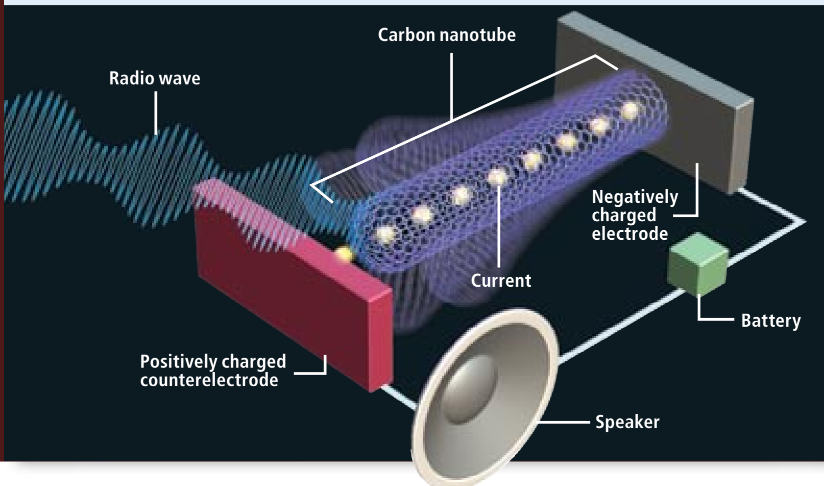
SHELTER PRODUCTIONS (*photo*); KURSTEN BRACCHI (*prop styling*); ANTHONY ISAMBERT FOR HALLEY RESOURCES (*grooming*)

[GOOD VIBRATIONS]

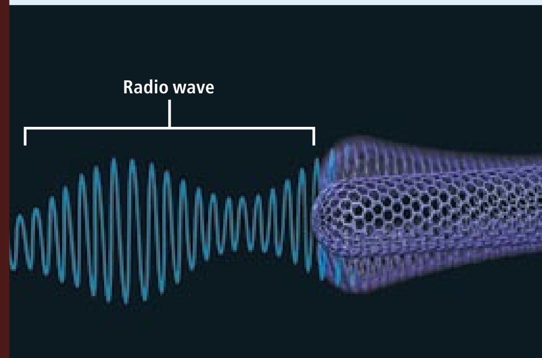
Anatomy of the Tiniest Radio

Just one nanotube can perform all the functions of a standard radio with many parts. Its tiny dimension enables it to vibrate rapidly in the presence of a radio signal. Connected to an electrical circuit, this nanoantenna can then be tweaked to tune, amplify and isolate just the audio component from the rest of the radio wave so that the sounds of the Beach Boys or George Frideric Handel can be discerned.

NANOTUBE RADIO



RECEPTION



Antenna of nanodimensions detects a radio wave by vibrating at the same frequency as the rapidly oscillating signal.

During the course of some experiments aimed at producing a nanotube mass sensor, one of Zettl's graduate students, Kenneth Jensen, found that if one end of a carbon nanotube was planted on a surface, creating a cantilever, the beam would vibrate when a molecule landed on its free end. Molecules of different masses would make the beam vibrate at different frequencies. When Zettl noticed that some of these frequencies included those in the commercial radio band, the idea of using the cantilevered nanotube to make a radio became virtually irresistible.

A bare-bones radio, Zettl knew, has four essential parts: an antenna that picks up the electromagnetic signal; a tuner that selects the desired frequency from among all those being broadcast; an amplifier that increases the strength of the signal; and a demodulator that separates the informational signal from the carrier wave on which it is transmitted. The informational component is then sent to an external speaker, which turns that part of the signal into audible tones.

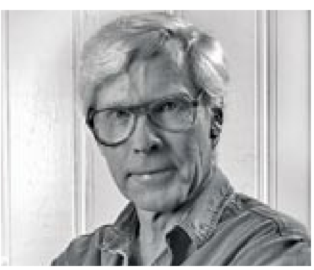
The carbon nanotube that was to be the core of the device proved to be a combination of such extremely favorable chemical, geometric and electrical properties that when it was placed between a set of electrodes, the miniature element alone accomplished all four functions simultaneously. No other parts were needed.

Zettl and Jensen began by working out an overall design in which a multiwalled carbon nanotube would be built on the tip of an electrode, an arrangement in which the nanotube would resemble a flagpole on a mountaintop. They decided on a multiwalled tube because it was a bit bigger than other kinds and was also easier to mount on the electrode surface, although they later constructed a version with a single-walled one as well. The tube, which would be about 500 nanometers long and 10 nanometers in diameter (roughly the size and shape of some viruses), would be placed on the electrode using nanomanipulation methods or directly grown on the electrode by a technique called chemical vapor deposition, in which layers of carbon precipitate out of an ionized gas.

Some distance away from the tip, rounded off in the shape of a hemispherical buckyball, would be a counterelectrode. A small direct-current (DC) voltage would be applied across the electrodes, creating a flow of electrons from the nanotube tip to the counterelectrode. The idea was that electromagnetic waves from an incoming radio transmission would impinge on the nanotube, causing it to physically vibrate in tune with the variations of the electromagnetic signal. Vibrating in sync with the incoming radio waves, the nanotube would be acting as an antenna but one that operates differently from that of a conventional radio.

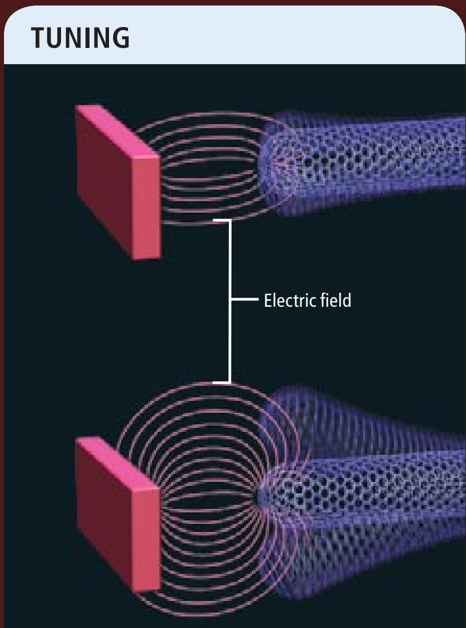
In a normal radio, the antenna picks up incoming signals electronically, meaning that the incoming waves induce an electric current within the antenna, which remains stationary. In the nanoradio, in contrast, the nanotube is so slen-

[THE AUTHOR]

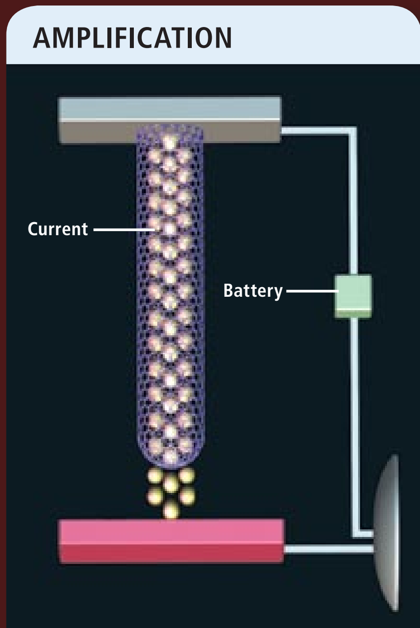


Ed Regis has written seven science books, including the recent *What Is Life?: Investigating the Nature of Life in the Age of Synthetic Biology,* which is about the attempt to build an artificial living cell. He and his wife live in the mountains in Maryland near Camp David.

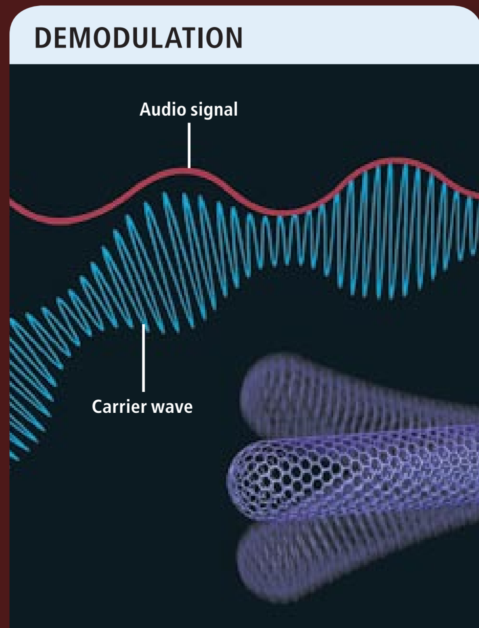
COURTESY OF PEPI KHARA (*Regis*); GEORGE RETSECK (*illustrations*)



Strength of an electric field can be adjusted to let the nanotube be tensioned like a guitar string so that it vibrates only at the proper frequency.



A large flow of electrons from the nanotube tip amplifies the signal in the presence of a small voltage from a battery.



The vibrating nanotube alters the current in a way that retains just the audio frequencies of the radio wave.

der and slight a charged object that the incoming electromagnetic waves are sufficient to push it back and forth mechanically.

"The nanoworld is weird—different things dominate," Zettl describes. "Gravity plays no role whatsoever, and inertial effects are basically nonexistent because things are just so small that residual electrical fields can play a dominant role."

The nanotube's vibrations, in turn, would set up a change in the current flowing from the nanotube tip to the counterelectrode: technically a field-emission current. Field emission is a quantum-mechanical phenomenon in which a small applied voltage produces a large flow of electrons from the surface of an object—a needle tip, say. Because of the way field emission works, the nanotube was expected to function not only as an antenna but also as an amplifier. The small-scale electromagnetic wave hitting the nanotube would cause a big spray of electrons to be released from its vibrating free end. That electron spray would amplify the incoming signal.

Next came demodulation, the process of separating a radio station's carrier-wave frequency from the informational message—voice or music—that is coded on top of it. In an amplitude-modulation (AM) radio broadcast, for example, this separation is achieved by a rectification and filtering circuit that responds to the amplitude and ignores (filters out) the frequency of the carrier-wave signal. These functions, too, Zettl's team reasoned, could be accomplished in the nanotube radio: when a nanotube mechanically vibrates in tune with a carrier wave's frequency, it also responds to the coded informational wave. Fortunately, rectification is an inherent attribute of quantum-mechanical field emission, meaning that the current coming off the nanotube varies only with the coded or modulated informational wave, whereas the carrier wave drops out of the picture. It would be demodulation for free—no separate circuitry required.

In short, an incoming electromagnetic signal would cause the nanotube, now acting as an antenna, to vibrate. Its vibrating end would amplify the signal, and its field-emission property of built-in rectification would separate (or demodulate) the carrier wave from the informational wave. The counterelectrode would then detect the changes in the field-emission current and send a song or news broadcast to an audio loudspeaker, which would convert the signal into sound waves.

Doing the Experiment

That, anyway, was the theory. In January 2007 Zettl, Jensen and two other Berkeley researchers, Jeff Weldon and Henry Garcia, performed the actual experiment. They mounted a multiwalled carbon nanotube on a silicon electrode and placed a counterelectrode about a micron away, connecting the two by wire. They also attached a DC battery to the apparatus to set up a small field-emission current between the nano-

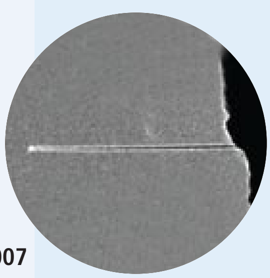
The working element of the radio would be the size and shape of some viruses.

VANISHING RADIOS

1931

1954

2003



2007

Radio waves are invisible, and now radios are, too, shrinking from a big box down to the size of a vibrating needlelike nanotube that can be viewed only through a high-powered microscope.

tube tip and the counterelectrode. To actually see what would happen during the course of a radio transmission from a nearby antenna, they placed their device inside a high-resolution transmission electron microscope (TEM). Then they started broadcasting.

According to the well-worn tale, the first message sent by telephone was the request, "Mr. Watson, come here. I want to see you," spoken by Alexander Graham Bell in 1876. The first wireless transmission, sent by Guglielmo Marconi in 1894, was a radio wave that made a bell ring 30 feet away. And in January 2007 the first successful operation of Zettl's carbon nanotube radio was the radio's reception of the music for "Layla," by Eric Clapton (while playing with Derek and the Dominos).

"It was fantastic," Zettl recalls of the experience. "I mean, it was spectacular. We could watch the nanotube [in the TEM], and the fact that you could see this molecular structure vibrating and hear it at the same time is kind of cool. I never thought I could *see* a radio operate!"

You can see the results for yourself, because the experimenters documented the entire process—audio and video—and converted the recording to a QuickTime movie that they posted on the Zettl Group's Web page, where anyone can download and play it for free. Later, they did the same with "Good Vibrations," by the Beach Boys; the "Main Title" theme from *Star Wars,* by John Williams; and the largo from *Xerxes,* the opera by George Frideric Handel. "This is the first song ever transmitted using radio," Zettl explains.

Hearing (and, yes, even watching) these tunes play is a surreal experience to witness. As the process starts up, a long, thin stationary nanotube appears against a featureless, grainy backdrop. The tube extends horizontally from a rocky-looking, irregular surface, next to a shorter nanotube that will remain untouched throughout by all the electromagnetic commotion taking place around it. (The shorter nanotube is insensitive to the broadcast because the frequency at which it resonates, which depends on its length, does not coincide with the frequency of the incoming transmission.)

Soon you hear a lot of static, but then the needle simply disappears in a vibrational blur as the song in question is dimly but recognizably heard above the background noise. It may sound like a broadcast from Neptune, but in fact it is the audible report of a countable number of carbon atoms moving in synchrony with the music.

Shortly after their initial success the experimenters removed the device from the TEM, made minor changes to the radio's configuration, and then were able to both broadcast and receive signals across the length of the laboratory, a distance of a few meters. They were also able to tune in different frequencies in real time, in effect "changing the station" as the radio played.

A nanotube radio can be tuned in two separate ways. One is by changing its length. While you can change the tone of a guitar string by bending it down against different frets, you can change the resonance frequency of a nanotube by shortening it—for example, by boiling atoms off the tip.

That, change, however, is irreversible. But just as there is a second method of varying a guitar string's pitch (namely, by varying its tension), so, too, with the nanotube. Varying the strength of the applied electric field will make the nanoradio respond to different frequencies of the radio band.

Their device did, in fact, perform all four of a radio's functions simultaneously: it was an antenna, amplifier, demodulator and tuner—all in one. That such a small and simple structure combined all these functions continues to amaze Zettl. How does he explain their almost magical convergence in a single elongated molecule of carbon?

"In electronics, often you have a trade-off: if you optimize this, then you lose something else. Here everything seems to just work for you, which is a little unusual. You don't see that often in science. It's one of those rare opportunities to see Murphy's Law not rearing its ugly head. Here everything that can go right is going right," he says.

Zettl and his colleagues withheld news of the nanoradio for several months, until it could be published in *Nano Letters,* a journal of the American Chemical Society. The apparatus had its formal debut online in October 2007 and then in the November print edition. In that same print issue, two independent researchers, Chris Rutherglen and Peter Burke, both at the University of California, Irvine, announced the use of a carbon nanotube to demodulate an AM signal. They called their piece "Carbon Nanotube Radio," but their radio was not an all-in-one device like Zettl's. In Rutherglen and Burke's setup, the antenna and amplification functions were provided by conventional, life-size desktop units.

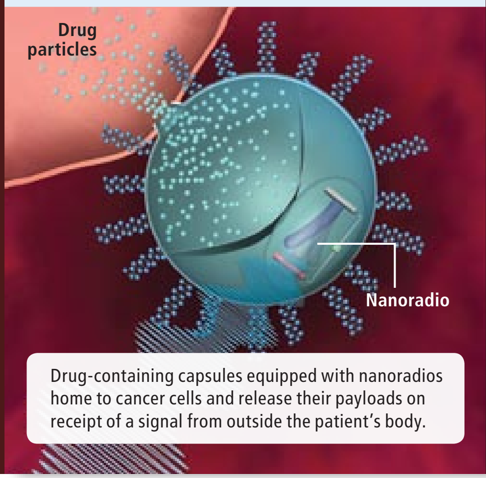
HEATHER GORDON (*vacuum tube radio, transistor radio* and *digital radio*); COURTESY OF ZETTL RESEARCH GROUP, LAWRENCE BERKELEY NATIONAL LABORATORY AND UNIVERSITY OF CALIFORNIA, BERKELEY (*nanoradio*)

[MORE THAN A TOY]

What to Do with a Radio You Can't See

The nanoradio is not just an alluring graduate project. The ability to send and receive signals from a microscopic apparatus will enable development of radically new types of drug delivery devices and robots that can assist in rescues at disaster sites.

DRUG DELIVERY



SEARCH AND RESCUE

GEORGE RETSECK

Burke, for his part, concedes that Zettl's all-in-one radio is "very elegant."

Lilliputian Drug Delivery Systems

Because it turns nanotechnology from a collection of theories, hopes and speculations into a practical, working appliance, the nanotube radio is potentially a transformative piece of equipment. Zettl, for one, is not bashful about foreseeing a bunch of killer apps made possible by the nanoradio: a whole new generation of communications devices, brain and muscle implants, and so on. Whereas some of these more futuristic applications will require a nontrivial amount of additional insight and engineering to make them into operational realities, others are more near term—in the form of radio-controlled drug delivery systems, for example.

One of the downsides of chemotherapy for shrinking invisible cancers that have spread or for treating inoperable ones is that the chemical agents used to kill cancer cells travel through the bloodstream to all parts of the body and often kill healthy cells as well as the malignant ones. A solution advanced by some physicians who have been in contact with Zettl would be to first inject packages that are molecularly targeted to cancer cells and that contain a chemo agent as well as a nanoradio; after allowing the packages time to find the tumors, radio-control signals would trigger release of the drug into the tumor cells for their destruction.

A second use would be to repair individual cells by injecting drugs into them. Zettl's group has moved in this direction by working on a fine-scale approach to nanoinjection in which the researchers punctured cell walls and membranes and put nanotube structures inside, where they released specific chemicals.

"The cells withstand that very nicely," Zettl says. "This nanoinjection technique works much better than the old technique where people used to try to use micropipettes that puncture cells and inject fluid. Those are way too crude and disruptive for most living cells." Zettl also foresees an application of his original nanotube mass sensor. Some types of explosives contain signature molecules of a known mass, and so a minuscule instrument that detects those molecules rapidly and reliably could replace the refrigerator-size explosives-sensing mass spectrometers now in use at some airport security checkpoints. No one is commercializing any of these devices as yet. Zettl, however, has patented his nanoradio, the nano mass sensor and other inventions that have come out of his Center of Integrated Nanomechanical Systems and has begun licensing the technology for others to develop.

Perhaps not surprisingly, some of Zettl's more recent achievements in the nanoworld seem to have plumbed the very limits of the Lilliputian. In July 2008 he announced in *Nature* that he and his group had coaxed an electron microscope to image individual atoms of hydrogen, nature's smallest atom. In the downward direction, there is nowhere left to go. ■

➥ MORE TO EXPLORE

Nanotube Radio. Alex Zettl et al. in *Nano Letters,* Vol. 7, No. 11, pages 3508–3511; 2007.

An Atomic-Resolution Nanomechanical Mass Sensor. Alex Zettl et al. in *Nature Nanotechnology.* Published online on July 20, 2008.

Images and movies of the University of California, Berkeley, group's nanotube radio can be found at **www.physics.berkeley.edu/research/zettl/projects/nanoradio/radio.html**

Saving NEW BRAIN CELLS

Fresh neurons arise in the adult brain every day. New research suggests that the cells ultimately help with learning complex tasks—and the more they are challenged, the more they flourish

BY TRACEY J. SHORS

If you watch TV, read magazines or surf the Web, you have probably encountered advertisements urging you to exercise your mind. Various brain fitness programs encourage people to stay mentally limber by giving their brain a daily workout—doing everything from memorizing lists and solving puzzles to estimating the number of trees in Central Park.

It sounds a bit gimmicky, but such programs may have a real basis in neurobiology. Recent work, albeit mostly in rats, indicates that learning enhances the survival of new neurons in the adult brain. And the more engaging and challenging the problem, the greater the number of neurons that stick around. These neurons are then presumably available to aid in situations that tax the mind. It seems, then, that a mental workout can buff up the brain, much as physical exercise builds up the body.

The findings may be particularly interesting to intellectual couch potatoes whose brains could benefit from a few cerebral sit-ups. More important, though, the results lend some support to the notion that people who are in the early stages of Alzheimer's disease or who have other forms of dementia might slow their cognitive decline by keeping their minds actively engaged.

It's a New Neuron!

