Not Enough Sunshine? Vitamin D Fights Cancer

SCIENTIFIC AMERICAN

When UNIVERSES COLLIDE
page 52

November 2007 www.SciAm.com

Do We Need NEW NUKES?

A *special report* on nuclear arsenals and replacing warheads

Save Neurons

Possible Therapies for Lou Gehrig's Disease

From Flight to Bright

Butterfly Wings Improve Electronic Displays

In Case of Emergency...

Science Saves Disaster Victims

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The ominous mushroom cloud was modeled by artist Jean-Francois Podevin. The shape in the upper right corner is a representation of a Calabi-Yau space, a higher-dimensional shape that has cosmological significance, generated by computer scientist Andrew J. Hanson of Indiana University.

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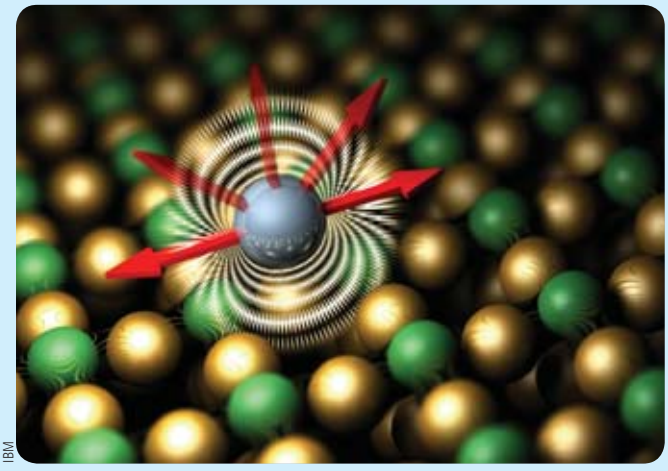

IBM

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Physicists say that it is theoretically possible to design a container that would be invisible, along with anything inside it—even you.

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Why cats prefer meaty wet food and disdain sugar.

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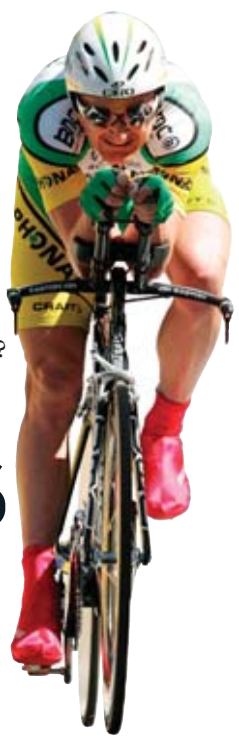

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The Best Defense

You can't be too safe. Or can you?

Reverence for the sun deity Huitzilopochtli thrived among the Aztec peoples of Mesoamerica as late as the 16th century. But students of history know that the true zenith of sun worship occurred in the 1970s, when engineers at Caltech constructed the first fully solar-powered George Hamilton and millions knelt at the feet of their fierce, tawny goddess Farrah Fawcett, whose gleaming tusks and shining blonde nimbus were foretold by Montezuma.

Widespread opinion held in those days that nothing could be more natural and invigorating than to start one's summer by getting a nice light sunburn—just to establish a good tanning base for the season, mind you. If you saw beachgoers slathering their skin with something, chances are strong that it was baby oil. For those of us so irredeemably untannable as to need protection against the sun, a bit of searching at the pharmacy might turn up a sunscreen with an SPF as high as 15.

Then those killjoy dermatologists began insistently connecting solar exposure to melanomas and other skin cancers, and America's love affair with the sun slowly set. Fashion certainly has not changed so far as to uphold pallor as the ideal for beauty, but a more healthy moderation has taken hold. Sunbathers know not to bake until blistered and always to wear protection. Almost everyone has heard and internalized some form of the advice, "You can't be too careful with the sun."

Then again, maybe you can. Beginning on page 62, researchers John H. White and Luz E. Tavera-Mendoza describe the many ways in which vitamin D contributes to human health, from building strong bones to fighting inflammation. Astonishing numbers of people who live in temperate climates may suffer subtly from deficiencies of it, in part because our modern lifestyles prevent us from getting enough sunlight for our bodies to make the vitamin abundantly. Epidemiological evidence hints that too little vitamin D might contribute to the incidence of certain cancers, immune disorders and even infectious diseases. Consequently, while quite wisely shunning sun exposure for the sake of our skins, some of us may have crossed the line and raised our risks for other problems. A little moderation may offer superior defense.

But on the subject of defense, no threat is potentially more grave than that posed by nuclear weapons. Our special report, beginning on page 74, looks at the state of the world's nuclear arsenals, which remain terrifying to contemplate. The graphics speak volumes about who truly poses a danger to whom and what even a single nuclear explosion can do.

Nevertheless, thanks to nonproliferation and disarmament treaties, most of the world's nuclear warheads are aging. Now the U.S. military is looking to replace old W-76 warheads, a pillar of the nation's defenses, with newer, "more reliable" ones. Aside from whether other nations might see that move as a treaty violation, some critics worry how trustworthy such weapons will be when they cannot be tested. David Biello has the details in the second half of our report, starting on page 80; see also our comments on the larger problem of U.S. nuclear strategy (or lack of one) in SciAm Perspectives, on page 37. Then ask yourself: How much nuclear defense is too much?

FLYNN LARSEN (*Rennie*); JAMES PORTO (*sunbather*)

JOHN RENNIE
editor in chief

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Faith Debate ▪ Stormy Weather ▪ Snoozing Mice

JULY 2007

"When religion tries to explain reality, it unsuccessfully competes with science."
—Thomas Bradley POWAY, CALIF.

Religion's Roles

The dialogue between Lawrence M. Krauss and Richard Dawkins on religion in "Should Science Speak to Faith?" is almost as frustrating as Pat Robertson and Jerry Falwell discussing cosmology. Both authors seem to assume that Christian fundamentalism provides a paradigm for all religion, which is sufficiently defined by its collision with biology and cosmology. Other faiths and Christian groups have never had such problems with science.

Religion is also about purpose, value and identity, the meaning of existence, the significance of human life, and the critique of our moral values. Slavery was abolished when Christians finally understood its incompatibility with their teachings. And if religion has known sin, so have science and atheism. Ask J. Robert Oppenheimer and Aleksandr Solzhenitsyn.

Ron Partridge
England

I think the disagreement about whether religion complements or competes with science arises from religion's being multipurpose. When it tries to explain reality, it unsuccessfully competes with science. When it acts as a social organization, it can complement science. With advances in psychology and sociology, this latter function could be disappearing, which may explain why some religious leaders have been aggressively attacking science.

Thomas Bradley
Poway, Calif.

Mean Seasons

Although human activity broadly is considered to contribute to climate change, Kevin E. Trenberth goes much further than this in stating unequivocally in "Warmer Oceans, Stronger Hurricanes" that global warming is caused by humans.

Also, it is ironic that, despite Trenberth's assertion that 2004 and 2005 were the worst years for frequency and intensity of hurricanes, only one of the storms in the "Worst Cyclones" sidebar (Katrina) was in that time frame.

Bryon Moyer
Sunnyvale, Calif.

TRENBERTH REPLIES: *According to the 2007 Intergovernmental Panel on Climate Change report, the warming of the past 50 years is with greater than 90 percent probability caused by human activity [see "The Physical Science behind Climate Change," by William Collins, Robert Colman, James Haywood, Martin R. Manning and Philip Mote; SCIENTIFIC AMERICAN, August 2007]. This assertion can be proved by running climate models with and without observed changes in the composition of the atmosphere, taking into account their veracity and influences on the climate system such as the sun. Climate fluctuates naturally on geologic timescales mainly because of variations in Earth's orbit, but in the past century such effects have been tiny.*

The 2005 North Atlantic hurricane season was the most active on record by many measures. For instance, it featured the largest number of named storms (28) and hurricanes (15), including Dennis, the strongest recorded storm for July and the earliest fourth-named storm of any season. It was the first season to have

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four Category 5 storms, including the most intense storms on record in the Atlantic (Wilma) and the Gulf of Mexico (Rita), along with Katrina. Furthermore, six of the eight most damaging storms on record for the U.S. occurred between August 2004 and September 2005 (Charley, Ivan, Frances, Katrina, Rita and Wilma).

2004 AND 2005 saw a rise in the number of intense storms such as Hurricane Katrina.

RICK WILKING *Reuters/Corbis*

Perchance to Dream?

In "The Memory Code," Joe Z. Tsien describes how he and his colleagues have converted binary code recordings of coordinated activities of large populations of neurons in the mouse hippocampus that can be attributed to specific experiences. I would like to suggest he continue such measurements when the mouse sleeps.

Such experimentation could shed light on the mechanism and functions of dreams. Finding the same neuronal discharges during sleep would suggest that mice have dreams. One might then measure how often dreams recur; whether neuronal activities change during this state; and whether they are associated with, or are shaped by, different but similar experiences (which could indicate that during dreaming transformation of the neuronal discharges associated with specific experiences occurs).

Rudolf Morant
ZeTuP Tumor Center, St. Gallen and Chur, Switzerland

TSIEN REPLIES: *These are good suggestions and a natural extension of our original research. We have indeed collected sleep-recording data and are actually analyzing mountains of it. We expect to publish some of those results in about a year.*

Asset Advice

In "The Prospects for *Homo economicus*" [Skeptic], Michael Shermer's scenario in which $20,000 can be made selling Google stock that has doubled in value or Ford stock that has lost half its value leaves out tax implications. With a long-term capital gains tax of 15 percent and a state tax of 10 percent, you would have to sell $22,857 of Google to net $20,000. Selling Ford for $20,000 would yield that amount (there is no tax on a loss), but ignoring the minor tax impact of the $3,000 maximum allowable deduction for capital losses, you would not recover your loss.

essential 2

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As a tax attorney, I would suggest selling $6,666.67 of Ford and $13,333.33 of Google, which would result in gains being offset by losses for a net taxable gain of $0.

John A. Young
via e-mail

ERRATA "The Evolution of Cats," by Stephen J. O'Brien and Warren E. Johnson, incorrectly states that the Toba volcanic eruptions of 73,000 years ago occurred on Borneo. The correct location is Sumatra.

"Should Science Speak to Faith?" by Lawrence M. Krauss and Richard Dawkins, gives the distance from New York to San Francisco as 3,400 miles. The distance is 2,565 miles by air.

Letters to the Editor

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First Satellite ▪ Canine Treachery ▪ Unlucky Ship

Compiled by Daniel C. Schlenoff

NOVEMBER 1957

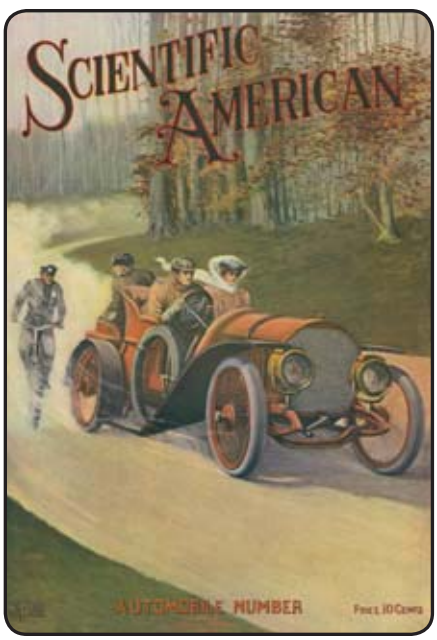
SPACE AGE BEGINS—"The earth's first man-made satellite, called *sputnik* (Russian for 'fellow traveler'), became spaceborne around midnight (Moscow time) on October 4. The U.S.S.R. gave no advance notice of the launching, and in the first days of sputnik's flight little information about the satellite was released to the rest of the world. The 'bird' itself was a sphere with a diameter of 58 centimeters (about 23 inches). It carried two radio transmitters. Whether the bird carried other instruments was not clear: Soviet scientists said the satellite was recording temperature, and U.S. scientists were certain that it was transmitting coded signals."

SUBJECTIVE PROBABILITY—"No single feature of our lives is more charged with anxiety or passionate beliefs than a gamble such as the toss of a coin to decide an issue. Our experiments in subjective probability give us a glimpse into the mind of the gambler. He seems unable to detach his prediction of an event from outcomes of similar events in the past, although in a sense he may 'know' that the new event is entirely independent of those previous outcomes. Like many children, he is apt to treat luck and ill luck as stores which can be used up, and to think that success in guessing is due to the possession of some uncanny shrewdness or occult power which acts like a divining rod."

NOVEMBER 1907

VALUABLE ROADS—"Good roads in the Mississippi Valley pay better than almost anywhere else in the country, owing to the vivid contrast between them and the natural poor roads. The increase in valuation of property along the line of macadam roads in this section has been up to sixty per cent, and many new, thriving towns are to-day making strenuous efforts to attract settlers and investors through improving roads. It has proved an economical success to increase road taxation in order to secure higher real estate values."

PERFECT CARS—"Nothing at the two fall automobile shows indicates so surely that the automobile has reached the final stage of its development, as the fact that novelties of type are conspicuous by their absence. Outside of the buggy-type machine and the two-engine automobile, there is very little among the exhibits which can be called a radical departure from the all-prevailing type [*see illustration*]."



NEWEST SPEEDY MOTORCAR leaves the weary bicycle-riding constable in the dust, 1907

To see images of more cars from 1907, go to **www.SciAm.com/ontheweb**

FEAR OF DOGS—"The only use for the Eskimo dog is for transportation in winter. Years of training have made this savage beast into an admirable sledge dog, capable of performing marvelous journeys. All the time, however, he has remained a wild animal, as savage as a wolf. Every year one hears of his murderous attacks. Last winter, on a sledge journey which was protracted by blizzards, the pack of dogs fell upon their drivers, and devoured the whole family. For over a year Dr. Grenfell has been hard at work promoting the introduction of the Lapland reindeer into Newfoundland and Labrador, to supplant the treacherous dogs. The reindeer will furnish the population with food, both milk and meat, and also with the best transportation."

NOVEMBER 1857

BUST—"The recent financial crisis, which fell upon us so suddenly, has been very disastrous in its results to the industry of our country. Manufactures have been paralyzed, and no one but an eye-witness can have a conception of their complete and overwhelming prostration. Factories are closed, forge fires are extinguished; the hammer, the saw, the spindle and loom are silent; and men walk about the streets with anxious, care-worn countenances, for although they have willing hearts and ready hands, there is no work for them to do."

LEVIATHAN—"An attempt was made to launch the Great Eastern, the colossal steamship, into the river Thames, London. It was the first and only trial, and the effort to move her beyond a few feet totally failed, and the gigantic vessel, which should have been a 'monster of the deep,' remains as firm, if not firmer, than ever upon the river's bank. When the ship seemed to slip some three or four feet, the men at the windlass madly tried to hold it, but the heavy iron handle flew round like lightning, striking them and hurling five or six high into the air as if they had been blown up by some powerful explosion."

[EDITORS' NOTE: Two men were killed in the accident; the ship was not launched until January 31, 1858.]

SCIENTIFIC AMERICAN, VOL. XCVII, NO. 19, NOVEMBER 9, 1907

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Cosmic Radiation ▪ Smoking and Genes ▪ Shrubs 1, Grasses 0 ▪ Corona Heat

Compiled by Philip Yam

Radiation Redux

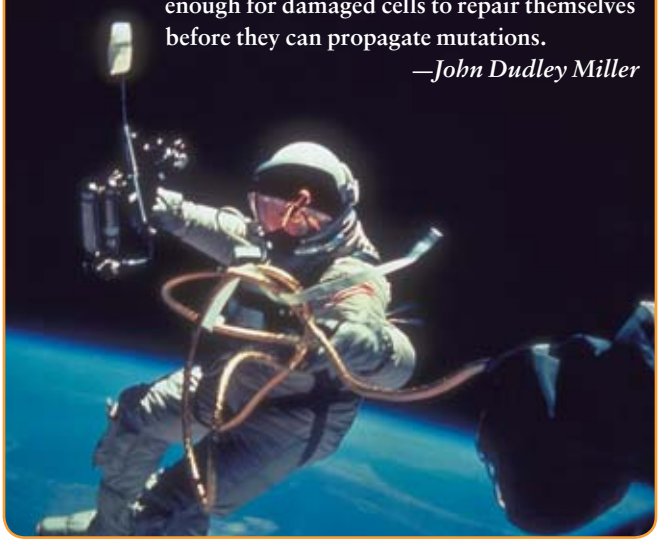
NASA has worried that cosmic rays could undermine a human voyage to Mars [see "Shielding Space Travelers"; SciAm, March 2006]. New simulations and calculations, though, suggest that such lengthy exposure to space radiation may pose only half the health risk that NASA had expected.

The best U.S. space radiation simulations take place at Brookhaven National Laboratory's Booster accelerator, where a facility for space research opened in 2003. The device sends beams of protons, iron and other cosmic elements down a 100-meter-long tunnel to strike human cells, mice and rats. Biologists then assess DNA damage. The Booster has enabled NASA to conduct regular, more realistic experiments beyond the one-week-a-year timetable of the past.

One interesting preliminary finding, according to Brookhaven radiobiologist Betsy Sutherland, is that the lower a proton's energy, the more damage it does. Apparently, lower-energy protons, which travel more slowly, have more time to interact with tissues. In lowering its assessment of risk, NASA also factored in astronauts' better-than-average health and switched from "whole-body" radiosensitivity to organ-by-organ measurements, where new studies have found lower risks for lungs, breasts and the blood system.

Such analyses, if they prove correct, could mean that Mars mission astronauts might not need radioprotective drugs at all, says Francis Cucinotta, NASA's chief scientist for human radiation research. For solar storms and other acute risks, he adds, "we might want to carry them just in case." Possible drugs include retinoids—vitamins that work as antioxidants—and compounds that delay cell division long enough for damaged cells to repair themselves before they can propagate mutations.

—John Dudley Miller



Tobacco Turnoff

The dangers of tobacco smoking are well known [see "Big Tobacco's Worst Nightmare"; SciAm, July 1998]. But the risks persist even after quitting. A possible explanation: smoking permanently affects some genes. Researchers came to this conclusion after analyzing lung samples from 24 current and former smokers and those who have never inhaled. Genes irreversibly affected include those that repair DNA and combat the development of lung cancer. The study appears in the August 29 *BMC Genomics*.

Shrubby Frontier

Scientists have observed how climate change has altered global ecosystems [see "Spring Forward"; SciAm, January 2004]. A five-year experiment reveals details of just how. Researchers exposed sections of a short-grass prairie to twice the amount of carbon dioxide it ordinarily would receive. The balance of plant species changed; the area became dominated by a 40 percent rise in woody shrubs, which metabolize CO_2 more efficiently than grasses do. The results, appearing in the September 11 *Proceedings of the National Academy of Sciences USA*, confirm the hypothesis that, in a CO_2-enriched world, woody shrubs will replace grasses on the American rangeland. The change could affect livestock and other grazers—certainly the deer and the antelope will have fewer places to play.

Heat Waves

Travel away from the sun's surface, and it actually gets hotter, increasing from 5,000 to two million degrees Celsius. Just how the sun's atmosphere, or corona, heats up so much has puzzled physicists [see "The Paradox of the Sun's Hot Corona"; SciAm, June 2001]. One proposed heating mechanism is magnetic oscillations. These oscillations, called Alfvén waves, would transport energy from the surface to the corona, which extends millions of kilometers. Astronomers have now detected Alfvén waves in the corona for the first time. In the August 31 *Science*, researchers describe how they measured these waves, which roughly follow the sun's magnetic field. The detected Alfvén waves alone do not carry enough energy to heat the corona to its blazing levels, but the team suspects that more accurate measurements will show that Alfvén waves are actually larger and able to deliver the heat.

SIGHTSEEING ARCHIVE/GETTY IMAGES (*astronaut*); STILL IMAGES/GETTY IMAGES (*cigarette*); TIM FITZHARRIS *Minden Pictures* (*grasslands*)

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BEHAVIOR

The Genetics of Politics

A study finds that biology strongly governs voter turnout BY CHARLES Q. CHOI

Aristotle once noted, "Man is by nature a political animal." What may be the first study to investigate this idea scientifically now controversially suggests that Aristotle may have been right—the desire to vote or abstain from politics might largely be hardwired into our biology.

When it comes to predicting who will vote, researchers have looked at "everything but the kitchen sink," says political scientist James Fowler of the University of California, San Diego. Theorists speculate on factors such as age, gender, race, marital status, education, income, home ownership, political knowledgeability and church attendance. But studies indicate that each one exerts only a small effect.

Fowler notes that people who vote often do so even when they know their lone ballot will not change the outcome of an election. "It's almost like voters are programmed to keep voting, even when their common sense tells them it is probably useless," he states. At the same time, "many people never vote, no matter what. So I started to wonder if there was something very basic at the biological level."

Fowler and his colleagues thus turned to identical and fraternal twins. If the decision to vote is based in part on genetics, they reasoned, identical twins should behave more alike than fraternal twins, because identical twins share all of their DNA, whereas fraternal twins share only half on average.

The researchers matched data from the Southern California Twin Registry with publicly accessible electronic voter registration and turnout records from Los Angeles County. Their analysis of voting histories for 326 identical and 196 fraternal twins suggests that genetics was responsible for 60 percent of differences in voting turnout between twin types, with the rest coming from environmental or other factors.

HARDWIRED? People may have a genetic predisposition to vote. The Miami citizens shown above used electronic ballots to pick candidates in 2004.

J. PAT CARTER *AP Photo*

Fowler and his colleagues also investigated a larger, more nationally representative database from the National Longitudinal Study of Adolescent Health, or Add Health. This study not only asked if participants voted but also inquired about participation in other political activities, such as whether they contributed to campaigns or attended political rallies or marches. The researchers' data on 442 identical and 364 fraternal Add Health twins indicate that genetics underlies 72 percent of differences in voting turnout and roughly 60 percent of differences in other political activity. Fowler, who presented the research at the American Political Science Association meeting in August, claims that preliminary results from the Twins Days festival in Twinsburg, Ohio, also support the findings.

Fowler adds that his team's work does not suggest that genetics can determine *whom* people will vote for, only whether or not they are likely to vote. He also emphasizes that environment most likely plays a significant role in voting: "There is still a lot we can do to shape political behavior in spite of our genetic tendencies."

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If genes do in part control voting, a single gene is unlikely to be responsible—hundreds of genes are probably involved, suggests behavioral geneticist Robert Plomin of King's College London. Fowler hypothesizes that because "we obviously did not vote in large-scale elections in the Pleistocene," the drive to vote or participate in politics may be linked with genes underlying more ancient behaviors, such as innate dispositions toward cooperation. The search for any such genes in our primate relatives could help determine "whether we share the neurobiological underpinnings of cooperation or whether humans are unique in this respect," Fowler adds.

Plomin states that "these findings are strong," but in his analysis of the same data, he concludes that genetics was responsible for 40, and not 60, percent of differences in voting turnout between twin types. Forty percent is still "a lot," he admits, and is also the average estimate of heritability seen in twin studies of personality, suggesting that voting is an example of a genetically influenced personality trait in general.

Behavioral neuroscientist Evan Balaban of McGill University, however, cautions that relying on twin studies as the sole evidence of links between genetics and behavior is a mistake. About two thirds of identical twins actually share the same bloodstream while fetuses, so greater similarities between twins could be attributable not only to sharing genes but "to sharing more similar levels of hormones and other compounds each fetus produces during development," he explains. "So there is a pattern of similarity these researchers have documented that needs to be explained, but genetics is not the only explanation for it."

Charles Q. Choi is a frequent contributor.

Political Races

If the decision to vote is strongly genetic in nature, that does not mean that some races are more likely to vote, emphasizes James Fowler of the University of California, San Diego. Genes vary far more among individuals within races than among races as a whole. "If genetic variation plays a role in voting, it is highly unlikely that it would explain any differences between individuals of different races," he asserts.

ENGINEERING

Repairs without Rivets

Carbon-fiber composites could lead to quick fixes for old bridges BY DAVID APPELL

Investigators still do not know exactly why the I-35W bridge collapsed into the Mississippi River in Minneapolis on August 1, killing 13 people and injuring about 100. But a succession of less spectacular failures over the years has raised concern among the country's bridge engineers. New materials promise to make routine repairs less costly and intrusive, an important consideration in an era in which money for infrastructure is tight. "The days of letting a bridge deteriorate and then simply replacing it are going away," says Mark Hirota, a consultant with Parsons Brinckerhoff and a former bridge engineer for the state of Oregon.

According to a 2005 study by the American Society of Civil Engineers, 27.1 percent of the nation's bridges are either structurally deficient or functionally obsolete—a total of more than 160,000 bridges. The estimated cost to repair these bridges is almost $10 billion a year over the next 20 years. Built in 1967, the Minneapolis structure was a deck truss bridge with multiple steel girders and had been a concern among the state's transportation officials for years. After the collapse, U.S. Secretary of Transportation Mary Peters quickly called for an inspection of all the nation's steel truss bridges similar to the I-35W span. A truss bridge, one of the oldest bridge types, is fairly simple in design and relatively cheap to build as compared with suspension and cable-stayed bridges, but engineers make no generalizations about types especially prone to sudden collapse.

Peters noted that initial inspections had raised concerns about stress on the I-35W bridge's gusset plates, devices that attach steel girders together (with rivets, in the case of the Minneapolis bridge—other options are welds or bolts). She also cautioned states to carefully consider the added stress that repair and construction projects can place on a bridge. Some engineers have recently raised concerns about an incomplete understanding of how gusset plates tear out and fail, such as those expressed in a 2006 paper in the *Canadian Journal of Civil Engineering* by Robert G. Driver of the University of Alberta and his colleagues.

Cracks develop in steel girders and gusset plates because of fatigue and corrosion, and those as small as one eighth of an inch in width can lead to tearing and subsequent structural failure. Traditionally, engineers weld or bolt steel cover plates across these and larger cracks, but this approach has several disadvantages: it adds weight to the bridge, can require costly heavy machinery such as cranes, and often requires traffic diversions.

A possible quick-fix alternative is a new carbon-fiber-reinforced polymer. "It works almost like a Band-Aid," says Hamid Saadatmanesh, a professor of civil engineer-

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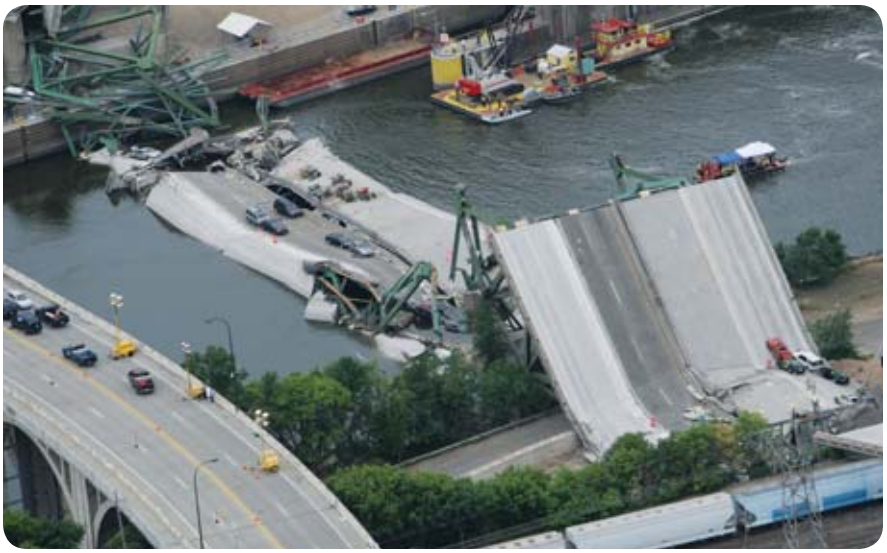

MANDEL NGAN *AFP/Getty Images*

ALL FALL DOWN: The collapse of the I-35W bridge in Minneapolis this past August has sparked concerns about the integrity of other spans.

ing at the University of Arizona. Saadatmanesh developed the material, called CarbonWrap, about six years ago and now sells it through CarbonWrap Solutions.

The polymer is made of woven filaments of glass, carbon and Kevlar, which are placed in a resin matrix. Its tensile strength—the force required to pull it apart—is about 200 tons per square inch, 10 times stronger than steel. The fiber costs $16 a pound and is attached to the bridge girders with a special epoxy. Patching a small girder crack would only cost about $200, including labor; doubling the layers increases the strength by about 30 percent.

"You don't need to drill holes," which can further weaken a structure, Saadatmanesh says. "Instead of taking eight hours" for a traditional patch, he adds, "you can do this in half an hour." In laboratory testing, Saadatmanesh says that CarbonWrap has held through the equivalent of about 10 million trips by a 35-ton truck. It resists corrosion, an important consideration given the galvanic currents that can be generated between metallic components on a bridge, and has withstood a pH 2.5 solution for two years. Steel would melt in just a few hours in such an acidic bath.

CarbonWrap has shored up water pipes and light poles, but it has yet to patch bridges—engineers are conservative by nature. "It takes a while to adopt a new thing," explains Taichiro Okazaki, a civil engineer at the University of Minnesota who is heading a team of researchers to examine the Minneapolis collapse. "New materials have to be very reliable, and it takes many years to develop trust." Bridge engineers have begun talking to Saadatmanesh's company, and Okazaki suggests that the first applications for CarbonWrap might be on small, lightly trafficked bridges, such as those found on golf courses. Such novel materials may play a crucial role in addressing the nation's aging infrastructure, although ultimately they cannot replace commitments to timely inspections, better designs and new bridges.

David Appell is based in Portland, Ore.

NANOTECH

A Simple Mimic

Water droplets encased in fat simulate cell membranes BY GARY STIX

A double layer of fat marks the property line that separates DNA, mitochondria, the endoplasmic reticulum and the rest of the elaborate internal machinery from everything that exists beyond the confines of a cell. Molecules of protein that poke through this lipid bilayer serve as communication channels for incoming and outgoing messages that regulate the body's most basic activities.

Biologists have tried for decades to produce a simple model of the cell's plasma membrane, particularly the openings to the outside world known as ion channels. The goal is not just academic. More than 60 ion-channel gene mutations have been linked to human diseases. Some drugs that target ion channels have achieved blockbuster status. Pharmaceutical companies could deploy such a model to simulate how new drugs interact with membrane proteins.

An ideal model has remained elusive. Some laboratories have focused on producing protocells—empty shells that are filled with cellular machinery that makes proteins or causes a fake cell to divide. Others have just created imitation cell membranes that simulate the electrical and chemical traffic at the cellular gateway. The most ambitious of these endeavors points toward a marriage of the work on protocells with membrane mimicry. It involves research at the University of Oxford and Duke University in which water droplets enveloped in a layer of fat come together to form bilayers into which membrane channels or pores can be inserted.

The droplets are manufactured by dis-

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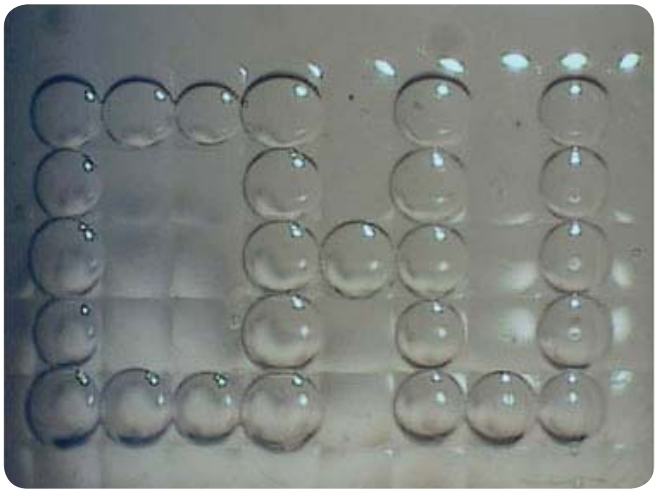
solving lipids in a small reservoir of oil. Water droplets measuring less than a millimeter across join the mix, causing the lipids to form a coating on the droplets of no more than half the thickness of a cell membrane. "These systems are very stable, like a robust soap bubble with a skin that's a biological surface," notes Matthew Holden, a postdoctoral fellow at the Oxford laboratory of chemist Hagan Bayley, where much of the research took place [see "Building Doors into Cells," by Hagan Bayley; SCIENTIFIC AMERICAN, September 1997].

Dubbed "liquid Lego," the droplets are intended to be a test bed for exploring the workings of not just a single cell membrane but an entire network of protocells. When a droplet joins with one of its neighbors, the two form the equivalent of a complete membrane. Ultimately, the team would like to engineer droplets with different characteristics, varying the pH of the water inside a droplet or the types of membrane channels used. Alternatively, different droplets may contain different drugs. The objective is to demonstrate how cells that constitute heart, brain or lung tissues communicate among themselves. "The new preparation of nanodrops holds enormous promise," says Bob Eisenberg, chairman of biophysics and physiology at Rush University Medical Center in Chicago. "It will allow manipulation of ion channels in new ways; it will allow systems to be built from arrays of drops that show interesting properties."

For the moment, simulating the pulsations of a heartbeat on a chip remains a dream, although the necessary tools are starting to come forth. In the June 16 online *Journal of the American Chemical Society,* Holden and his colleagues recount how they sent current through a chain of 16 droplets by plugging electrodes into various droplets along the network. They inserted bacterial pores (surrogates for ion channels) into the lipid protomembranes and also showed how electrodes could be used to add or remove droplets while keeping the network intact.

Two droplet experiments demonstrated the prospect of one day building autonomous systems that power themselves or make their own components. The paper describes a battery devised by infusing droplets with differing concentrations of ions and, separately, a current generated when droplets were infused with a membrane protein (bacteriorhodopsin) that causes protons to flow when exposed to green light.

The last unrealized step, of course, would be to insert DNA and organelles from a cell that could encode the desired ion channel from within the droplet. Then all scientists might have to do is just turn on the lights and watch the show.



WILLIAM HWANG *University of Oxford*

LIQUID LEGO: Fat-covered droplets snap together to form the initials for the University of Oxford, where these imitation cells, each of which holds 200 nanoliters of water, were first concocted.

HEALTH

Scared Off Silicone

Liability fears trump science for ulcer-beating injectable silicone BY MELINDA WENNER

Of the 20 million Americans suffering today from diabetes, one million will probably be killed by their feet. A diabetic foot ulcer and its attendant complications constitute a surer death sentence than colorectal cancer—just over half of all diagnosed patients survive for five years. More startling than these statistics, however, is that for 40 years, physicians have known about a safe medical procedure to prevent these ulcers. But the U.S. Food and Drug Administration has yet to approve the treatment.

Diabetics develop foot ulcers because of nerve damage. Injury to motor neurons deforms the feet, creating pressure points that are susceptible to harm during walking, and damage to sensory neurons prevents patients from feeling anything. "They lose the gift of pain," explains David Armstrong, a surgeon and a podiatric medicine expert at Rosalind Franklin University in Chicago. Unaware that anything is wrong, patients continue to walk and end up wearing out the protective fat pad between the skin and the bone in those areas. Eventually the skin erodes away, and an ulcer forms. They "wear a hole in their foot just like you or I might wear a hole in our shoe," Armstrong says. Left untreated, an ulcer can become infected or gangrenous and can lead to foot or leg amputation—if it does not cause sepsis, a blood infection, first.

The best way to prevent ulcers is to relieve pressure on the exposed parts of the feet. Doctors have historically prescribed

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special shoes or inserts, but few people remember to wear them because they are not in any pain, says Sol Balkin, a podiatrist who recently retired from the Los Angeles County + University of Southern California Medical Center. So, after seeing a hospital lecture in 1963 about the use of injectable liquid silicone to boost breast size, Balkin got an idea. What if he could inject a small amount of silicone into the ball of the foot to replace the lost fat pad and redistribute foot pressure—creating a kind of internal orthotic?

Balkin tested his idea on a few willing patients and was elated to find that it worked. "Essentially the silicone acts as a soft-tissue substitute," he explains. He began injecting more patients, following their symptoms for years and gathering postmortem data; in the meantime, a separate clinical trial was conducted in England. All the peer-reviewed studies revealed that the injections safely and effectively prevent ulcers, although sometimes patients require boosters.

The treatment, however, has yet to make it to market, and, as Balkin contends, it's all politics. In 1998 silicone manufacturer Dow Corning (which also sponsored one of Balkin's studies) settled a multibillion-dollar class-action lawsuit after allegations that silicone breast implants caused immune disorders and cancer—a suit that forced Corning out of the medical silicone implant business entirely. Silicone had become synonymous with poison, an unfortunate association that has lingered despite evidence that the material is perfectly safe, says Dick Compton, CEO of NuSil, the world's biggest supplier of medical silicone for long-term implantation. "The safety of silicones, the information on that, is abundant," Compton maintains.

In 1999 the Institute of Medicine, an organization designed to provide evidence-based advice on health issues, largely debunked any association between silicone, immune disorders and cancer. But the FDA has been slow to respond—it finally lifted its ban on cosmetic silicone breast implants in November 2006—and the agency admits that it still "has serious safety concerns about liquid injectable silicone," according to FDA spokesperson Josephine Tropea. Only one product, an injectable liquid silicone treatment for retinal detachment, has been approved to date. (Balkin has used injectable liquid silicone in an "off-label" manner to treat his patients.)

Despite the frustrations, Balkin never gave up—he continued to try to recruit companies to pursue FDA approval for his treatment. Four expressed interest, only to back out later because of fears over product liability. "They said, 'We don't want to go through what Dow Corning went through,'" Balkin recounts. It does not help that the product cannot be patented, he adds, because it is just liquid silicone.

But the tide may be turning. Balkin has started working with a Tennessee-based company that expects approval to market the treatment in Europe by the end of the year. Soon afterward the company plans to approach the FDA. Still, the agency may decide that additional studies are necessary, which could cost millions and take years to complete, Balkin says.

But he has a good feeling that this time, science might just prevail over politics. "To have lived through this, and hopefully live long enough to see it finally happen in my lifetime," says Balkin, who recently turned 82, "I'd be one happy guy, to say the least."

Melinda Wenner is based in New York City.

ENERGY

Rotor in Motor

Replacing aluminum with copper in electric motors saves energy BY STEVEN ASHLEY

A few percentage points of improvement in energy efficiency are rarely noteworthy, but those digits add up fast when the technology involved annually consumes several hundred billion kilowatt-hours of electricity worldwide. About two thirds of the juice used by American industry, for example, drives the countless electric motors running pumps, compressors, fans, conveyors and other devices in factories and plants nationwide, according to the U.S. Department of Energy. After a decade-long R&D effort, engineers have succeeded in wresting a bit more efficiency from these motors. And industry has just begun to take notice.

Small versions of so-called three-phase AC induction motors, which generate from one to 20 horsepower, can convert as much as 90 percent of the power they draw into rotary mechanical force. Today's standard designs feature rotors—rotating electromagnetic armatures—composed of die-cast aluminum, but motor engineers have

On the Road with Copper

Several innovative vehicles incorporate large, high-efficiency electric motors with die-cast copper rotors. The Tesla Roadster (*right*), a battery-powered electric sports car from Tesla Motors that can run from zero to 60 miles an hour in 3.9 seconds, owes its 200-mile driving range to a 250-horsepower copper-rotor motor. The U.S. Department of Defense's next-generation Heavy Expanded Mobility Tactical Truck, a multiton hybrid transport vehicle that can power field hospitals, command centers or airstrips, uses a 140-horsepower electric motor with a die-cast copper rotor to drive each wheel.

TESLA MOTORS

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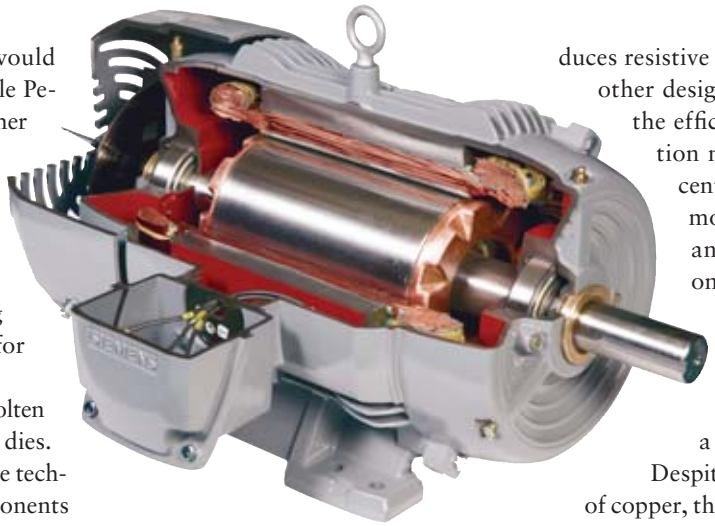
long known that copper rotors would save energy, says metallurgist Dale Peters. "Copper has substantially higher electrical conductivity than aluminum, which significantly cuts the resistive losses in rotors," he explains. "But copper melts at 1,083 degrees Celsius, significantly hotter than aluminum's melting point, which poses big problems for die casters."

In die casting, machines force molten metal into reusable steel molds, or dies. Manufacturers traditionally use the technique to fabricate the rotor components from aluminum. But when molten copper repeatedly contacts the cold steel of a casting die, Peters says, "the high heat causes the die to continually expand and contract," compromising its molding surface.

In the late 1990s Peters and other researchers at the Copper Development Association (CDA), an organization devoted to expanding the market for copper, established a program to find a reliable and cost-effective copper die-casting technique. CDA specialists first analyzed the phenomenon in detail using 3-D computer-modeling methods. In time, they realized that preheating the steel dies offered a solution. But because higher temperatures lower the durability of even heated steel dies, the team turned to tools made of heat-resistant nickel-base alloys.

The resulting die-cast copper rotor reduces resistive losses and, together with other design refinements, can boost the efficiency of small AC induction motors to around 93 percent. Moreover, the resulting motors are smaller, lighter and longer-lasting. At prices only about 5 percent higher than their premium predecessors, the new motors can often pay for themselves in less than a year.

Despite the high and rising cost of copper, the CDA has managed to encourage electric-motor manufacturers to start adopting the alternative. Companies such as Siemens and SEW Eurodrive now offer small, industrial copper-rotor electric motors, and four U.S. competitors are working to implement the technology. Most significantly for energy savings, though, motor makers in China, India, Japan and Brazil are gearing up to market the improved technology, a trend that is particularly important because non-U.S. motors of this class are typically much less energy efficient.



COPPER POWER: In replacing its aluminum counterparts, the distinctive copper rotor (*center*) results in an ultraefficient electric motor—the product of a long research effort led by a copper industry consortium.

SIEMENS ENERGY & AUTOMATION

GEOPHYSICS

Higher Power

Earth's heat keeps continents afloat and land above sea level BY SARAH SIMPSON

Topography seems easy to explain when beholding jagged summits such as Colorado's Rocky Mountains or California's Sierra Nevada range. After all, these mountains mark spots where the continent grew thick during violent collisions with other tectonic plates: the land crumpled and heaved skyward, like the hood of a car buckling in a head-on crash.

But surface-shaping geologic forces account for surprisingly little of the planet's highs and lows. About half of North America's elevation actually results from the planet's internal heat. Minus that warmth, most land would sink below sea level, say University of Utah geophysicists Derrick Hasterok and David S. Chapman. Based on their recent calculations, parts of the Rockies and high Sierras would shrink to mere islands, whereas cities such as New York, Los Angeles and even mile-high Denver would slip 200 meters (700 feet) or more underwater.

Scientists have long known that heat must be part of the reason that the continental crust, which is about 40 kilometers thick on average, floats like foam atop the denser rocks of the mantle underneath. Although the crust's temperature varies from place to place, its bottom side is an estimated 400 degrees Celsius at its coldest. About 60 percent of that heat rises from the earth's fiery interior; the rest builds up from the decay of radioactive elements. And, like most materials, the rocky crust expands—and thus floats higher—the hotter it is.

But despite this seemingly simple relation between temperature and elevation, observed topography correlates poorly with the measurable heat flow. In other words, hotter does not always mean higher, Hasterok explains. Such discrepancies exist because the makeup of continental crust, which also varies from one region to the next, exerts its own influence on buoyancy; some rock types are denser than others, regardless of temperature.

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BEYOND THE BLACK BOX

The Forensics of Airplane Crashes

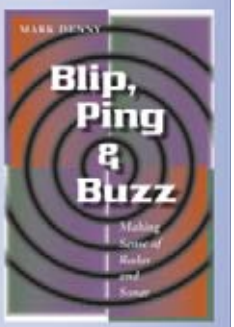
GEORGE BIBEL

Shows how crash investigators use physics, aerodynamics, and mechanical engineering to determine the probable cause of a crash and how resulting safety recommendations are incorporated to make flying safer.

BLIP, PING, AND BUZZ

Making Sense of Radar and Sonar

MARK DENNY



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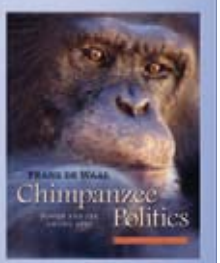

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The other complicating factor is the crust's variable thickness: geologic forces not only pile up mountains in some places but also stretch the crust thin in others.

To isolate heat's role, Hasterok and Chapman came up with calculations that strip away the effects of composition and thickness for 36 geologic provinces across North America. For the resulting elevations, which reflect the thermal contribution alone, hotter usually does mean higher. The Colorado Plateau sits about 1,500 meters (5,000 feet) higher than the Great Plains even though the same rocky types underlie the two regions, mainly because the crust below the plateau is an estimated 150 degrees C warmer than the crust below the plains.

"If the elevation doesn't reflect the heat flow, then we know there's something else going on," Hasterok says. One region of crust under northern Canada, for example, is hotter than the thermal elevation suggests it should be—almost certainly because a higher-than-average concentration of radioactive isotopes is heating up rocks near the surface, Hasterok says. (To contribute to buoyancy in any notable way, that heat would have to warm a deeper part of the crust.) In

Stepping Up

Seattle could have been the U.S.'s other mile-high city: it would sit at an elevation of 1,813 meters (5,949 feet) above sea level were it not for a cold slab of seafloor beneath it. That slab, which is diving, or subducting, eastward underneath the Pacific Northwest, insulates that part of the continental crust from hotter temperatures below it. If that heat were allowed to rise, the crust would expand and become more buoyant: remove the slab, and Seattle shoots skyward.

BARRY SWEET *AP Photo*

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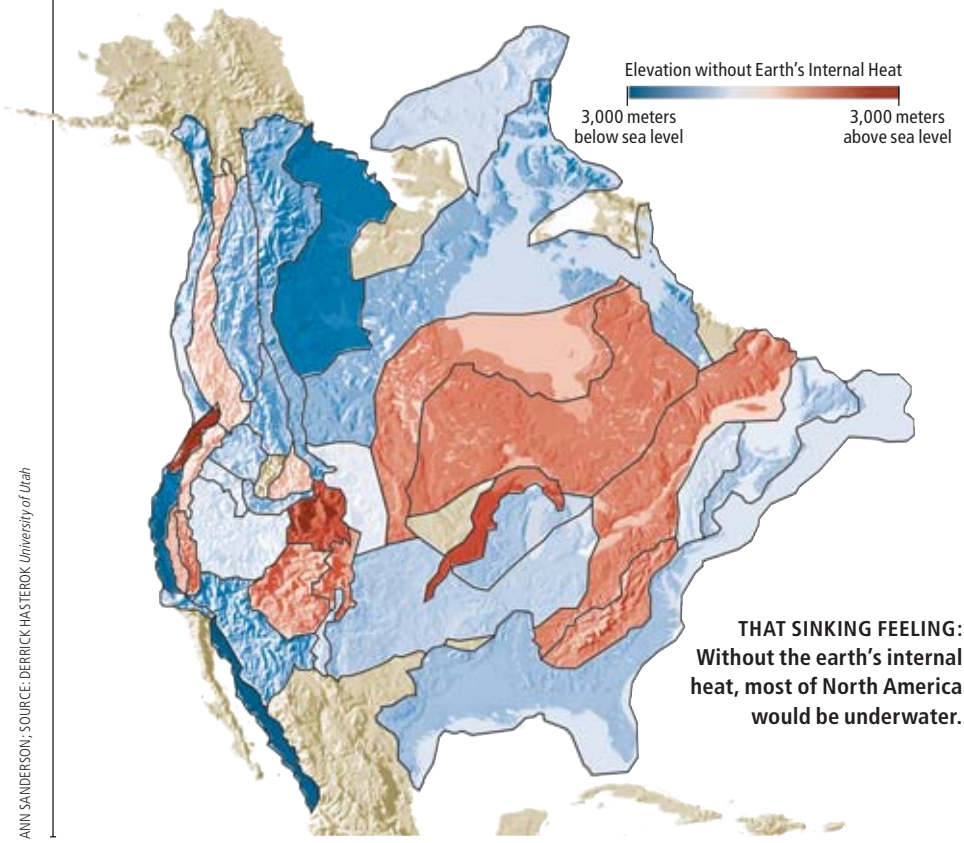

ANN SANDERSON; SOURCE: DERRICK HASTEROK *University of Utah*

THAT SINKING FEELING: **Without the earth's internal heat, most of North America would be underwater.**

general, then, regions that look hot relative to their thermal elevations could be good targets for uranium or thorium mining, Hasterok notes.

A mismatch between thermal elevation and heat flow can also tell scientists something about the timing of certain geologic events. That the thermal elevation of the Sierras is higher than expected suggests that a particularly hot chunk of mantle must be heating that part of the crust from below. That heat simply has not had enough time to rise all the way to the surface, where scientists can measure it directly.

Such insights into heat's contribution to elevation are critical for modeling how mountains are built and how oceans form, among other geologic processes, because crustal rocks tend to weaken—and become more likely to break or fold—the warmer they get. Hasterok and Chapman are already applying lessons from North America to decipher the ups and downs of the other continents as well.

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ASTROPHYSICS

Dark Riddles

Behavior of galaxy cluster may shift thinking about gravity BY GOVERT SCHILLING

Dark matter, the substance no one has ever seen, continues to baffle cosmologists. New observations of the distribution of dark matter in a distant cluster of galaxies may even force scientists to propose a fifth force of nature—or to rewrite the basics of Newtonian gravity. Little wonder that many researchers hope that the unsettling result will turn out to be an observational fluke.

Giant clusters of galaxies consist of two observable components. The galaxies themselves can be seen with large optical telescopes. The hot, tenuous gas in between the galaxies can be spied and mapped by x-ray satellites such as NASA's Chandra X-ray Observatory. But according to current wisdom, a galaxy cluster may have a third, invisible component: mysterious dark matter that pulls in the atoms from which stars and galaxies form. Dark matter can be charted only by the subtle way its gravity slightly bends light, altering the shapes of faint galaxies in the distant background. The ability to detect such "weak lensing" has seen major improvements during the past decade.

Last year researchers hailed observations of the "Bullet Cluster" as the first definitive proof of the existence of dark matter. The Bullet is actually two clusters in the process of merging. As expected, the colliding gas in the two clusters is dragged to the common center of gravity, while the individual galaxies move on relatively unimpeded. Crucially, weak-lensing observations revealed the existence of huge amounts of dark matter coinciding with the galaxies, not with the gas. That is exactly the prediction of popular theories, in which dark matter hardly interacts with itself and in which galaxies form and reside in regions where the dark matter density is highest.

But now another cluster spoils the party. At a distance of 2.4 billion light-years in the constellation of Orion, Abell 520 also consists of two colliding clusters. But according to a team led by Andisheh Mahdavi and Henk Hoekstra of the University of Victoria in British Columbia, the dark matter in Abell 520 does not appear to be tied to the galaxies. Instead the lensing observations—carried out with the 3.6-meter Canada-France-Hawaii Telescope on Mauna Kea in Hawaii—indicate that enormous amounts of dark matter are concentrated in the core of the colliding pair, where most of the hot gas is found but few galaxies are seen. As the team writes in its October 20 *Astrophysical Journal* paper, this dissociation between dark matter and galaxies "cannot be easily explained within the current ... dark matter paradigm."

"It's a remarkable result," says cosmologist David Spergel of Princeton University. "A conservative explanation would be that not all dark matter concentrations are efficient in the formation of stars and galaxies. The alternative is that dark matter interacts with itself in response to an unknown, fifth force of nature, which only involves dark matter." Under the influence of such an attractive force, two clouds of dark matter could no longer pass through each other unimpeded but would eventually be dragged like the hot cluster gas, ending up in the common center of gravity of the colliding clusters.

Post-doc and Visiting Professor Positions at Politecnico di Torino, Italy

In the framework of its strategy for the establishment of an "International Campus" in Turin, the Politecnico di Torino is looking for brilliant postdocs, young researchers, and visiting professors, wishing to collaborate in the projects of the institution.

For Postdocs and Researchers, the Politecnico proposes contracts of 2 years (renewable up to 4 years), with a financial support of approx. 1.500 Euros per month. Depending on the position, it is also contemplated an amount between 8.000 and 13.000 Euros, to partially cover the mobility costs.

Visiting professors contracts may last from 6 to 12 months, and the monthly support is of 4.500 Euros (submitted to taxes). An amount of 10.000 Euros is contemplated to partially cover the mobility costs.

The Call is open until November 30, 2007.
For more information please visit the Web page:
http://www.polito.it/visiting

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Robert Sanders of the University of Groningen in the Netherlands offers a third solution to the problem: modified Newtonian dynamics (MOND). Invented in the early 1980s by Mordehai Milgrom of the Weizmann Institute of Science in Rehovot, Israel, MOND proposes that the observed signatures of dark matter in fact result from a different behavior of the force of gravity. In particular, gravity in low-acceleration regions (such as the outskirts of galaxies) would weaken linearly with distance, not exponentially. Even in a MOND universe, some dark matter has to exist, but it could consist of "normal" particles, such as neutrinos, instead of mysterious, undetected stuff. Sanders says that he and Milgrom are writing a paper on how MOND can accommodate the cluster observations. "These new results—if they are real—could be an outstanding success for MOND," he states.