In the 1990s scientists rocked the field of neurobiology with the startling news that the mature mammalian brain is capable of sprouting new neurons. Biologists had long believed that this talent for neurogenesis was reserved for young, developing minds and was lost with age. But in the early part of the decade Elizabeth Gould, then at the Rockefeller University, demonstrated that new cells arise in the adult brain—particularly in a region called the hippocampus, which is involved in learning and memory. Similar reports soon followed in species from mice to marmosets, and by 1998 neuroscientists in the U.S. and Sweden had shown that neurogenesis also occurs in humans [see "New Nerve Cells for the Adult Brain," by Gerd Kempermann and Fred H. Gage; Scientific American, May 1999].

KEY CONCEPTS

- Thousands of new cells are generated in the adult brain every day, particularly in the hippocampus, a structure involved in learning and memory.
- Within a couple of weeks, most of those newborn neurons will die, unless the animal is challenged to learn something new. Learning—especially that involving a great deal of effort—can keep these new neurons alive.
- Although the neurons do not seem to be necessary for most types of learning, they may play a role in predicting the future based on past experience. Enhancing neurogenesis might therefore help slow cognitive decline and keep healthy brains fit.

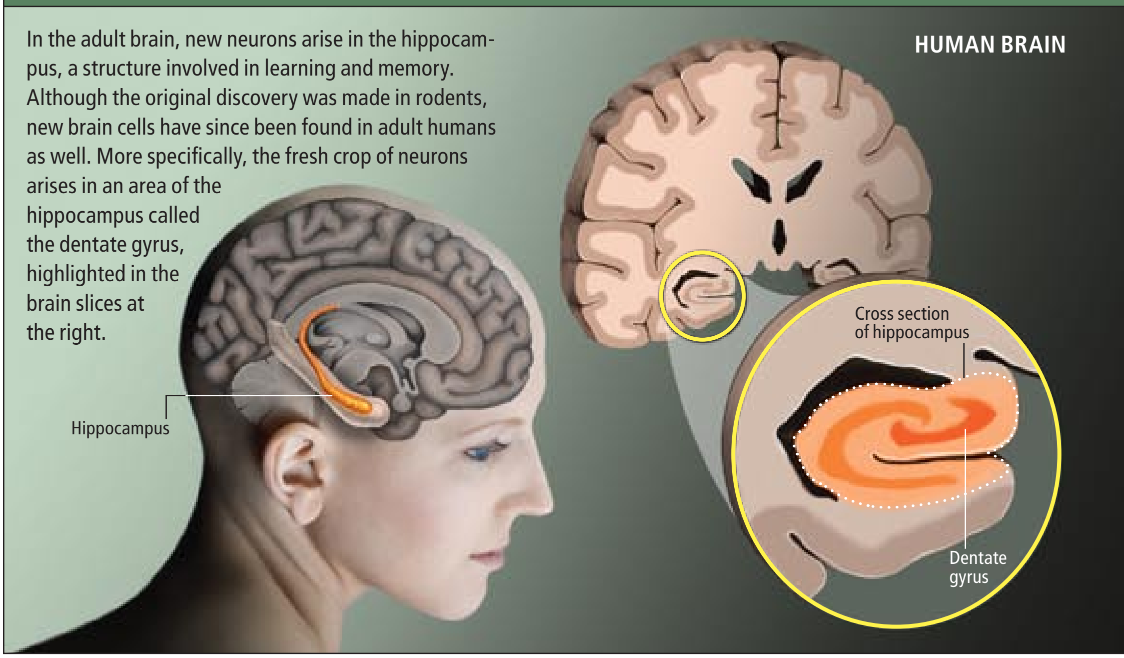
—The Editors

JANA LEON

The tasks that rescue the most neurons are the ones that are hardest to learn.

[BASICS]

WHERE NEW NEURONS FORM



In the adult brain, new neurons arise in the hippocampus, a structure involved in learning and memory. Although the original discovery was made in rodents, new brain cells have since been found in adult humans as well. More specifically, the fresh crop of neurons arises in an area of the hippocampus called the dentate gyrus, highlighted in the brain slices at the right.

In rodents, studies of neurogenesis generally involve injecting the animals with a drug called BrdU (bromodeoxyuridine), which marks newly formed cells, making them stand out when viewed under a microscope. Those studies indicate that in rats, between 5,000 and 10,000 new neurons arise in the hippocampus every day. (Although the human hippocampus also welcomes new neurons, we do not know how many.)

The cells are not generated like clockwork, however. Instead their production can be influenced by a number of different environmental factors. For example, alcohol consumption has been shown to retard the generation of new brain cells. And their birth rate can be enhanced by exercise. Rats and mice that log time on a running wheel can kick out twice as many new cells as mice that lead a more sedentary life. Even eating blueberries seems to goose the generation of new neurons in the rat hippocampus.

Use It or Lose It

Exercise and other actions may help produce extra brain cells. But those new recruits do not necessarily stick around. Many if not most of them disappear within just a few weeks of arising. Of course, most cells in the body do not survive indefinitely. So the fact that these cells die is, in itself, not shocking. But their quick demise is a bit of a puzzler. Why would the brain go through the trouble of producing new cells only to have them disappear rapidly?

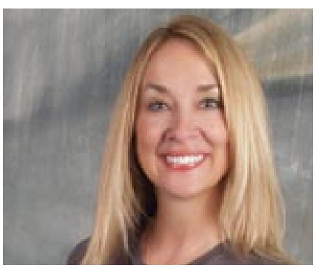
From our work in rats, the answer seems to be: they are made "just in case." If the animals are cognitively challenged, the cells will linger. If not, they will fade away. Gould, who is now at Princeton University, and I made this discovery in 1999, when we performed a series of experiments looking at the effect of learning on the survival of newborn neurons in the hippocampus of rat brains.

The learning task we used, called trace eyeblink conditioning [*see box on page 50*], is in some ways similar to the experiments in which Pavlov's dogs started to salivate when they heard a sound they associated with the arrival of dinner. In eyeblink conditioning, an animal hears a tone and then, some fixed time later (usually 500 milliseconds, or half a second), gets hit with a puff of air or a mild stimulation of the eyelid, which causes the animal to blink.

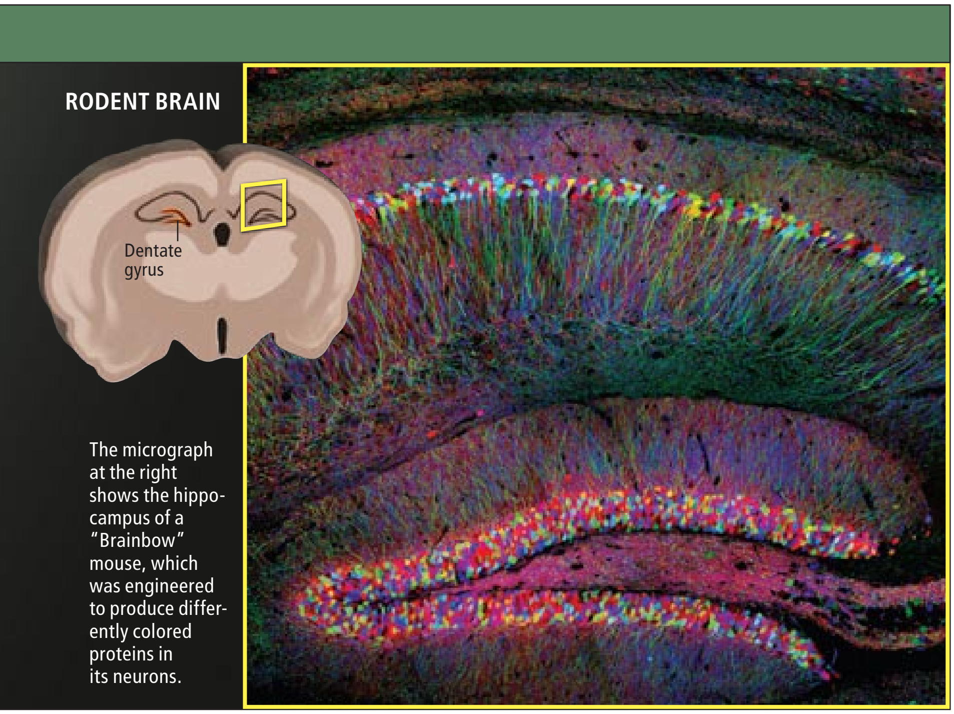
After enough trials—usually several hundred—the animal makes a mental connection between the tone and the eye stimulation: it learns to anticipate when the stimulus will arrive and to blink just before that happens. This "conditioned" response indicates that the animal has learned to associate the two events together in time. The rats' accomplishment may sound trivial, but the setup provides a good way to measure "anticipatory learning" in animals—the ability to predict the future based on what has happened in the past.

To examine the connection between learning

[THE AUTHOR]



Tracey J. Shors, a professor in the department of psychology and the Center for Collaborative Neuroscience at Rutgers University, has had a long-standing interest in the neurobiology of learning and memory. Working with Elizabeth Gould of Princeton University, a discoverer of adult neurogenesis, Shors showed that learning enhances the survival of new neurons in the hippocampus and that these neural recruits seem to be involved in some aspects of learning. Some 10 years later Shors continues to ponder the question: "Neurogenesis: What's learning got to do with it?"



The micrograph at the right shows the hippocampus of a "Brainbow" mouse, which was engineered to produce differently colored proteins in its neurons.

and neurogenesis, all the animals were injected with BrdU at the start of the experiments. One week later half the rats were recruited into the eyeblink training program; the others lounged in their home cages. After four or five days of training, we found that the rats that had learned to time their blink properly retained more BrdU-labeled neurons in the hippocampus than did the animals that had simply remained in their cages. We concluded that learning this task rescued cells that would otherwise have died. In the animals that received no training, very few of the newborn cells that had been labeled with BrdU at the start of the experiment could be seen at the end. And the better the animal learned, the more new neurons it retained. The same thing happens in animals that have learned to navigate a maze.

When we first started doing the eyeblink studies in the late 1990s, we examined the effects of training in animals that had learned well: in other words, rats that learned to blink within, say, 50 milliseconds of the eyelid stimulation—and did so in more than 60 percent of the trials. More recently, we asked whether animals that failed to learn—or that learned poorly—also retained new neurons after training. They did not. In studies published in 2007, rats that went through some 800 trials but never learned to anticipate the eyelid stimulation had just as few new neurons as the animals that never left their cages.

We also conducted eyeblink experiments in which we limited the animals' opportunity to learn. This time we gave rats only one day—200 trials—to get it right. In this situation, some animals learned to anticipate the stimulus, and others did not. Again, the rats that learned retained more of the new neurons than the rats that did not, even though all went through the same training. These data imply that it is the process of learning—and not simply the exercise of training or exposure to a different cage or a different routine—that rescues new neurons from death.

No Pain, No Gain

Although learning must occur if newborn hippocampal neurons are to survive, not all types of learning work. For example, training an animal to swim over to a platform that is visible in a pool of water does not enhance cell survival. Nor does training an animal to recognize that two stimuli, such as a tone and an eyeblink stimulus, occur almost simultaneously.

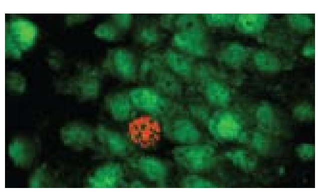
The reason these tasks fail to rescue new cells from death, we surmise, is that they do not require much thought. Swimming to a visible platform is something rats do readily. After all, they do not want to drown. And if eyelid stimulation overlaps in time with a tone, the animals do not need to form a memory trace of an event that happened in the past—the sound of the tone—to help them predict when the eyeblink stimulus will occur. They simply respond when they hear the sound.

We think that the tasks that rescue the most new neurons are the ones that are hardest to learn, requiring the most mental effort to master. To test this hypothesis, we took a task that is a bit of a no-brainer and made it a little more challenging. We started with the easy eyeblink task, in which the tone precedes but still overlaps in time with the eyelid stimulation. Learning that connection, as indicated above, does not typically rescue new neurons. Then we made this task more challenging by greatly extending the duration of the tone so that now the stimulus arrived toward the end of a very long sound.

Learning when to blink in this task is more difficult than in the easy test, because in this case blinking soon after the tone begins, like runners taking off after hearing the starting pistol, is not the correct response. The task is also more difficult than the standard, 500-millisecond trace test because the animal cannot use the

VIEWING NEW NEURONS

The chemical BrdU marks cells that are born after an animal has been exposed to the substance. The image below highlights one newborn cell—the BrdU shows up as red, and the green peeking through identifies the cell as a neuron. Mature neurons surround the new one.



COURTESY OF JEAN LIVET, TAMILY WEISSMAN, JOSHUA SANES AND JEFF LICHTMAN *Harvard University (hippocampus)*; COURTESY OF BENEDETTA LEUNER *(BrdU)*

It appears there is a critical window of time in which learning can save new neurons.

end of the tone as a signal to "get ready." Rather the rat must keep track of exactly when the tone started and estimate when the eyelid stimulation will occur—a real challenge for all animals, including humans. And we found that this challenge rescues as many, and sometimes more, new neurons than does the standard trace conditioning task.

Interestingly enough, among the animals that learned in our conditioning tasks those that were a bit slow—in that they required more trials to learn how to master a task—ended up with more new neurons than animals that learned fast. Thus, it seems that new neurons in the hippocampus respond best to learning that requires a concerted effort.

Timing Counts

Why effortful learning should be critical is not clear. One theory is that tasks requiring more thought—or taking longer periods of training to learn—activate more vigorously the networks of hippocampal nerve cells that include these newborn neurons, and that such activation is key. I tend to favor this hypothesis for a couple of reasons.

First, a number of investigators have demonstrated that tasks involving learning, such as the classical eyeblink conditioning test, generally increase the excitability of neurons in the hippocampus, making them become much more active. Furthermore, this hippocampal hustle and bustle goes hand in hand with learning: the animals that show the most activation are the ones that best learn the task.

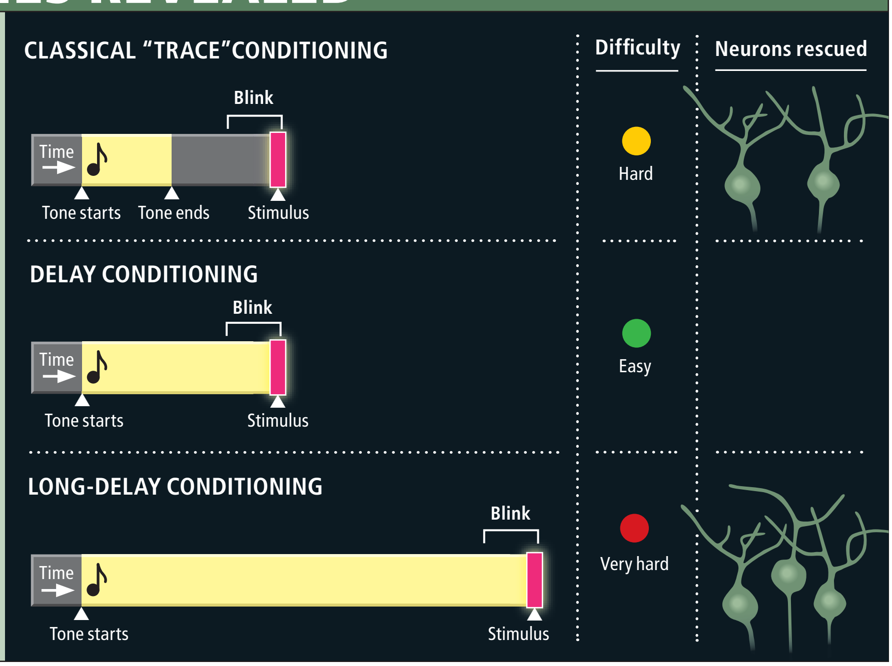
Next, it appears there is a critical window of time in which learning can save newborn neurons—in rodents, between about one week and two weeks after the cells arise. One recent study in rats reported, for instance, that learning can rescue cells when the cells are seven to 10 days old. Training that occurs after that time is too late: the neurons are already dying off. And training before that time is too early to help. This learning window corresponds to the period when these newborn cells, which start life unspecialized, begin to differentiate into neurons—sprouting signal-detecting dendrites (which receive impulses from other parts of the brain) and axons (which carry messages to a neighboring region of the hippocampus called CA3). Around this time they also begin to re-

[LEARNING TESTS]

WHAT RAT STUDIES REVEALED

The author and her colleagues relied on "eyeblink conditioning" experiments to discover that working hard to learn something enhances the survival of new neurons. They began with a classical form of the experiment (*top*), in which an animal hears a tone that is followed half a second later by a stimulus that will make it blink. After several hundred trials, most animals learn to blink just before the stimulus arrives. Because the tone and the blink-inducing stimulus are separated in time, figuring out when to blink is difficult; this task rescues a large fraction of newborn neurons.

Rats master readily an easier version of the test—in which the blink stimulus overlaps with the tone (*middle*); this task does not enhance survival of new neurons. Making conditions more challenging—by having the rat wait much longer before the stimulus arrives (*bottom*)—rescues more neurons than even the classical approach does.

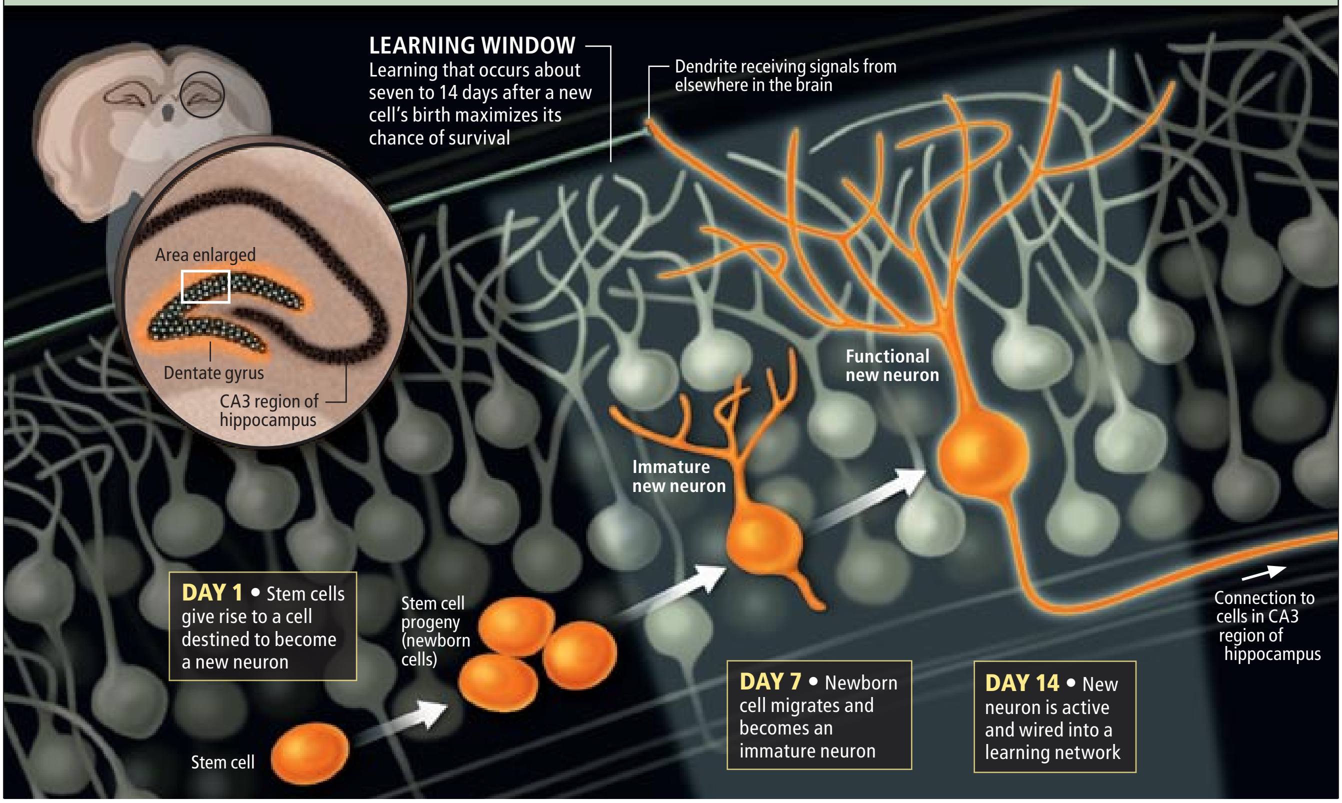


NIGEL CATTLIN *Photo Researchers, Inc.* (*rat*); JEN CHRISTIANSEN (*illustrations*)

[HYPOTHESIS]

HOW LEARNING HELPS TO SAVE NEW NEURONS

During their first week of life, newborn hippocampal cells migrate from the edge of the dentate gyrus in to a deeper area, where they mature and become wired into a network of neurons. Learning that occurs when the cells are between about one to two weeks old enhances their survival—perhaps exerting this effect by stimulating existing neurons, which in turn release signals that foster maturation of young cells. In the absence of learning during the maturation period, most new hippocampal cells will die.



spond appropriately to certain neurotransmitters—the chemicals that carry communications between nerve cells.