X-RAY: NASA/CXC/UVIC./A. MAHDAVI ET AL.; OPTICAL/LENSING: CFHT/UVIC./A. MAHDAVI ET AL.

A MYSTERIOUS MATTER: A composite image of galaxy cluster Abell 520 shows amid the galaxies a distribution of dark matter (*blue*) and hot gases (*pink*) that may suggest a fifth force of nature.

If they are real, indeed. Douglas Clowe, now at Ohio University, has his doubts. Last year Clowe was the lead author of the paper on the Bullet Cluster. "We have separate [weak-lensing] data on Abell 520," he notes, "and our results do not agree with those of Mahdavi's team." Clowe argues that the statistical significance of Mahdavi's results is not particularly impressive. Spergel agrees that the Abell 520 results are "suggestive but not yet convincing." Luckily, new Hubble Space Telescope observations of Abell 520 are in the pipeline. As Clowe puts it: "If they confirm the ground-based observations, it's time to start worrying."

Govert Schilling writes about space science from Amersfoort, the Netherlands.

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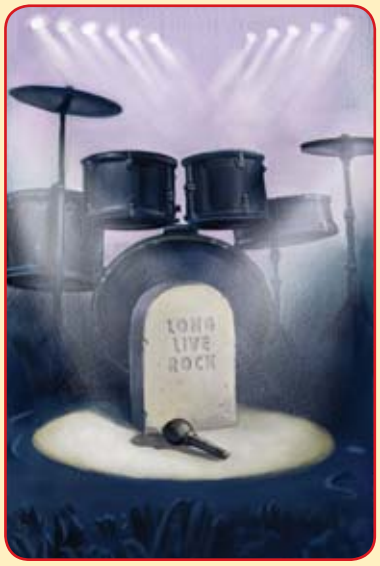
Data Points



Live Fast, Die Young

Living fast is a rock 'n' roll cliché, and now scientists have quantified that speed. They analyzed the fates of European and North American musicians who became famous between 1956 and 1999, based on the artists' appearance in a 2000 poll of the all-time top 1,000 albums. The genres covered were rock, punk, rap, R&B, electronica and new age. Although the celebrities studied do not affect overall mortality statistics, the scientists worry that their risky behaviors could negatively influence their millions of fans.

Number of famous musicians studied: 1,064

Number who died by 2005: 100

Median age of death of:
North American celebrity: 41.78
European celebrity: 35.18

Percent of deaths related to drug and alcohol use: 31

Risk of early death compared with general population (within first 25 years of fame):
1.7 times

SOURCE: Journal of Epidemiology and Community Health, *October 2007*

PHYSICS

Molecules with Antimatter

For decades, researchers have known that the electron and its antiparticle, the positron, can join together to form a short-lived, hydrogenlike atom dubbed positronium. Now scientists at the University of California, Riverside, have managed to get two positronium atoms to stick together to form a molecule—di-positronium. The researchers first collected some 20 million positrons in an electromagnetic trap. They then fired the positrons in an intense nanosecond-long burst onto a microscopic spot on a thin, porous silica film. The positrons diffused into the pores, pulling in electrons and forming roughly 100,000 molecules of di-positronium. Investigating these molecules could open up new studies of antimatter and explain why so little of it exists in the universe. The gamma rays generated when electrons and positrons eventually collide might also be used to develop directed-energy weapons or to help ignite fusion reactions in nuclear power plants.

Make more sense of the matter in the September 13 *Nature*. —*Charles Q. Choi*

PERCEPTION

Explaining Out-of-Body Experiences

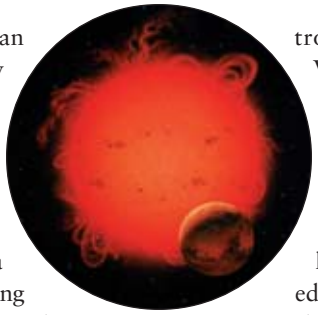
SCI AM

Video cameras can create an out-of-body sensation. Researchers had volunteers sit in front of two cameras set to film their backs. A special headset displayed the images from the left camera to the left eye and the right camera to the right eye. An experimenter then simultaneously stroked a subject's chest and performed a similar motion just below the cameras' view, chest level. Subjects reported being overcome by the strange sensation that they were sitting where the cameras were rather than in their own bodies. Another experiment persuaded subjects that they were not standing where they really were. The findings suggest that the consciousness of a self in our body is based on the brain processing and correlating inputs from the various senses. These results, described in the August 24 *Science*, further indicate that self-consciousness begins with the awareness of a self in a particular body. —*David Biello*

ASTRONOMY

Red Giant Survival

SCI AM



Astronomers have detected an exoplanet that most likely survived the red giant phase of its parent star. V391 Pegasi belongs to a class of subdwarf stars that vary in brightness every few minutes. Researchers noticed a regular variation in the timing of these pulsations, which indicates the presence of a planet at least 3.2 times the mass of Jupiter. The nature of subdwarfs implies that the planet once orbited about one Earth-sun distance, or astronomical unit (AU), from V391 Pegasi; the gap closed to 0.3 AU during the star's red giant phase. After V391 Pegasi lost its outer mass to become a dwarf—it has shrunk from 0.9 to 0.5 solar mass—the planet migrated farther away.

The finding, which arguably supports the theory that Earth might survive the sun's red giant phase (as it might appear in the illustration), is in the September 13 *Nature*. —*JR Minkel*

LYNETTE COOK *Photo Researchers, Inc. (red giant star)*; ILLUSTRATION BY MATT COLLINS

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In Brief

SQUATTERS FOR SUBURBIA

The detritus of human habitation reveals that Tell Brak, an ancient city in northeastern Syria, was urbanized more than 7,000 years ago and boasted suburbs most likely filled with immigrants as far back as 6,200 years ago. Instead of an ancient ruler willing a city into existence, analysis of clay potsherds show a more haphazard, perhaps squatter-promoted growth pattern. All told, the city swelled to cover 130 hectares (321 acres) by 3400 B.C., according to a paper in the August 31 *Science*. —*David Biello*

BEE BUG

A mystery illness last winter wiped out 45 percent of bees among nearly one quarter of commercial U.S. beekeepers. Sophisticated genetic analyses have revealed the presence of an obscure bee bug, the Israeli acute paralysis virus, in almost all beekeeping operations affected by "colony collapse disorder" but in only a single healthy one. Pesticides and other stressors may have contributed to hives' vulnerability to the virus, which apparently spread from Australia three years ago.

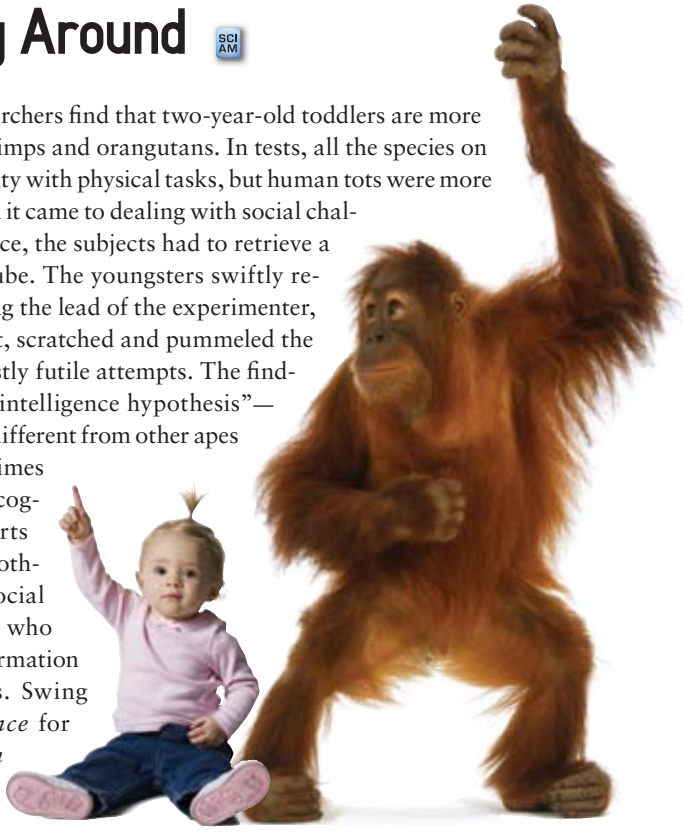
—*JR Minkel*

VENUS-SAFE MICROCHIP

NASA not only aims for better rocket ships but also for better rocket chips. Past microchips could not withstand more than a few hours of searing heat before failing. Electronics engineer Phil Neudeck of the NASA Glenn Research Center and his colleagues have now built a chip that can continuously operate for 1,700 hours at 500 degrees Celsius, at least 100 times longer than before. This heat resistance could lead to circuitry capable of withstanding the heat of the surface of Venus or, nearer to Earth, the heat of jet engines or oil well drills. —*Charles Q. Choi*

EVOLUTION

No Monkeying Around

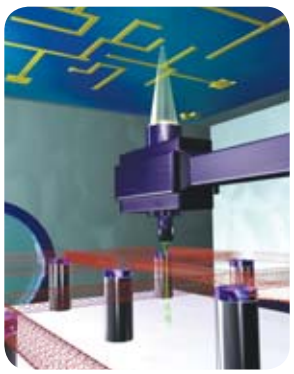


Score one for the tykes—researchers find that two-year-old toddlers are more socially mature than adult chimps and orangutans. In tests, all the species on average showed a similar facility with physical tasks, but human tots were more than twice as competent when it came to dealing with social challenges. In one task, for instance, the subjects had to retrieve a piece of food from inside a tube. The youngsters swiftly removed the morsel by following the lead of the experimenter, but the chimps and orangs bit, scratched and pummeled the container in a number of mostly futile attempts. The finding contradicts the "general intelligence hypothesis"—which states that humans are different from other apes because our brains are three times bigger, allowing for greater cognitive skills. Instead it supports the "cultural intelligence hypothesis," in which heightened social skills are unique to humans, who needed them to exchange information within groups and cultures. Swing open the September 7 *Science* for more. —*Nikhil Swaminathan*

NANOTECH

Cross-Circuiting to Nanotubes

Carbon nanotubes would make ideal wires in advanced microchips, because electricity can flow through them more quickly than it can through silicon. But a method to easily integrate such tiny, sticky, floppy strands into circuits has proved elusive. Now scientists report the first simple, inexpensive technique for building large-scale networks of single-walled carbon nanotubes. The process, developed by Yael Hanein of Tel Aviv University and her colleagues, first involves growing nanotubes between catalytic spots on top of silicon pillars. The nanotubes form a horizontal network between the spots, and the properties of the nanotubes can be tailored based on the catalysts selected. The method can create circuit patterns consisting of hundreds of nanotubes, and the extraordinarily strong nanotubes can then be stamped onto a variety of surfaces, such as silicon or plastic.



CARBON NANOTUBE NETWORK could be grown across pillars, then mapped and stamped onto an electronic circuit.

The researchers describe the results in the September 12 *Nano Letters*.

—*Charles Q. Choi*

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COURTESY OF ZEEV ABRAMS AND YAEL HANEIN *Tel Aviv University* (*nanotubes*); DON FARRALL (*bee*), GERRY ELLIS (*honeycomb*), NICOLE HILL (*baby*) AND DAVE KING (*orangutan*) *Getty Images*

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SciAm Perspectives

Build Diplomacy, Not Bombs

The U.S. needs a new defense strategy, not new nuclear warheads

BY THE EDITORS

The global nuclear weapons scene is changing, yet the U.S. is promoting a costly program to replace its warheads according to an outdated cold war policy. More thinking should precede more spending.

In July the secretaries of defense, state and energy issued a simple three-page document saying that the country's strategy is to deter aggression and that nuclear weapons play the essential role. The statement calls for replacing thousands of aging warheads with new Reliable Replacement Warheads (RRWs), with the insistence that the swap does not violate the Nuclear Non-Proliferation Treaty because it does not provide any new military capability—a position some nations dispute (see "A Need for New Warheads?" by David Biello, on page 80). The note also benevolently rationalizes that such a swap would "assure our allies that the U.S. nuclear arsenal continues to serve as the ultimate guarantor of their security, thus obviating any need for them to develop nuclear weapons of their own."

This view hardly amounts to enlightened policy. The statement itself acknowledges as much in the very first paragraph, noting that "every American administration since President Truman's day has formulated U.S. national security policy in much the same terms."

Indeed, in the decades since World War II, the U.S. has maintained thousands of nuclear warheads that could be launched at a moment's notice. According to the original strategy, this capability would deter other nations from building nuclear arsenals, because if one country launched its missiles the U.S. would, too, assuring mutual destruction. Rational or not, such a strategy fit a world in which two superpowers had stockpiled enough warheads to destroy the planet.

But today nine countries have nuclear weapons, and the portrait of enemies and allies is much more complex. Although Russia is annoyed at America's interest in building an antimissile defense system—to the point of testing, in September, the largest nonnuclear bomb ever built—it is also a partner in a wider war against terrorism. China has targeted more of its missiles at the U.S., and yet it is one of only a few countries to declare that it will not use nuclear weapons unless it is first attacked with them. In September, North Korea, on the verge of joining the fearsome fraternity, said it would disable its atomic programs if the U.S. lifted economic sanctions and removed its name from America's list of countries accused of sponsoring terrorism. Iran, meanwhile, is operating more and more centrifuges to enrich uranium but has no missile or bomber that could reach the U.S.

Furthermore, military experts acknowledge that the most likely nuclear attack on American soil would be a dirty bomb in a terrorist's suitcase or van. How would the U.S. respond—by carpet bombing Afghanistan with nuclear warheads? Clearly, neither al Qaeda nor Iran is deterred by a huge U.S. stockpile.

Even though the 2002 Moscow Treaty on Strategic Offensive Reductions specifies that the U.S. and Russia must each reduce their stockpiles of "operationally deployed" warheads to less than 2,200 by 2012, American defense laboratories say the country must refurbish old warheads through the RRW program. Critics say the program is nothing more than job security for lab personnel. Gradually replacing warheads with upgraded models will cost many billions of dollars, including $21 billion to retrofit industrial infrastructure. Experts disagree over whether an upgrade is even needed. Others note that the new warheads could not be tested, according to the Comprehensive Nuclear Test Ban Treaty, so no one would know if they are "better" or even reliable; therefore, military commanders would not trust them.

Both Democrats and Republicans on Capitol Hill have expressed skepticism about the RRW program, noting that without a modernized defense strategy, funding the program is irresponsible. Change is clearly in order. The U.S. might even consider leading the world toward abolishing nuclear weapons. Former secretaries of state Henry Kissinger and George Shultz, former secretary of defense William Perry and former senator Sam Nunn of

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THE EDITORS' BLOG

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Emotions Recalled in the Sea of Tranquility

Posted by George Musser, Sept. 5, 2007

Last night I saw a preview of *In the Shadow of the Moon,* the new feature-length documentary about the Apollo moon landings. I admit it: I'm a space buff. But I think the movie will appeal even to people who aren't. Its innovation is to explore the emotions of the astronauts, recalled after nearly four decades of reflection.

What emerges defies the stereotype of laconic test-pilot jocks. Here was a group of men, chosen for grace under pressure, who were profoundly moved by their experiences. You feel they could be your own grandfathers, with all their warmth and idiosyncrasies. The filmmaker, David Sington, captures them with a simple style of documentary filmmaking, a perfect antidote to the age of irony: no computer graphics, no opinionated or golly-gee-whiz narration—just the astronauts, in their own words, and the NASA footage, unadorned.

Today I sat in on a series of roundtable interviews with Buzz Aldrin (*Apollo 11*), Alan Bean (*12*), Edgar Mitchell (*14*) and Charlie Duke (*16*). What a pleasure to meet people who are humbled by their celebrity and can never quite get over the fact that anyone cares what they did. Mitchell said he welcomed the opportunity the film gave him to rethink what the events meant to him: "I was too busy at the time to think about how I felt." Aldrin says that dealing with emotions will be one of the great challenges of the space program as it plans to set up long-term bases on the moon and eventually Mars: "The compatibility of people together may be our most serious obstacle to success."

To be sure, the film had its weak points. It neglects the engineers and other behind-the-scenes guys who made the mission possible. The close-up shots of the astronauts' faces are charming at first, but by the umpteenth time I found them a little tiresome. There's also an awkward beat when John Young claims Gus Grissom said he was afraid to complain about poor wiring in the *Apollo 1* capsule, for fear the agency would

continued on page 42

Georgia (who chaired the Senate Committee on Armed Services) have all recently argued for the elimination of such weapons. As arms-control experts note, if the U.S. thinks it needs new nuclear weapons, then it is easy for other countries to believe that they are in need of them, too.

Antiproliferation efforts have succeeded frequently. In the 1980s South Africa built six nuclear bombs, then dismantled them and joined the nonproliferation treaty. Thirteen other nations have terminated active nuclear weapons programs. Even the cantankerous Libyan leader Mu'ammar Muhammad al-Gadhafi announced in 2003 that his country would end its program. A high-profile cut in the U.S. arsenal could recapture some of the moral high ground that antiproliferation efforts thrive on, without eroding the nation's ability to assuredly destroy any country that would attack it. ■

Sustainable Developments

Climate Change and the Law

Even the Bush administration has started to recognize U.S. legal obligations to fight global warming

BY JEFFREY D. SACHS

Global negotiations on stabilizing greenhouse gas emissions in the period after 2012 will commence in Bali in December. The main emitters—including Brazil, Canada, China, the European Union, India, Mexico, South Africa and the U.S.—have recently affirmed their commitment to reach a "comprehensive agreement" in these negotiations. They have also promised to contribute their "fair share" to stabilize greenhouse gases to prevent "dangerous anthropogenic interference with the climate system."

The Supreme Court struck down all the EPA's defenses for inaction.

Of course, one of the biggest obstacles, if not the very biggest, to such an international agreement has been the U.S. itself. The U.S. not only has failed to ratify the Kyoto Protocol—the international framework to limit emissions up to the year 2012—but also has failed to put forward any meaningful stabilization strategy in its place. One of the most shocking aspects of the U.S. failure has been the country's disregard for both international and domestic law. Yet this lawlessness looks set to change.

In recent years the unilateralist foreign policy of the U.S. government has shamelessly ignored or contravened countless aspects of international law, ranging from the Geneva convention to multilateral environmental treaties to which the U.S. is a signatory.

This brazenness has infected the very core of policy discussions in our country. Consider an opinion piece by two distinguished professors of law at the University of Chicago, who argued in the *Financial Times* on August 5 that the U.S. has no obligations to control greenhouse gases and that if other countries don't like how the U.S. behaves, they might think about paying the U.S. to cut its emissions.

BRUCE GILBERT/EARTH INSTITUTE

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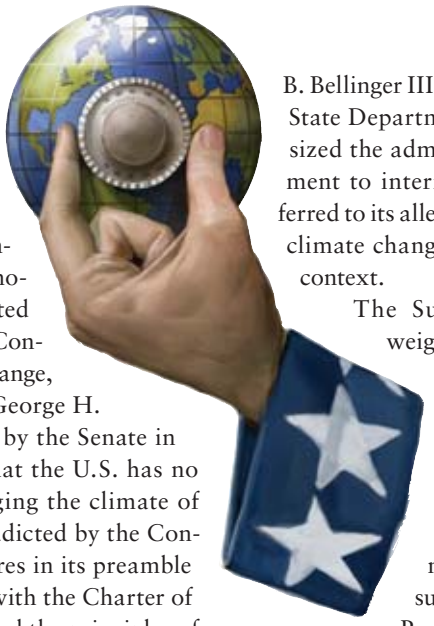

Stunningly, the law professors completely neglected that the U.S. is already bound to take steps to stabilize greenhouse gases in the atmosphere under the United Nations Framework Convention on Climate Change, signed by President George H. W. Bush and ratified by the Senate in 1992. Their claim that the U.S. has no duty to avoid damaging the climate of others is flatly contradicted by the Convention, which declares in its preamble that "in accordance with the Charter of the United Nations and the principles of international law.... [States have] the responsibility to ensure that activities within their jurisdiction or control do not cause damage to the environment of other States or areas beyond the limits of national jurisdiction."

Ironically, those law professors are running away from international law even faster than the Bush administration. John B. Bellinger III, a legal adviser to the State Department, recently emphasized the administration's commitment to international law and referred to its allegiance to a post-2012 climate change framework in that context.

The Supreme Court also weighed in recently to affirm that U.S. domestic law compels stronger federal action to mitigate climate change. Massachusetts, among a number of plaintiffs, sued the Environmental Protection Agency for its failure to regulate the emission of carbon dioxide by automobiles. The court firmly struck down all the EPA's defenses for inaction: it noted that the EPA is obliged to regulate any deleterious pollutant emitted by motor vehicles; that carbon dioxide clearly falls within that category; that Massachusetts had standing to sue because climate change was already claiming part of the state's coastline; and that the state was vulnerable to considerably greater coastal losses this century if climate change is not mitigated. Moreover, it emphasized that mitigating U.S. auto emissions would have a meaningful effect on the pace of climate change.

The obligation to limit greenhouse gas emissions is therefore already the law of the land, and it's high time we began respecting those laws. We should do so not only because it is important that we honor our legal commitments but because we made those commitments for reasons of our own survival and well-being. Even an administration that has dragged its feet for seven years is finally beginning to face that reality. ■

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

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

MATT COLLINS

Forum

Don't Wreck the Mars Program

Devoting all the funding to just one mission would be a mistake

BY ROBERT ZUBRIN

In the mid-1990s the U.S. embarked on a new strategy for exploring the Red Planet. In response to the 1993 failure of the Mars Observer mission—a billion-dollar, decade-in-the-making probe that mysteriously lost contact with ground controllers just before it was scheduled to go into orbit around the planet—NASA administrator Daniel Goldin decided to shift to smaller, less expensive spacecraft and create a sustained exploration campaign by sending one or two probes to Mars at every launch opportunity. (These opportunities come every two years or so, when Earth and Mars are properly aligned.) The new strategy spread out the inherent risk of interplanetary travel and ensured that the engineering experience and scientific data acquired by one mission could be rapidly used by the next. The approach has proved a brilliant success, putting three NASA spacecraft into orbit around Mars and three rovers on the planet's surface (Pathfinder, Spirit and Opportunity). The Phoenix Mars Lander, which left Earth in August, is expected to reach the Red Planet next May, and NASA plans to launch the Mars Science Lab in 2009.

Subsequent missions are in jeopardy, however. Alan Stern, associate administrator for NASA's Science Mission Directorate, warned in July that at least one of the future Mars probes may have to be scrapped to free up funding for a much costlier mission, tentatively scheduled for the 2018–2020 period, that would collect samples of Martian rock and bring them to Earth. Moreover, highly placed scientists and program leaders report that the new plan may actually require the sacrifice of all other Mars spacecraft after 2009.

Putting aside the question of whether the redirected funds would actually be de-

COURTESY OF ROBERT ZUBRIN

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retaliate. It was this wiring that killed Grissom and his crewmates in a fire on January 27, 1967. The film doesn't go anywhere with Young's remark, leaving the audience not knowing what to think. Was there a conspiracy? Were NASA officials any less dedicated and human than the astronauts themselves?

Humans, Chimps and Genes

Posted by Christopher Mims, Sept. 5, 2007

Proponents of Evo-Devo, whose practitioners inquire into the developmental significance of various genes and in so doing have discovered that, among other things, some genes have much more power to shape body plans than others, like to point to the supposed similarity between humans and chimps—about 99 percent shared DNA—to illustrate the power of just a few genes to effect radical changes in the phenotype of an animal.

This finding in no way diminishes Evo-Devologists' (Evo-Devonators?) findings, but they might have to find a different handy example to hang their hat on.

Humans may have as little as 99 percent of their genes in common with one another, and, by the same analysis, as little as 95 percent of their genes in common with chimpanzees.

The results came out of a detailed analysis, published in *PLoS Biology,* of J. Craig Venter's genome by—get ready to get meta—J. Craig Venter himself. (With the help, no doubt, of dozens of his minions at Celera Genomics and/or the J. Craig Venter Institute.)

In the analysis, Venter compared his own genome with the "standard" genome produced by the official, government-sponsored Human Genome Project (which used a mix of different individuals' DNA). A second, as yet unpublished analysis of the genome of James Watson, co-discoverer of DNA, yielded similar results.

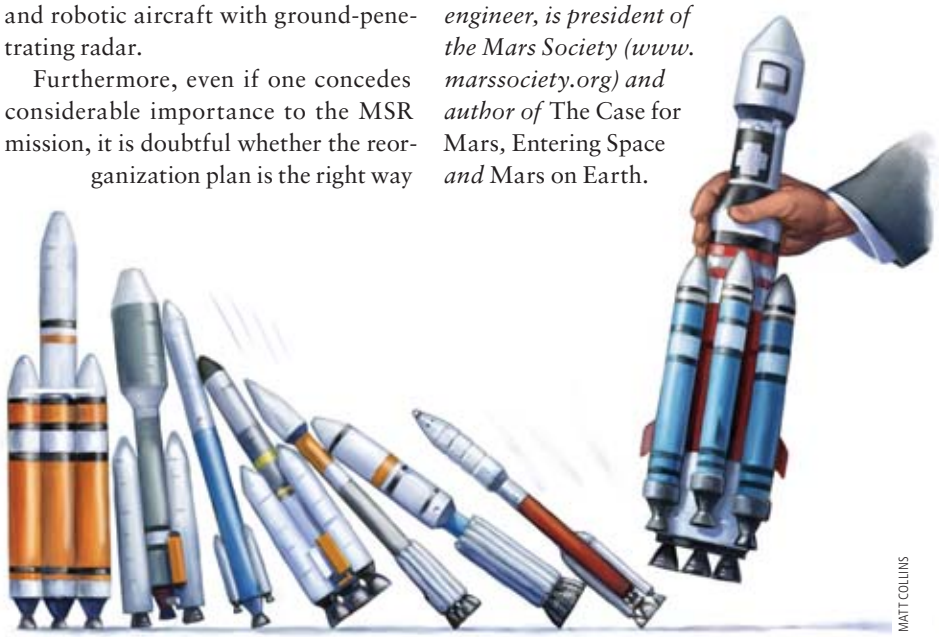
No telling what this ultimately really means, given that both the original value for how similar humans are to one another—99.9 percent similar—and the new value are somewhat arbitrary numbers until we know what all those genes do. I recommend you check back at this blog in about 50 years.

voted to the Mars Sample Return (MSR) mission, such a reorganization would be a very bad idea. A one-shot mission to bring Martian rocks to Earth for laboratory analysis is not really a good way to address the central question of Mars science. The Red Planet is a critical test bed for the hypothesis that life is likely to arise wherever the appropriate physical conditions—notably, the presence of liquid water—prevail on a planet for a sufficiently long time. Scientists now know that Mars probably had standing bodies of water on its surface between three billion and four billion years ago, when there was already plentiful microbial life on Earth. Because asteroid and comet impacts facilitate the transfer of rocks between Mars and Earth, the discovery of microfossils on the Martian surface would not in itself prove that life arose independently on Mars. To settle the question, researchers would need to find living organisms on the planet and examine their biochemistry. These organisms, if they exist, are most likely to be found in groundwater. Thus, the most important goal of the exploration program is to identify sites on Mars where groundwater is within practical drilling distance of the surface. This task can best be done not with an MSR mission but with a comprehensive scouting program involving orbiters, rovers, drillers and robotic aircraft with ground-penetrating radar.

Furthermore, even if one concedes considerable importance to the MSR mission, it is doubtful whether the reorganization plan is the right way to get there. If NASA halts its Mars exploration for a decade, all the best people will leave the team and be replaced by those who enjoy drawing charts and schedules. Instead of wrecking the current Mars program and hoping for the best, the space agency should build on it. New orbital spacecraft and aircraft should extend the reconnaissance of the Red Planet and identify sites containing potential fossils and near-surface groundwater. With such discoveries building well-justified public interest, NASA will be able to ask for extra funding to add an MSR mission to the queue. While the space agency is preparing the mission, it can send rovers and drillers to the most promising sites and cache samples that could reveal the truth about life on Mars. In addition to providing major scientific discoveries, such a mission might well give NASA the boost it needs to send human explorers to the Red Planet.

The Mars exploration program is one of the brightest jewels in the crown of American science; indeed, it represents one of the great cultural accomplishments of contemporary human civilization. It should not be discarded lightly. Rather than breaking from it, we should build on it. That is the way to Mars. ■

Robert Zubrin, an astronautical engineer, is president of the Mars Society (www.marssociety.org) and author of The Case for Mars, Entering Space *and* Mars on Earth.



MATT COLLINS

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Skeptic

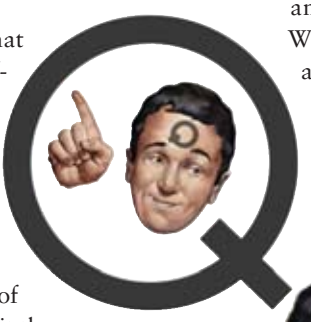
Weirdonomics and Quirkology

How the curious science of the oddities of everyday life yields new insights

BY MICHAEL SHERMER

Using an index finger, trace the capital letter Q on your forehead. Which way did the tail of the Q slant?

What an odd thing to ask someone to do. Exploring weird things and why people believe them, however, is what I do for a living. Coming at science from the margins allows us to make an illuminating contrast between the normal and the paranormal, the natural and the supernatural, and the anomalous and the usual. The master at putting uncanny things to the experimental test—the man I call the Mythbuster of Magical Thinking—is University of Hertfordshire psychologist Richard Wiseman. His new book, *Quirkology: How We Discover the Big Truths in Small Things* (Basic, 2007), presents the results of his numerous (and often hilarious) experiments on all matters peculiar.



For instance, Wiseman explains that the Q test is a quick measure of "self-monitoring." High self-monitors tend to draw the letter Q with the tail slanting to their left, so that someone facing them can read it. By temperament, they tend to focus outwardly: they are concerned with how other people see them, enjoy being the center of attention and adapt their actions to suit the situation. They are also skilled at manipulating others, Wiseman says, which makes them good at deception. And self-deception, apparently, which he discovered when he told these subjects what the experiment is supposed to measure—given that high self-monitors tended to claim (and apparently believe) that they traced the Q the opposite direction to how they actually drew it.

If that is not quirky enough, Wiseman once spent a day in London's King's Cross railway station asking the following question of individuals and of couples reuniting in a passionate embrace: "Excuse me, do you mind taking part in a psychology experiment? How many seconds have passed since I just said the words 'Excuse me?'" Wiseman discovered that people in love significantly underestimated the passing of time. In other words, as the poets already know, times passes quickly when you're in love.

Paranormal anomalies have long been a target of Wiseman's experimental bow. To test the psychology of ghostly experiences, for example, Wiseman spent 10 days at Hampton Court Palace in London, having individuals walk through specific locations and describe any unusual experiences. He discovered that people who have a vivid imagination and are easily hypnotized reported a sensed presence and an uneasy feeling in the exact same locations where those with dry imaginations reported nothing. In a related study, Wiseman's psychologist colleague James Houran of Southern Illinois University had subjects walk through an abandoned cinema and describe how it made them feel. One group of subjects was told that the building was haunted, and the other group was told that it was being renovated. The "haunted" group reported significantly more unusual experiences than the other group did.

In search of a normal explanation for such apparently paranormal enigmas, Wiseman conducted an experiment in a London concert hall in which he had participants listen to and rate the emotional experience of a performance by acclaimed Russian pianist GéNIA. At two different times during the performance, Wiseman piped in extremely low frequency infrasound waves that are inaudible to the human ear but are known to cause an internal vibratory feeling in the head and chest that can be experienced in a deeply emotional way. (NASA once tested infrasound waves on astronauts to measure the effect of rocket engines during launch.) He found that 22 percent of the 400 subjects noted unusual experiences during the infrasound conditions, reporting such feelings as "shivering on my wrist, odd feeling in stomach"; "increased heart rate, ears fluttering, anxious"; "felt like being in a jet before it takes off"; and "preorgasmic tension in body and arms, but not in legs."

Other quirkiness reported by Wiseman includes why there are a disproportionate number of marine biologists called Dr. Fish (names do matter, it turns out); the best wording of a donation solicitation (adding "even a penny helps" doubles the giving rate); superior pickup lines (not boring, such as "Do you come here often?" but silly, such as "If you were a pizza topping, what would you be?"); the most effective personal ads (a 70 to 30 ratio between "this is me" and "this is what I'm looking for"); and the world's funniest joke: "Two hunters are out in the woods when one of them collapses…," which I'll finish next month, when I explain what weirdonomics and quirkology reveal about how science actually works. ■

Michael Shermer is publisher of Skeptic *(www.skeptic.com). His latest book is* Why Darwin Matters.

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Anti Gravity

Profit Tears

Some may cry about cleaning up spilled milk

BY STEVE MIRSKY

Here's what she said: "If China were to revalue its currency, or China is to start making, say, toys that don't have lead in them or food that isn't poisonous, their costs of production are going to go up, and that means prices at Wal-Mart here in the United States are going to go up, too."

That was CNBC's Erin Burnett, apparently a graduate of the Milo Minderbinder School of Business, speaking on the air on August 10. For anyone unacquainted with Milo, he was the man responsible for making sure that World War II was good business in Joseph Heller's masterwork *Catch-22*. Milo's grand free-trade organization is called M&M Enterprises. The first M is for Milo, the second M is for Minderbinder and the ampersand is "to nullify any impression that the syndicate is a one-man operation."

M&M Enterprises is a true multinational conglomerate—Minderbinder even makes a deal with the Germans to have Americans bomb their own base, to save money on all sides. Of course, such an action is so outrageous that there are inevitable consequences. "This time Milo had gone too far.... High-ranking government officials poured in to investigate and Congressmen denounced the atrocity in stentorian wrath and clamored for punishment. Mothers with children in the service organized into militant groups and demanded revenge. Not one voice was raised in his defense. Decent people everywhere were affronted, and Milo was all washed up until he opened his books to the public and disclosed the tremendous profit he had made."

In another venture, Minderbinder corners the market on Egyptian cotton. Then he finds that he can't sell off the bumper crop for conventional use in textiles. He approaches *Catch-22*'s central character, Yossarian, and asks him to taste something

FLYNN LARSEN

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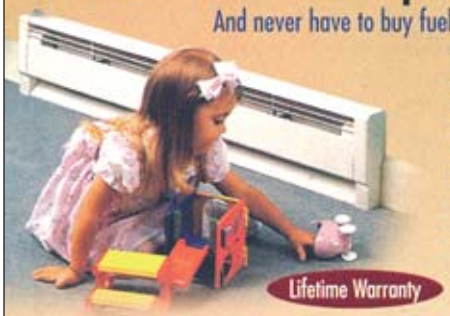

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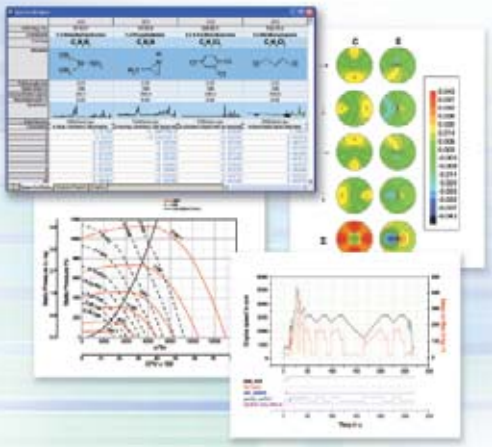

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soft, round and brown. "What is it?" Yossarian asks, while taking a bite. "Chocolate-covered cotton," Milo replies. Yossarian gags, spits and asks, "Have you gone crazy?" To which Milo responds, "Give it a chance … it can't be that bad." "It's even worse," Yossarian says. Later, Milo tries one more time. "I was joking," he says. "It's really cotton candy, delicious cotton candy." But no matter what he calls it, it's still indigestible.

Back to the indigestible comments of Ms. Burnett, who later attempted a clarification of her warning that nontoxic toys and nonpoisonous foods might eat into the profit margin: "Nobody wants children to play with toys that are not safe. Nobody wants that. I don't want that. You don't want that. But safety and quality come with a price." Note for future damage control: the sentiment rings truer without the "but." As in, simply, "safety and quality come with a price."

In an admittedly nonscientific poll, 100 percent of people I surveyed were indeed willing to pay a bit extra for food that wasn't poisoned. As for the toddler toxicity—as I write in early September, yet another three quarters of a million tainted toys were just recalled by Mattel—it's not entirely clear that safety would actually even cost more. Lead is added to paint to make the colors brighter and shinier. So it's possible that an unleaded dog for Barbie's Dream Puppy House might actually be cheaper, albeit the possessor of a slightly less lustrous coat. Which would make the fake dog that much more realistic—real dogs were recently treated to pet food laced with an additive produced in China that included melamine. That chemical is a fire retardant that has the added benefit of making food appear to have more protein content.

Lenin famously said, "The Capitalists will sell us the rope with which we will hang them." Even he might have been impressed by economics gurus warning us about the fiscal dangers of *not* poisoning our children with products from a communist country. But business is business. As when Milo buys eggs for seven cents each, sells them at five cents each and still somehow makes a profit. "I don't make the profit," he explains. "The syndicate makes the profit. And everybody has a share."

MATT COLLINS

One additional note: in this space back in February 2006, we discussed how Idaho Senator Larry Craig (once named "Legislator of the Year" by the National Hydropower Association) managed to shut down a salmon-counting center in Oregon because it implicated a local hydroelectric system in driving down the salmon population. Perhaps the senator would be willing to take a wider stance on this issue now that he has been relegated to endangered status. ■

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The Forgotten Code Cracker

In the 1960s Marshall W. Nirenberg deciphered the genetic code, the combination of the A, T, G and C nucleotides that specify amino acids. So why do people think that Francis Crick did it? BY ED REGIS

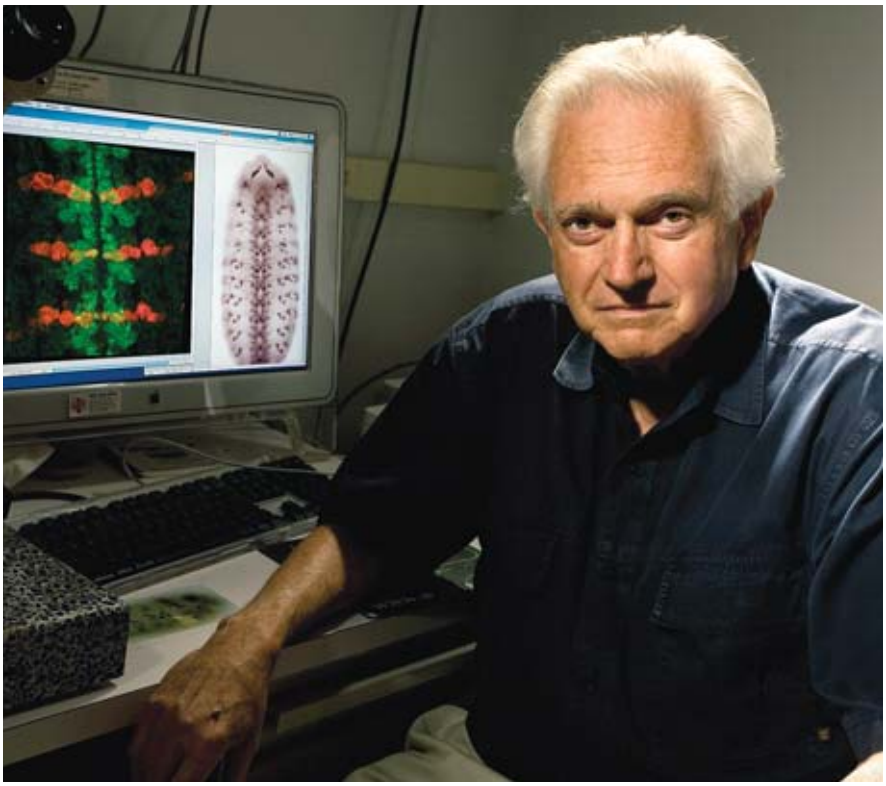
In the summer of 2006 Marshall W. Nirenberg chanced on a just published biography of a prominent molecular biologist. It was entitled *Francis Crick: Discoverer of the Genetic Code*.

"That's awful!" he thought. "It's wrong—it's really and truly wrong!"

Nirenberg himself, along with two other scientists, had received the Nobel Prize in Physiology or Medicine in 1968 "for their interpretation of the genetic code and its function in protein synthesis," and neither of his co-winners happened to be named Crick. (They were in fact Robert W. Holley and Har Gobind Khorana.)

The incident was testimony to the inconstancy of fame. And it was by no means an isolated example, as Nirenberg knew from the long and bitter experience of seeing similar misattributions elsewhere. The breaking of the genetic code was one of the most important advances in molecular biology, secondary only to the discovery of the double-helical structure of DNA in 1953 by Crick and James D. Watson. But whereas they are household names, Marshall Nirenberg certainly is not.

Nirenberg, 80, is now a laboratory chief at the National Institutes of Health, where he has spent his entire career. His otherwise standard-issue science office is distinguished by framed copies of his lab notebooks tabulating the results of his genetic code work. Many of the original documents and some of the instruments he used in this research are on display on the first floor of the NIH Clinical Center, in the exhibit "Breaking the Genetic Code."



KAY CHERNUSH

"People had hypothesized that there was a genetic code in the 1950s," Nirenberg says. "But nobody knew how proteins were synthesized. Nobody knew how it was done."

When Nirenberg arrived at the NIH in 1957 as a biochemistry postdoc, cracking the genetic code was not the first item on his agenda. Ambitious as he was, deciphering the language of life seemed too daunting a project—at least initially.

Consider the problem. The information inside a DNA molecule is encoded by the nucleotide bases adenine, thymine, guanine and cytosine (A, T, G and C). The full sequence of those four nucleotides, which run in nearly endless combinations up and down the strands, constitutes a molecular message for building an organism. Each

MARSHALL W. NIRENBERG

GENETIC CODE BUSTER: His deciphering of the genetic code provided science with what James Watson has called "the Rosetta Stone of Life."

MODEST MODUS: A winner of the 1968 Nobel Prize in Physiology or Medicine, he helped to lay the foundation of molecular biology but never sought fame: "[Francis] Crick told me I was stupid because I never was after the limelight."

ON HIS RESEARCH SHIFT: "I went into neurobiology because there are only two systems in biology where information is stored and retrieved: genes and the brain."

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three-letter sequence of nucleotides (or codon) stands for a specific amino acid. GCA, for example, codes for alanine, one of the 20 different amino acids found in animal organisms. Cellular machinery strings together the amino acids to form the proteins that make up a living being. The task of deciphering the genetic code, then, was reduced to the problem of finding out which exact three-letter sequences stood for which precise amino acid.

In 1955 Crick himself tried to solve the problem, not by experimenting but essentially by thinking, just as a cryptanalyst might try to crack a coded message. He got nowhere and abandoned the attempt. (People today may attribute the discovery of the code to Crick because of his theoretical efforts and because in 1966, based on the experiments of others, he drew up one of the first charts of the complete code.)

Nirenberg started work on the code around 1960, but he had to confront a preliminary problem first. "My question was, Is DNA read directly to protein?" DNA, he knew, resided in the cell nucleus, whereas protein synthesis took place in the cytoplasm. Therefore, either DNA itself exited the nucleus, or some intermediate molecule did—what we now know as messenger RNA. "So the question I was asking was, Does messenger RNA exist? And I thought if I made a cell-free protein-synthesizing system from *E. coli* and added DNA to it, or RNA, then I would see if they stimulated protein synthesis."

The so-called cell-free system is one of the stranger tools of experimental biology. Also known as cell sap, it is a mass of cells denuded of their membranes, the result being a quantity of free cytoplasm in which the original cellular organelles and other structures remain largely intact and functional. In late 1960 Nirenberg and Heinrich Matthaei, who had joined Nirenberg's lab, found that putting RNA into the cell-free system caused it to synthesize proteins but that adding DNA did not.

RNA, then, was the molecule that directed protein production. At some point Nirenberg hypothesized that if he could introduce a specific, known RNA triplet into a cell-free system, and if the system responded by synthesizing a distinct amino acid, then he would have a key to unlocking the genetic code. Others at the NIH were making strings of synthetic nucleotides, long-chain molecules that repeated the same base: AAAAA … (also known as poly-A); TTTTT … (poly-T); and so on.

Nirenberg got hold of a quantity of poly-U (in RNA, uracil replaces DNA's thymine), and he wrote up an experimental protocol for Matthaei to carry out. And so it happened that late one night in May 1961, Matthaei added a quantity of poly-U into a cell-free system.

He somehow became the Forgotten Father of the Genetic Code.

It was a historic moment: the cell sap reacted by churning out the amino acid phenylalanine. One codon had been deciphered, and the triplet UUU became the first word in the chemical dictionary of life. "That was really staggering," Nirenberg recalls today.

He announced the result in August 1961 at a biochemical congress in Moscow. Soon afterward Nirenberg had competition: Nobelist Severo Ochoa of the New York University School of Medicine set up his own lab and started deciphering the code, too. Ochoa continued until 1964, when at a meeting of the American Chemical Society both he and Nirenberg spoke. At that point, each scientist had discovered the base compositions, but not the sequences, of many of the codons. Ochoa spoke first and reported the compositions of some of them. "I was the next speaker," Nirenberg remembers. "I described a simple assay that could be used to determine the nucleotide sequences of RNA codons. Ochoa then stopped working on the genetic code."

By 1966, with the aid of key contributions from Holley and Khorana, Nirenberg had identified both the compositions and base sequences of all the genetic code's 64 trinucleotides. For this achievement, he shared the Nobel Prize in 1968; however, he somehow became the Forgotten Father of the Genetic Code.

Why? "Personality, I guess," Nirenberg says. "I'm shy, retiring. I like to work, and I've never gone out of my way to try to publicize myself. Crick told me I was stupid because I never was after the limelight." In addition, Watson and Crick's discovery yielded a simple, visually stunning image: a gleaming molecular spiral staircase. The genetic code, in contrast, was a mazeworks of forbidding chemical names, codons and complex molecular functions—a publicist's nightmare.

In Nirenberg's own mind, anyway, he had better things to do than burnish his reputation. He turned his talents to the brain. In particular, he wanted to discover how axons and dendrites found one another during embryonic development and how they wired up correctly.

To find out, he and his colleagues established thousands of nerve cell lines, including cells that were hybrids of muscle and nerve. He found that by electrically stimulating a nerve cell, he could record a response across a synapse with striated muscle cells—the cell-level equivalent of Luigi Galvani's getting frog muscles to move in the 18th century. Experiments on fruit flies revealed the existence of four new genes, *NK-1* through *NK-4*, that regulate the differentiation of embryonic nerve cells called neuroblasts.

Nirenberg has racked up 71 publications in neurobiology over the past 20 years. But for all that productivity, those studies will likely never eclipse his cracking of the language of A, T, G and C. That he is not well known for it does not seem to faze him. "Deciphering the genetic code was fantastic fun," he says. "I mean, it was really thrilling." Fame may be fleeting, but the genetic code will endure for as long as there is life. ■

Ed Regis is the author of seven science books, including his forthcoming What Is Life? *(Farrar, Straus and Giroux, 2008).*

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◀ **YOU CAN ALMOST FEEL IT IN YOUR STOMACH:** As universes move through the extra dimensions of space (*shown here in a highly stylized way*), they may expand in size, accounting for various cosmological mysteries. Warning: You must be shorter than 10^{-18} meter to ride.

JEAN-FRANCOIS PODEVIN

The Great Cosmic *Roller-Coaster Ride*

Could cosmic inflation be a sign that our universe is embedded in a far vaster realm?

By Cliff Burgess and Fernando Quevedo

You might not think that cosmologists could feel claustrophobic in a universe that is 46 billion light-years in radius and filled with sextillions of stars. But one of the emerging themes of 21st-century cosmology is that the known universe, the sum of all we can see, may just be a tiny region in the full extent of space. Various types of parallel universes that make up a grand "multiverse" often arise as side effects of cosmological theories [see "Parallel Universes," by Max Tegmark; Scientific American, May 2003]. We have little hope of ever directly observing those other universes, though, because they are either too far away or somehow detached from our own universe.

Some parallel universes, however, could be separate from but still able to interact with ours, in which case we could detect their direct effects. The possibility of these worlds came to cosmologists' attention by way of string theory, the lead-

KEY CONCEPTS

- String theory is the leading candidate for a fundamental theory of nature, but it lacks decisive experimental tests. Cosmic inflation is the leading description of the universe's first instants, but it lacks an explanation in terms of fundamental physics. Might string theory and inflation be the solution to each other's problems?
- As parallel universes postulated by string theory bump into one another or higher dimensions of space get reshaped, the space within our universe may be driven to expand at an accelerated rate.

—The Editors

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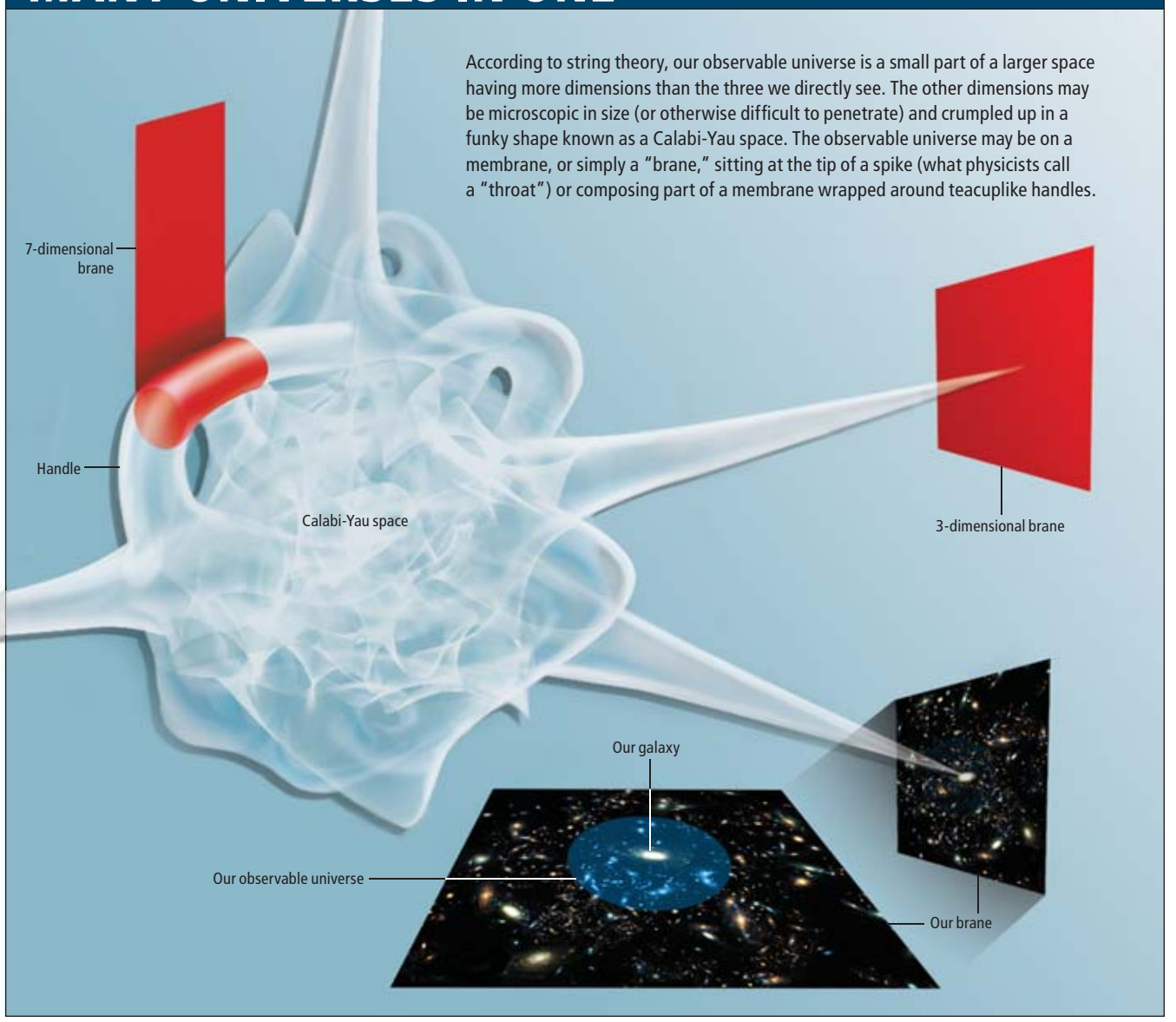
[THE BASICS]

MANY UNIVERSES IN ONE



ing candidate for the foundational laws of nature. Although the eponymous strings of string theory are extremely small, the principles governing their properties also predict new kinds of larger membranelike objects—"branes," for short. In particular, our universe may be a three-dimensional brane in its own right, living inside a nine-dimensional space. The reshaping of higher-dimensional space and collisions between different universes may have led to some of the features that astronomers observe today.

String theory has received some unfavorable press of late. The criticisms are varied and beyond the scope of this article, but the most pertinent is that it has yet to be tested experimentally. That is a legitimate worry. It is less a criticism of string theory, though, than a restatement of the general difficulty of testing theories about extremely small scales. All proposed foundational laws encounter the same problem, including other proposals such as loop quantum gravity [see "Atoms of Space and Time," by Lee Smolin; SCIENTIFIC AMERICAN, January 2004]. String theorists continue to seek ways to test their theory. One approach with promise is to study how it might explain mysterious aspects of our universe, foremost among which is the way the pace of cosmic expansion has changed over time.