These observations suggest that the new cells must be somewhat mature and wired into networks with other neurons in the brain before they can respond to learning. When learning is difficult, neurons throughout the hippocampus—including the new recruits—are fully engaged. And these recruits survive. But if the animal is not challenged, the new neurons lack the stimulation they need to survive and then simply fade away.

What Do They Do?

So thousands of new cells arise in the hippocampus every day, and if an animal is challenged to learn, these cells stay around. But what function do they perform? They cannot, of course, help with learning in real time as they arise. Much learning occurs almost instantaneously (over the course of seconds, if not less). Faced with a new task, the brain cannot very well wait around a week or so for new neurons to be born, mature and hook up into functional networks before an animal can begin to learn. My colleagues and I suspected that the stockpiled cells influence some aspects of learning later on.

To test that idea, we decided to get rid of newborn brain cells. If these cells become important for learning, we reasoned, animals that lacked them would be less successful students. Of course, excising every single new cell from an animal's brain would be technically impossible. Instead we prevented the cells from being generated in the first place by treating rats for several weeks with a drug called MAM, which stops cells from dividing. Then the animals hit the classroom.

Rats treated with MAM, we found, were poor students in the standard, 500-millisecond trace eyeblink conditioning task. They had a difficult time learning to anticipate the stimulus. Yet the treated animals performed well on many other learning tasks that depend on the

JEN CHRISTIANSEN

WHAT HELPS, WHAT HURTS

Learning promotes the survival of new neurons but does not affect the number of cells produced. Other interventions, however, have been found to influence the generation of neurons in rodents.

BOOSTERS

Exercise

Antidepressants

Blueberries

BLOCKERS

Alcohol

Nicotine

hippocampus, such as the Morris water maze. In this task, rats are dropped into a pool of opaque liquid through which they must swim until they find a submerged platform. The walls of the pool are marked with spatial cues that help the animals navigate. Rats bereft of recently born neurons caught on just as quickly as their untreated mates.

In our hands, animals that were treated with MAM also learned to remember the place in which an emotional experience occurred. For example, rats that received a mildly unpleasant stimulus to the foot when placed into a particular cage froze the moment they were put back there. This type of emotional learning, known as contextual fear conditioning, also depends on the hippocampus, but it did not give our treated animals any problems.

All told, the learning abilities of rats with few new neurons were relatively unimpaired. The animals did seem to have trouble learning more difficult associations, such as figuring out that a sound always precedes a stimulation to the eyelid by half a second. We surmise, therefore, that if the new neurons are necessary for learning at all, they come into play only in a select set of situations, apparently those involving some cognitive effort.

Biologically speaking, that kind of specialization makes sense: an animal would not want to rely on producing and developing an entire cohort of new neurons to respond to situations that will affect its immediate survival. So presumably the added cells, once they mature, are used to fine-tune or boost problem-solving skills that already exist. In the lingo of psychology, enhancement of such skills is called "learning to learn."

Could neurogenesis somehow be exploited for preventing or treating disorders that bring about cognitive decline?

What about My Brain?

All the studies discussed thus far were conducted in laboratory animals—either mice or rats. What would happen in humans who did not produce new neurons in the hippocampus? Modern medicine, sadly, provides us with a population of ready-made subjects: people who are undergoing systemic drug treatment (chemotherapy) for cancer. Like treatment with MAM, chemotherapy impairs the cell division required for generating new cells. It is perhaps no coincidence, then, that people who have had chemotherapy often complain that they have trouble learning and remembering things, a syndrome sometimes referred to colloquially as "chemobrain."

In some ways, the observation fits our animal data. Like rodents who show very mild or limited cognitive impairment after MAM treatment, people undergoing chemotherapy function quite well under most circumstances. They get dressed, go to work, make meals, socialize with friends and family, and otherwise continue to live their lives. Which makes sense. Given the findings in laboratory animals, one would *not* expect profound or pervasive deficits in basic cognitive functions. Rather one would expect selective deficits in more difficult types of learning processes—the kinds of things everyone finds challenging, such as multitasking that calls for juggling multiple projects while trying to process new information.

To establish that neurogenesis plays a role in human learning, investigators need to develop noninvasive methods for detecting new neurons in the living brain, and they need to find reversible ways to prevent the cells' maturation during the learning process. The former methods are

WHAT'S NEXT?

Much remains to be discovered about how learning affects the survival of new neurons in the hippocampus. First, we would like to determine the molecular mechanisms by which cognitive challenges save new cells. Which neurotransmitters are involved? Which receptor proteins? And when exactly do those mechanisms operate? Does learning help new neurons to become integrated into neuronal networks, or does it promote the survival of those that are already connected? Further, how do neurons produced in the mature brain contribute to the ability to gain knowledge?

Those kinds of studies are being done in animals. But we would also like to understand more about neurogenesis in humans—both in healthy individuals and in people with diseases such as Alzheimer's.

To do that, we will need noninvasive ways to monitor the birth and death of newborn neurons in the human brain. Armed with that ability, we could begin to address some interesting issues, such as how much neurogenesis goes on in a healthy human brain versus a brain afflicted by Alzheimer's. Ultimately, we could also examine whether an intervention such as gene therapy could increase the numbers of new neurons generated in the human hippocampus—and whether particular brain-exercising activities would help keep those new neurons around.

—T.S.

JEN CHRISTIANSEN

being developed, and the latter are likely to be some time off.

Suppose, for the moment, though, that having a ready supply of new neurons on tap does help to keep the human brain intellectually limber. Could neurogenesis, then, somehow be exploited for preventing or treating disorders that bring about cognitive decline?

Consider the case of Alzheimer's, in which degeneration of hippocampal neurons leads to a progressive loss of memory and of learning ability. People with Alzheimer's do continue to produce new neurons, but it seems that many of the cells do not survive to become fully mature. Perhaps the process of neurogenesis and neuronal maturation is impaired in these individuals. Or perhaps the new cells do not survive because the disease hampers the ability to learn.

Yet some findings offer hope, at least for those in the early stages of dementia. As mentioned earlier, studies in healthy animals and people suggest that simple actions such as aerobic exercise can boost the production of new neurons. In addition, antidepressants have been found to be powerful modulators of neurogenesis. And a study in 2007 found that chronic treatment with antidepressants increases daily living and global functioning in patients with Alzheimer's—a hint, at least, that such therapy might promote production and survival of new neurons in patients.

Anecdotal accounts suggest that effortful learning may also help some patients. I recently presented our animal data at a meeting about Alzheimer's and other forms of dementia. The clinicians in the audience were intrigued by our findings indicating that efforts to learn something difficult help to preserve freshly minted nerve cells. They report having seen benefits from such exertions in their patients. And they note that patients who can fully engage themselves in cognitively demanding activities may be able to delay the progression of this mind-robbing disease.

That said, it would be foolish to think that cognitive engagement combined with antidepressants or physical activity could completely reverse the damage done by a disease such as Alzheimer's, which kills many more brain cells than just new ones. It could be, though, that such activities might slow the rate of cognitive decline—in people grappling with degenerative diseases and, perhaps, in all our brains as we grow older.

They say you can't teach an old dog new tricks, and certainly as adults, many of us find it painful to learn something completely new. But if we want to keep our brains in shape, it probably would not hurt to learn a new language, take up tap dancing, or tackle some fast gaming after your Wii Fit workout—and it might even help. ■

THE MORE CHALLENGING a cognitive task is, the more new neurons it is likely to rescue, if findings from rodents hold true in humans.

➡ MORE TO EXPLORE

Learning Enhances Adult Neurogenesis in the Hippocampal Formation. Elizabeth Gould, Anna Beylin, Patima Tanapat, Alison Reeves and Tracey J. Shors in *Nature Neuroscience,* Vol. 2, No. 3, pages 260–265; March 1999.

Neurogenesis in the Adult Is Involved in the Formation of Trace Memories. Tracey J. Shors, George Miesegaes, Anna Beylin, Mingrui Zhao, Tracy Rydel and Elizabeth Gould in *Nature,* Vol. 410, pages 372–376; March 15, 2001.

Neurogenesis, Learning and Associative Strength. Jaylyn Waddell and Tracey J. Shors in *European Journal of Neuroscience,* Vol. 27, No. 11, pages 3020–3028; June 2008.

PHOTOALTO *Getty Images*; PHOTOILLUSTRATION BY JEN CHRISTIANSEN (*book title*)

THE POWER OF RENEWA

BLES

The need to tackle global climate change and energy security makes developing alternatives to fossil fuels crucial.

HERE IS HOW THEY STACK UP

BY MATTHEW L. WALD

Illustrations by Don Foley

Renewable energy, such as from photovoltaic electricity and ethanol, today supplies less than 7 percent of U.S. consumption. If we leave aside hydroelectric power, it is under 4.5 percent. Globally, renewables provide only about 3.5 percent of electricity and even less of transportation fuels.

But increasing that fraction for the U.S.—as seems necessary for managing greenhouse gases, trade deficits and dependence on foreign suppliers—has at least three tricky components. The obvious one is how to capture the energy of wind, sun and crops economically. After that, the energy has to be moved from where it is easily gathered, such as the sunny American Southwest or the windy High Plains, to the places it can be used. And the third is to convert it into convenient forms. Most prominently in the last category, electricity for transportation has to be loaded into cars and trucks, either through batteries or perhaps as hydrogen.

In some ways, the field is galloping ahead. A recent study sponsored by the United Nations found that global investment in renewable energy in 2007 was $148.4 billion, up 60 percent from 2006. But new wind turbines and solar cells are joining an infrastructure with coal-fired power plants that seem to run more hours every year and that are multiplying as well.

And although solar energy and especially wind have declined steeply in price over the past few years, they are competitive only when given subsidies or mandates. U.S. residential customers pay an average of 11 cents per kilowatt-hour (kWh) for power from a mix of coal, natural gas, nuclear and hydroelectric sources, but renewables are far pricier. Of course, all forms of energy get a carrot-and-stick treatment from governments, whether to provide work for coal miners or to prove that splitting the atom is useful for something besides bombs. But in many places, renewables get something even better: quotas. And rising prices for traditional fuels could help, raising the market to reach the renewables' costs.

A carbon charge would also help; each $10 tax on a ton of carbon dioxide emitted would raise the price of a kilowatt-hour from a coal-fired power plant by about a penny. But the scale of the transformation is immense; in energy content, coal production is about 70 times larger than wind-energy production. The numbers for oil and natural gas are similarly daunting.

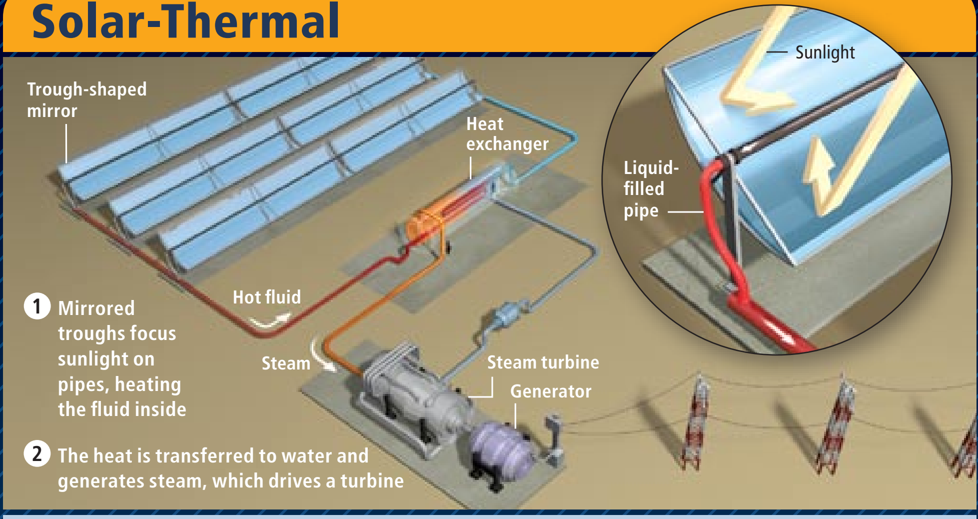
On the following pages is an overview of the elements of an energy system with a large contribution from renewables and the ways they might fit together.

JUSTIN SULLIVAN *Getty Images* (*electric car*); LESTER LEFKOWITZ (*solar panels*); SCOTT OLSON *Getty Images* (*ethanol sign*); ARCTIC-IMAGES/CORBIS (*geothermal plant*); GEORGE FREY *Getty Images* (*wind turbine*)

Generating Electric Power

No technology provides a one-size-

Solar-Thermal

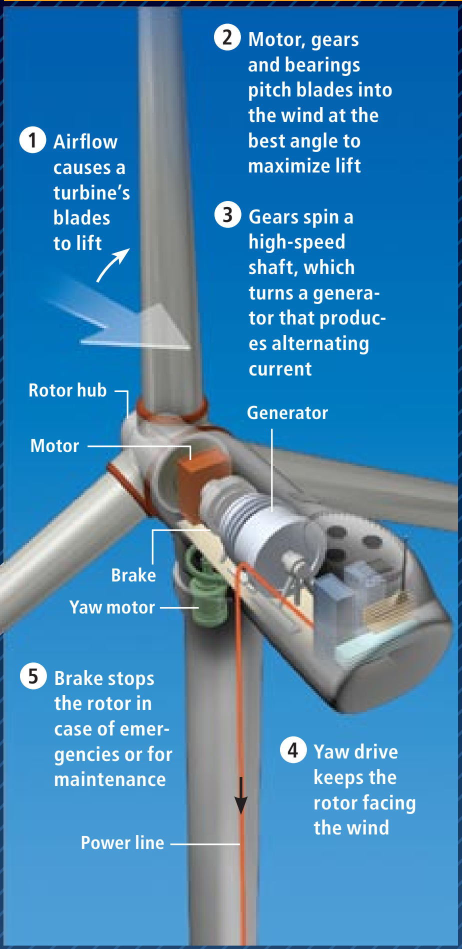


In solar-thermal, a trough-shaped mirror that tracks the sun over the course of the day focuses light to heat an oil- or water-based fluid in a black pipe. The pipe snakes over miles to a heat exchanger, which makes steam to drive a turbine. The system can be built as an adjunct to a natural gas–fired plant, so that gas can make steam during cloudy periods or after sunset. Future models may substitute molten sodium as the working fluid, which would allow higher temperatures without requiring higher pressures.

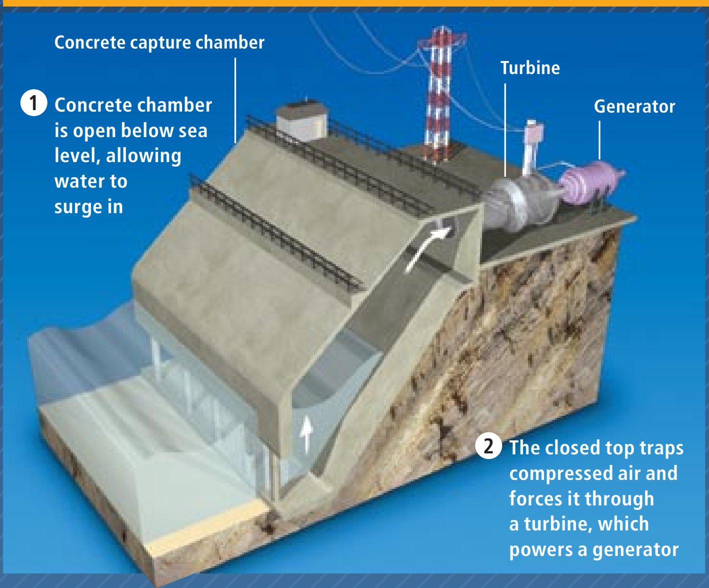
A variant is a "power tower," which looks a bit like a water tower but is filled with molten sodium and heated by a vast array of mirrors, some at a distance of a kilometer. The sodium can be connected to an insulated tank and can store enough heat to run around the clock or at least well into high-demand times.

STATUS	Trough systems are commercial; power towers have been demonstrated
PRICE	19.9–28.1 cents/kWh (for trough)
ADVANTAGES	May be the most amenable to storage of renewables
DRAWBACKS	Needs flat land; best resources may be distant from existing transmission; disturbs pristine desert environments; may require cooling water, which is hard to find in deserts, the sunniest areas

Wind



Ocean Wave Power



Hydroelectric has been developed as far as it can go, given environmental concerns about dams. But the Pacific Northwest coast could produce 40 to 70 kilowatts per meter, according to the Department of Energy. Harnessing ocean power is a long way behind wind, solar and geothermal, however. Inventors have been filing for wave-energy patents for two centuries.

One technique is to build a steel or concrete column, open to the ocean below the water line but closed at the top. The rise and fall with each wave alternately pressurizes and depressurizes the air at the top, which can drive a turbine; Wavegen in Scotland, partly owned by Siemens, the giant electrical company, recently opened a 100-kilowatt generator based on this system. Another design harnesses the energy of a rising and falling float.

STATUS	Demonstrated but not ready for prime time
PRICE	Too early to estimate
ADVANTAGES	Transmission lines are usually short
DRAWBACKS	Building durable structures in areas of strong surf is expensive

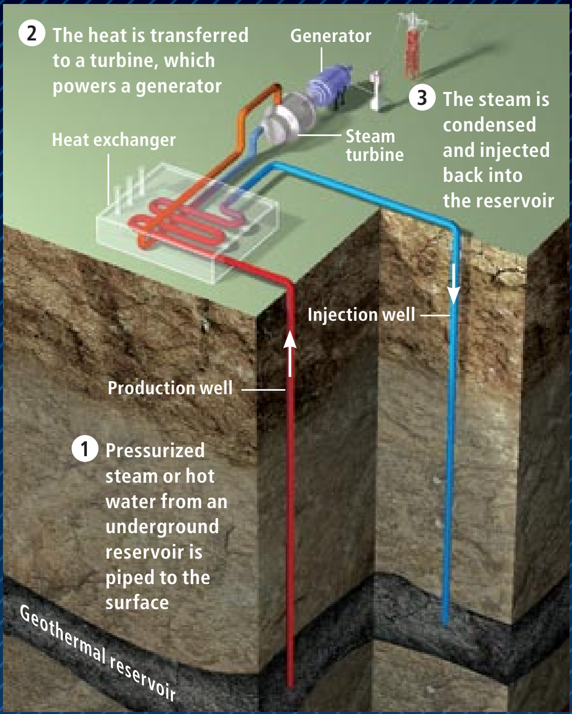
fits-all solution, but a combination can create a robust energy supply.

Wind is the most promising, most advanced—and perhaps most problematic of the renewable energy sources. In 2007 developers installed more than 5,000 megawatts in the U.S., raising the installed base by 46 percent. But the kilowatt-hour contribution was much smaller, because even on a good site wind produces only about 28 percent of the energy that would result from around-the-clock production. Worse, wind works best at night, when demand is low.

Technology is trimming costs, partly by making wind machines bigger. The latest are six megawatts, which would run several shopping centers. On a machine that big, each blade is about 65 meters, the approximate wingspan of a Boeing 747. New models are highly efficient, capturing about half the energy in the air that passes through them.

STATUS	Commercial; growing rapidly
PRICE	6.1–8.4 cents/kWh (but transmission can push those amounts higher)
ADVANTAGES	Offers greatest energy-producing potential; no need for cooling water
DRAWBACKS	Production correlates poorly with load; some object to the appearance and sound of the machines and transmission towers; threat to some birds and bats; may interfere with aerial surveillance radars; best sites are not near population centers

Geothermal

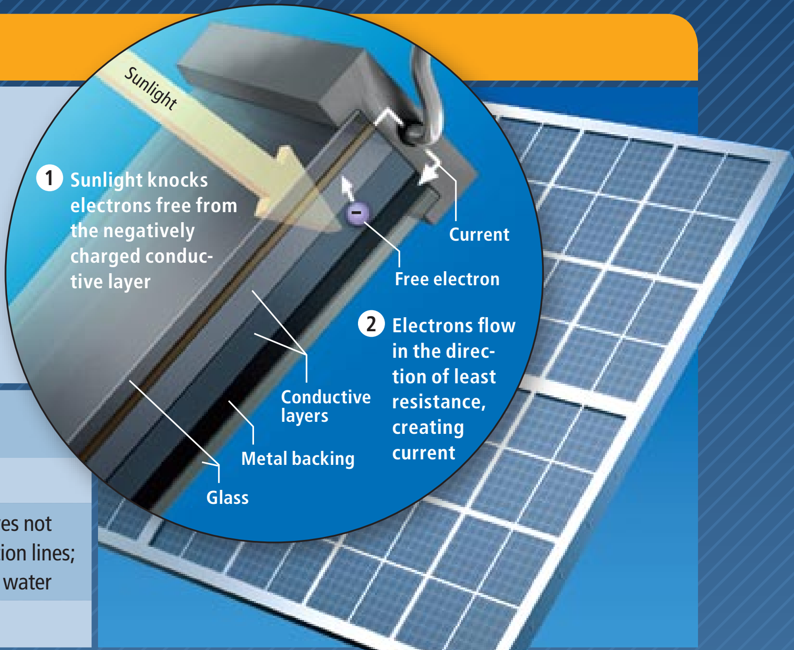


Unlike wind or solar, geothermal works on demand. "The heat in the earth is there; you can bank on it," says Steven Chu, director of Lawrence Berkeley National Laboratory and President Barack Obama's nominee for energy secretary. The plants generally run around the clock. Not every location has hot rock, but Hawaii generates a quarter of its energy that way and California, 6 percent. Geothermal installations use hot water that flows up by itself, but vast areas of the U.S. have "hot dry rock," proponents say, requiring only water injection through a deep well. Most systems use a heat exchanger to boil clean water for steam to spin a turbine.

STATUS	Commercial but small
PRICE	6.2–7.6 cents/kWh
ADVANTAGES	Supply is reliable enough to be used for base-load power
DRAWBACKS	The steam from underground water can have nasty components, which will rot heat exchangers and, if released, pollute the air; location is at the whim of nature and often not convenient to existing power lines

Solar-Photovoltaic

Two layers of semiconductor materials, one with extra electrons and the other with extra "holes," are sandwiched together in photovoltaic panels. When the material absorbs sunlight, excess electrons move from one layer to the other, creating an electric current. The effect was first observed 169 years ago, but scientists and engineers are still working to optimize it. The first practical use was in the space program, and cells are widely used off the grid but are not now competitive with fossil fuel or even other renewables on the grid. Photovoltaics can be incorporated into new construction, as roofing tiles or building facade materials, at lower cost.



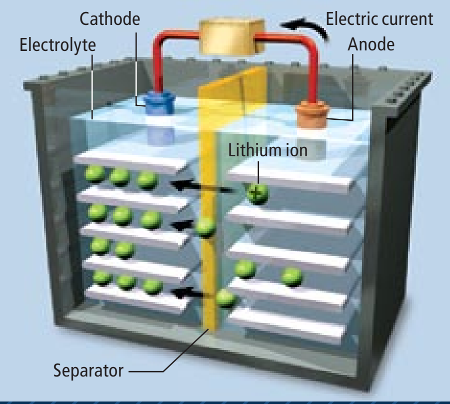
STATUS	Commercial but competitive in grid applications only when demanded by quota or heavily subsidized
PRICE	46.9–70.5 cents/kWh
ADVANTAGES	Can be deployed in electrically congested urban areas, where it saves not only the cost of generation but also the cost of laying new distribution lines; peak production matches peak load fairly well; no need for cooling water
DRAWBACKS	If you have to ask, you can't afford it; production is very small

Storing and Delivering Renewable Power

Intermittent sources of energy, such as wind and sun, require energy storage and delivery systems. Several candidates exist.

Automotive Batteries

Automakers want a lithium-ion battery that will endure 15 years and 5,000 charge cycles, far more than the familiar lithium ions in today's consumer devices. The goal is a price of $300 per usable kilowatt-hour of storage for a battery that would run a car for 40 miles, assuming a little more than three miles per kilowatt-hour. General Motors plans to market a plug-in hybrid in 2010; Ford's version is five years away. In this case, the voice in the car whining, "Are we there yet?" may not be the kid in the backseat; it may be the driver.

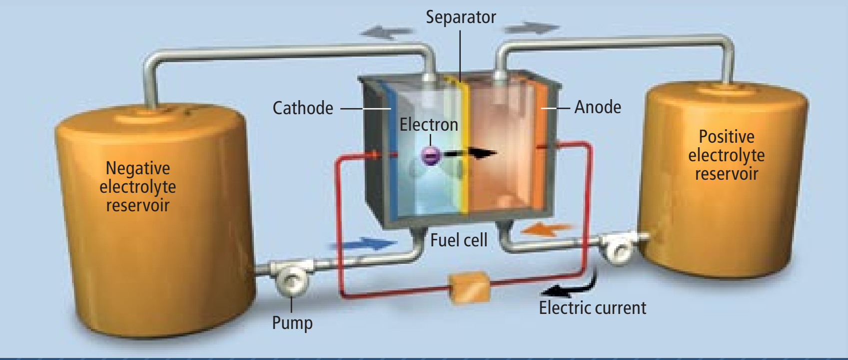


Fuel Cells

Electricity from any source, such as solar, wind and even coal, can be used to break up water molecules into their hydrogen and oxygen components in a device called an electrolyzer. The hydrogen can then be run through a fuel cell to make electricity. A downside of fuel cells, however, is that they have a capital cost in the thousands of dollars per kilowatt of capacity, and the round-trip efficiency through the electrolyzer to the fuel cell and then back into current is less than 50 percent—meaning that for every two kilowatt-hours put in the bank, only one comes back out again.

Stationary Batteries

A Vancouver-based company, VRB Power Systems, sells "flow batteries," with tanks to hold hundreds of gallons of electrolytes. Run in one direction, the system absorbs energy; in the other, it gives it back, in megawatt-hour quantities. It costs $500 to $600 to store a kilowatt-hour, and the round-trip efficiency is 65 to 75 percent—meaning the battery loses 25 to 35 percent of the electricity put into it. This system would raise the price of the solar kilowatt-hour by 50 percent or more.

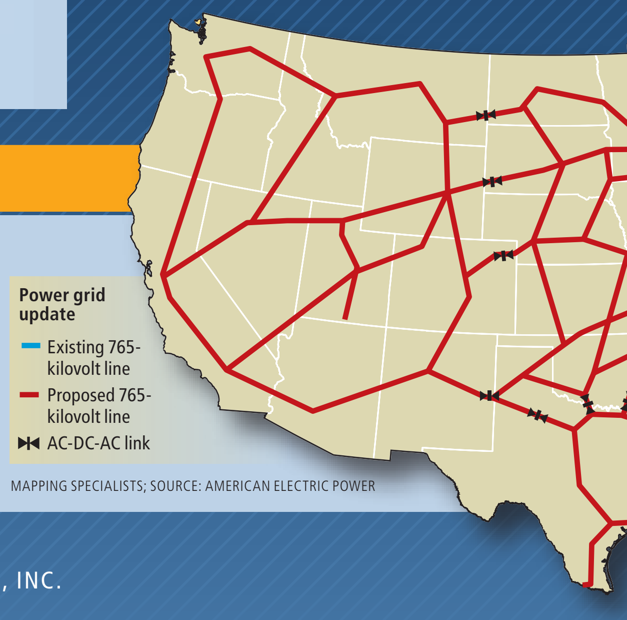


Compressed Air

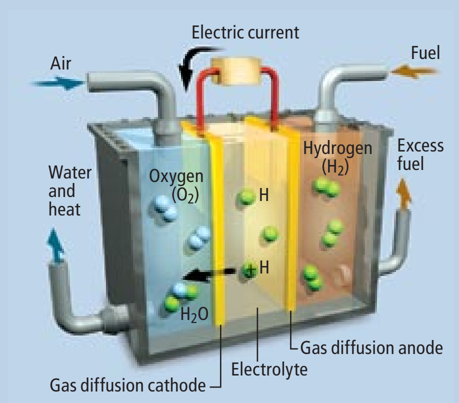
The Alabama Energy Cooperative opened a compressed-air energy storage plant in 1991, using coal plants that ordinarily would be idle at night, to pump air into a hollowed-out salt dome at a pressure of more than 1,000 pounds per square inch. When extra power is needed in daytime, compressed air is inserted into a combustion turbine fired by natural gas. Ordinarily the turbine compresses its own air, and the most efficient generator today requires 6,000 British thermal units (Btu) of natural gas to produce a kilowatt-hour. Compressed air storage, in contrast, cuts natural gas use by one third.

Electricity Transmission

Intermittent sources are less troublesome if they feed a bigger grid; a region with 100 scattered installations of wind and solar could count on some average level of input. But the existing grid cannot handle bulk power transfers over huge distances. A solution could be a new high-voltage "backbone," akin to an interstate highway system for the grid, according to the Department of Energy last year. It would comprise about 19,000 miles of transmission, with 130-foot towers, at $2.6 million a mile. Voltage would be pushed up to 765,000 volts to reduce line losses. No new technology is involved, but the system requires two things that the U.S. does not now have: a national commitment to integrating the electricity system on a continental scale and about $60 billion to pay for it.



MAPPING SPECIALISTS; SOURCE: AMERICAN ELECTRIC POWER



Ice Storage

Ice Energy, a company based in California, sells equipment that yields 500-gallon blocks of ice at night, in building basements. Making ice at night is easier than doing so during the day, because the temperature of the outdoor air, to which the compressor must release the heat, is generally lower than it is earlier in the day. The resulting ice is used to cool the building during the daytime. The effect is to use energy produced at night, such as from wind power, to do work when it is needed during the daytime.

Renewable Transportation Fuels

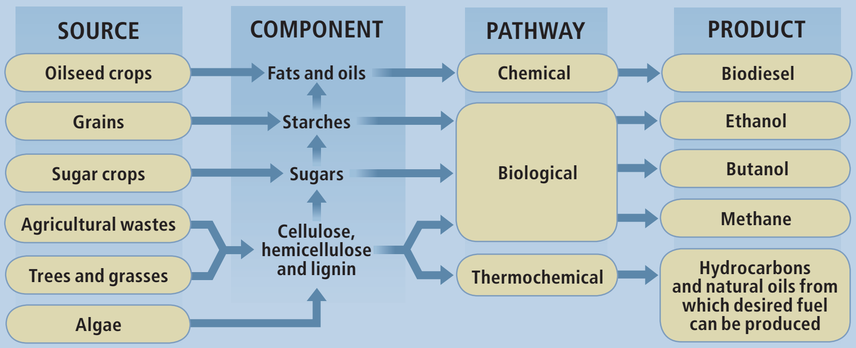
Three main pathways exist for making liquid transportation fuels from renewables. The first is simply to burn plant oils, most often soy or palm, in diesel engines. In the U.S., to be legal the oil must be converted to a chemical form called an ester. The process is simple, but the scale is limited, and the entire enterprise is caught up in the food-versus-fuel debate.

Equally simple is to let yeast digest sugars and produce alcohol, but that, likewise, is limited in scale and puts the corner filling station in competition with the supermarket for the output of the field.

Tremendous volumes of sugars, however, are tied up in nonfood crops and in the nonedible part of plants that are grown as food, such as wheat straw and corn stalks. This cellulosic material contains conventional six-carbon sugars as well as five-carbon sugars, which ordinary yeast does not like.

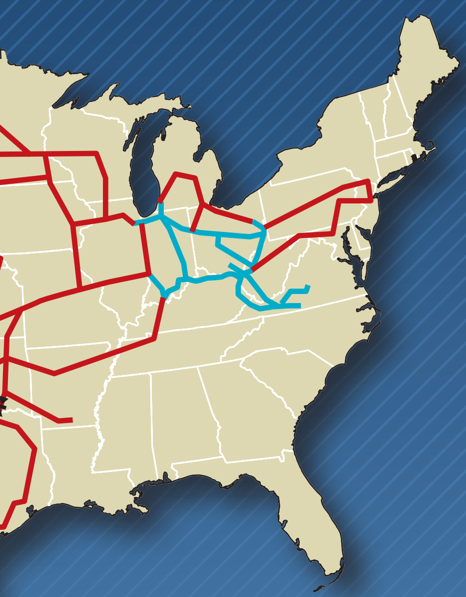
To unlock these sugars for the third pathway, some pilot-scale plants use steam or acids, or a combination. Another option is enzymes from gene-altered bacteria or fungi. To convert the sugars to liquid fuel, some use catalytic processes, and others turn to yeasts, often genetically altered as well. Some simply break down cellulosic material into a fuel gas of carbon monoxide and hydrogen, then re-form that into hydrocarbon molecules, such as ethanol, other alcohols or other liquids. Feedstocks include forest detritus, such as chips, bark and pinecones; paper and plastics from household garbage; and agricultural wastes.

Although all these methods have been shown to work on a lab or pilot scale, successful commercial operation remains elusive. Incentives and quotas are spurring many efforts, however.



SOURCE: "BIOFUELS FOR TRANSPORTATION," BY NAOMI PENA AND JOHN SHEEHAN, IN *CDM INVESTMENT NEWSLETTER,* NR. 3/2007

STATUS	Struggling toward commercial operation
PRICE	Not established; the target is uncertain because gasoline and diesel prices are so volatile
ADVANTAGES	Some biofuels are low- or zero-carbon; reduces reliance on overseas oil
DRAWBACKS	Some fuels put pressure on food prices; production of biofuels from corn requires copious amounts of fossil fuels, so total energy and carbon advantages are small; most biofuels are less energy-dense than gasoline, yielding fewer miles per gallon



Matthew L. Wald is a reporter at the *New York Times,* where he has covered energy topics since 1979. He has written about oil refining, electricity production, electric and hybrid automobiles, and air pollution. Wald is currently based in Washington, D.C., where he also tracks transportation safety and other subjects. This article is his fourth for *Scientific American.*

➡ MORE TO EXPLORE

Department of Energy scenario for meeting 20 percent of electric needs with wind by 2030: **www1.eere.energy.gov/windandhydro**

Hybrid power plant to be built in California that produces energy from solar power when it is available and natural gas when it is not: **www.inlandenergy.com**

Information on compressed-air energy storage: **www.solarfeeds.com/index.php?option=com_content&view=article&id=3256:compressed-air-energy-storage-further-along&catid=80:80&Itemid=173**

Renewable Fuels Association facts on cellulosic ethanol: **www.ethanolrfa.org/resource/cellulosic**

NEW TACTICS AGAINST TUBERCULOSIS

The pandemic is growing in many places, and strains resistant to all existing drugs are emerging. To fight back, biologists are applying a host of cutting-edge drug development strategies

By Clifton E. Barry III and Maija S. Cheung

KEY CONCEPTS

- Tuberculosis is second only to HIV as the worldwide cause of death from infection, and the pandemic is growing in many places.
- TB is caused by a bacterium. Most cases are treatable, but strains resistant to first- and second-line drugs are on the rise.
- Conventional approaches to developing new antibiotics and vaccines against the disease have mostly failed.
- New tools are enabling scientists to study the TB-causing bacterium in greater detail, offering unprecedented insight into the interactions between pathogen and host. The results are exposing promising new targets for drug therapy.

—The Editors

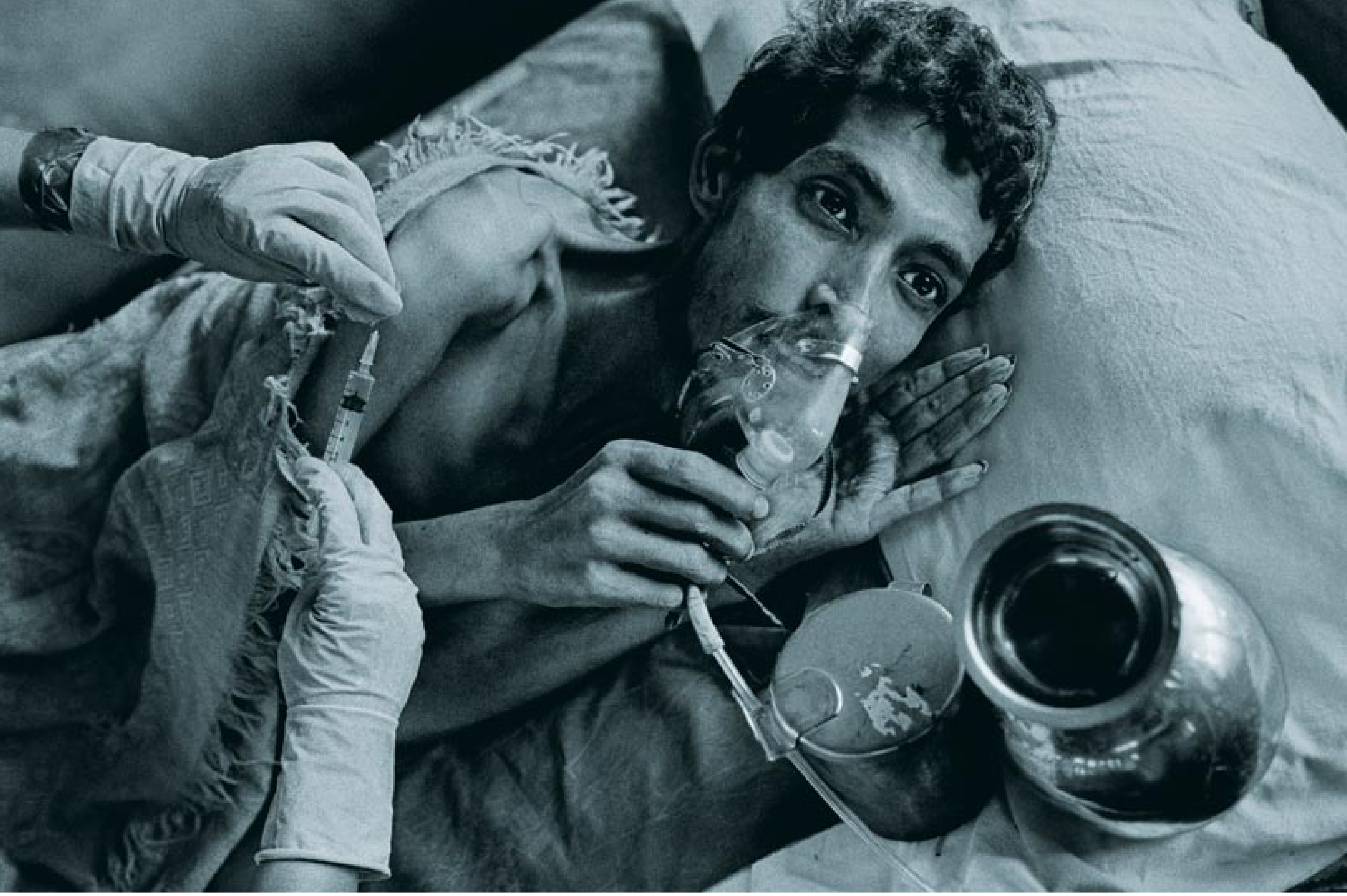
Bubonic plague, smallpox, polio, HIV—the timeline of history is punctuated with diseases that have shaped the social atmospheres of the eras, defined the scope of science and medicine, and stolen many great minds before their time. But there is one disease that seems to have stalked humanity far longer than any other: tuberculosis. Fossil evidence indicates that TB has haunted humans for more than half a million years. No one is exempt. It affects rich and poor, young and old, risk takers and the abstinent. Simply by coughing, spitting or even talking, an infected individual can spread the bacterium that causes the disease.

Today TB ranks second only to HIV among infectious killers worldwide, claiming nearly two million lives annually, even though existing drugs can actually cure most cases of the disease. The problem is that many people lack access to the medicines, and those who can obtain the drugs often fail to complete the lengthy treatment regimen.

Additionally, TB is evolving faster than our therapies are. In recent years, investigators have observed a worrying rise in the number of cases resistant to more than one of the first-line drugs used to treat the illness. Even more alarming, we have begun to see the emergence of strains that are resistant to every last one of the antibiotic defenses.

The disease is particularly devastating for the developing nations, where some 90 percent of cases and 98 percent of TB deaths occur. Beyond bringing untold suffering and sorrow there, TB harms entire economies. With 75 percent of cases arising in people between the ages of 15 and 54, TB will rob the world's poorest countries of an estimated $1 trillion to $3 trillion over the next 10 years. Furthermore, the disease forces these struggling nations to divert precious resources from other important areas into health care. But the developed world would be mistaken to consider itself safe: although the incidence there is comparatively low, that situation could change if a highly resistant strain were to gain traction.

As bleak as this state of affairs is, we have reason to be hopeful. Cutting-edge biomolecular technologies are enabling researchers to study the complex interactions between the TB bacterium and the body in unprecedented detail, generating insights that are informing the development of novel diagnostic tests and drug therapies.