Going for a Ride

Next year will be the 10th anniversary of the announcement that the universe is expanding at

DON DIXON

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an ever quickening pace, driven by some unidentified constituent known as dark energy. Most cosmologists think that an even faster period of accelerated expansion, known as inflation, also occurred long before atoms, let alone galaxies, came into being. The universe's temperature shortly after this early inflationary period was billions of times higher than any yet observed on Earth. Cosmologists and elementary particle physicists find themselves making common cause to try to learn the fundamental laws of physics at such high temperatures. This cross-fertilization of ideas is stimulating a thorough rethinking of the early universe in terms of string theory.

The concept of inflation emerged to explain a number of simple yet puzzling observations. Many of these involve the cosmic microwave background radiation (CMBR), a fossil relic of the hot early universe. For instance, the CMBR reveals that our early universe was almost perfectly uniform—which is strange because none of the usual processes that homogenize matter (such as fluid flow) would have had time to operate. In the early 1980s Alan H. Guth, now at the Massachusetts Institute of Technology, found that an extremely rapid period of expansion could account for this homogeneity. Such an accelerating expansion diluted any preexisting matter and smoothed out deviations in density [see "The Inflationary Universe," by Alan H. Guth and Paul J. Steinhardt; Scientific American, May 1984, and "The Self-Reproducing Inflationary Universe," by Andrei Linde; Scientific American, November 1994].

Equally important, it did not make the universe exactly homogeneous. The energy density of space during the inflationary period fluctuated because of the intrinsically statistical quantum laws that govern nature over subatomic distances. Like a giant photocopy machine, inflation enlarged these small quantum fluctuations to astronomical size, giving rise to predictable fluctuations in density later in cosmic history.

What is seen in the CMBR reproduces the predictions of inflationary theory with spectacular accuracy. This observational success has made inflation the leading proposal for how the universe behaved at very early times. Upcoming satellites, such as the European Space Agency's Planck observatory that is scheduled for launch next year, will look for corroborating evidence.

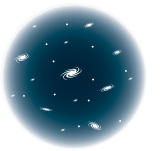
But do the laws of physics actually produce this inflation? Here the story gets murkier. It is notoriously difficult to get a universe full of regular forms of matter to accelerate in its expansion. Such a speedup takes a type of energy with a very unusual set of properties: its energy density must be positive and remain almost constant even as the universe dramatically expands, but the energy density must then suddenly decrease to allow inflation to end.

At first sight, it seems impossible for the energy density of anything to remain constant, because the expansion of space should dilute it. But a special source of energy, called a scalar field, can avoid this dilution. You can think of a scalar field as an extremely primitive substance that fills space, rather like a gas, except that it does not behave like any gas you have ever seen. It is similar to but simpler than the better-known electromagnetic and gravitational fields. The term "scalar field" simply means that it is described by a single number, its magnitude, that can vary from location to location within space. In contrast, a magnetic field is a vector field, which has both a magnitude and a direction (toward the north magnetic pole) at each point in space. A weather report provides examples of both types of field: temperature and pressure are scalars, whereas wind velocity is a vector.

The scalar field that drove inflation, dubbed the "inflaton" field, evidently caused the expansion to accelerate for a long period before switching off abruptly. The dynamics were like the first moments of a roller-coaster ride. The coaster initially climbs slowly along a gentle hill. ("Slowly" is a relative term; the process was still very fast in human terms.) Then comes the breathtaking plunge during which potential energy is converted to kinetic energy and ultimately heat. This behavior is not easy to reproduce theoretically. Physicists have made a variety of proposals over the past 25 years, but none has yet emerged as compelling. The search is hampered by our ignorance of what might be going on at the incredibly high energies that are likely to be relevant.

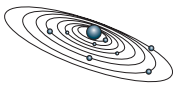
POWERS OF TEN

Natural phenomena occur on many scales. The fine details tend not to affect the large-scale workings, making it hard to test quantum theories of gravity such as string theory. But cosmic inflation allows the absurdly small to affect the astronomically big.



10^{26} meter: Observable universe

10^{21} meter: Milky Way galaxy



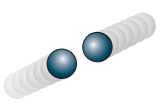
10^{13} meter: Solar system

10^{7} meter: Earth

10^{-2} meter: Insect

10^{-10} meter: Atom

10^{-15} meter: Atomic nucleus



10^{-18} meter: Smallest distance probed by particle accelerators

10^{-18} to 10^{-35} meter: Typical size of fundamental strings and of extra dimensions

10^{-35} meter: Minimum meaningful length in nature

?

Brane Bogglers

During the 1980s, as inflation was gaining credence, an independent line of reasoning was making progress toward reducing our ignorance on that very issue. String theory proposes that subatomic particles are actually tiny one-dimensional objects like miniature rubber bands. Some of these strings form loops (so-called closed strings), but others are short segments with two ends (open strings). The theory

MELISSA THOMAS

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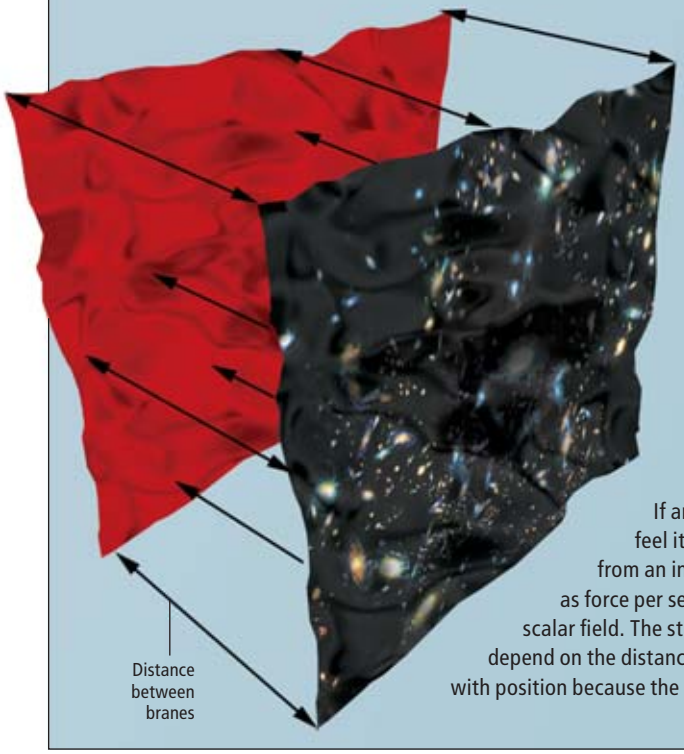
[SCALAR FIELDS]

HOW OTHER BRANES AFFECT US



If another universe came near our own, we might feel its influence. The force it exerted would be coming from an indefinable direction, so we would not perceive it as force per se. What we would detect would be a so-called scalar field. The strength of this field at any particular place would depend on the distance to the other universe, which would vary slightly with position because the two branes would not be perfectly parallel.

SCHEMATIC PLOT OF INTERBRANE DISTANCE (SCALAR FIELD)

The energy represented by such a field could have driven inflation, a huge expansion in the size of our universe early in cosmic history. Inflation, in turn, would have magnified stringy effects to cosmic size. (A similar upturn in the expansion rate may also have started recently, caused by dark energy.)

To account for inflation, the scalar field's energy density had to remain nearly constant and then fall abruptly, like the plunge during a roller-coaster ride.

attributes all the elementary particles ever discovered, and many more undiscovered, to different styles of vibration of these types of strings. The best part of string theory is that, unlike other theories of elementary particles, it organically contains gravity within itself. That is, gravity emerges naturally from the theory without having been assumed at the outset.

If the theory is correct, space is not quite what it appears to be. In particular, the theory predicts that space has precisely nine dimensions (so spacetime has 10 dimensions once time is included), which represent six more than the usual three of length, breadth and height. Those extra dimensions are invisible to us. For instance, they may be very small and we may be oblivious to them simply because we cannot fit into them. A parking lot may have a hairline fracture, adding a third dimension (depth) to the pavement surface, but if the fracture is small, you will never notice it. Even string theorists have difficulty visualizing nine dimensions, but if the history of physics has taught us anything, it is that the true nature of the world may lie beyond our ability to visualize directly.

Despite its name, the theory is not just about strings. It also contains another kind of object called a Dirichlet brane—D-brane, for short. D-branes are large, massive surfaces that float within space. They act like slippery sheets of flypaper: the ends of open strings move on them but cannot be pulled off. Subatomic particles such as electrons and protons may be nothing more than open strings and, if so, are stuck to a brane. Only a few hypothetical particles, such as the graviton (which transmits the force of gravity), must be closed strings and are thus able to move completely freely through the extra dimensions. This distinction offers a second reason not to see the extra dimensions: our instruments may be built of particles that are trapped on a brane. If so, future instruments might be able to use gravitons to reach out into the extra dimensions.

D-branes can have any number of dimensions up to nine. A zero-dimensional D-brane (D0-brane) is a special type of particle, a D1-brane is a special type of string (not the same as a fundamental string), a D2-brane is a membrane or a wall, a D3-brane is a volume with height, depth and width, and so on. Our entire observed universe could be trapped on such a brane—a so-called brane world. Other brane worlds may float around out there, each being a universe to those trapped onboard. Because branes can move in the extra dimensions, they can behave

[THE AUTHORS]

Cliff Burgess and Fernando Quevedo met in the early 1980s as graduate students of the famous physicist Steven Weinberg. They have worked together ever since, mostly on the question of how to relate string theory to real live observable physics. Burgess is a researcher at the Perimeter Institute in Waterloo, Ontario, and a professor at McMaster University in nearby Hamilton. He received a Killam Fellowship in 2005. Quevedo is a professor at the University of Cambridge and a recipient of a Guggenheim Fellowship, among other awards. He has been active in developing science in his home country of Guatemala.

JENS LANGEN (*Burgess*); ELISA QUEVEDO (*Quevedo*); MELISSA THOMAS (*graphs*)

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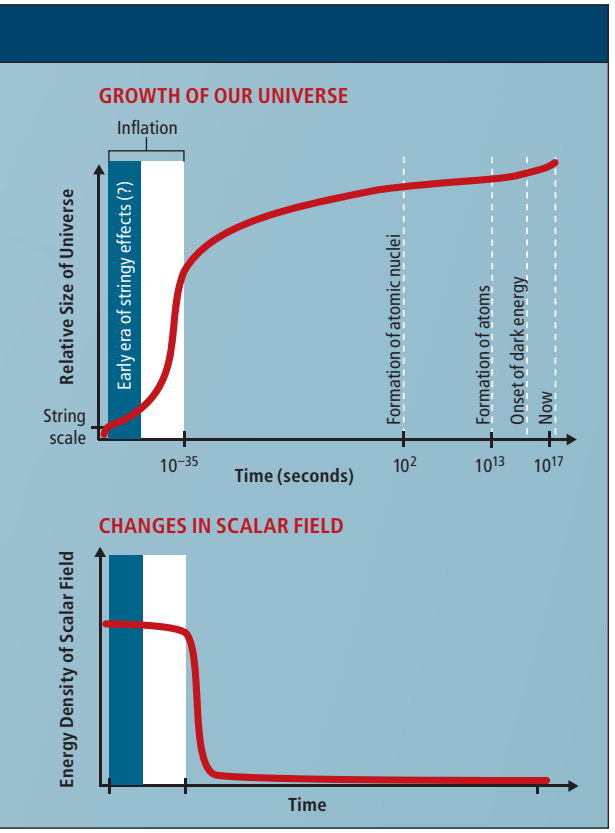

like particles. They can move, collide, annihilate, and even form systems of branes orbiting around one another like planets.

Although these concepts are provocative, the acid test of a theory comes when it is confronted with experiments. Here string theory has disappointed because it has not yet been possible to test it experimentally, despite more than 20 years of continued investigation. It has proved hard to find a smoking gun—a prediction that, when tested, would decisively tell us whether or not the world is made of strings. Even the Large Hadron Collider (LHC)—which is now nearing completion at CERN, the European laboratory for particle physics near Geneva—may not be powerful enough.

Seeing the Unseen Dimensions

Which brings us back to inflation. If inflation occurs at the high energies where the stringy nature of particles becomes conspicuous, it may provide the very experimental tests that string theorists have been looking for. In the past few years, physicists have begun to investigate whether string theory could explain inflation. Unfortunately, this goal is easier to state than achieve.

To be more specific, physicists are checking whether string theory predicts a scalar field with two properties. First, its potential energy must be large, positive and roughly constant, so as to drive inflation with vigor. Second, this potential energy must be able to convert abruptly into kinetic energy—the exhilarating roller-coaster plunge at the end of inflation.

The good news is that string theory predicts no shortage of scalar fields. Such fields are a kind of consolation prize for creatures such as ourselves who are stuck in three dimensions: although we cannot peer into the extra dimensions, we perceive them indirectly as scalar fields. The situation is analogous to taking an airplane ride with all the window shades lowered. You cannot see the third dimension (altitude), but you can feel its effects when your ears pop. The change in pressure (a scalar field) is an indirect way of perceiving the dimension.

Air pressure represents the weight of the column of atmosphere above your head. What do the scalar fields of string theory represent? Some correspond to the size or shape of space in the unseen directions and are known by the mathematical term of geometric "moduli" fields. Others represent the distance between brane worlds. For instance, if our D3-brane approached another D3-brane, the distance between the two could vary slightly with location because of ripples in each brane. Physicists in Toronto might measure a scalar field value of 1 and physicists in Cambridge a value of 2, in which case they could conclude that the neighboring brane is twice as far from Cambridge as from Toronto.

To push two branes together or contort extra-dimensional space takes energy, which can be described by a scalar field. Such energy might cause branes to inflate, as first proposed by Georgi Dvali of New York University and Henry S.-H. Tye of Cornell University in 1998. The bad news is that the first calculations for the various scalar fields were not encouraging. Their energy density proved to be very low—too low to drive inflation. The energy profile more resembled a train sitting on level ground than a slowly climbing roller coaster.

Introducing Antibranes

That is where the problem stood when the two of us—together with Mahbub Majumdar, then at the University of Cambridge, and Govindan Rajesh, Ren-Jie Zhang and the late Detlef Nolte, all then at the Institute for Advanced Study in Princeton, N.J.—began thinking about it in

STRINGLISH

STRING THEORY
A candidate unified theory of all physical forces and particles.

INFLATION
A period of accelerated cosmic expansion early in the history of the universe.

OBSERVABLE UNIVERSE
The sum of all we can see. Also called "our universe."

OTHER UNIVERSE
An unobserved region of spacetime, perhaps having distinct properties and laws of physics.

CALABI-YAU
Six-dimensional shape of hidden dimensions.

BRANE
Short for "membrane." It can be a two-dimensional sheet (like an ordinary membrane) or a lower- or higher-dimensional variant.

FIELD
A form of energy that fills space like a fog.

SCALAR FIELD
A field described by a single number at every position. Examples: temperature, inflaton field.

MODULI
Scalar fields that describe the size and shape of hidden space dimensions.

ANNIHILATE
To convert completely to radiation, as happens when matter and antimatter or branes and antibranes collide.

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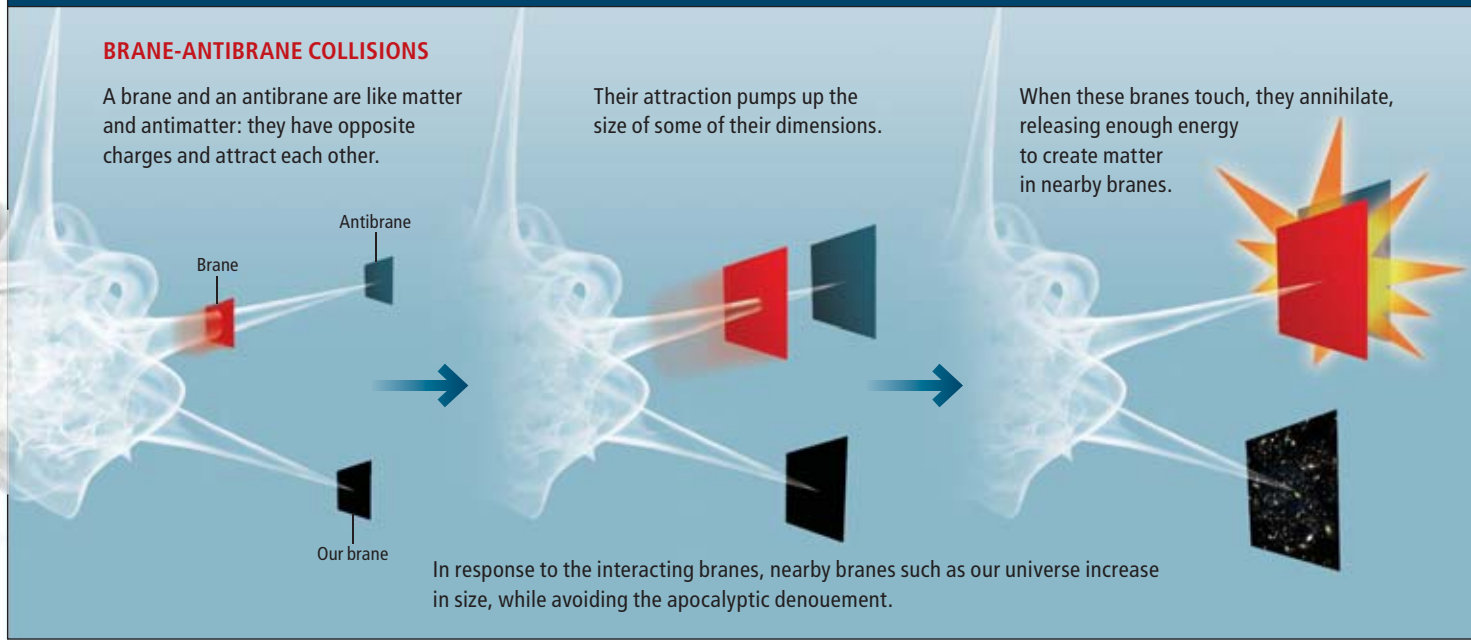
[TWO SCENARIOS]

INFLATION FROM BRANES



WHAT'S NEXT

- Tests of gravitational-wave predictions by the Planck satellite and proposed gravitational-wave detectors
- Telescope searches for cosmic strings
- Theoretical work to understand the initial moment of the big bang
- Continued efforts to determine whether string theory can explain inflation
- Study of the possibility of communicating with other universes

2001. Dvali, Sviatoslav Solganik of N.Y.U. and Qaisar Shafi of the University of Delaware developed a related approach at the same time.

Our innovation was to consider both branes and antibranes. Antibranes are to branes what antimatter is to matter. They attract each other, much as electrons attract their antiparticles (positrons). If a brane came near an antibrane, the two would pull each other together. The energy inside the branes could provide the positive energy needed to start inflation, and their mutual attraction could provide the reason for it to end, with the brane and antibrane colliding to annihilate each other in a grand explosion. Fortunately, our universe does not have to be annihilated to benefit from this inflationary process. When branes attract and annihilate, the effects spill over into nearby branes.

When we calculated the attractive force in this model, it was too strong to explain inflation, but the model was a proof of principle, showing how a steady process could have an abrupt ending that might fill our universe with particles. Our hypothesis of antibranes also inspired new thinking on the long-standing question of why our universe is three-dimensional [*see box on opposite page*].

The next level of refinement was to ask what happens when space itself, not just the branes within it, becomes dynamic. In our initial efforts, we had assumed the size and shape of extra-dimensional space to be fixed as the branes moved around. That was a serious omission, because space bends in response to matter, but an understandable one, because in 2001 nobody knew how to compute this extra-dimensional bending explicitly within string theory.

Space Warps

Within two years the situation changed dramatically. In 2003 a new theoretical framework known as KKLT, for its creators' initials, was developed by Shamit Kachru, Renata Kallosh and Andrei Linde of Stanford University, together with Sandip Trivedi of the Tata Institute of Fundamental Research in Mumbai. Their framework describes the circumstances in which the geometry of the extra dimensions is very stiff and so does not flex too much as things move around within it. It predicts a huge number of possible configurations for the extra dimensions, each corresponding to a different possible universe. The set of possibilities is known as the string theory landscape. Each possibility might be realized in its own region of the multiverse [see "The String Theory Landscape," by Raphael Bousso and Joseph Polchinski; SCIENTIFIC AMERICAN, September 2004].

Within the KKLT framework, inflation can happen in at least two ways. First, it could result from the gravitational response of extra dimensions to brane-antibrane motion. The extra-dimensional geometry can be very peculiar, resembling an octopus with several elongations,

DON DIXON

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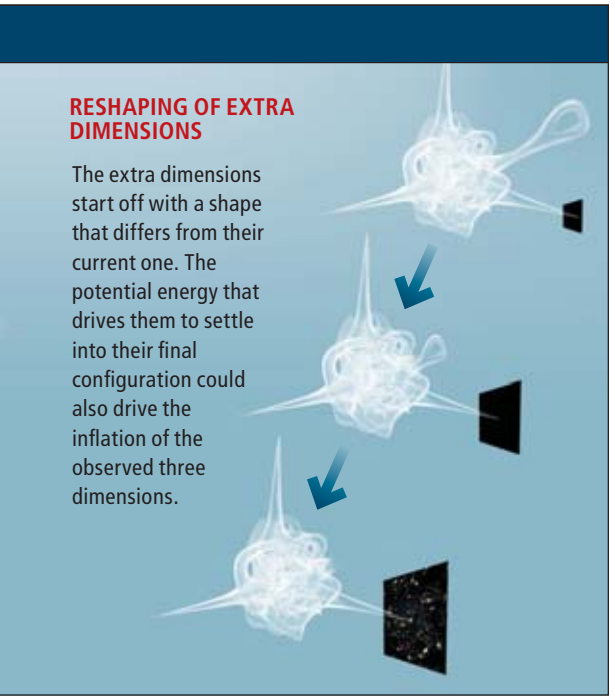

or "throats." If a brane moves along one of these throats, its motion through the warped dimensions weakens the brane-antibrane attraction. This weakening enables the slow-roll process that gives rise to inflation, perhaps solving the main problem with our original proposal.

Second, inflation could be driven purely by changes in the geometry of the extra dimensions, without the need for mobile branes at all. Two years ago we and our colleagues presented the first stringy inflationary scenario along the second of these lines. This general process is called moduli inflation because moduli fields, which describe the geometry, act as the inflatons. As the extra dimensions settle into their current configuration, the three normal dimensions expand at an accelerated pace. In essence, the universe sculpts itself. Moduli inflation thus relates the size of the dimensions we see to the size and shape of those we cannot.

Strings in the Sky

The stringy inflation models, unlike many other aspects of string theory, might be tested observationally in the near future. Cosmologists have long thought that inflation would produce gravitational waves, ripples in the fabric of space and time. String theory may alter this prediction, because the existing stringy inflation models predict unobservably weak gravitational waves. The Planck satellite will be more sensitive to primordial gravitational waves than current instruments are. If it were to detect such waves, it would rule out all the models of string inflation proposed so far.

Also, some brane inflation models predict large linear structures known as cosmic strings, which naturally arise in the aftermath of brane-antibrane annihilation. These strings could come in several types: D1-branes or fundamental strings blown up to enormous size, or a combination of the two. If they exist, astronomers should be able to detect them by the way they distort the light coming from galaxies.

Despite the theoretical progress, many open questions remain. Whether inflation indeed occurred is not entirely settled. If improved observations cast doubt on it, cosmologists will have to turn to alternative pictures of the very early universe. String theory has inspired several such alternatives, in which our universe existed before the big bang, perhaps as part of a perpetual cycle of creation and destruction [see "The Myth of the Beginning of Time," by Gabriele Veneziano; Scientific American, May 2004]. The difficulty in these cases is to describe properly the transition that marks the moment of the big bang.

In summary, string theory provides two general mechanisms for obtaining cosmic inflation: the collision of branes and the reshaping of extra-dimensional spacetime. For the first time, physicists have been able to derive concrete models of cosmic inflation rather than being forced to make uncontrolled, ad hoc assumptions. The progress is very encouraging. String theory, born of efforts to explain phenomena at minuscule scales, may be writ large across the sky. ■

MORE TO EXPLORE

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On Inflation in String Theory. Renata Kallosh. **http://arxiv.org/abs/hep-th/0702059**

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Why Is Our Universe 3-D?

When a brane and antibrane meet, they do not annihilate directly to energy. Instead they first fragment into shards. These shards are smaller branes and antibranes; they occupy two fewer dimensions than the original ones did. For instance, if the initial brane and antibrane spanned seven spatial dimensions (a D7-brane and antibrane), they fragment into many D5-branes and antibranes. These shards, in turn, annihilate into D3-branes and antibranes and thence into D1-branes. Only at that point do they vanish altogether.

The cascade of brane-antibrane annihilation tends to remove large branes, which easily find their antibrane doppelgangers and so annihilate. Smaller branes, such as the D3 and D1 varieties, have greater difficulty bumping into antibranes in the vastness of nine-dimensional space. Lisa Randall of Harvard University and Andreas Karch of the University of Washington generalized our results to include nine expanding dimensions. This process may help explain why most branes, like ours, tend to have fairly few dimensions. —*C.B. and F.Q.*

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Cell Defenses and the Sunshine Vitamin

Scientists now recognize that vitamin D does much more than build strong bones and that many people are not getting enough of it. Is widespread D deficiency contributing to major illnesses?

By Luz E. Tavera-Mendoza and John H. White

JAMES PORTO

KEY CONCEPTS

- Vitamin D, long associated only with its role in bone formation, is actually active throughout the human body, powerfully influencing immune system responses and cell defenses.
- It can be obtained from food or manufactured by human skin exposed to sunlight. Measures of vitamin D levels show, however, that many people have too little of it circulating in their blood to protect health.
- Clear associations between low vitamin D levels and cancers, autoimmunity, infectious diseases and other conditions suggest that current daily intake recommendations for this critical nutrient need revision.

—The Editors

It was called the sunshine cure, and in the early 20th century, before the era of antibiotics, it was the only effective therapy for tuberculosis known. No one knew *why* it worked, just that TB patients sent to rest in sunny locales were often restored to health. The same "treatment" had been discovered in 1822 for another historic scourge, rickets—a deforming childhood condition caused by an inability to make hardened bone. Rickets had been on the rise in 18th- and 19th-century Europe, coinciding with industrialization and the movement of people from the countryside to the polluted cities, when a Warsaw doctor observed that the problem was relatively rare in rural Polish children. He began experimenting with city children and found that he could cure their rickets with exposure to sunshine alone.

By 1824 German scientists found that cod-liver oil also had excellent antirickets properties, although that treatment did not catch on widely, in part because the possibility that a food might contain unseen micronutrients important to health was not yet understood by doctors. And nearly a century would pass before scientists made the connection between such dietary cures for rickets and the beneficial effects of sunshine. Early 20th-century researchers showed that irradiated skin, when fed to rats with artificially induced rickets, had the same curative properties as cod-liver oil. The critical common element in the skin and the oil was finally identified in 1922 and dubbed vitamin D. By then the idea of "vital amines," or vitamins, was a popular new scientific topic, and subsequent research into the functions of vitamin D in the body was very much shaped by D's image as one of those essential micronutrients that humans can obtain only from food.

The association with rickets also steered most vitamin D research for the next 50 years toward understanding the molecule's role in bone building and how it acts in the kidneys, intestines and the skeleton itself to help control the flow of calcium into and

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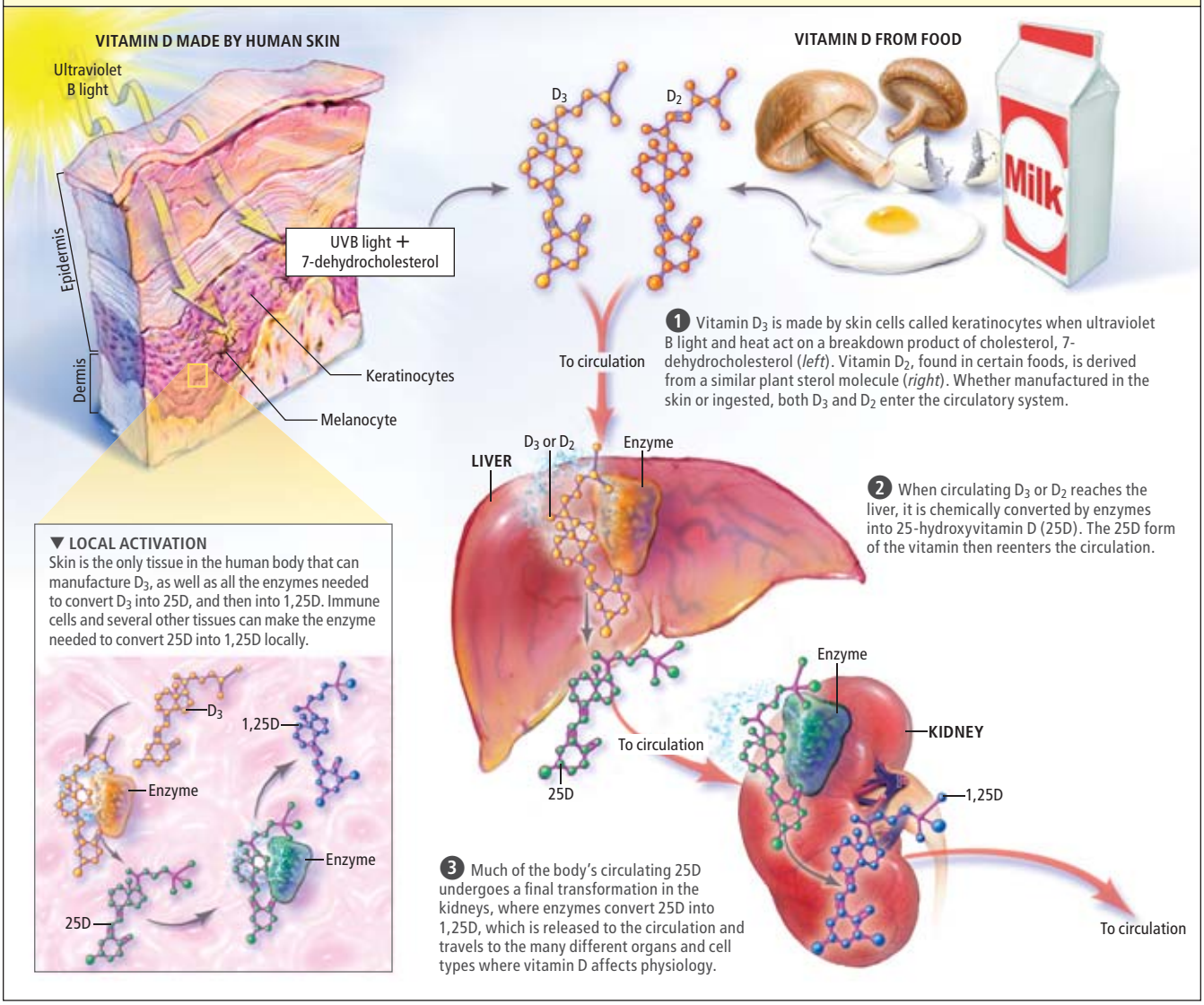
[THE BASICS]

THE MAKING OF AN ACTIVE VITAMIN

The term "vitamin D" refers to two slightly different molecules—D_3, manufactured by human skin, and D_2, which originates in plants and which people can obtain from food. Both versions of D must undergo stages of conversion by enzymes to reach a biologically active form, known as 1,25D.



ANDREW SWIFT

out of bones from the bloodstream. In the past quarter century, however, studies of vitamin D's function have broadened, revealing that the so-called sunshine vitamin does far more than build bones. Extensive evidence now shows that D has potent anticancer actions and also serves as an important regulator of immune system responses. Moreover, many of D's newly recognized benefits are maximized when it is present in the bloodstream at levels considerably higher than those found in many populations. These findings, together with epidemiological data linking low vitamin D levels to disease, support the possibility that widespread vitamin D deficiency is contributing to a number of serious illnesses.

A Versatile Switch

To make sense of new findings about vitamin D, it pays to first review what D actually is and how it is used in the human body. People can obtain the molecule known as vitamin D from limited food sources, such as fatty fish and fish oil, and, today, from dietary supplements. But we can also make it ourselves, through a chemical reaction that happens in the skin when it is exposed to ultraviolet B (UVB) light. Strictly speaking, then, vitamin D is not a vitamin at all, because with moderate UVB exposure, we do not need to get it from food. In temperate regions of the world, however, UVB light is insufficient to induce adequate vitamin D synthesis in the skin

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for up to six months of the year, and then dietary sources of vitamin D become essential [*see box on opposite page*].

The term "vitamin D" generally refers collectively to the two very similar molecules that come from each of those sources. Vitamin D_3, which is also known as cholecalciferol, is created by skin cells called keratinocytes from a breakdown product of cholesterol, 7-dehydrocholesterol, in response to UVB light. Vitamin D_2, or ergocalciferol, is derived from a similar plant sterol, and the resulting molecule has slight structural differences that distinguish it from D_3. Neither version has any biological activity in the body, however. First, either molecule must be modified by a series of related enzymes in a process called hydroxylation, which adds two thirds of a water molecule to generate 25-hydroxyvitamin D (25D).

That conversion takes place primarily in the liver, but various cell types within the skin are also capable of performing the transformation locally. The 25D made by the liver is nonetheless the major form of vitamin D circulating in the bloodstream. When it is needed in the body, a final conversion to the biologically active form is required—25D is further hydroxylated and becomes 1,25-dihydroxyvitamin D (1,25D). The enzyme that performs this task, 1alpha-hydroxylase, was first discovered in the kidney, and renal processing is responsible for generating much of the body's circulating 1,25D supply.

Once again, however, scientists now realize that many other tissues, including cells of the immune system and the skin, can also make that enzyme and perform the 25D conversion themselves. Skin is therefore unique among organs in that it is capable of manufacturing biologically active 1,25D in the presence of UVB light from start to finish, although local production of 1,25D from circulating 25D in other tissues is a substantial source of vitamin D's biological activity in the body that was not appreciated until very recently. Once the breadth of D's activity is considered, though, it becomes easy to see why the ability to make its active form for local use might be important to certain types of cells.

The 1,25D molecule functions as a switch that can turn genes "on" or "off" in virtually every tissue in the human body. This form of D acts by attaching to a protein known as the vitamin D receptor (VDR), which serves as a so-called transcription factor inside a cell's nucleus. Once bound by 1,25D, the VDR protein seeks out a companion protein, the retinoid-x receptor (RXR), and the complex they form binds to a specific region of the cell's DNA adjacent to a target gene. Their attachment to the DNA induces cellular machinery to begin transcribing the nearby gene into a form that the cell will translate into a protein [*see box on page 68*].

By causing a cell to make a particular protein, 1,25D alters cellular function, and this ability to trigger gene activity in different cells is the basis of vitamin D's widespread physiological effects. Because D is a substance manufactured in one tissue and circulates through the body influencing many other tissues, it is also technically a hormone. In fact, the VDR belongs to a family of proteins known as nuclear receptors that respond to powerful steroidal hormones such as estrogen and testosterone.

At least 1,000 different genes are believed to be regulated by 1,25D, including several involved in the body's calcium processing that account for D's well-known role in bone formation. Over the past two decades, however, scientists have identified many other genes influenced by vitamin D activity in the body, including genes with critical roles in a variety of cellular defenses.

Fortification by D

Since the 1980s various lines of evidence have pointed to vitamin D's protective effect against cancer. Many epidemiological studies have shown a strong inverse relation between exposure to sunlight and the incidence of certain types of cancer. Studies in animals and cell cultures have supported that association and helped to pinpoint the mechanisms that may be involved.

In a mouse model of head and neck cancer, for example, a compound called EB1089, which is a synthetic analogue of 1,25D, reduced tumor growth by 80 percent. Similar results have been attained in animal models of breast and prostate cancer. Identifying the genes activated by this synthetic version of D has helped explain these responses. Uncontrolled proliferation, or growth, is a hallmark of tumor cells, and EB1089 was shown to suppress the cells' ability to multiply by altering the activity of a number of different genes. One gene ramped up by the compound—*GADD45*α—is well known for triggering growth arrest in normal cells whose DNA is damaged, thereby reducing their risk for becoming cancerous. In addition, EB1089 activates

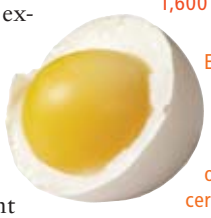
SOURCES OF VITAMIN D

Vitamins D_3 and D_2 occur naturally in some foods, and both versions of the vitamin are added to certain "fortified" products. Foods provide relatively small doses of D compared with amounts made by the skin in response to UVB light. (IU = international units.)

Cod-liver oil (1 tbsp): 1,360 IU D_3

Cooked tuna, sardines, mackerel or salmon (3–3.5 oz): 200–360 IU D_3

Shiitake mushrooms (fresh, 3.5 oz): 100 IU D_2 (dried, 3.5 oz): 1,600 IU D_2



Egg yolk: 20 IU D_3 or D_2

Fortified dairy products, orange juice or cereals (one serving): 60–100 IU D_3 or D_2

Full-body exposure to UVB (15 to 20 minutes at midday in summer, fair skin): 10,000 IU D_3

JAMES PORTO

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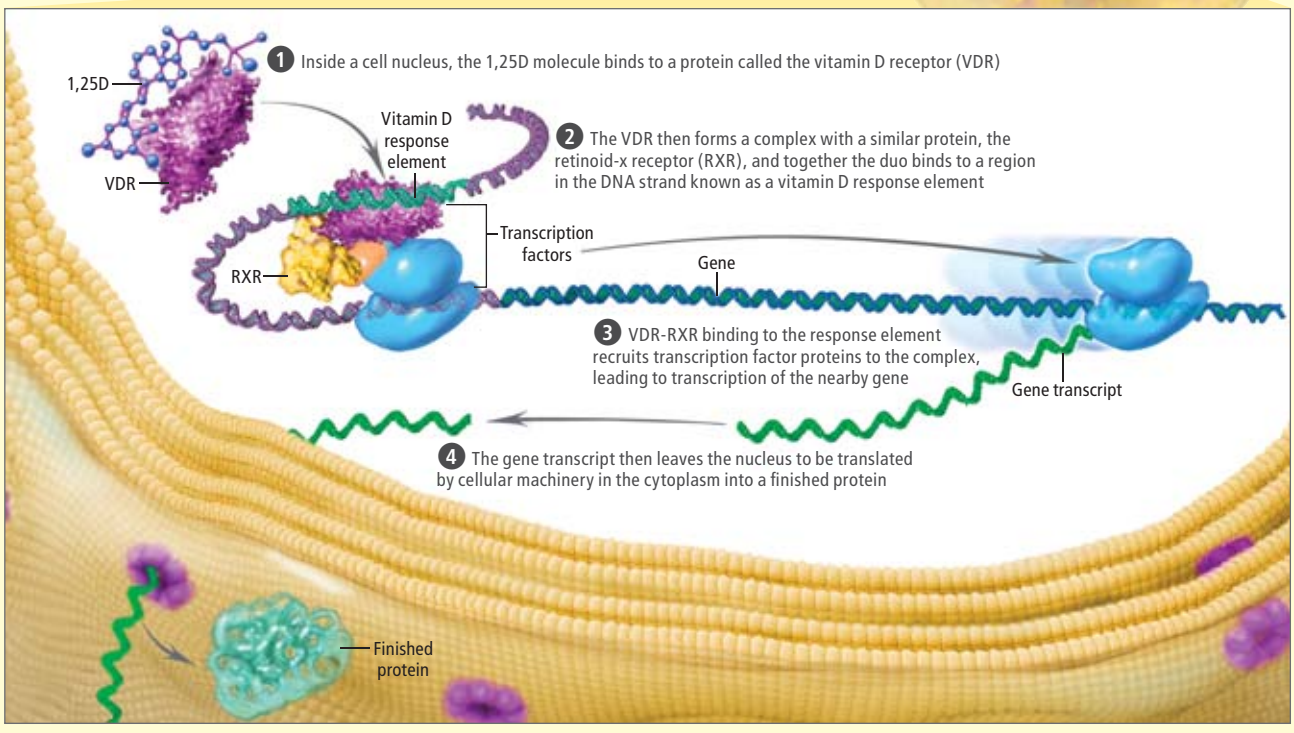
[D IN ACTION]

A BROAD-ACTING GENE SWITCH

The biologically active form of vitamin D—1,25D—turns "on" certain genes, leading to the manufacture of the proteins they encode. Those proteins may have local or widespread physiological effects. More than 1,000 different genes, in at least a dozen tissues and cell types throughout the body, are thought to be regulated by 1,25D.



TISSUES AFFECTED BY VITAMIN D

The VDR receptor protein (*above*) is found in many body tissues as well as circulating immune cells, indicating a role for active vitamin D in regulating gene activity in those locations. The list below includes some of the tissues and cells where 1,25D action has been established.

- Bone
- Brain
- Breast
- Fat
- Intestine
- Immune cells
- Kidneys
- Liver
- Nerves
- Pancreas
- Parathyroid gland
- Prostate
- Skin keratinocytes

genes that direct tumor cells to become more differentiated, a mature state that limits a cell's ability to proliferate.

Another dozen genes involved in a cell's energy management and self-detoxification have also been linked to EB1089's antitumor actions. That experimental compound, which was chemically designed to have 1,25D-like activity without causing toxic levels of calcium to build up in the bloodstream and body tissues, is one of several potential cancer therapies developed by pharmaceutical companies to harness vitamin D's powerful antitumor properties.

Indeed, our laboratory group at McGill University was also investigating D's cancer-related actions in 2004 when we inadvertently hit on a completely different form of physiological defense governed by 1,25D. Many of the genes regulated by vitamin D have been discovered in recent years by scientists scanning parts of the human genome, looking for vitamin D response elements (VDREs)—the distinctive sequences of DNA code that lie adjacent to genes, to which the VDR-RXR protein complex binds. In collaboration with Sylvie Mader of the University of Montreal, we used a computer algorithm designed to scan the entire genome, seeking out VDREs and mapping their positions relative to nearby genes.

Although these mapping studies did help us to better understand some of the anticancer actions of vitamin D, they also revealed VDREs lying close to two genes that encode antimicrobial peptides called cathelicidin and defensin beta 2. These small proteins act as natural antibiotics against a wide spectrum of bacteria, viruses and fungi. We pursued this lead with studies in cultured human cells and found that exposure to 1,25D caused a relatively modest increase in the cells' manufacture of the defensin beta 2 peptide. But in a number of different cell types—including immune system cells and keratinocytes—the rise in cathelicidin production was dramatic. We next demonstrated that immune cells treated with 1,25D, when exposed to pathogenic bacteria, released factors—presumably cathelicidin—that killed off the bacteria.

ANDREW SWIFT

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Philip Liu and Robert Modlin of the University of California, Los Angeles, and their collaborators substantially advanced this line of investigation last year by showing that human immune cells respond to bacterial cell walls by manufacturing both VDR proteins and the enzyme that converts circulating 25D into the biologically active 1,25D. In the group's experiments, these events induced the immune cells to start producing cathelicidin and to demonstrate antimicrobial activity against a variety of bacteria, including one that is perhaps the most intriguing: *Mycobacterium tuberculosis*. Thus, for the first time, the group revealed a plausible basis for the mysterious efficacy of the tuberculosis sunshine cure: the sun-soaked convalescents' vitamin D boost could have provided their immune cells with the raw material needed to generate a natural antibiotic that fought off the TB bacteria.

As gaps in our understanding of vitamin D physiology are filled in, researchers have come to appreciate that a number of D's protective actions in the body might have evolved from functions originating at the molecule's source, in the skin. The growth-arresting influence of 1,25D on cancer cells makes sense in this light because excess UVB exposure is known to damage the DNA of skin cells, which can lead them to become cancerous. Some have also speculated that the antimicrobial response regulated by vitamin D is an adaptation that might have evolved to compensate for D's role in suppressing certain other immune system reactions—specifically, those that lead to excessive inflammation. As many of us know too well from experience, excessive UVB exposure causes sunburned skin, which at the tissue level results in fluid buildup and inflammation. Although a limited amount of inflammation is a beneficial mechanism for wound healing and helps the immune system fight off infection, too much inflammation causes its own havoc.

Perhaps not surprisingly, then, an impressive body of work now shows that 1,25D also acts as an anti-inflammatory agent that functions by influencing immune cell interactions. For example, different subtypes of immune cells communicate by secreting factors called cytokines to initiate a particular type of immune response. Vitamin D has been shown to repress exaggerated inflammatory responses by inhibiting that cytokine cross talk.

Direct evidence of vitamin D's natural role in preventing inflammation came first from animal experiments in the early 1990s, which showed that mice treated with 1,25D were protected from the inflammation normally associated with wounds and the chemical irritant dinitrobenzene, whereas vitamin D–deficient mice were hypersensitive to those same insults. This immune-suppressing function of vitamin D immediately suggested a range of new therapeutic possibilities for using vitamin D or its analogues in the control of autoimmune diseases thought to be caused by overactive cytokine responses, such as autoimmune diabetes, multiple sclerosis (MS) and inflammatory bowel disease.

Since that time, scientists have realized that many cell types, including immune cells, are capable of using circulating 1,25D and of converting circulating 25D to the active form of the vitamin, confirming that the anti-inflammatory actions of 1,25D are not restricted to skin cells nor simply to the context of sunburn.

Epidemic Deficiency?

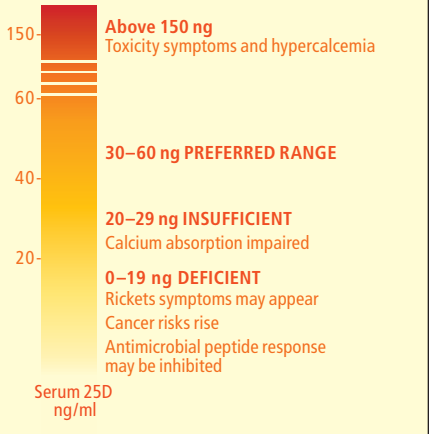
Recognition that 1,25D has a broad range of biological activities far beyond its role in calcium homeostasis has thrown into sharp relief a large body of epidemiological evidence that low vitamin D levels correlate strongly with certain types of disease, among them cancers, autoimmune conditions and even infectious diseases, such as influenza, as well as with seasonal variations in illness rates. In addition, many of the noted physiological responses to vitamin D seen both in the laboratory and in clinical studies are optimized only when circulating concentrations of 25D are higher than is typical in many populations. Members of the vitamin D research community are therefore coming to a widespread consensus that substantial numbers of people in temperate regions of the world have

[THE AUTHORS]

Luz E. Tavera-Mendoza and **John H. White** worked together in White's laboratory at McGill University investigating the molecular activities of vitamin D in human cells. They have uncovered aspects of the vitamin's role in cancer prevention and discovered, with their collaborators, that D regulates certain genes involved in cell responses to microbial invaders. Tavera-Mendoza is now a postdoctoral fellow at Harvard Medical School studying vitamin D and breast cancer. Having witnessed vitamin D's health-protecting actions firsthand in the lab, both authors take supplements during the parts of the year when sunlight is too weak in the northern cities where they reside to produce adequate amounts in skin. White takes 4,000 international units of D_3 daily during those "vitamin D winter" months, and Tavera-Mendoza takes 1,000.

HOW MUCH 25D IS DESIRABLE?

Estimates of vitamin D available to the body are based on measurements of 25D concentrations in blood serum. Levels between 30 and 45 nanograms per milliliter of serum are considered minimally sufficient for bone health, although some beneficial cellular responses to D are optimized at higher concentrations. Below 30 ng/ml, health risks increase; above 150 ng/ml, excess calcium buildup in blood and tissues and symptoms of toxicity are possible.



ANA PALIJAN (*photographs*); LUCY READING-IKKANDA (*graph*)

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levels of vitamin D that are well below optimal concentrations for health, particularly during winter months.

UVB light penetrates the atmosphere more directly in the tropics than in more temperate regions of the planet, which receive substantial amounts of it only during the summer. Because most people obtain vitamin D mainly through UVB exposure, circulating 25D levels in populations generally diminish with increasing latitude, although variations at a given latitude do arise because of differing ethnicities and diets, as well as variations in local climate and elevation. Consistent with vitamin D's observed gene-regulatory activities, a clear association is seen between increasing latitude and increased risk of several illnesses, most conspicuously autoimmune diseases such as MS.

A chronic progressive illness, MS is caused by immune cell assaults on the protective myelin sheath that surrounds nerve fibers of the central nervous system. Its incidence is significantly higher in areas farthest from the equator in North America, Europe and Australia, and convincing evidence suggests that this pattern results from decreased UVB exposure. Disease progression and symptom flare-ups in MS sufferers also display well-established seasonal variations, with the highest disease activity in the spring (when circulating 25D levels would be lowest following the winter) and the least disease activity in the fall, after the summertime boost of D_3. For example, scientists at the University of Southern California found an inverse relation among 79 pairs of identical twins between increased sun exposure during childhood and a lifetime risk of developing MS. The twins who spent more time outdoors as children had as much as 57 percent lower risk of developing the condition.

Similar patterns of risk for illness have been documented for autoimmune diabetes and for Crohn's disease, an inflammatory autoimmune intestinal condition, as well as for certain types of malignancy. Population rates of cancers of the bladder, breast, colon, ovary and rectum increase twofold from south to north in the U.S., for instance.

In addition to the many studies correlating sun exposure with disease incidence, recent investigations have made similar connections between disease risk and direct measurements of circulating 25D concentrations in blood serum. An enormous survey by researchers at the Harvard School of Public Health looked at the stored serum samples of some seven million U.S. Army and Navy personnel as well as their health records to see which individuals had developed MS between 1992 and 2004. The researchers found a significantly lower risk of later developing the disease in the group with high serum 25D levels at the time the sample was taken. Soldiers with serum 25D concentrations above 40 nanograms per milliliter had a 62 percent lower risk than the soldiers whose concentrations were 25 ng/ml or below.

Measuring circulating levels of 25D is the usual method of gauging vitamin D availability in the body. Generally agreed on health standards, based largely on bone-forming needs, hold circulating 25D levels of 30 to 45 ng/ml to be minimally sufficient. Serum vitamin D concentrations below between 21 and 29 ng/ml are considered insufficient and often accompanied by decreased bone density. Some symptoms of rickets may appear when concentrations fall below 20 ng/ml, and the risk of colon cancer rises.

Such low concentrations are unfortunately all too common, especially in winter. In February and March of 2005, for example, a survey of 420 healthy females across northern Europe—in Denmark (Copenhagen: 55° latitude), Finland (Helsinki: 60°), Ireland (Cork: 52°) and Poland (Warsaw: 52°)—found that 92 percent of adolescent girls in these countries had 25D levels less than 20 ng/ml and that 37 percent of the girls were severely deficient, with 25D levels of less than 10 ng/ml. Among the older women tested, 37 percent were found to be vitamin D deficient and 17 percent were severely deficient.

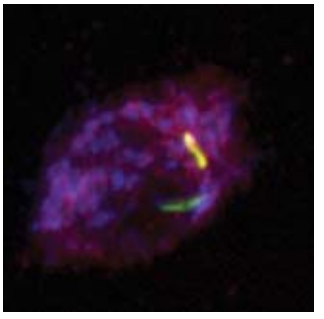
Beyond latitude, several factors can contribute to vitamin D deficiency, and primary among these is race. White skin synthesizes vitamin D six times faster than dark skin because higher levels of melanin in darker skin block UV penetration [see "Skin Deep," by Nina G. Jablonski and George Chaplin; Scientific American, October 2002]. As a result, African-Americans generally have levels of 25D that are approximately half those of whites in the U.S. In fact, data gathered for the U.S. National Health and Nutrition Examination Survey showed that 42 percent of African-American women tested were seriously 25D deficient, with serum concentrations of less than 15 ng/ml.

Increased public awareness that excessive exposure to sunlight causes skin damage is undoubtedly contributing to vitamin D deficiency as well. When properly applied, topical sunscreens reduce vitamin D produced in the skin

D MAKES A DIFFERENCE

Growing evidence suggests that chronically low levels of vitamin D raise a person's risk for certain major illnesses. Examples of findings based on a population's blood serum D levels or UV exposure include:

- 30% to 50% higher risk for breast, prostate and colon cancers at serum 25D levels below 20 ng/ml
- Five times higher risk of ovarian cancer among women living at high latitudes (for example, Norway and Iceland) than women living at equatorial regions
- 77% lower risk for all cancers among Nebraska women age 55 and older taking 1,100 IU of D_3 daily over a three-year period compared with a placebo group
- 62% lower risk for multiple sclerosis at serum 25D levels above 40 ng/ml than at 25 ng/ml or less
- 80% lower lifetime risk for autoimmune (type 1) diabetes in Finnish children given 2,000 IU of D_3 daily during first year of life



PHILIP LIU, MARIA TERESA OCHOA AND ROBERT MODLIN *Division of Dermatology, Department of Medicine, U.C.L.A.*

▲ **IMMUNE CELL treated with 1,25D responds to infection by tuberculosis bacteria (*green* and *yellow*) by making antimicrobial cathelicidin peptides (*red*).**

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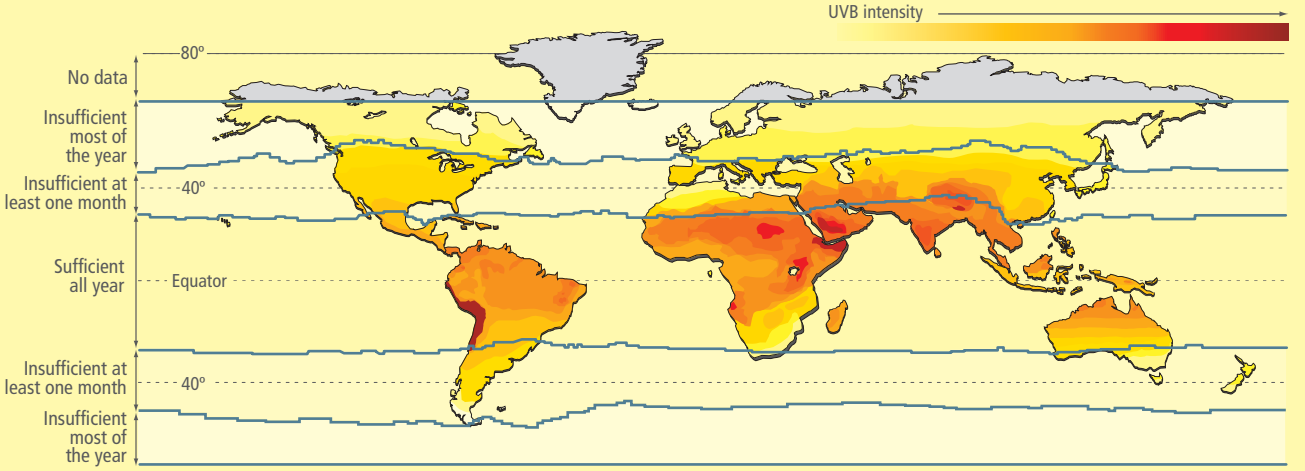
[GLOBAL PROBLEM]

VITAMIN D WINTER

Exposure to UVB radiation in sunlight is the single greatest source of vitamin D for most individuals, so location and season affect a population's risk of deficiency. For periods of the year known as vitamin D winter, UVB intensity is too weak at some latitudes even to induce vitamin D synthesis in the skin. Because ozone blocks UVB rays, the rays are most intense nearest the equator, where sunlight travels the least distance through the earth's atmosphere, and vitamin D synthesis is possible year-round. An increasing angle of penetration at higher latitudes weakens UVB intensity until it is insufficient, especially during winter, for making vitamin D.



by more than 98 percent. Enough vitamin D for good health can be synthesized in skin with sun exposure that might produce at most a slight pinkness, however. For most fair- and medium-skinned people in North America, this takes five to 15 minutes of sunlight between 10:00 A.M. and 3:00 P.M. during the summertime.