MODERN PLAGUE: **Every year tuberculosis kills nearly two million people and infects some eight million more. Here a patient in Mumbai, India, is treated for a highly drug-resistant form of the disease.**

JAMES NACHTWEY VII

A Short-Lived Success

First identified by German physician Robert Koch in 1882, *Mycobacterium tuberculosis* (*Mtb*), the rod-shaped bacterium that causes tuberculosis, exists in both latent and active forms. In a latent infection, the immune system prevents the bacteria from multiplying, thus keeping them from disrupting tissues. Individuals with this form show no symptoms and are not contagious. Latent *Mtb* may persist for months, years or even decades without multiplying or making its host ill. Ninety percent of people infected with *Mtb* never develop active TB disease. But 10 percent of them do develop the active form, particularly those with weakened immune systems, such as young children and individuals who have HIV or are undergoing chemotherapy.

In people with active TB, the bacteria outpace the immune system, rapidly multiplying and spreading out to attack the organs. Primarily an aerobic bacterium, meaning it prefers environments rich in oxygen, *Mtb* has a special affinity for the lungs. Indeed, some 75 percent of patients with active TB exhibit the pulmonary variety of the disease. As the bacteria multiply, they destroy the lung tissue, commonly causing the host to develop such symptoms as a severe cough, chest pain and the coughing up of blood. But other organs are vulnerable, too. In fact, active TB can affect nearly every organ in the body. In children, TB can invade the cerebrospinal column, where it provokes a high fever with systemic shock—a condition known as meningitis. Left untreated, half of people with active TB die of it, most from lung destruction.

A century ago society had no way to combat TB, save for limiting its spread by sequestering affected individuals in sanatoriums. Back then TB, often called "consumption," was widespread even in places that today have a relatively low incidence of the scourge, such as North America and western Europe. Scientists began to gain on the disease in 1921, when a vaccine made by French immunologists Albert Calmette and Camille Guérin, both at the Pasteur Institute in Paris, first entered into public use. (Initially believed to protect against both adult and childhood forms of the disease, the BCG vaccine, as it is known, was later shown through an extensive series of tests to confer consistent protection against only severe childhood forms.)

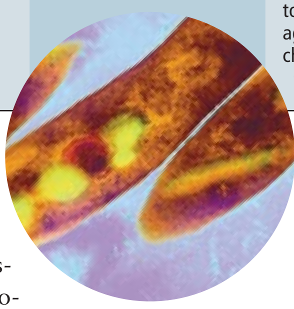
Twenty-two years later a team led by American microbiologist Selman Waksman developed

HUMAN VS. MICROBE

Tuberculosis has dogged humankind for millennia. Here are some key events in this long-standing battle between people and pathogen.

500,000 years ago
By that time, TB had begun infecting human ancestors.

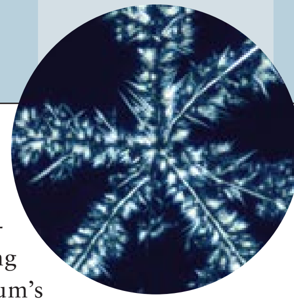
1882
Robert Koch identifies *Mycobacterium tuberculosis* (*Mtb*) as the cause of TB.



1908
Albert Calmette and Camille Guérin develop the BCG vaccine against TB, which is later shown to consistently protect against only severe childhood forms of the disease.

1921
BCG vaccine enters public use.

1943
A team led by Selman Waksman creates the first effective antibiotic against TB: streptomycin.



streptomycin, which despite causing some side effects was the first effective therapy for TB. Waksman's achievement opened the door for the creation in the 1950s of a rapid succession of antibiotics that compensated for streptomycin's weaknesses.

Together these developments brought the era of sanatoriums to a close and significantly lowered the incidence of TB in countries that had the money and infrastructure to tackle the problem. By the 1970s many experts believed that TB had been almost completely eradicated. In reality, however, with international travel on the rise, the largest epidemics were just beginning. To make matters worse, those who would be hit hardest were those who could least afford it: residents of the poorest nations, who would soon also be facing a new and costly killer—HIV.

Today more than half a century after the debut of the first anti-TB drugs, the World Health Organization estimates that fully a third of the world's population (more than two billion people) is infected with *Mtb*. On average, eight million of these carriers a year will develop active TB, and each will infect between 10 and 15 more individuals annually, maintaining the pandemic.

The picture becomes even more frightening when one considers the rising incidence of HIV. People who have latent TB and are HIV-positive are 30 to 50 times more likely than their HIV-negative counterparts to develop active TB, because HIV leaves their immune systems unable to keep TB in check. In fact, TB is the leading cause of death among HIV-positive individuals, claiming the lives of one out of every three worldwide and one out of every two in sub-Saharan Africa, where health care is especially hard to come by. Even if HIV-positive individuals have access to anti-TB drugs, their health will likely deteriorate because dangerous interactions between antiretroviral therapy and first-line TB drugs often force patients to suspend their antiretroviral therapy until the TB is under control.

FAMOUS VICTIMS

Tuberculosis has claimed the lives of many luminaries. Among them are:

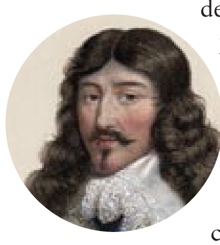
All three Brontë sisters

Anton Chekhov

Frederic Chopin

John Keats

Louis XIII of France



Molière

George Orwell

Cardinal Richelieu

Jean-Jacques Rousseau

Erwin Schrödinger

Henry David Thoreau

The Latest Challenge

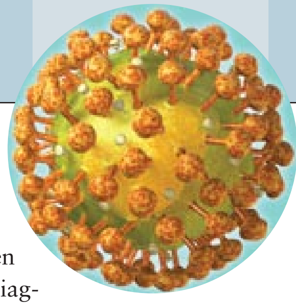
Perhaps the most disquieting aspect of the present pandemic, however, is the growing problem of the TB bacterium's resistance to antibiotics. To understand how this predicament came to be, consider how TB is treated. The current treatment course, which was developed in the 1960s, is a demanding regimen consisting of four first-line drugs created in the 1950s and 1960s: isoniazid, ethambutol, pyrazinamide and rifampin. Patients who follow the regimen as directed take an average of 130 doses of the drugs, ideally under direct observation by a health care worker. This combination is extremely effective against active, drug-susceptible TB as long as patients are compliant and complete the entire six- to nine-month course.

Drug-resistant strains develop when patients do not complete the full protocol, whether because they start feeling better or because their drug supply is interrupted for some reason. Inconsistent use of antibiotics gives the bacteria time to evolve into a drug-resistant form. Once a drug-resistant strain has developed in one person, that individual can spread the resistant version to others. (For this reason, some authorities argue that it is better to not undergo treatment than to undergo incomplete treatment.)

According to the World Health Organization, nearly 5 percent of the roughly eight million new TB cases that occur every year involve strains of *Mtb* that are resistant to the two most commonly used drugs in the current first-line regimen: isoniazid and rifampin. Most cases of this so-called multidrug-resistant TB (MDR-TB) are treatable, but they require therapy for up to two years with second-line anti-TB drugs that produce severe side effects. Moreover, MDR-TB treatment can cost up to

SCIENCE SOURCE *Photo Researchers, Inc.* (*tuberculosis bacteria*); DAVID PARKER *Photo Researchers, Inc.* (*streptomycin*); ROGER HARRIS *Photo Researchers, Inc.* (*HIV*); MICHAEL NICHOLSON *Corbis* (*Louis XIII*); THE GALLERY COLLECTION *Corbis* (*Chopin*); THE GRANGER COLLECTION (*Orwell*)

1960s	1970s	1981	1998	2005	2006
Current TB treatment course, which employs four different drugs over a six- to nine-month period, is developed.	TB is widely believed to have been nearly eradicated.	Scientists identify HIV, which leaves people additionally vulnerable to TB.	TB genome is sequenced.	Improved diagnostic test receives U.S. Food and Drug Administration approval.	Outbreak of extensively drug-resistant TB in KwaZulu-Natal, South Africa.



1,400 times more than regular treatment. Given that most MDR-TB occurs in impoverished countries, this expensive treatment is often not an option. Failure to properly diagnose MDR-TB, along with the high cost of treatment, means that only an estimated 2 percent of MDR-TB cases worldwide are being treated appropriately.

Worst of all, over the past few years health surveys have revealed an even more ominous threat, that of extensively drug-resistant TB (XDR-TB). This type, which made headlines in 2006 following an outbreak in KwaZulu-Natal, South Africa, is resistant to virtually all the highly effective drugs used in second-line therapy. Although XDR-TB is less common than MDR-TB, the possibility that XDR-TB will evolve and spread looms wherever second-line TB drugs are in use. World Health Organization records indicate that 49 countries had confirmed cases as of June 2008. That is a minimum figure, though, because very few countries have laboratories equipped to diagnose XDR-TB.

A Trickling Drug Pipeline

To say that scientists erred in assuming that the first-line drugs from the 1950s would be sufficient to combat TB is a profound understatement. But with the overwhelming majority of TB patients concentrated in some of the world's poorest countries, large pharmaceutical companies have had little incentive since then to invest heavily in research and development for new drugs. And the prevailing wisdom among the greater pharmaceutical conglomerates is still that the cost of drug development—$115 million to $240 million and seven to 10 years per drug—far outweighs the potential global market for such products.

Thanks to government programs and private philanthropic organizations such as the Bill and Melinda Gates Foundation, however, many efforts are under way to create TB antibiotics to both treat drug-resistant cases and reduce the time that it takes to treat normal TB cases.

As a result, a few promising agents are currently in early clinical trials. One such agent, known as SQ109, inhibits cell wall synthesis. It recently completed phase I (safety) clinical trials. Another drug candidate is PA-824, a compound whose ability to attack *Mtb* in both its actively dividing stage and its slow-growing one has generated hopes that the drug could significantly reduce the time needed to treat the disease. PA-824 is in phase II clinical trials, which look at efficacy.

Unfortunately, the odds are against these candidates: historically, fewer than 10 percent of antibiotics that enter early clinical trials garner approval—a success rate that derives in large part from the outmoded logic used to discover these drugs. Fifteen years ago developing new antibiotics was mostly a matter of following a simple formula: identify enzymes that are essential to bacteria survival and that do not have any counterparts in humans; screen libraries of compounds for potent inhibitors of these enzymes; chemically synthesize derivatives of those inhibitors; then optimize the compounds for druglike properties, such as the ability to get from the stomach to the bloodstream. Yet even the large pharmaceutical companies, masters of developing medicines to treat nearly any disease, have been spectacularly unsuccessful in producing new antibiotics using this approach.

For its part, the TB battleground is littered with the corpses of drug candidates that failed. Many of these compounds were highly specific and potent inhibitors of key TB enzymes. In some cases, although they effectively foiled isolated enzymes, they flopped when tested on whole bacterial cells. In others, the compounds thwarted whole bacteria in test tubes (in vitro) but missed their mark when tested in infected animals. TB offers perhaps the most extreme example of the troubling disconnect between the in vitro and in vivo effects of antibiotics. Most of the time investigators have absolutely no idea why drug candidates fail. The crux of

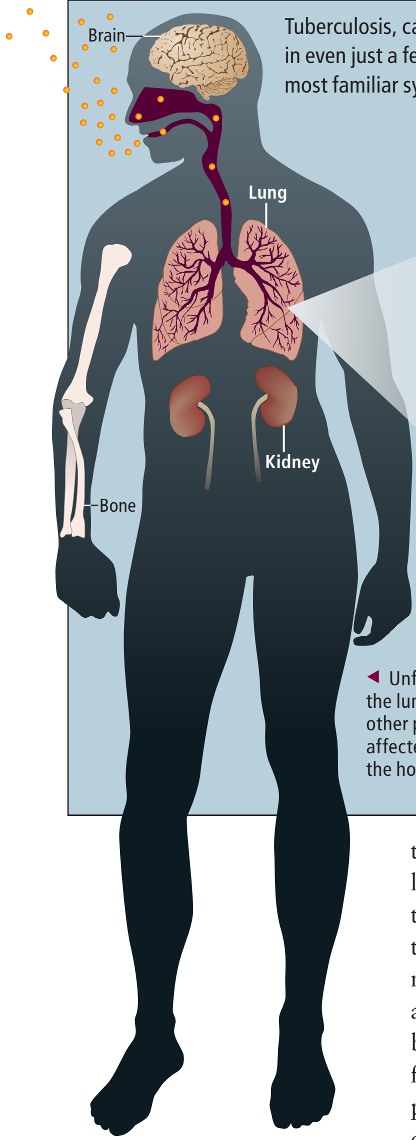
SOBERING FACTS

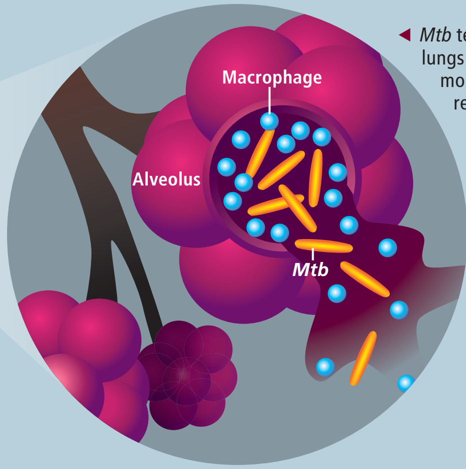
- A third of the world's population is infected with the TB bacterium; **one in 10** of them will become sick with active TB in their lifetime.
- On average, nearly **four in 10** TB cases are not being correctly detected and treated.
- TB is responsible for a death **every 20 seconds**.
- An estimated **490,000** new cases of TB resistant to first-line drugs and 40,000 cases of TB resistant to second-line drugs occur every year.

[INFECTION BASICS]

AN ILL WIND

Tuberculosis, caused by the bacterium *Mtb*, occurs in both latent and active forms. People can become infected by breathing in even just a few *Mtb* bacteria released into the air when those with active TB cough, spit or talk. *Mtb* causes coughing, the most familiar symptom, because it accumulates abundantly in the lungs, but it can harm other organs as well (*diagram*).

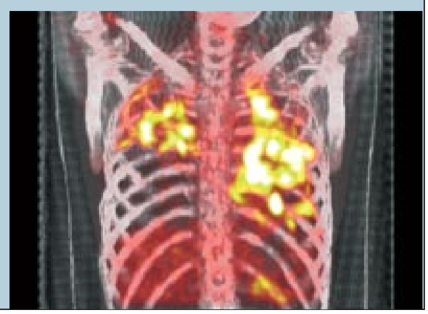




◀ *Mtb* tends to concentrate in the air sacs, or alveoli, of the lungs because it prefers environments rich in oxygen. In most people, the immune system is able to keep bacterial replication in check, dispatching defensive cells known as macrophages to the site of infection, where they form a shell around the bacteria. But in 10 percent of infected individuals, *Mtb* breaks down the shell, after which it can begin to multiply.

◀ Unfettered by the immune system, the bacteria destroy the tissue of the lungs; some may also make their way into the bloodstream and infect other parts of the body, including the brain, kidneys and bone. Eventually affected organs may sustain so much damage they cease to function, and the host dies.

▼ Scan highlights *Mtb* infection in lung.



COURTESY OF CLIFTON E. BARRY III (*PET-CT lung scan*); MELISSA THOMAS (*illustrations*)

the problem is that bacteria are autonomous life-forms, selected throughout evolution for their ability to adapt and respond to external threats. Like modern aircraft, they have all manner of redundancies, bypasses, fail-safes and emergency backup systems. As Jeff Goldblum's character in *Jurassic Park* puts it, life finds a way. Until we truly appreciate the complexities of how TB interacts with humans, new drugs against it will remain elusive. The good news is that we are making progress on that front.

Insights from "Omics"

A key turning point in our TB education came in 1998 with the sequencing of the DNA code "letters" in the *Mtb* genome—a project in which one of us (Barry) participated. That sequence, and those of related organisms, has yielded a trove of insights. Perhaps most importantly, the results showed that of all the enzymes and chemical reactions that are required for TB to survive in a human, we were considering only a third of them in our in vitro (test tube) tests. We learned, for instance, that *Mtb* devotes a huge amount of its genome to coding for proteins that synthesize and degrade lipids, suggesting that some of those proteins might be worth considering as drug targets. Analysis of the TB genome also hinted that, contrary to conventional wisdom, the bacterium is perfectly capable of living in the absence of air—a suggestion now verified. Under such anaerobic conditions, *Mtb*'s metabolism slows down, making it intrinsically less sensitive to existing antibiotics. Targeting the metabolic elements that remain active under these circumstances is one of the most promising strategies for shortening treatment time.

Translating the information we have gleaned from the genome into discoveries that can help save the lives of people who contract TB has neither been simple nor straightforward. But recently researchers have used those data to make significant advances in diagnostic tests for the disease. Diagnosis can be complicated by the effects of the childhood vaccine, which is given to more than half of all infants born around the world. The vaccine contains a strain of *Mtb* that has lost its virulence yet is still able to induce a child's immune system to react against the TB bacterium. Vexingly, though, the predominant test for TB cannot distinguish between immune responses elicited by virulent *Mtb* and the vaccine form. Hence, the test results for someone who is infected look exactly like the results for someone who has been vaccinated.

While the *Mtb* genome was undergoing sequencing, scientists in Seattle discovered that a large stretch of DNA was missing from the bacterial strain used in the vaccine. Shortly thereafter, independent research teams at the Pasteur Institute, the Albert Einstein College of Medicine and the University of Washington showed that the missing genes were essential to virulence. The deleted region in the vaccine strain thus offered investigators a strategy for improving the specificity of the test. A test that searched only for an immune response directed against the virulence factors absent from the vaccine strain, the researchers reasoned, should be able to distinguish infected individuals from those who had been vaccinated. In fact, just such a test was developed and approved by the U.S. Food and Drug Administration in 2005, and many recent studies have confirmed its accuracy. Unfortunately, so far the cost of the test is high, which restricts its use to the First World.

The *Mtb* genome is not the only new source of data able to provide insight into the TB bacterium's potential vulnerabilities. Scientists can now study all kinds of cell components and processes—from all the proteins in a cell (a discipline known as proteomics) to the amount of messenger RNA (the templates from which proteins are made) made from every gene ("transcriptomics") to the intermediate and final products of cell metabolism ("metabolomics"). These fields are still in their infancy, but already they have borne fruit. Last November, Barry coauthored a paper in *Science* reporting that when TB was treated with PA-824, the bacterial transcriptome reacted exactly as if it had just been poisoned with potassium cyanide. This finding was a vital clue that in metabolizing the drug, *Mtb* releases nitric oxide, a defensive molecule normally made by immune cells in the human body. Armed with this knowledge, we and others are now synthesizing compounds that stimulate the release of larger amounts of nitric oxide than are elicited by PA-824 and so should be even more potent against *Mtb*.

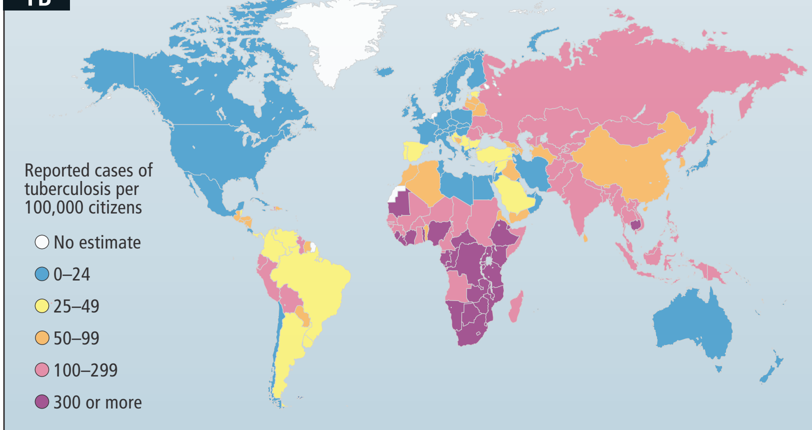
Complementing those approaches, structural genomics seeks to uncover the three-dimensional structure of every protein in *Mtb*—work that can both help identify the still-mysterious functions of many *Mtb* proteins and aid the design and synthesis of drugs targeting particular sites on critical proteins. So promising is this line of inquiry that a global consortium with members

[AFFECTED NATIONS]

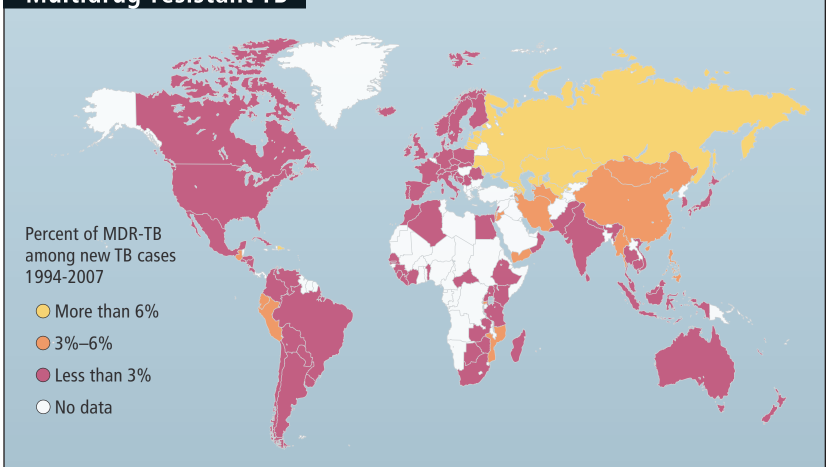
WORLDWIDE RESISTANCE

Tuberculosis occurs in virtually every country in the world, although it is most widespread in developing nations. The incidence of TB caused by strains of *Mtb* resistant to two or more of the first-line drugs for the disease—so-called multidrug-resistant TB (MDR-TB)—has been rising as a result of improper use of antibiotics. Worse still is extensively drug-resistant TB (XDR-TB)—a largely untreatable form identified in 2006; as of June 2008, 49 countries had confirmed cases. Sadly, that figure most likely underestimates XDR-TB's prevalence.