Vitamin D supplements could address the high prevalence of vitamin D deficiency in temperate zones, but how much people should take is still a subject of debate. The American Academy of Pediatrics recommends a minimum daily intake (RDI) of 200 international units (IU) for children, which many researchers have argued is suboptimal, even for rickets prevention. The RDI for adults in North America and Europe currently ranges between 200 IU and 600 IU, depending on age. After reviewing multiple studies comparing vitamin D intake and the serum concentrations of 25D produced, Harvard School of Public Health researchers and others concluded last year that the current RDIs are inadequate. They suggested that no less than half of U.S. adults needed to consume at least 1,000 IU of vitamin D_3 daily to raise their serum 25D concentrations to the minimum healthy level of 30 ng/ml. No rule of thumb exists for calculating the serum 25D levels generated by supplements, because individual responses can vary and may depend in part on the extent of deficiency. A study of pregnant women showed, for example, that daily doses of 6,400 IU raised serum 25D levels dramatically until they reached about 40 ng/ml and then leveled off. Vitamin D_2 has also been found to be less effective than D_3 at raising and sustaining serum 25D concentrations over time.

Toxic vitamin D overdose through supplementation is certainly possible, although it is generally seen when doses of 40,000 IU or more of D have been taken daily for an extended period. Sunshine-induced vitamin D toxicity has never been observed, however. To put this in perspective, an adult woman with white skin exposed to summer sun while wearing a bikini generates about 10,000 IU of vitamin D in 15 to 20 minutes. Longer exposures do not generate higher amounts of vitamin D, because UVB light also degrades the vitamin, preventing too much of it from building up in the skin.

Accumulating evidence suggests that the subtle and longer-term effects of even slight vitamin D deficiency may be multifold and manifested later in life, in the form of increased frequency of bone fractures and enhanced susceptibility to infection and autoimmune diseases, as well as elevated frequencies of certain cancers. The research strongly implies that at the very least the general public would benefit substantially from greater awareness of the broad physiological benefits of vitamin D, a sound medical consensus on sensible sun exposure and a clear indication of optimal recommended daily intakes of vitamin D from dietary sources. ■

MORE TO EXPLORE

Unraveling the Enigma of Vitamin D. Beyond Discovery Series, National Academy of Sciences, 2003. **www.beyonddiscovery.org/content/view.article.asp?a=414**

1,25-Dihydroxyvitamin D_3 Is a Direct Inducer of Antimicrobial Peptide Gene Expression. Tian-Tian Wang et al. in *Journal of Immunology,* Vol. 173, pages 2909–2912; 2004.

The Pleiotropic Actions of Vitamin D. Roberto Lin and John H. White in *BioEssays,* Vol. 26, No. 1, pages 21–28; January 2004.

The Urgent Need to Recommend an Intake of Vitamin D That Is Effective. Reinhold Vieth et al. in *American Journal of Clinical Nutrition,* Vol. 85, No. 3, pages 649–650; March 2007.

Vitamin D Deficiency. Michael F. Holick in *New England Journal of Medicine,* Vol. 357, No. 3, pages 266–281; July 19, 2007.

LUCY READING-IKKANDA

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NUCLEAR

Countries are altering their nuclear arsenals, prompting the U.S. to refurbish its own warheads

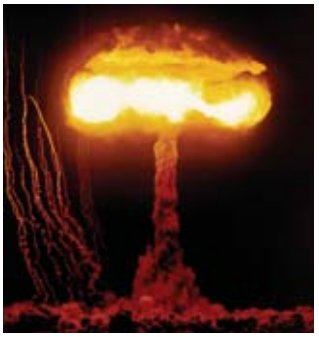
EDITORS' INTRODUCTION

Unleashing a nuclear bomb would cause untold death and disfigurement. But society tends to forget. It has been more than 60 years since the U.S. dropped two terrible bombs on Japan and more than 15 years since the cold war between the U.S. and the former Soviet Union ended, and government commitment to avoiding nuclear war may be fading.

Although the likelihood of a missile exchange between the U.S. and Russia has lessened considerably, it has not vanished. Worry that other nuclear confrontations might occur has risen recently. Intelligence reports indicate that China is retargeting more of its missiles at the U.S. Iran continues to expand its uranium-enrichment facilities; it insists that this work is aimed only at generating electricity, but few nations believe that claim. India is broadening its ability to launch nuclear weapons from land, air and sea, and Pakistan is responding in kind. And even though North Korea indicated in September that it would disable its atomic programs, international negotiators are not yet convinced and the country continues to test longer-range missiles.

The changing threats pose many questions: Who can harm whom? How badly? What, if anything, should the U.S. do in response? Answers appear on the following pages. In a nutshell:

- Nine countries can now deliver nuclear warheads on ballistic missiles, and Iran wants to join this club. Several nations could hit targets anywhere in the world, but regional salvos might be more likely.
- Today's weapons would exact greater death and injury than the bomb dropped on Hiroshima. Simulations performed for SCIENTIFIC AMERICAN of a one-megaton payload detonated above Manhattan show that millions of people would die from the resulting explosion, mass fires and radiation. Other cities worldwide would fare just as badly.
- The U.S. has embarked on a 25-year program to replace thousands of aging W76 nuclear warheads, which military officials say could be degrading. Proponents claim that the substitute weapon—the Reliable Replacement Warhead (RRW)—is essential to maintaining the U.S. stockpile as a credible deterrent. Critics argue that the RRW is a waste of billions of dollars and could goad other nations into a renewed nuclear arms race.



TEST: **A mushroom cloud was produced by an atomic bomb dropped onto the Nevada desert on June 4, 1953.**

U.S. DEPARTMENT OF ENERGY *Photo Researchers, Inc. (cloud)*; COURTESY OF NATIONAL NUCLEAR SECURITY ADMINISTRATION *(missile launch)*; C. MAYHEW AND R. SIMMON *NASA/GSFC, NOAA/NGDC AND DMSP DIGITAL ARCHIVE (night map)*; SLIM FILMS *(photocomposition)*

Nuclear Report Table of Contents

■ Missile Ranges **76** ■ Warhead Arsenals **77** ■ Destroying New York **78** ■ Sick Survivors **79** ■ A Need for New Warheads? **80**

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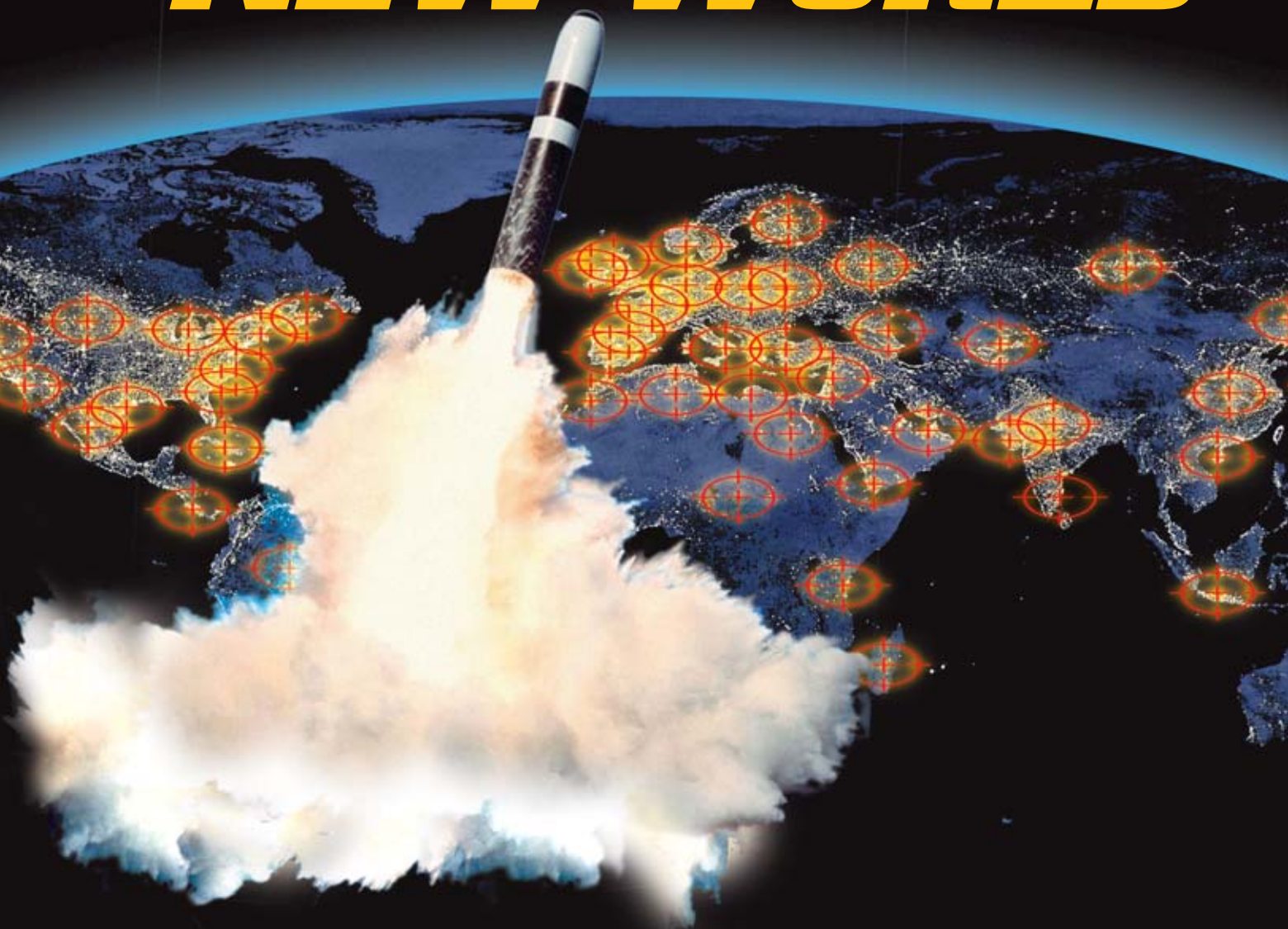
WEAPONS IN A NEW WORLD



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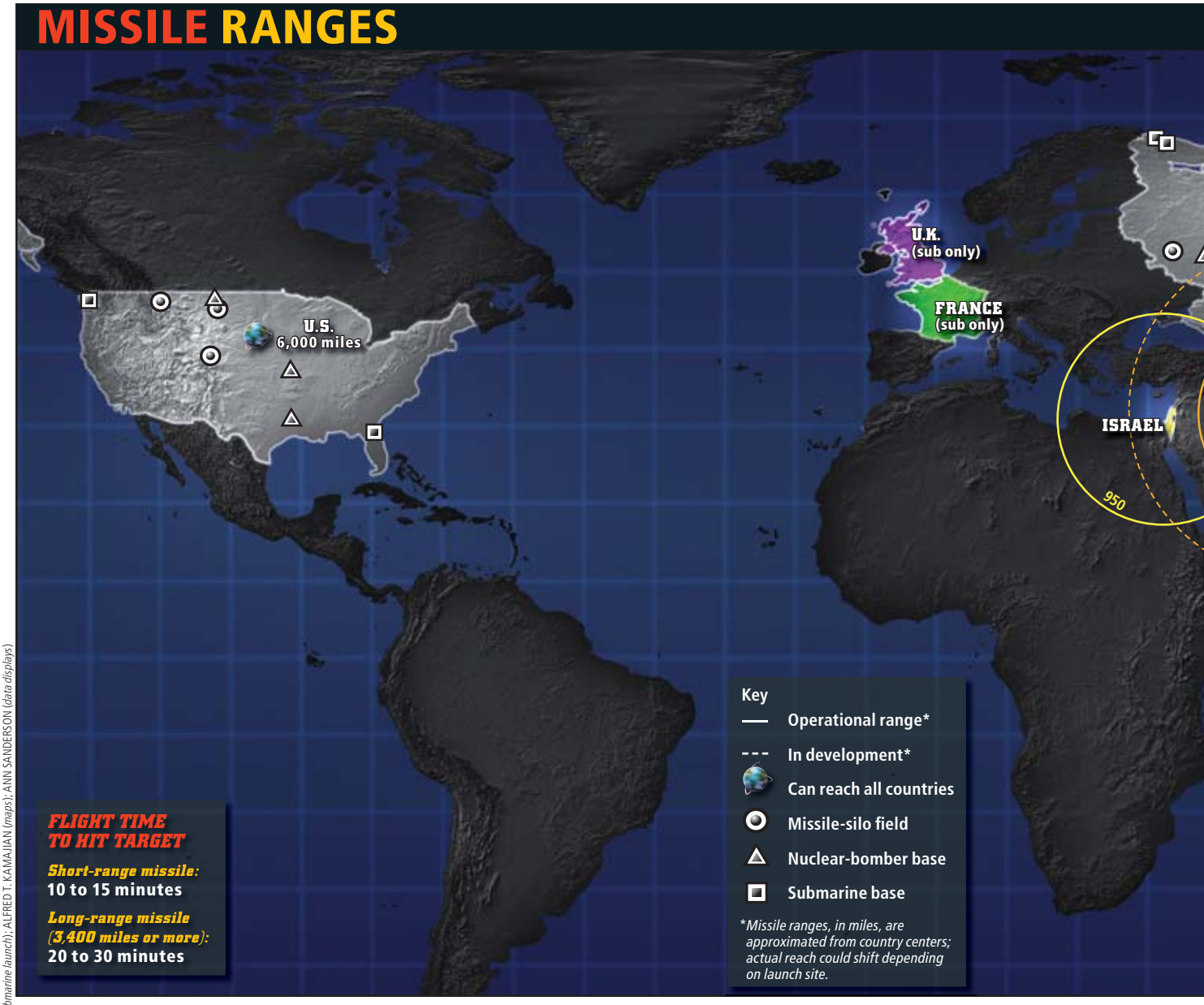
The NUCLEAR THREAT

BY MARK FISCHETTI

Nine countries could kill many people on a moment's notice by launching missiles carrying nuclear warheads. A 10th, Iran, may be weaponizing uranium. The U.S., Russia and China can bomb virtually any country with long-range ballistic missiles and, along with France and the U.K., could do the same using submarines [*see these two pages*]. The effects of even one bomb could far exceed the horror of Hiroshima and Nagasaki [*see pages 78 and 79*].

MISSILE RANGES



SUBMARINE ATTACK RANGE

Five countries could wreak havoc with nuclear warheads launched from submarines, which can roam almost anywhere.

CHINA NEWSPHOTO/REUTERS/CORBIS (*submarine launch*); ALFRED T. KAMAJIAN (*maps*); ANN SANDERSON (*data displays*)

SOURCES (pages 76 and 77): Center for American Progress; Natural Resources Defense Council; Carnegie Endowment for International Peace; Federation of American Scientists; MILNET: Strategic Missiles

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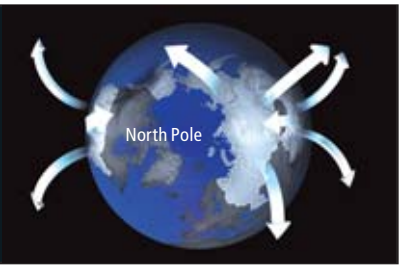
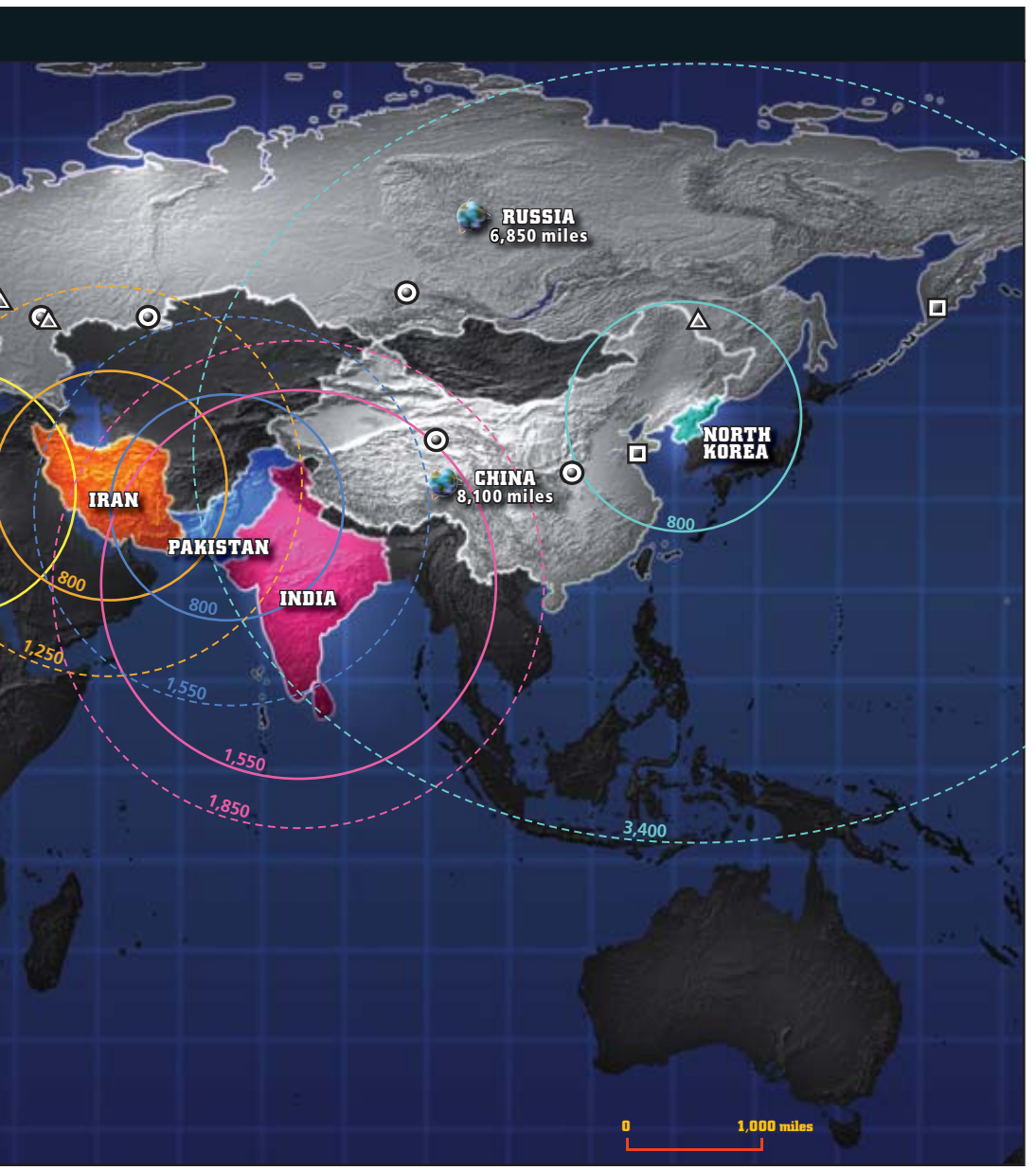
GLOBAL REACH

Ballistic missiles launched from the U.S., Russia and China can reach most landmasses by traveling along various trajectories, including those over the North Pole region.

	Range in miles
China	8,100
Russia	6,850
U.S.	6,000





WARHEAD ARSENALS

Russia*	5,800 operational (ready to deploy)	15,000 Stockpiled
U.S.*	5,700 operational	9,900
France		350
China		200
U.K.		200
Israel		80
Pakistan		60
India		50
North Korea		<10
Iran		In development?

**The Moscow Treaty on Strategic Offensive Reductions limits Russia and the U.S. to a maximum of 2,200 "operationally deployed" warheads by 2012.*

CONVENTIONAL WARFARE

Eighteen countries have ballistic missiles but no nuclear weapons. The ranges are all below 500 miles, except for Saudi Arabia, at 1,600 miles.

- Afghanistan
- Armenia
- Bahrain
- Belarus
- Egypt
- Greece
- Iraq
- Kazakhstan
- Libya
- Saudi Arabia
- Slovakia
- South Korea
- Syria
- Taiwan
- Turkey
- Turkmenistan
- Ukraine
- United Arab Emirates

CHUNG SUNG-JUN Getty Images (Scud missile)

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DESTROYING NEW YORK

The pressure wave from a one-megaton hydrogen bomb detonated 2,950 feet above the center of Manhattan (*top*) would cripple structures within a three-mile radius; intense heat from the blast would ignite mass fires and inflict third-degree burns across the city. Most radiation would stream into the atmosphere, however, leaving little radioactive fallout. The same bomb detonated at ground level (*bottom*) would cause destruction and burns only 60 to 90 percent as far but would kick up vast quantities of radioactive particles, resulting in a heavy fallout plume.

AIRBURST: DAMAGE

STRENGTH OF PRESSURE WAVE

9 pounds per square inch (psi): severe damage to steel-framed buildings

5 psi: severe damage to wood-framed buildings

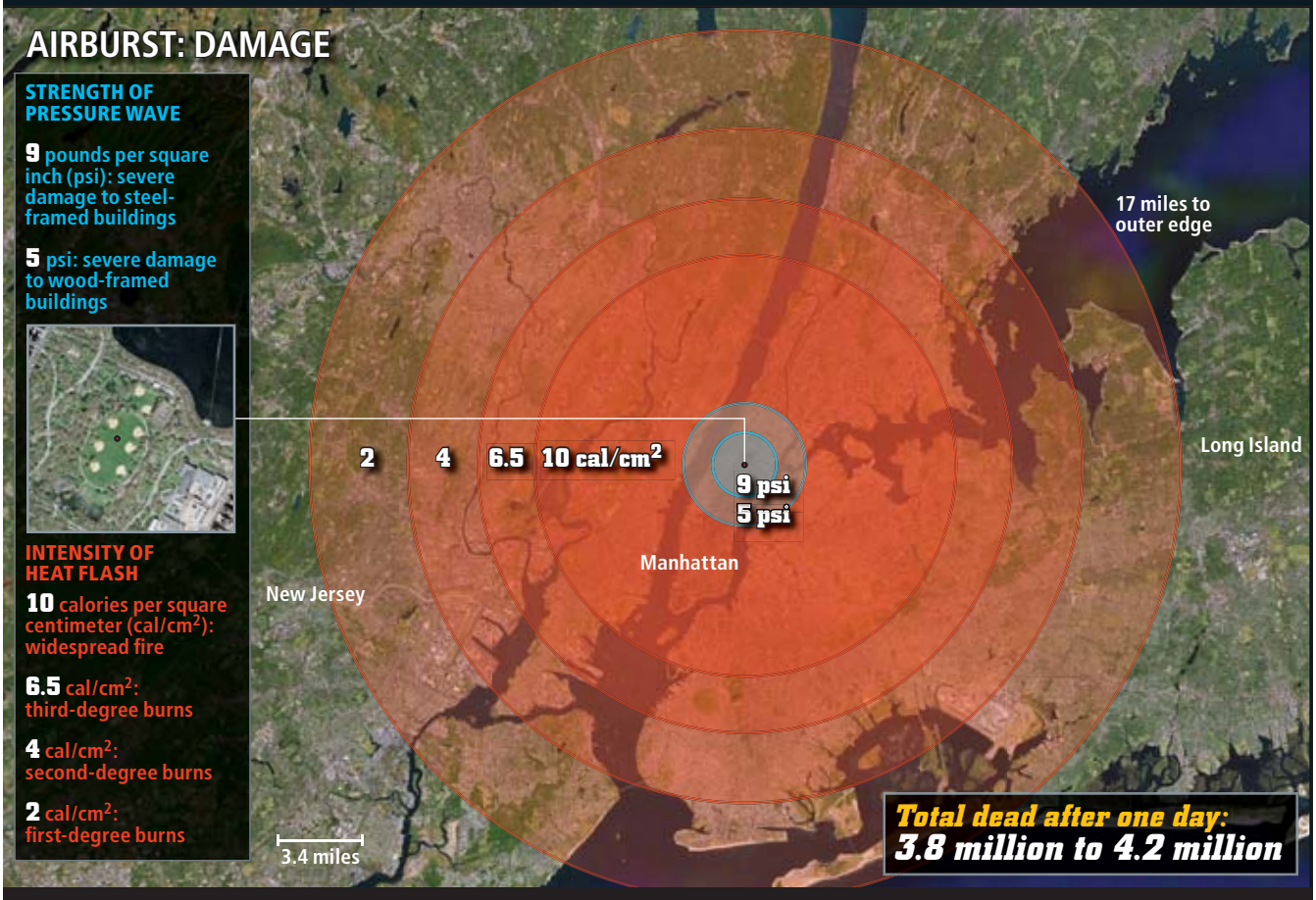
INTENSITY OF HEAT FLASH

10 calories per square centimeter (cal/cm^2): widespread fire

6.5 cal/cm^2: third-degree burns

4 cal/cm^2: second-degree burns

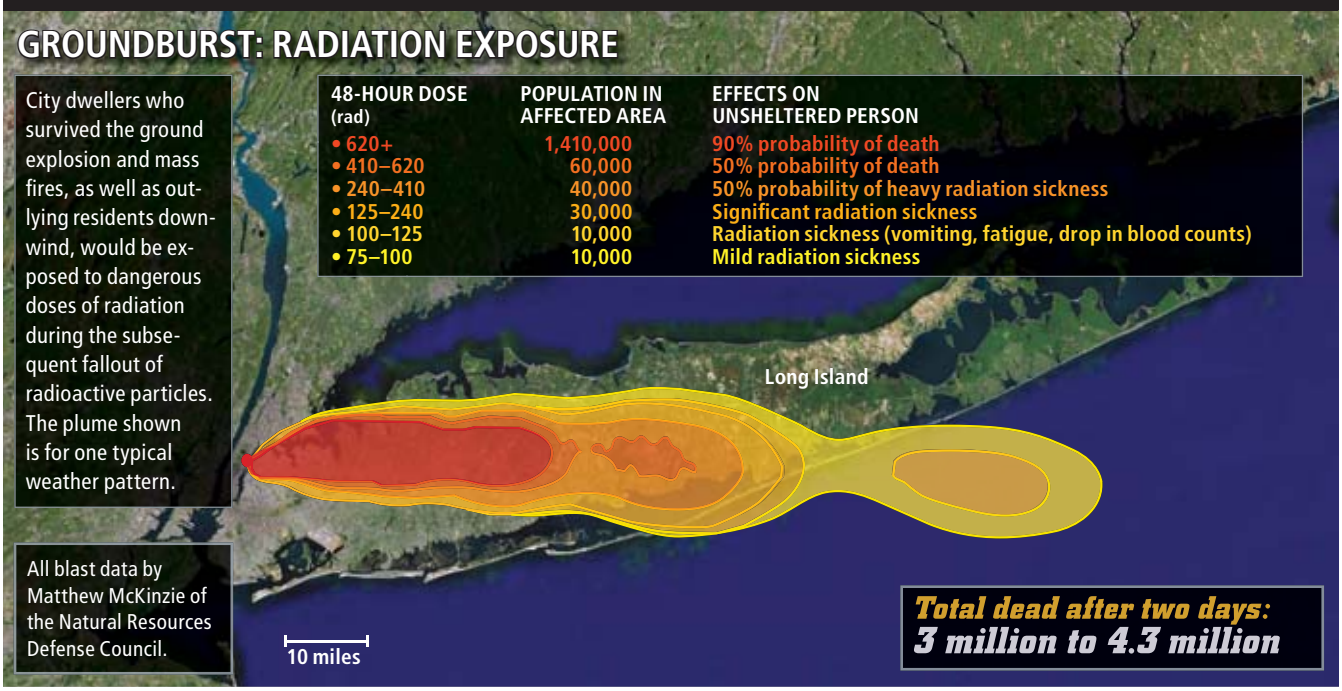
2 cal/cm^2: first-degree burns



GROUNDBURST: RADIATION EXPOSURE

City dwellers who survived the ground explosion and mass fires, as well as outlying residents downwind, would be exposed to dangerous doses of radiation during the subsequent fallout of radioactive particles. The plume shown is for one typical weather pattern.