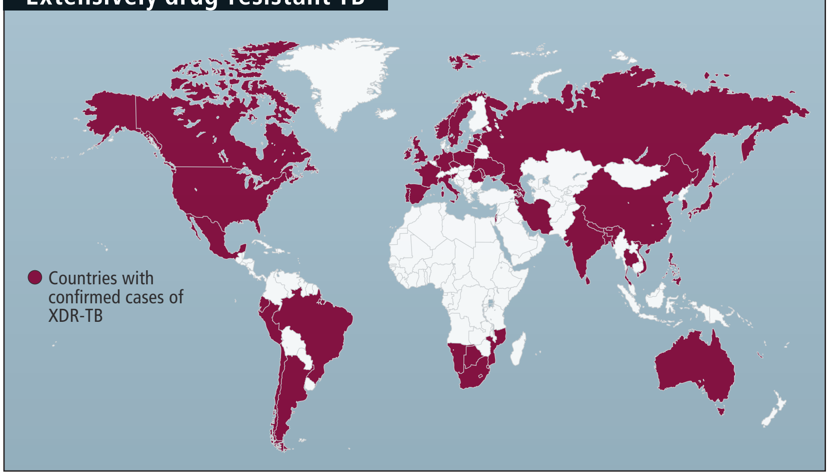
TB



Multidrug-resistant TB



Extensively drug-resistant TB



MELISSA THOMAS (*illustrations*); SOURCES: CLIFTON E. BARRY III AND WORLD HEALTH ORGANIZATION

[A WAY FORWARD]

PROMISING TREATMENT STRATEGIES

The first-line drugs currently used to treat tuberculosis were developed in the 1950s and 1960s. The six- to nine-month regimen is demanding, and failure to comply with it completely has led to the emergence of resistant forms of TB. Developing agents that are easier to administer and cheaper and that hit the *Mtb* bacterium in new ways is critical.

TODAY:
Traditional trial-and-error approaches to identifying drugs against TB have produced some new candidates now in clinical trials.

DRUG/DRUG CLASS	HOW IT WORKS AGAINST TB	STAGE OF DEVELOPMENT
Fluoroquinolones (already approved for treating other conditions)	Inhibits DNA replication	Phase III trials (largest tests of efficacy)
Nitroimidazoles (PA-824/OPC67683)	Inhibits cell wall synthesis and cell respiration	Phase II (efficacy)
Diarylquinoline (TMC207)	Inhibits synthesis of the energy storage molecule ATP	Phase II
Oxazolidinones	Inhibits protein synthesis	Phase II
SQ109	Inhibits cell wall synthesis	Phase I (safety)

from 17 countries is focusing its efforts entirely on the structural genomics of *Mtb*. Thus far the consortium has helped determine the structure of about 10 percent of the organism's proteins.

Another "omics" branch worth noting is chemical genomics, a very recently established field of research that effectively reverses the standard process of drug discovery. Instead of starting with a protein of known function and looking for a compound that inhibits its activity, investigators begin with a compound known to have a desirable trait—such as an ability to inhibit *Mtb* reproduction in cell cultures—and work backward to identify the microbial enzyme impaired by the substance. The compounds can be anything from molecules synthesized in a chemistry lab to products isolated from plants, microbes and even animals. The starting chemical in this case serves strictly to reveal vulnerable enzymes or biological processes, which scientists may then identify as targets for drug development.

What makes this approach so appealing is that it allows us to harness the power of natural selection in our quest to thwart *Mtb*. Before *Mtb* and other mycobacteria found humans to be such appealing hosts, they occupied environmental niches where they had to compete with countless other bacteria for food in a constant arms race. Bacterial ecosystems have therefore undergone multiple rounds of natural selection, and in most cases other bacteria have evolved ways of keeping the mycobacteria in check, as is evident from the diversity of bacteria types in these ecosystems. If researchers could tap into the amazing reservoir of weapons that these competitor bacteria have evolved—applying modern omics tools to identify the defensive molecules, screen them for their anti-TB potential and pinpoint their molecular targets in *Mtb*—we could well uncover entirely new classes of drugs. We could then select those agents that knock out the pathogen's whole system, as opposed to just a single process for which *Mtb* likely has a workaround.

A Model Bacterium

To reap the full benefits of the omics revolution, we need information technology tools capable of making sense of the vast data sets generated by omics experiments. In fact, the development of such tools has become a discipline unto itself, called bioinformatics. And only with these tools can researchers hope to clear another obstacle to drug development: that posed by so-called emergent properties—behaviors of biological systems that cannot be predicted from the basic biochemical properties of their components.

To borrow an example from neuroscience, consciousness is believed to be an emergent property of brain biochemistry. In the case of in vitro *Mtb*, one emergent property is a tendency of the bacteria to form "cords"—serpentine arrays

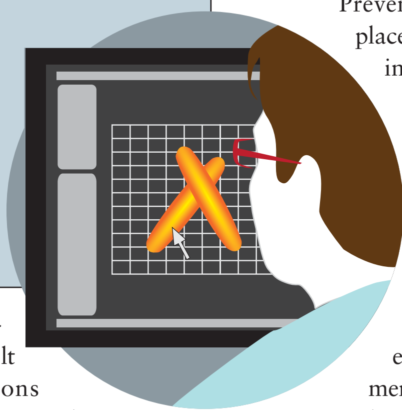
[THE AUTHORS]


Clifton E. Barry III is chief of the tuberculosis research section at the National Institutes of Health in the Institute of Allergy and Infectious Diseases (NIAID), which he joined in 1991. Barry's research group studies all aspects of tuberculosis drug discovery and genomics and runs a clinical trials program involving patients with highly drug-resistant TB in South Korea. **Maija S. Cheung** is a fellow at NIAID. A graduate of Middlebury College, Cheung plans to go to medical school to study global public health and infectious disease.

COURTESY OF SEOKYONG LEE (*Barry*); COURTESY OF MAIJA S. CHEUNG (*Cheung*)

FUTURE:
More recently, scientists have begun trying to understand *Mtb* in far greater detail by studying its genome and other cell components—work that is yielding fresh insights into how the bacterium establishes infection in humans and what its vulnerabilities are. Researchers should be able to inhibit synthesis of ATP much more effectively than drugs now in development can. Likewise, they can probably find compounds that stimulate the bacterium to release even more nitric oxide, which shuts down the cell's ability to breathe, than existing agents do. Blocking synthesis of niacin, the cell's main energy transporter, is another tactic with considerable potential.

FAR FUTURE:
Ultimately, investigators want to create an in silico model of *Mtb*—a computer model that behaves exactly like its real counterpart does in a human. Such a model would enable researchers to predict the organism's responses to various compounds with far greater precision than is currently feasible.



MELISSA THOMAS *(illustration)*

that have a ropelike appearance; these cords result from complex interactions among molecules on the bacterial surface, and their development is not predictable from the properties of the molecules involved. Correspondingly, in a human host, the interactions among such surface molecules and the cells of the immune system result in the formation of a granuloma—a large aggregate of host cells and bacteria that is very difficult for drugs to penetrate. The granuloma, too, is an emergent property of the interaction between *Mtb* and its host.

With the aid of bioinformatics, we hope to ascertain how all 4,000 of *Mtb*'s genes, their corresponding proteins and the bacterium's metabolic by-products react when *Mtb* is treated with a new drug in vitro. Moreover, in the past 10 years we have begun piecing together exactly how the bacterium operates inside of TB patients, as opposed to in vitro. The ultimate goal is to replicate *Mtb* in silico—that is, produce a computer simulation of the bacterium that behaves just like the real thing does in the body. The significance of such an achievement cannot be overstated, because it will enable investigators to accurately predict which bacterial components make the best drug targets and which drug candidates will likely hit those targets most effectively.

To achieve this objective, scientists will need to trace in exquisite detail all of the organism's biochemical pathways (series of reactions) and identify more of the emergent properties that arise from the operation of these pathways. The task is enormous: we still do not know what perhaps a third of *Mtb*'s proteins do in the first place, never mind what their associated pathways are or what emergent properties they spawn. But based on the current rate of progress, we are confident that within the next 20 years we will see a complete in silico bacterium that acts exactly like its counterpart growing in a test tube in the lab—and maybe even in a human being.

Preventing TB infection in the first place is, of course, better than treating people after they have become sick. To that end, efforts to create a vaccine that confers better protection against the disease than does the BCG vaccine are under way. Some developers are trying to improve the existing vaccine; others are attempting to make entirely new ones. But for the moment, the work is mostly doomed to trial and error because we do not understand why the current vaccine does not work nor how to predict what will work without testing candidates in humans.

In other diseases for which vaccines are available, surviving an initial infection provides immunity to future infection. In TB, however, initial infection does not offer any such protection. A vaccine that is based simply on an attenuated version of TB therefore will not work. And whereas drug development would be greatly accelerated by the development of an in silico bacterium alone, enhanced vaccine development would require both an in silico bacterium and an in silico human to be successful. Such an arrangement would allow us to systematically explore the effects on humans of altering the bacterium.

In his book *The Tipping Point,* Malcolm Gladwell defines said point as "the level at which the momentum for change becomes unstoppable." Never has the need for better diagnostic tests, drug therapies and vaccines against TB been greater. Much work remains to be done, but with the genomes of both *Homo sapiens* and *Mycobacterium tuberculosis* decoded and with an unprecedented amount of brainpower now trained on the problem, the momentum for change truly is unstoppable. ■

IN THE TRENCHES

New drugs will be critical for combating TB, but public health officials cannot afford to wait until they are available. In the meantime, programs such as the World Health Organization's Stop TB Partnership are working to stem the pandemic by improving quality control at testing facilities, enhancing patient supervision and support, assuring drug supply and educating the public about care, among other tactics. The program aims to reduce the number of deaths from TB by more than half by 2015.

➥ MORE TO EXPLORE

The Forgotten Plague: How the Battle against Tuberculosis Was Won—and Lost. Frank Ryan. Little, Brown, 1993.

The Magic Mountain. Thomas Mann. Translated by John E. Woods. Alfred A. Knopf, 1995.

Building a Better Tuberculosis Vaccine. Douglas B. Young in *Nature Medicine,* Vol. 9, No. 5, pages 503–504; 2003.

Multidrug Resistant Tuberculosis in Russia. Merrill Goozner in ScientificAmerican.com; August 28, 2008. Available at **www.SciAm.com/report.cfm?id=tuberculosis-in-russia**

PA-824 Kills Nonreplicating *Mycobacterium tuberculosis* by Intracellular NO Release. Ramandeep Singh et al. in *Science,* Vol. 322, pages 1392–1395; November 28, 2008.

Tuberculosis information from the World Health Organization is available at **www.who.int/tb/en**

MONITORING FOR NUCLEAR EXPLOSIONS

Detecting a test of a nuclear weapon has become so effective and reliable that no nation could expect to get away with secretly exploding a device having military significance

By Paul G. Richards and Won-Young Kim

KEY CONCEPTS

- Seismic monitoring can now detect a nuclear explosion with a yield of a kiloton or more anywhere on Earth. In many places, detection is far more sensitive than that.
- President Barack Obama is likely to ask the U.S. Senate to reconsider its 1999 vote against the Comprehensive Nuclear-Test-Ban Treaty (CTBT).
- Treaty opponents have argued that some signatories would cheat by testing explosive nuclear weapons in secret, putting noncheaters at risk.
- The objection that secret tests could go undetected is no longer seriously credible.

—The Editors

As president, I will reach out to the Senate to secure the ratification of the CTBT [Comprehensive Nuclear-Test-Ban Treaty] at the earliest practical date and will then launch a diplomatic effort to bring onboard other states whose ratifications are required for the treaty to enter into force.

—Barack Obama, September 10, 2008

As this article goes to press, Iran's nuclear program is rapidly expanding its capacity to enrich uranium. The terrorist attacks in Mumbai, India, last November have once more raised the specter of a nuclear weapons exchange between India and Pakistan—a "regional war" that could kill tens of millions of both countries' citizens and lead to severe change in global climate. North Korea, having joined the nuclear club with its first successful explosive test of a fission weapon on October 9, 2006, has reportedly separated enough weapons-grade uranium to build at least half a dozen atomic bombs. Eight countries have openly tested nuclear weapons, and Israel is presumed to have them as well. The possibility that terrorists could get their hands on such weapons is the worst nightmare of the U.S. Department of Homeland Security and its counterparts around the world.

Yet there are hopeful signs for reducing nuclear tensions as well. By the end of 2008, 180 countries had signed the Comprehensive Nuclear-Test-Ban Treaty (CTBT), which forbids all nuclear explosions, including the explosive testing of nuclear weapons. That treaty, adopted by the United Nations General Assembly in September 1996 and promptly signed by President Bill Clinton and many other world leaders, aims to restrict the further development of nuclear weapons by countries that have them and to prevent countries that do not possess them from building them with any confidence that the devices will work on the battlefield.

Even though the CTBT has not yet come into force, every nation that signed it—including the U.S. and Russia—has maintained a moratorium on nuclear weapons testing at least since the U.N. voted to adopt it. (The three nations that have tested nuclear weapons since 1996—India, North Korea and Pakistan—have not signed the treaty. For a brief historical and political background on the CTBT, see the box on page 76.)

FRANCE EXPLODED this nuclear weapon at Mururoa Atoll in French Polynesia on July 3, 1970. Atmospheric explosions are now banned by treaty and relatively easy to detect. Most monitoring efforts today focus on detecting explosions underground.

In the U.S. this moratorium on testing has continued despite serious opposition to the treaty itself. In 1999 the U.S. Senate declined to give its constitutional "advice and consent" to the ratification of the agreement, and soon after the 2000 election President George W. Bush declared the CTBT not to be in the interests of national security.

The reason some senators voted against the treaty was concern about whether adequate tools exist for detecting attempts at clandestine nuclear testing—and thereby pinpointing treaty violations. Why renounce testing, the argument goes, if the U.S. cannot tell whether other countries are cheating? While we sleep, other countries could secretly conduct tests that would increase their ability to harm the interests of the U.S. and its allies.

In our view, those concerns about monitoring are groundless—and have been for several years. The scientific and technical community has developed a well-honed ability to monitor militarily significant nuclear test explosions anywhere in the world, above ground or below, and to distinguish them from mine collapses, earthquakes, and other natural or nonnuclear phenomena. For example, the yield of the North Korean test conducted underground in 2006 was less than a kiloton (the equivalent of 1,000 tons of TNT). Yet it was promptly detected and identified. Given such demonstrated capabilities, as well as continuing improvements in monitoring, the concerns about clandestine nuclear testing no longer provide defensible grounds for opposing the CTBT.

Learning What to Look For

The science of monitoring nuclear explosions is as old as nuclear testing itself. From the beginning, the major rationale for the U.S. to monitor was to collect basic information about the capabilities of potential adversaries. A second important reason has been to support international treaties on nuclear arms control. If each country that is party to a comprehensive test ban has reason to believe that any attempt to hide a nuclear test will very likely fail, the fear of international sanctions may deter the country from testing at all. More than 2,000 explosive nuclear tests have been conducted since the end of World War II—in the atmosphere, underwater and underground. From that record inves-

NO PLACE TO HIDE

Monitoring aims to ensure that trying to conceal a nuclear explosion is a fool's errand. Among many ways the explosions signal their existence are:

- Seismic waves, which travel through solid rock
- Hydroacoustic waves, sound waves that can travel great distances through the oceans
- Infrasound, low-frequency sound that propagates thousands of miles through air
- Airborne radioactive particles and gases
- Shifts in ground level, particularly from an underground explosive test, detectable from space
- Light flashes bright enough to be seen from space
- X-rays visible from space

SYGMA/CORBIS (*nuclear explosion*); LUCY READING-IKKANDA (*icons*) tigators have gained vast experience in acquiring and interpreting the signals of a nuclear blast.

Nuclear test explosions generate a variety of potentially detectable signals. An explosion in the atmosphere, for instance, emits an intense flash of light, which can be imaged by satellite. The roar of an explosion quickly dissipates at frequencies in the range of human hearing, but at "infrasound" frequencies—lower than 20 hertz—sound waves travel vast distances in air. Infrasonic "listening" posts equipped with microbarometers detect the very small changes in atmospheric pressure that make up the infrasound signal.

Radioactive isotopes of certain stable elements are created by all nuclear explosions, and in an atmospheric test they are blown high into the air as gases. As they cool, some of them, such as radioactive xenon, remain in the gas phase as a telltale sign of a nuclear explosion. Others condense and combine with dust to form particles that can drift around the world. As early as 1948, the U.S. Air Force monitored American atmospheric test explosions in the Pacific and confirmed that such radioactive particles are big enough to collect by pumping air through filter paper similar to that used for making coffee.

Radioisotope detection soon proved its worth. On September 3, 1949, a WB-29 bomber flying east of Kamchatka Peninsula gathered data proving that, four days earlier, the U.S.S.R. had become the second country in the world to test a nuclear device. The mix of isotopes in the debris—notably plutonium and uranium 238—told a story of its own: the Soviets had tested a bomb that was almost an exact copy of the 21-kiloton explosive the U.S. had dropped on Nagasaki.

Quite early in the U.S. nuclear program, explosions were tested underwater as well as in the atmosphere. Sound travels very efficiently in water, particularly when the sound energy is trapped by slight changes in temperature and salinity that define the so-called sound fixing and ranging channel: the SOFAR layer. It became obvious that underwater explosions with a yield as small as a few millionths of a kiloton could therefore be monitored with hydrophones, or underwater microphones, by placing them near the SOFAR layer in seawater between 2,000 and 4,000 feet deep.

Seismic Monitoring

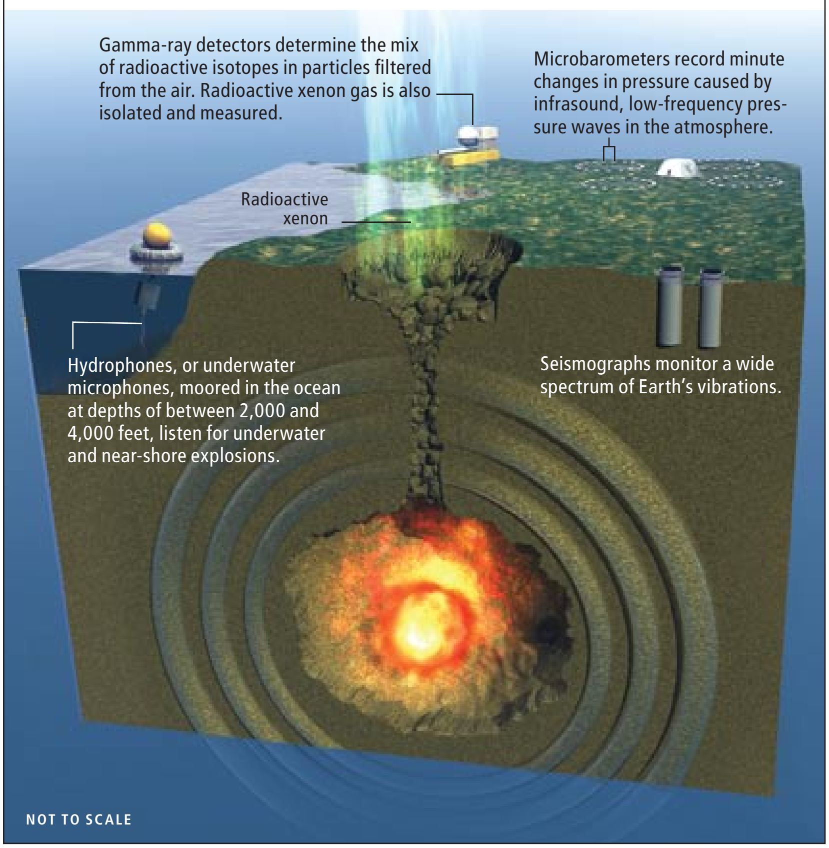
In 1963, following long and intense negotiations, the U.S., the Soviet Union and the U.K. (the first three members of the "nuclear club") signed the Limited Test Ban Treaty. The LTBT banned nuclear testing in outer space, in the atmosphere and underwater. Parties to the treaty, however, could still test nuclear explosions underground. For that reason, the information conveyed by seismic waves—elastic wave energy that travels through Earth as a result of an impact, collapse, slippage, explosion or other force that impinges on the planet—quickly became a major focus of the monitoring community. Fortunately, the sensors needed for detecting earthquakes can do double duty in detecting bomb blasts. But learning how to distinguish earthquakes from bomb blasts took several years, and refinements of that work continue to this day.

The main difficulty arises from the great variety and number of earthquakes, chemical explosions and other nonnuclear phenomena generating seismic signals every day. Any good mon-

[HOW IT'S DONE]

Monitoring Technologies That Support the CTBT

The International Monitoring System (IMS) set up by the Comprehensive Nuclear-Test-Ban Treaty (CTBT) Organization in Vienna incorporates detectors that search for four kinds of characteristic signals of a nuclear explosion (*below*), particularly a device exploded underground.



ALFRED T. KAMAJIAN

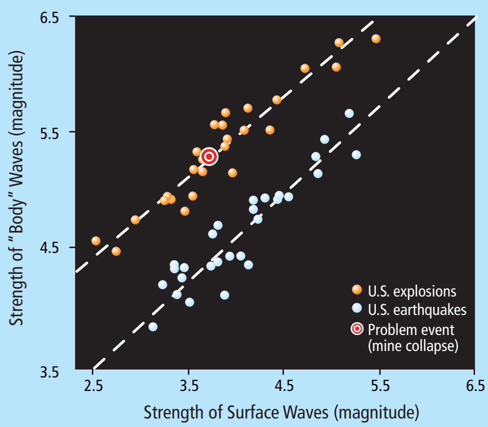
[SCREENING DATA]

How to Tell a Blast from a Crash

Distinguishing the seismic signals of a nuclear explosion from those of other seismic events is one of the main challenges for monitoring; misidentifications can lead to false accusations and international incidents. Identifying a reliable seismic difference between an underground explosion and the collapse of a large mine was an important advance of recent years.

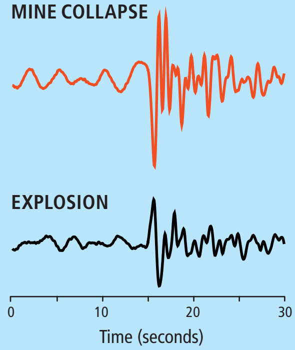
The collapse of a mine in southwestern Wyoming sent long-range seismic "body" waves around the world. (Body waves pass through the solid interior of Earth.) The waves were picked up by seismic stations at least 2,000 miles away (*squares*).

MISTAKEN IDENTITY?



Underground explosions (*orange circles*) are readily distinguishable from earthquakes (*light blue circles*) by the ratio of the strengths of two kinds of seismic waves: body waves and surface waves. The graph shows how explosions and earthquakes tend to fall into separate populations. By that discriminant, however, the Wyoming mine collapse (*red target*) looked much like a nuclear explosion.

On further study, seismologists noted that the seismogram of the body wave from the mine collapse begins with a deep trough, whereas that from a nuclear explosion begins with a sharp peak (*below*). Both were made at College Station, Alaska. The downward motion recorded in the seismogram of the mine collapse reflects the initial implosion of rock surrounding the center of the event.



MAPPING SPECIALISTS (*globe*); LILA RUBENSTEIN (*graph*); LUCY READING-IKKANDA (*seismograms*); SOURCE: "DISCRIMINATING BETWEEN LARGE MINE COLLAPSES AND EXPLOSIONS USING TELESEISMIC P WAVES," BY DAVID BOWERS AND WILLIAM R. WALTER, IN *PURE AND APPLIED GEOPHYSICS*, VOL. 159, NO. 4; FEBRUARY 2002

itoring network cannot avoid detecting those signals. Worldwide, for instance, more than 600 earthquakes a day eventually find their way into an international summary report, and mining operations in industrialized countries explode millions of tons of blasting agents a year. In all, about 25 seismic events above a magnitude of four take place every day, and that number goes up by a factor of about 10 for each drop of one unit in magnitude (say, from 25 to 250 events a day for a drop in magnitude from four to three).

At most locations on Earth, magnitude 4 corresponds to an explosive yield of less than a kiloton for an underground explosive device packed inside a small cavity in hard rock, from which seismic signals radiate efficiently. In other locations the rock is softer and more of the energy from the explosion is absorbed, reducing its measured seismic magnitude. Some policy makers have worried that a country might try to reduce the seismic signal by modifying the immediate environment of the test. For example, a large cavity hollowed out of rock could partly muffle the seismic waves from a blast, but for any militarily useful test explosion the cavity would have to be so big it would collapse or attract attention in other ways—for example, the excavated material would have to be concealed from satellites. The risk of discovery would be very high.

In practice, with seismic monitoring alone, all nuclear explosions down to yields of one kiloton can be detected with 90 percent reliability by examining between about 50 and 100 seismic events a day. To detect nuclear explosions with lower yields, the number of seismic events that must be examined goes up. Even one kiloton, however, is quite small for a nuclear explosion, and according to a 2002 report by the U.S. National Academy of Sciences, a test of that size would be of little use to a testing country attempting to make larger nuclear weapons—particularly if the country had little prior experience with nuclear testing [*see box on page 75*].

Where to Focus, What to Ignore

Monitoring a nuclear explosion begins with the detection of signals, followed by an attempt to gather and associate all the signals recorded by various monitoring stations that originate from

A GUIDE TO ACRONYMS

AEDS Atomic Energy Detection System

AFTAC Air Force Technical Applications Center

CTBT Comprehensive Nuclear-Test-Ban Treaty

IMS International Monitoring System

IRIS Incorporated Research Institutions for Seismology

LTBT Limited Test Ban Treaty

NPT Treaty on the Non-Proliferation of Nuclear Weapons

[FINDING CHEATERS]

How Monitoring for the Treaty Covers Earth

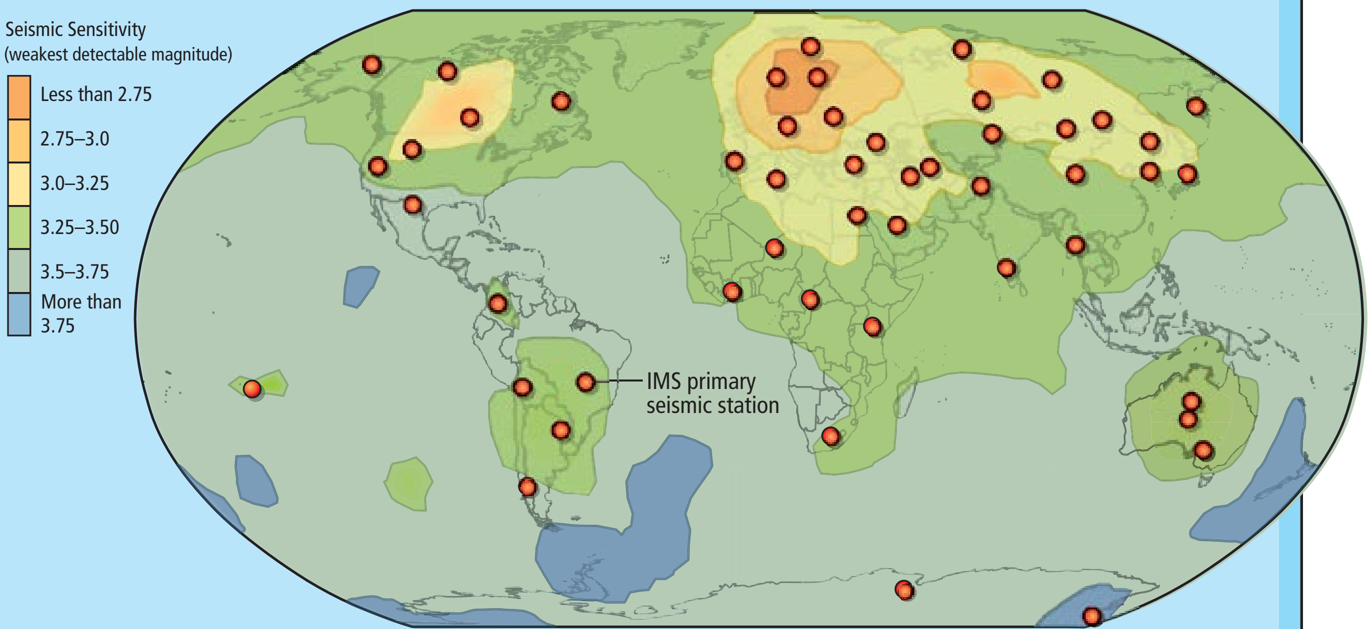
The IMS primary seismic network can detect a nuclear explosion that generates seismic waves of approximately magnitude 3.75 anywhere in the world—which is sensitive enough to monitor any test explosion likely to give militarily useful information. But the IMS is taking no chances catching cheaters. As the map shows (*below*), for explosions in most parts of the world the network is sensitive enough to monitor far weaker seismic signals.

The extra margin of sensitivity is important because the seismic signal strength depends on many factors, other than explosive "yield," that a rogue state might manipulate to hide a test, including the kind of rock that surrounds the explosion (*table at right*). Yield is usually expressed as the mass of TNT, in kilotons, that would explode with equivalent energy.

Rough Yields of Underground Explosions Corresponding to Seismic Magnitudes

Seismic magnitude	Yield in hard rock (kilotons)	Yield in soft rock (kilotons)
2.75	0.005	0.04
3.0	0.01	0.08
3.25	0.03	0.2
3.5	0.05	0.3
3.75	0.1	0.6

DETECTION THRESHOLDS BY REGION



the same event. The final steps are to estimate the location of the event, primarily from the differences in the arrival times of signals at different stations, and to identify it. For example, did it have the characteristics of a meteor breaking up in the atmosphere, a mining blast, a test of a nuclear weapon? And if the latter, how big was it? What was its yield? What country carried it out?

The vast majority of seismic events can be classified automatically by computer algorithms; only the hard cases are flagged by the software for human intervention. Specialists have been monitoring earthquakes and mine blasts for many years and have thereby become well acquainted with the way many of their features are reflected in the seismic record. That knowledge, in turn, has helped inform efforts to identify nuclear test explosions. In particular, several kinds of seismic events became touchstones as protocols were developed for identifying a particular event as a nuclear explosion.

One kind of event was a series of mine collapses—one in 1989 in Germany and two more in 1995, one in Russia and the other in the U.S. Seismic stations throughout the world detected all three, but the data raised concerns because at great distances the classic method of distinguishing explosions from other seismic events was incorrectly suggesting the events were underground explosions. In that classical method, seismologists compare the strength of long-wavelength seismic waves traveling over Earth's surface with that of body waves, which pass deep through the planetary interior. For example, a shallow earthquake and an underground explosion might set off body waves of the same strength, but if so, the surface waves from the earthquake would be significantly stronger than they would be for the underground explosion.

MAPPING SPECIALISTS

A closer analysis of the seismic waves from the mine collapses showed that those waves could not have come from an explosion, because they began with a trough rather than a peak: the ground had initially moved inward toward the source rather than outward, just as one would expect from a mine collapse [*see box at top of page 73*]. The episode was important because it showed that such an event could be reliably distinguished from an underground explosion on the basis of seismic recordings alone.

A second event illustrated the importance of the seismic distinction between two kinds of body waves for monitoring nuclear explosions. In 1997 a small seismic shock of magnitude 3.5, along with an even smaller aftershock, was detected below the Kara Sea, near Russia's former nuclear test site on the Arctic island of Novaya Zemlya. Were the Russians violating their obligations as a signatory of the CTBT?

The surface waves from the event were too small to measure reliably, and so once again the classic method of identifying an explosion—comparing the strength of the long-wavelength surface waves with that of the body waves—could not be applied. But the detection of "regional" seismic waves, which pass through the upper mantle and crust of Earth and which can be measured within about 1,000 miles of an event, resolved the issue. They enabled seismologists to distinguish compressional, or *P*, waves from shear, or *S*, waves generated by the event. (*P*-waves travel as oscillating regions of compression and rarefaction along the same direction in which the waves propagate; *S*-waves oscillate at right angles to the propagation direction.)

It was known that the *P*-waves from an explosion are typically stronger than the *S*-waves, but that distinction was just beginning to be applied at frequencies above five hertz. This time the measured ratio of the strengths of the *P*- and *S*-waves at high frequency—and the fact that the main shock had an aftershock—showed that the Kara Sea event was an earthquake.

More Eyes to Catch Cheaters

A third touchstone event, the North Korean nuclear test explosion of October 9, 2006, illustrated the importance of recording seismic waves as close as possible to their source. The blast left traces on sensors worldwide even though its yield was estimated at less than a kiloton. But regional seismic data were required to determine that the signals came from an explosion and not from an earthquake. In the event, the world was well prepared. Several seismic stations were close by, including one in the network of the International Monitoring System (IMS), the CTBT's own system for monitoring nuclear explosions.

After the seismic detection of the Korean test and the announcement of the test by North Korea, radioactive matter in the air and on the ground in Asia, as well as downwind across the Pacific Ocean at an IMS station in Canada, decisively confirmed the explosion as nuclear. Detecting the radioactivity was itself highly reassuring. The topography of the North Korean test site suggests that the explosion was deeper than most other subkiloton tests. Yet the test still leaked radioactive material.

Experience with these and other special seismic events has shown that the best seismic data for resolving a specific monitoring issue can sometimes come from stations that are not part of any treaty-monitoring network. Those stations, built with other goals in mind, can provide the dense coverage that makes it possible to strengthen the evidence derived from dedicated monitoring networks. Monitoring stations in the Korean region, for instance, are so dense that underground explosions with a yield

[THE AUTHORS]

Paul G. Richards (*left*) is Mellon Professor of the Natural Sciences at the Lamont-Doherty Earth Observatory at Columbia University. Since the mid-1980s his work has focused on using seismological methods to study nuclear weapons test explosions and their implications in both the scientific and political worlds. **Won-Young Kim** (*right*) is a Doherty Senior Research Scientist, also at Lamont-Doherty. His research focuses on the analysis of "regional" seismic signals from sources within about 2,000 miles to study earthquakes and to identify sources of underground explosions.

COURTESY OF LAMONT-DOHERTY EARTH OBSERVATORY, COLUMBIA UNIVERSITY (*Richards*); BRUCE GILBERT/EARTH INSTITUTE (*Kim*)

WHAT GOOD IS A TEST?

If the risk were taken to try to evade CTBT monitoring systems with a secretly conducted nuclear explosion, countries relatively experienced with nuclear testing would learn nothing that would add much to the nuclear threat they already pose to the U.S., and countries inexperienced with testing could expect to learn very little beyond what could be achieved with an untested weapon. Here is what inexperienced countries might learn by testing at various explosive yields:

Yield (kilotons)	**Detectable?**	**Purpose or Plausible Achievement**
Less than 0.0001	Unlikely	One-point safety tests* (with difficulty)
Between 0.0001 and 0.01	Unlikely	One-point safety tests
Between 0.01 and 1–2	Probably; concealable in some circumstances	Some improvement in weight and efficiency of "unboosted"† fission weapons; proof test of compact weapons yielding as much as 2 kilotons
Between 1–2 and 20	Almost always	Development of low-yield boosted fission weapon; eventual development and full testing of low-yield thermonuclear (fusion) weapon; proof test of fission weapon with yield as high as 20 kilotons

* A one-point safety test seeks to prove that no nuclear explosion would take place even if the chemical explosive that surrounds the fissionable material is accidentally set off at a single point.

† A boosted weapon incorporates tritium and deuterium to increase the number of neutrons, causing more fission in the nuclear explosive and thus greater yield.

SOURCE: *TECHNICAL ISSUES RELATED TO THE COMPREHENSIVE NUCLEAR TEST BAN TREATY.* NATIONAL ACADEMY OF SCIENCES. NATIONAL ACADEMIES PRESS, 2002.

[TIMELINE]

Fifty Years of Nuclear Testing and Monitoring

- **July 16, 1945:** World's first test of a nuclear device is conducted by exploding a bomb on a tower at Trinity site, Alamogordo, N.M.
- **August 6, 1945:** First atomic bomb is dropped on Hiroshima; three days later a second atomic bomb is dropped on Nagasaki.

- **1947:** General Dwight D. Eisenhower orders an effort to monitor the nuclear tests of other countries.
- **August 29, 1949:** The U.S.S.R. becomes the second nation in the world to test a nuclear device (also in the atmosphere).
- **September 3, 1949:** The Soviet explosion is detected by an American plane that collects radioactive debris in the upper atmosphere. It is the first nuclear explosion monitored by a country other than the testing power.
- **October 3, 1952:** The U.K. becomes the third nuclear weapons state, when it explodes its first nuclear device (also in the air).
- **Mid-1950s:** Many national and international groups bring public attention to the genetic hazards of radioactive materials produced by the continuing nuclear testing.
- **September 19, 1957:** First underground nuclear test explosion is conducted at the Nevada test site.
- **February 13, 1960:** France tests its first nuclear device.
- **October 31, 1961:** The Soviet Union explodes the largest device ever tested, the "Big John," with a yield of more than 50 megatons. It was promptly detected all around the world.
- **August 5, 1963:** Limited Test Ban Treaty is signed by the U.K., the U.S. and the U.S.S.R., banning testing in the atmosphere, underwater and in space. China and France refuse to sign.
- **October 16, 1964:** China tests its first nuclear device, becoming the fifth nation to do so.
- **July 1, 1968:** Sixty-one countries sign the Non-Proliferation Treaty, prohibiting the transfer of nuclear weapons technology to nonnuclear weapons states. India, Israel, North Korea and Pakistan refuse to sign.
- **May 18, 1974:** India tests its first nuclear device (underground).
- **1992:** The U.S. under President George H. W. Bush declares a moratorium on all nuclear testing.
- **September 10, 1996:** The United Nations General Assembly votes in favor of the Comprehensive Nuclear-Test-Ban Treaty (CTBT), which prohibits all nuclear test explosions.
- **September 24, 1996:** President Bill Clinton signs the CTBT for the U.S. By the end of that day 66 nations, including the four other nuclear weapons states (China, France, Russia and the U.K.) sign the treaty. India, North Korea and Pakistan do not sign.
- **May 11 and 13, 1998:** India conducts two sets of underground nuclear tests, breaking a de facto global moratorium on testing that had prevailed since the CTBT was opened for signatures in 1996.
- **May 28, 1998:** In response to India's renewed testing, Pakistan conducts two sets of its own underground nuclear tests.
- **October 13, 1999:** U.S. Senate votes to withhold its advice and consent to the CTBT.
- **2001:** Shortly after taking office, President George W. Bush declares the CTBT is not in U.S. interests. He continues the U.S. moratorium on testing.
- **October 9, 2006:** North Korea tests its first nuclear device (underground).
- **December 31, 2008:** 180 countries have signed the CTBT, including 41 of 44 countries that must sign it before it can go into force. Only India, North Korea and Pakistan remain holdouts.

as low as a few percent of a kiloton can be detected there.

Well-tested networks of seismic stations for rapidly analyzing, assembling and distributing large amounts of seismic data already exist, quite independently of the IMS. Thousands of seismometers have been set up throughout the world to evaluate earthquake hazards and to determine our planet's internal structure. In the U.S., the U.S. Geological Survey and the Incorporated Research Institutions for Seismology, a consortium of more than 100 American universities, are jointly building and operating seismic data systems. As of the end of 2008, IRIS was receiving current seismic data from 71 networks that operate 1,797 stations, including 474 outside the U.S. An international group, the Federation of Digital Seismic Networks, plays a huge and still growing role in the data collection. Such networks are well suited to picking up unanticipated nuclear test explosions, as well as high-quality regional signals from events that might seem suspicious if they were analyzed by a sparse global network alone. Those data can thereby supplement data from the IMS and the various national treaty-monitoring networks.

One network of particular note among all the foregoing networks is the monitoring system the U.S. still maintains specifically for detecting nuclear explosions. The Atomic Energy Detection System (AEDS) is operated by the Air Force Technical Applications Center (AFTAC) out of Patrick Air Force Base in Florida and includes an extensive global network of seismometers. AFTAC reports on the data from the AEDS network within the U.S. government. If the CTBT finally goes into force and the AEDS or some other national facility detects a suspicious event, such data can be presented in an international forum, thereby augmenting information gathered by the IMS.

How Low Must You Go?

Even though existing technologies can ferret out rather small bomb tests and technical advances in monitoring will undoubtedly continue, one practical caveat must be made. It is obviously not possible to detect explosions of every size, with 100 percent reliability, all the way down to zero explosive yield. In this sense, monitoring is imperfect. But does it really matter that a technologically sophisticated country could perhaps conceal a very small nuclear explosion from the rest of the world, even though the

KEYSTONE/GETTY IMAGES (*newspaper*); BETTMANN/CORBIS (*explosion*)

[BACKGROUND]

A Brief History of the CTBT

The Comprehensive Nuclear-Test-Ban Treaty (CTBT) is closely related to the Non-Proliferation Treaty (NPT), which went into effect in 1970 and is now agreed to by more than 180 countries. In signing the NPT, nations undertook not to allow nuclear weapons technology to pass from the nuclear to the nonnuclear weapons states.

Throughout the NPT negotiations, most nonnuclear states wanted a complementary set of commitments from the nuclear states that they would not further develop their nuclear weapons technology. The CTBT is the most detailed and far-reaching of these commitments. Yet despite its many signatories, the CTBT cannot go into effect until it is both signed and ratified by 44 countries that, during the final negotiations, were understood to have some capability to run nuclear reactors. As of the beginning of 2009, 35 of those 44 countries had ratified—including Russia and almost all NATO members. Among the nine holdouts are six that have signed but not ratified (China, Egypt, Indonesia, Iran, Israel and the U.S.) and three that have not even signed (India, North Korea and Pakistan).

The 1999 defeat of the CTBT in the U.S. Senate placed the treaty in the limbo it occupies in the U.S. today. When George W. Bush took office, he did not revoke Bill Clinton's signing (*right*), but he did state his opposition to the treaty. The Bush administration also cut off part of the U.S. share of funds for the CTBT's International Monitoring System. There was never any possibility that the treaty would come before the full Senate for reconsideration as long as Bush was in office. With new information, however, including input from the Obama administration, the Senate could reconsider the treaty and conduct a second vote.

—***P.G.R. and W.-Y.K.***

GREG GIBSON *AP Photo*

explosion served no practical purpose in a nuclear weapons program? The goal of monitoring systems is to ensure that the yield of a successfully concealed nuclear test explosion would have to be so low that the test would lack military utility.

In the 1950s President Dwight D. Eisenhower was willing to agree to a comprehensive test ban even if monitoring was not sensitive enough to detect explosions with yields less than a few kilotons. Today monitoring is much more effective. Is the CTBT worth scuttling if a nuclear device of less than a kiloton might in principle be exploded without being detected? The 2002 analysis by the National Academy of Sciences argues that, on the contrary, ratifying the CTBT would be a positive development for U.S. national security.

Nevertheless, some leaders in the military and in nuclear weapons laboratories have opposed the CTBT. They argue that it prevents the U.S. from verifying the continuing viability of its current nuclear arsenal or from developing more sophisticated nuclear weapons. But the reliability of proven designs in the U.S. stockpile of nuclear weapons does not, in practice, depend on a program of nuclear test explosions. Rather reliability is ensured by nonexplosive testing that is not restricted by the CTBT. As for new nuclear weapons, the CTBT is an impediment—just as it was intended to be—and its restrictions on U.S. weapons development must be weighed politically against the merits of the restrictions it imposes on all signatories.

Our discussion has touched on several important technical issues related to weapons development and monitoring that arise as the U.S. judges whether ratifying the CTBT is in the national interest. Unfortunately, individuals and organizations with strong opinions on the CTBT have sometimes turned such issues—the assessment of monitoring capability in particular—into a surrogate battleground for an overall political evaluation of the treaty itself and the trade-offs it implies. We would urge, instead, that the main debate focus on the merits of the treaty directly and remain separate from technical, professional reviews of monitoring capability.

If the CTBT finally does go into force, the de facto moratorium on international testing would become formally established. The treaty could then become what it was always intended to be: a vital step in strengthening global efforts to prevent the proliferation of nuclear weapons and a new nuclear arms race. ■

MORE TO EXPLORE

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Toward a Nuclear-Free World. George P. Shultz, William J. Perry, Henry A. Kissinger and Sam Nunn in *Wall Street Journal Commentary;* January 15, 2008.

CTBT Monitoring: A Vital Activity for Our Profession. Paul G. Richards in *Seismological Research Letters,* Vol. 79, No. 3, pages 375–378; May 2008.

The Comprehensive Test Ban Treaty: Effectively Verifiable. David Hafemeister in *Arms Control Today,* Vol. 38; October 2008. Available at **www.armscontrol.org/print/3391**

For more information about monitoring technologies, the history of nuclear testing, the development of the CTBT and the Preparatory Commission for the CTBT Organization in Vienna, visit **www.ctbto.org**

Escape from the Killing Fields

As the world warms up, some species cannot move to cooler climes in time to survive. Camille Parmesan thinks humans should help—even if it means creating invasive species BY DAVID APPELL

Camille Parmesan didn't mind having her early work denigrated by Rush Limbaugh during his on-air program. "Actually, I was quite pleased with that," she says of the radio show host, who derided her studies on the geographic shifts of a butterfly species because of climate change. "I thought if I got his goat that heavily, then I must be making an impact."

That was in 1996, and since then she has become one of the leading conservation biologists monitoring what rapid climate change is doing to the world's plants and animals. Like many of her colleagues, she warns anyone who will listen of the ecological dangers. But unlike her colleagues, she is lately suggesting a way of saving threatened species that is still unthinkable to many biologists: assisting their migration and colonization.

The controversial approach, she argues, may be the only way to save imperiled species that cannot adapt to the unnatural rate of today's changes or escape to appropriate climes. Transplantation should be done, she says, even if it risks engendering new diseases and pests or other unintended consequences. Some scientists have begun to take her seriously, meeting to discuss the issue and building models that go beyond simple climate projections.

Parmesan did not hold such a view when she published her now famous 1996 study on the plight of Edith's checkerspot butterfly—a delicate creature colored with brown, orange and white spots, sometimes no more than a centimeter across. She had spent almost five years trekking into the backcountry along the Pacific coast, from Mexico to Canada, crawling under the insect's plant, a type of snapdragon. Only once did she get chased off the land, in Baja California by someone who acted like "a typical drug lord," she recalls.

The checkerspot is very sensitive to temperature because its host plant dries out in warm temperatures, eliminating the insect's food source while in its caterpillar stage. Scientists already knew that human development and climate were driving down its populations, but Parmesan's systematic science startled everyone: three fourths of the populations at the lowest latitudes had become extinct, whereas only 20 percent of those in Canada had disappeared. Populations at higher altitudes were only one third as likely to go extinct as those at lower, warmer heights.

Soon Parmesan, now at the University of Texas at Austin, noticed similar trends among butterflies in Europe, where records of their domains go back much further. Subsequent analyses conducted with colleagues such as David Easterling of the National Climatic Data Center in Asheville, N.C., and Gary Yohe of Wesleyan University uncovered evidence of climate change nearly everywhere they looked. For instance, plants and animals have shifted their ranges by about six kilometers per decade toward the poles during the past quarter of a century. Spring events, such as blooming, frog breeding and migrant bird arrivals, have advanced 2.3 days per decade. Tropical pathogens are moving up in latitude and striking species not adapted to deal

COURTESY OF MICHAEL C. SINGER

CAMILLE PARMESAN

CALL IN THE MOVERS: Advocates "assisted migration," in which humans actively transplant species to help them escape ecological shifts caused by rapid climate change.

BUSY FUTURE: Earth has warmed by 0.7 degree Celsius from preindustrial times, causing 40 percent of species to shift their ranges. Parmesan thinks that with "business as usual" energy production, the number will approach 100 percent, with up to 75 percent of species affected negatively.

with them. About two thirds of the 110 known harlequin frog species in Costa Rica are believed to be extinct, their temperature-weakened immune systems devastated by a lethal fungus—itself taking advantage of warmer temperatures.

Last December scientists announced the probable extinction of the first mammal because of climate change: the white lemuroid possum, now gone from Queensland, Australia. The possum, which lived only above 1,000 meters in altitude, could be killed by as little as five hours in temperatures greater than 30 degrees Celsius (86 degrees Fahrenheit). Although precise predictions are not yet possible, Chris D. Thomas of the University of Leeds in England and his colleagues have found that even under midrange global-warming scenarios, 15 to 37 percent of terrestrial species will be "committed to extinction" by 2050. Add that to existing threats from habitat destruction and migration barriers from towns and highways, and the future

IN TROUBLE: **Edith's checkerspot butterflies, seen here mating, are vanishing as rising temperatures dry out their food source.**

COURTESY OF CAMILLE PARMESAN

of the world's biodiversity looks increasingly thin and vanilla.

"As soon as I started to see what an impact climate change was having on wild species and documenting wild species going extinct," Parmesan says, she began to think about how the species might be saved. Short of the world's governments paying heed and cutting greenhouse gas emissions sharply to enable Earth to cool down, she and a few others began pondering alternative actions—in particular, human assistance. She sees assisted migration, as the concept has come to be called, as the only hope to save at least some species—though certainly only a small minority of those in peril. Jessica J. Hellmann, a conservation biologist at the University of Notre Dame, believes that most assisted migrations will require an advocate who favors a particular species for sentimental or, especially, economic reasons. (Parmesan understandably has several western butterfly species in mind.) Timber companies are already taking climate change into account when planting new trees to be harvested decades hence.

One amateur group, the Torreya Guardians, are attempting to "rewild" the endangered Florida torreya, a conifer tree. Native only to a 65-kilometer length of the Apalachicola River, it began to decline in the 1950s, probably because of fungal pathogens, and is thought to be "left behind" in a habitat hole that has prevented its migration northward. A few dozen seedlings were planted on private land near Waynesville, N.C., last July, with more expected.

Such assisted migration, Parmesan acknowledges, horrifies some conservation biologists: "They spend a good bit of time working against invasive species, and one big cause of species being endangered is being outcompeted by invasive species." In the particular case of the Torreya Guardians, "many biologists are queasy about it because they feel they didn't do the groundwork to see how it would impact the [new] community," she says. So she advocates systematic studies of threatened species' habitats—where they thrive and why and what might threaten them.

Better theoretical tools will certainly help. Today's efforts, called climate envelope models, simply consider the temperature, precipitation levels and soil types that a species prefers, then feed that into a standard climate model to predict where a species might naturally migrate, sans human obstacles and assistance. Hellmann is working on a model that incorporates biological elements, such as genetics and competition among species—what other species might be attracted or at risk, evolutionary responses, and so on—because populations often vary genetically across a species' range. With such data, Hellmann remarks, "we can perhaps get rules of thumb that can help set population priorities."

Assisted migration is a more active idea in academia than among traditional conservation organizations. For example, the Nature Conservancy is studying the idea. "Assisted migration is a relatively drastic option," says Patrick Gonzalez, a climate change expert at the organization, "but might come about if all of our other options fail and a species is in danger of extinction. But it entails a lot of risks."

Such caution frustrates Parmesan, who was a co-author on a 2008 paper in *Science* proposing a "decision framework" for assessing the possible relocation of endangered species. "If we do nothing, we're also risking biodiversity. Conservation managers have the attitude that doing nothing is good, and my approach is that doing nothing is bad," she explains.

But she is more dismayed by policy makers. In its last months in office, the Bush administration altered the Endangered Species Act to explicitly exclude climate change from factors that would necessitate independent, multiagency studies of species proposed to be protected. Parmesan's reaction was, she says, "mostly unprintable. It's in defiance of what every conservation organization is moving toward." John Kostyak of the National Wildlife Federation says that "chances are very good" for the Obama administration to reverse the regulation, although it could take as long as a year.

No matter what the White House does to tackle climate change, the world's ecosystems are in for more of a shock. Parmesan's call will surely only grow louder. ■

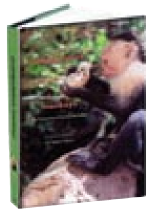
David Appell is based in St. Helens, Ore.

Monks and Monkeys

BY MICHELLE PRESS

➔ MANIPULATIVE MONKEYS: THE CAPUCHINS OF LOMAS BARBUDAL

by Susan Perry, with Joseph H. Manson. Harvard University Press, 2008 ($45)



Looking for a good species in which to investigate the evolution of intelligence, Susan Perry and her husband, Joseph H. Manson, primatologists at the University of California, Los Angeles, came upon the capuchins. These New World monkeys have brains larger for their body size than any primate except humans, and since 1990 the couple has followed the lives of four generations of capuchins in a Costa Rican rain forest. The monkeys' tonsured head and striking cowl grant them a vague resemblance to the monks for whom they were named. Their world may be almost as structured and ritualistic. Not only do they interact in byzantine ways, but they evince an excellent understanding of who is friends with whom and under what circumstances. Much of their considerable intellectual creativity is expressed through devising unique rituals for testing and maintaining friendships, including sticking their fingers up one another's noses and forming totem poles of up to four monkeys piled high to frighten enemies.

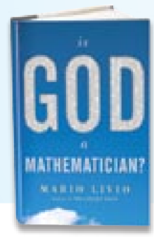
The book is immense fun to read, as Perry melds tales of the rigors of rain forest research

EXCERPT

➔ IS GOD A MATHEMATICIAN?

by Mario Livio. Simon & Schuster, 2009 ($26)

For centuries, mathematicians have been uncannily accurate in predicting the physical world. Astrophysicist Mario Livio tries to explain why. In a book with a question for the title, it is hard to resist quoting an entire paragraph of questions, but in response to what you are wondering, yes, Livio provides answers as well.

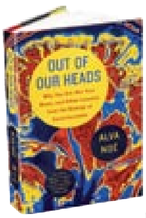


▪ You Are Not Your Brain ▪ Miraculous Anticipation?

with surprising revelations about these complex creatures.

➡ OUT OF OUR HEADS: WHY YOU ARE NOT YOUR BRAIN, AND OTHER LESSONS FROM THE BIOLOGY OF CONSCIOUSNESS

by Alva Noë. Hill and Wang, 2009 ($25)



Alva Noë, a University of California, Berkeley, philosopher and cognitive scientist, argues that after decades of concerted effort on the part of neuroscientists, psychologists and philosophers "only one proposition about how the brain makes us conscious … has emerged unchallenged: we don't have a clue." The reason we have been unable to explain the neural basis of consciousness, he says, is that it does not take place in the brain. Consciousness is not something that happens inside us but something we achieve—it is more like dancing than it is like the digestive process. To understand consciousness—the fact that we think and feel and that a world shows up for us—we need to look at a larger system of which the brain is only one element. Consciousness requires the joint operation of brain, body and world. "You are not your brain. The brain, rather, is part of what you are."

NOTABLE BOOKS: ASTRONOMY

1 **The Pluto Files: The Rise and Fall of America's Favorite Planet**
by Neil deGrasse Tyson. W. W. Norton, 2009 ($23.95)
Tyson chronicles this country's irrational love affair with an extraterrestrial underdog.

2 **Joseph Cornell and Astronomy: A Case for the Stars**
by Kirsten Hoving. Princeton University Press, 2008 ($49.50)
The master of the assemblage box, artist Joseph Cornell (1903–1972) had an intense fascination with astronomy and the cutting-edge discoveries made during his lifetime.

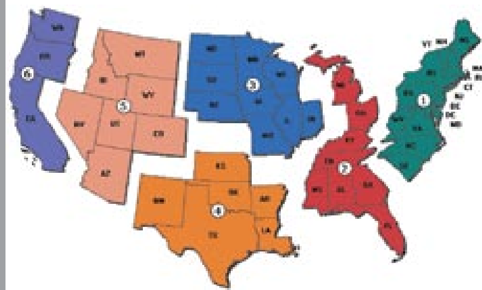
3 **People and the Sky: Our Ancestors and the Cosmos**
by Anthony Aveni. Thames and Hudson, 2008 ($29.95)
Ancient societies depended on signals in the sky for sustenance, navigation, social cohesion and political authority.

4 **Hubble: Imaging Space and Time**
by David Devorkin and Robert W. Smith. Smithsonian Air and Space Museum, in association with National Geographic, 2008 ($50)
Stunning photographs; spare, intelligent text.

HUBBLE view of Saturn, 1996

AURA/STSCI/NASA

"The unreasonable effectiveness of mathematics creates many intriguing puzzles: Does mathematics have an existence that is entirely independent of the human mind? In other words, are we merely *discovering* mathematical verities, just as astronomers discover previously unknown galaxies? Or, is mathematics nothing but a human *invention?* If mathematics indeed exists in some abstract fairyland, what is the relation between this mystical world and physical reality? How does the human brain, with its known limitations, gain access to such an immutable world, outside of space and time? On the other hand, if mathematics is merely a human invention and it has no existence outside our minds, how can we explain the fact that the invention of so many mathematical truths miraculously anticipated questions about the cosmos and human life not even posed until many centuries later?"



Q How do **spacecraft orient themselves** in the absence of magnetic poles? Is there any truth to the system they use on Star Trek?

—S. Messick, Oklahoma City

Christopher Potts, a navigation engineer at the NASA Jet Propulsion Laboratory in Pasadena, Calif., shows the way:

Without an ever present magnetic field to rely on, as compass users have on Earth, those of us responsible for spacecraft navigation must utilize a three-dimensional Cartesian coordinate system, or frame, of our own devising.

One common frame currently used in deep space is called the Earth Mean Equator and Equinox of Epoch J2000, abbreviated as EME2000. Its name is so involved because it captures the many elements required to define a three-dimensional coordinate system: a reference body (Earth); a reference plane (the mean equator, an idealized equator that does not include the small nodding motion, or nutation, of Earth's axis); a reference direction (the vernal equinox, a line from Earth to the sun on the first day of spring); and a reference time (J2000, or January 1, 2000, at 12:00:00 Ephemeris Time, a uniform timescale used for planetary motion calculations). The reference body and reference plane define the *x-y* plane of the frame. The *z*-axis is perpendicular to the plane, generally along the body's axis of rotation. A reference time is required because the reference planes experience subtle motion caused by gravitational forces of the other bodies in the solar system.

VOYAGER probe, two of which took flight in 1977, in an artist's rendition.

Using the defined coordinate frame, a spacecraft must be able to both determine and control its orientation. Instead of a compass, spacecraft sensors use the sun and stars to determine the craft's orientation relative to the coordinate frame. Desired directions can be specified in several ways with respect to the defined frame, but two angular measurements are commonly used. In astronomy, right ascension and declination identify directions in the sky. Right ascension is an angular measurement in the reference plane, and declination measures the angle above or below the reference plane.

Although the specifics may vary, determining directions in spaceflight relies on the basic principles of defining a reference frame and using measurements to determine orientation relative to that frame. As for the system on *Star Trek* (such as heading 294, mark 37), I doubt this method finds any current use in deep-space navigation. But by specifying two measurements, at least there is enough information to properly aim the warp drive.

Q How long will **global uranium** deposits fuel the world's nuclear reactors at present consumption rates?

—G. Peck, Seward, Alaska

Steve Fetter, dean of the University of Maryland's School of Public Policy, supplies an answer:

If the Nuclear Energy Agency (NEA) has accurately estimated the planet's economically accessible uranium resources, reactors could run more than 200 years at current rates of consumption.

Most of the 2.8 trillion kilowatt-hours of electricity generated worldwide from nuclear power every year is produced in light-water reactors (LWRs) using low-enriched uranium (LEU) fuel. About 10 metric tons of natural uranium go into producing a metric ton of LEU, which can then be used to generate about 400 million kilowatt-hours of electricity, so present-day reactors require about 70,000 metric tons of natural uranium a year.

According to the NEA, identified uranium resources total 5.5 million metric tons, and an additional 10.5 million metric tons remain undiscovered—a roughly 230-year supply at today's consumption rate in total. Further exploration and improvements in extraction technology are likely to at least double this estimate over time.

Using more enrichment work could reduce the uranium needs of LWRs by as much as 30 percent per metric ton of LEU. And separating plutonium and uranium from spent LEU and using them to make fresh fuel could reduce requirements by another 30 percent. Taking both steps would cut the uranium requirements of an LWR in half.

Two technologies could greatly extend the uranium supply itself. Neither is economical now, but both could be in the future if the price of uranium increases substantially. First, the extraction of uranium from seawater would make available 4.5 billion metric tons of uranium—a 60,000-year supply at present rates. Second, fuel-recycling fast-breeder reactors, which generate more fuel than they consume, would use less than 1 percent of the uranium needed for current LWRs. Breeder reactors could match today's nuclear output for 30,000 years using only the NEA-estimated supplies. ■

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NASA (*spacecraft*); ED DARACK (*nuclear plant*)

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