48-HOUR DOSE (rad)	POPULATION IN AFFECTED AREA	EFFECTS ON UNSHELTERED PERSON
• 620+	1,410,000	90% probability of death
• 410–620	60,000	50% probability of death
• 240–410	40,000	50% probability of heavy radiation sickness
• 125–240	30,000	Significant radiation sickness
• 100–125	10,000	Radiation sickness (vomiting, fatigue, drop in blood counts)
• 75–100	10,000	Mild radiation sickness



All blast data by Matthew McKinzie of the Natural Resources Defense Council.

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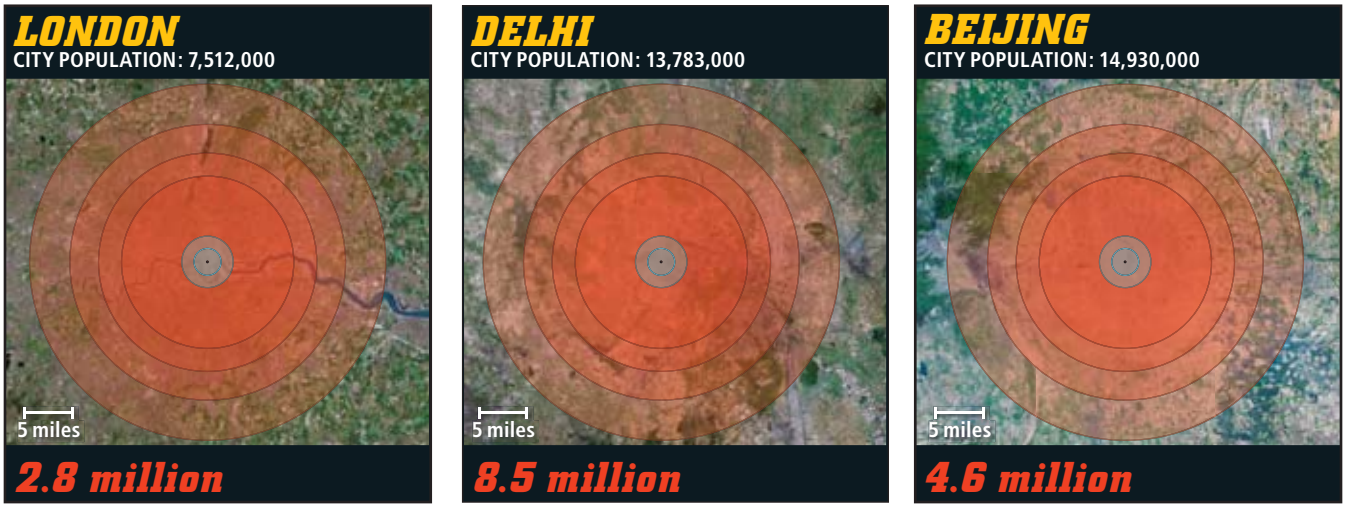
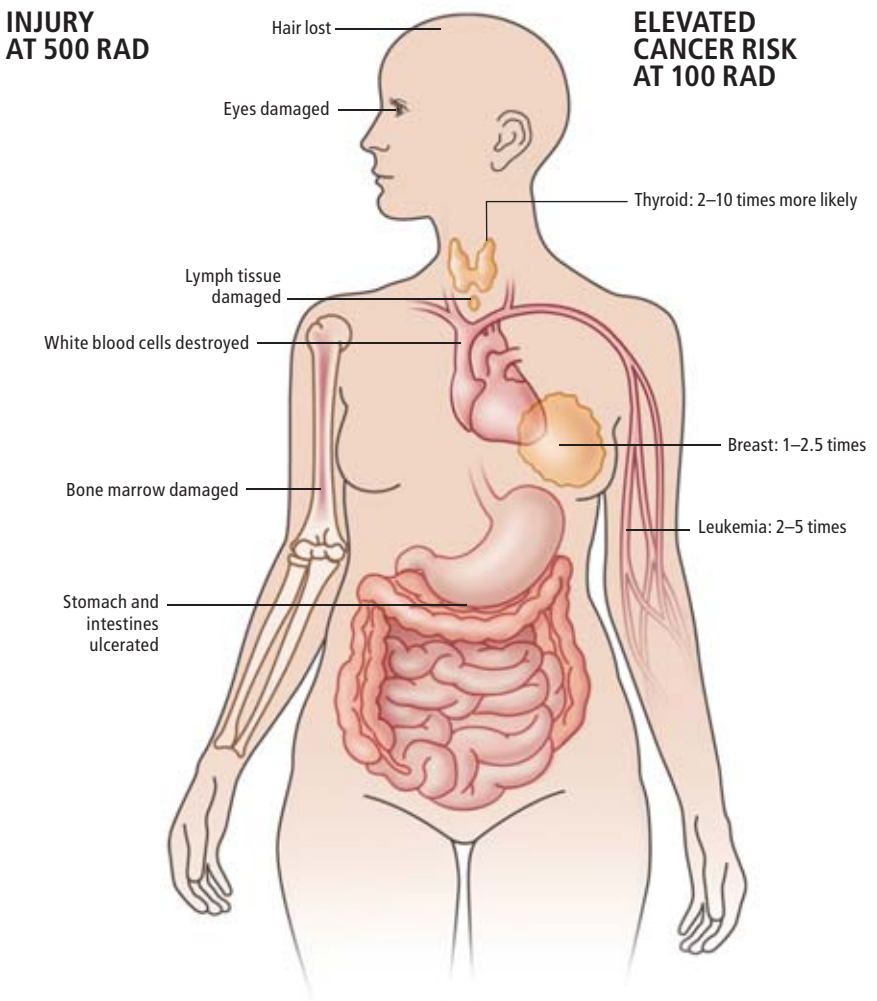
CASUALTIES FROM A SIMILAR ONE-MEGATON AIRBURST



SICK SURVIVORS

Although millions of people would die quickly in a large nuclear blast, millions more would be maimed, burned and otherwise hurt. If they survived these injuries, they would still face serious consequences from radiation exposure.



"People came fleeing.... One after another they were almost unrecognizable. The skin ... was hanging from their hands and from their chins; their faces were red and so swollen that you could hardly tell where their eyes and mouths were."

—Hiroshima survivor in The Making of the Atomic Bomb, *by Richard Rhodes*

"I have been hospitalized 10 times by radiation diseases, three times ... my family called to my bedside. I have to admit I am getting bored with death."

—Hiroshima survivor Sanao Tsuboi, quoted by Torcuil Crichton in "Hiroshima: The Legacy," U.K. Sunday Herald; *July 31, 2005*

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A Need for New WARHEADS?

The U.S. government's proposal to build the first new nuclear warhead in two decades raises a host of questions

By David Biello

JARGON BUSTER

RRW1, W76
Reliable Replacement Warhead, proposed as a successor for W76 nuclear weapons at the end of their planned 30-year service life. The "1" presumes a series of such replacements that would match the capabilities of their precursors.

NNSA
National Nuclear Security Agency, a branch of the Department of Energy that oversees U.S. nuclear weapons. It has offered a variety of rationales for building RRW1s.

PRIMARY, SECONDARY
RRW1 would use a previously tested primary—a fissile nuclear pit that detonates first, to flood the secondary bomb with radiation to yield a thermonuclear explosion. Proponents say that using a tested primary ensures reliability without the need for confirmation by blowing up the entire warhead.

At this very moment, hundreds of U.S. nuclear warheads and bombs are poised to strike targets in Russia and elsewhere. Despite the demise of the Soviet Union in 1991—and thus the end of the cold war policy of mutually assured destruction—the U.S. maintains a stockpile of roughly 10,000 nuclear weapons. Russia, China, France, India, Israel, Pakistan and the U.K. are now all U.S. allies or, at worst, nonbelligerent competitors. All but Russia possess only limited nuclear arsenals. North Korea and Iran, whose relations with the U.S. are more strained, do not yet have the capability to inflict massive nuclear harm on this nation. Indeed, the most pressing nuclear hazard appears to be a "dirty bomb"—a conventional bomb packed with radioactive material—or a small nuclear explosive. A massive nuclear arsenal may provide little deterrent against the use of such weapons by terrorists or nonstate entities.

As part of its obligations under the Moscow Treaty on Strategic Offensive Reductions, the U.S. plans to reduce its total number of active nuclear weapons to between 1,700 and 2,200 warheads and bombs. At the same time, the U.S. Department of Energy and the Department of Defense, worried that aging warheads may not operate optimally after years of storage, want to replace some of them. First on the list is the W76, which makes up a third of the available warheads; the oldest W76s will reach the end of their 30-year life span in 2008. An individual W76 nuclear explosive generates 100 kilotons of force when detonated, equal to 100,000 tons of TNT; it is designed to obliterate "soft targets," such as ports, garrisons and factories.

Three years ago the DOE and DOD launched the Reliable Replacement Warhead (RRW) program. In March, Lawrence Livermore National Laboratory won the RRW program's initial competition to design the nation's first nuclear warhead in 20 years. As a replacement designed to match the explosive-yield capabilities of the W76, the weapon, called the RRW1, would not fulfill a new strategic role in a post–cold war world, and many observers question the need for it. The W76 is currently undergoing a life-extension program that will refurbish as many as 2,000 of the warheads, and concerns about the reliability of aging plutonium components in this warhead and others have proved unfounded [*see box on page 83*].

Yet the National Nuclear Security Adminis-

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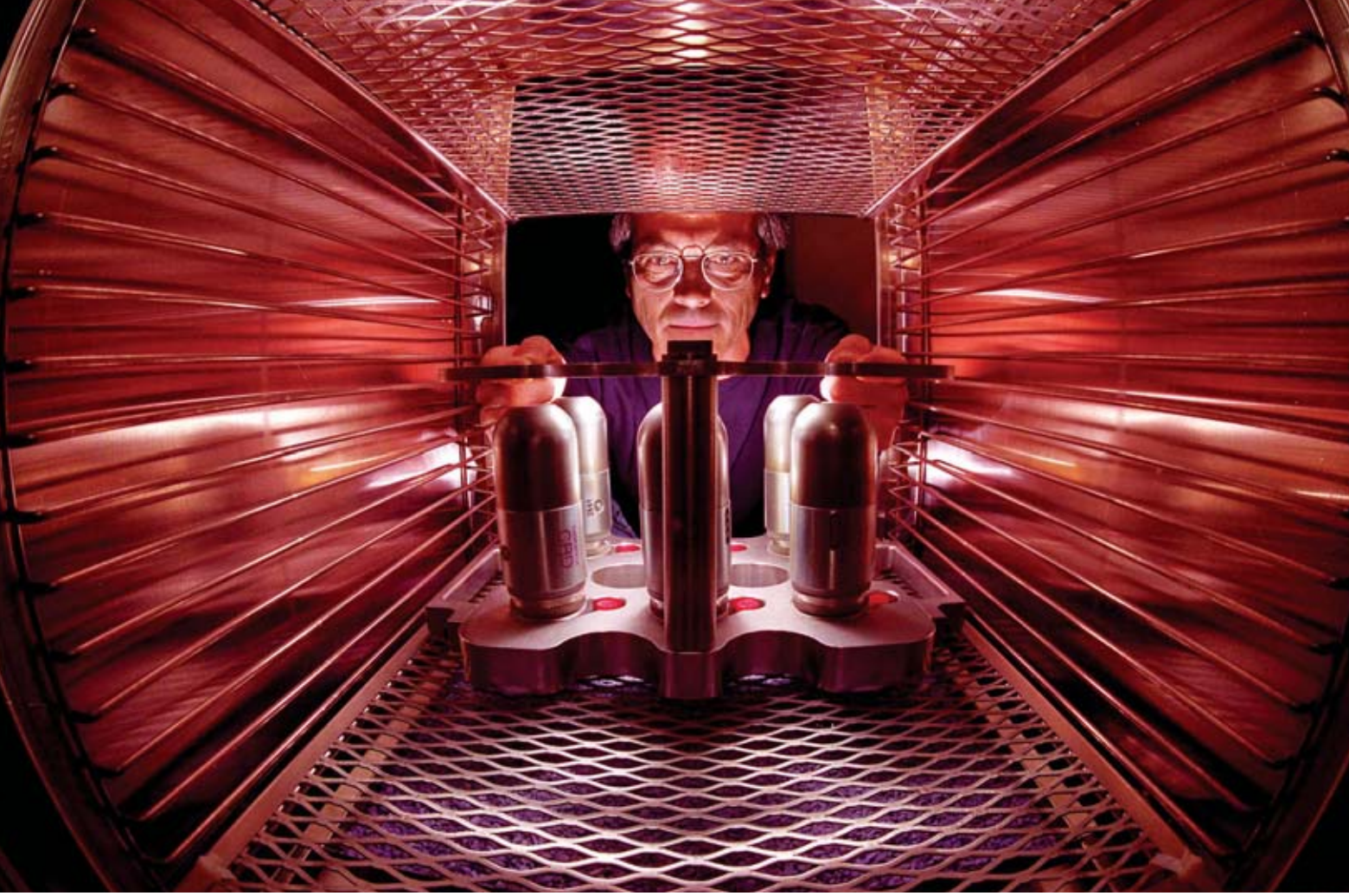

TECHNICIAN TESTS neutron pulse tubes at Sandia National Laboratories for the W76 nuclear warheads, as part of the life-extension program for the 30-year-old weapons.

tration (NNSA)—the branch of the DOE in charge of the nation's nuclear weapons—has offered a variety of other rationales, including reducing the risk of a return to nuclear testing and creating a weapon that cuts the use of toxic materials. Although funding of the RRW effort has not been approved, and parts of the program have already been cut or questioned by members of Congress, a cost estimate and production plan will be completed by the end of this year. As the stockpile continues to age, the questions facing the government remain: What is the purpose of the U.S. nuclear arsenal, what should it be composed of and how many weapons are necessary?

Same Old, Same Old?

One government defense of the new weapon is that it would not require testing; President Bill Clinton codified a 1992 moratorium on nuclear testing. NNSA officials emphasize that the RRW1 is based on a previously tested weapon, although it adds a host of new components. "It's new in the sense that we've never done this before, but it's not new in the traditional arms-control sense," says John Harvey, director of policy planning staff at the NNSA. "It will have the same form and function as the current weapon."

In fact, the Livermore design triumphed because it is based on a former design, one detonated during the more than 1,000 nuclear tests conducted before the U.S. moratorium. The weapon's key component—the plutonium pit—"was nuclear-tested four times," notes Bruce Goodwin, Livermore's associate director for defense and nuclear technologies. "It's the exquisite test pedigree of the baseline for this design that gives very high confidence that it will work as expected."

The new warhead would work much the same way as any other fusion bomb. The fissile nuclear pit, or primary, explodes and floods surrounding chemical compounds, known as the secondary, with radiation. This radiation triggers a fusion reaction between the tritium and deuterium isotopes of hydrogen produced by the irradiated compound. A thermonuclear explosion follows.

Only a few types of primaries have been tested. "It's the SKUA9 design," Goodwin says. The SKUA9 was one of a series of primaries that Livermore created during the most recent nuclear testing program in the 1980s, solely to examine the viability of options for secondaries; it

OHIO-CLASS ballistic missile submarines carry W76 nuclear warheads.

RANDY MONTOYA (*top*); CHRIS OTSEN *U.S. Navy/Zuma Press/Newscom* (*bottom*)

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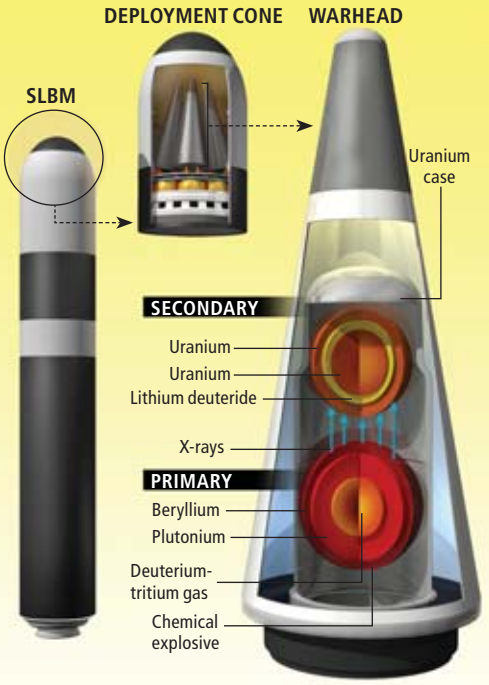
[HOW IT WORKS]

A ONE-TWO PUNCH

Modern nuclear warheads are fusion bombs—essentially fission bombs wrapped in specific elements that can undergo fusion when the conditions are right.

First, shaped explosives surrounding the primary, a fissile nuclear pit, detonate, compressing plutonium that is under neutron bombardment from a special trigger. The plutonium splits apart into smaller elements, releasing energy.

This energy, in the form of radiation, floods the secondary, a device containing elements primed to fuse. The radiation, helped along in some designs by another fission reaction it sets off, initiates fusion between tritium and deuterium isotopes of hydrogen in the lithium-deuteride fuel. This fusion feeds on itself, and a thermonuclear fireball follows.



was never produced in a weapon. As a result of this prior testing and computer modeling, the RRW1 would require no further detonations, according to the NNSA and Livermore.

The RRW1's design improvements will also provide increased confidence in the weapon's margin over the W76, says J. Stephen Rottler, vice president for weapons engineering and product realization at Sandia National Laboratories, which will be responsible for integrating the RRW1 into weapons systems such as missiles. ("Margin" describes a weapon's ability to avoid nuclear explosions of diminished yield; those with sufficient margin, for instance, should remain as powerful in late age as they are when they are first built.)

The new warhead will be bigger, thicker and heavier—and therefore less likely to fail, Rottler and Goodwin say. But critics note that margin could also be improved in existing weapons by changing the composition or mechanism of the so-called boost gas, gaseous tritium and deuterium around the pit that enhances its explosive potential. They also note that no nuclear weapon in the current U.S. arsenal has ever been manufactured without being detonated to confirm its operability. "Is there a military commander out there who will ever rely on something that has not been fully tested? So far that has not been the case," says Hans Kristensen, director of the nuclear information project at the Federation of American Scientists (FAS), which the creators of the original nuclear weapons founded in 1945.

Adds physicist Frank von Hippel of Princeton University: "You never know if you've made a mistake until you've tested the thing. The existing weapons have the merit of having been tested."

Building a Better Bomb

In addition to ensuring sufficient margin in the RRW1s, improvements by weapons designers are addressing another kind of reliability issue: that the bombs will not go off accidentally. The RRW1s will add new, heavier features, such as insensitive high explosives and advanced security technology. During the cold war, the military emphasized packing many warheads into one weapon to generate maximum explosive yield, while also minimizing its overall weight to enable maximum range. Today such considerations are no longer as crucial, designers say.

Another way to improve safety—that of handling these weapons in storage—is to add explosives, such as triaminotrinitrobenzene (TATB), that resist detonation from impact or heat except when properly triggered. "We have taken insensitive high explosives and slammed them into reinforced concrete blocks at Mach 4. They will not detonate," Livermore's Goodwin says. It is so secure, "you can put a gasoline fire out with it. If you put a blowtorch to it, you can get it to molder."

But clients in the armed forces have previously decided that such safety precautions are unnecessary. For example, the U.S. Navy declined to replace the conventional explosives in some of its Trident warheads in the early 1990s. "They decided it wasn't worth it," von Hippel says. "They were confident they could handle the warhead safely."

An additional safety upgrade in the RRW1, not available in the W76, is permissive action link (PAL), a computerized system that requires authorization to fire the weapon. "Under refurbishment, if we wanted to improve security interior to the warheads, we would have had to retrofit that into the warheads, which is difficult to do without nuclear testing," Harvey says.

Whether the armaments require costly additions such as PAL is an open question, however. Because the W76 is carried onboard submarines or stored in heavily secured stockpiles, it

NUCLEAR NUMBERS

15 kilotons

Equivalent to 15,000 tons of TNT. Amount of explosive force produced by the bomb dropped on Hiroshima, Japan, in 1945.

50 megatons

Record yield, equivalent to 50 million tons of TNT, produced by the Soviet Tsar Bomba in a 1961 test.

1 to 475 kilotons

Range of yields for active weapons in the U.S. arsenal. "Boosts" can increase yields.

DON FOLEY

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has little need for such features, critics note. And the life-extension program for other nuclear weapons, such as the B61 gravity bomb, has added security measures, such as increased encryption, without having to start a new design from scratch, Kristensen argues. "Here was a weapon that was designed back in the 1960s and 1970s, and when it was first deployed it did not have safety features," he says. "They refit it all on the weapon itself without having to rebuild it. This suggests that you can achieve extraordinarily high levels of safety in current designs without going to a new design."

The U.S. also spent millions of dollars upgrading the security of nuclear weapon storage sites after the September 11 terrorist attacks, leaving open the question of who is capable of improperly triggering such weapons. "I don't know anyone who believes that the physical security of U.S. nuclear weapons is in doubt," says Ivan Oelrich, FAS's vice president for strategic security programs. A panel of experts convened to evaluate the RRW program—the Nuclear Weapons Complex Assessment Committee of the American Association for the Advancement of Science (AAAS)—agrees. In its April assessment report the committee found no reason to believe that features such as PAL would "substantially reduce the current reliance on guns, guards and gates."

The NNSA says the new features are necessary for the small amount of time such weapons spend being trucked from site to site, to eliminate the threat of hijacking. "It gives us an extra measure that we think is prudent, particularly in transportation scenarios," Harvey says.

COSTS

$6.5 billion
Fiscal year 2008 cost for stockpile stewardship
—NNSA FY08 Budget Request

$21 billion
Cost to replace the present weapons complex
—George Allen, Director, Office of Transformation, NNSA

$5.8 trillion
Estimated cost of U.S. nuclear weapons program
—Stephen Schwartz, The Brookings Institution

The "Green" Nuclear Warhead

The RRW1 also would eliminate the need for some of the toxic substances often used in weapons, such as beryllium, a brittle, carcinogenic metal that reflects the neutrons released in a nuclear explosion and redirects them back to start a thermonuclear chain reaction. "Because of the release of the weight requirement, we are able to use materials that are heavier but more environmentally benign," Goodwin says. "We will be able to eliminate an entire [manufacturing] process that produces 96 percent radiological toxic waste that has to be buried and replace it with nontoxic waste that is 100 percent recyclable."

"You replace [beryllium] with something that quite honestly you could eat and be healthy," he adds. "It is in prosthetic body implants. It's about as biologically benign as any material can be." Because the exact specifications remain classified, however, Goodwin cannot reveal what the substance is or its exact role in the new weapon. And any nuclear weapon would still rely on plutonium, which can kill in hours if handled improperly.

Building a new warhead would entail refitting the nation's nuclear weapons–producing factories, such as Amarillo, Tex.–based Pantex, Kansas City Plant in Missouri, and Y-12 in Oak Ridge, Tenn. All are "antiques," as Goodwin calls them, some dating from the 1940s. The Bush administration unveiled plans in April for a complex to build all the components of new nuclear warheads—dubbed Complex 2030 for the year set for its completion.

Even if the Complex 2030 plans were scaled back, upgrades to the current infrastructure would be needed to carry out the RRW program, according to the AAAS panel, including at least a doubling of the current assembling and disassembling work at the Pantex plant as well as a significant increase in the amount of plutonium pits produced at the Los Alamos TA-55 facility, which began producing new primaries for the first time in 18 years in July. "We do have pit production capability but it's one-

[RELIABILITY CONCERNS]

TRUST BUT VERIFY

Concerns about the reliability of aging weapons first prompted the U.S.'s Reliable Replacement Warhead program. Some argued that older plutonium cores would degrade and impede the thermonuclear explosion they were designed to create. But subcritical tests, computer models and other analyses allayed those fears, and a government-commissioned independent review by a panel of scientists known as Jason estimates that the plutonium pits in the current W76 warheads will last a minimum of a century. Jason has therefore recommended that no action be taken other than continuing routine maintenance in the current life-extension program, such as replacing surrounding circuitry and parts as needed.

Some scientists, most prominently Richard Morse, a former group leader of bomb design as well as laser fusion at Los Alamos National Laboratory, argue that the W76 design itself is flawed. The thin uranium shell that surrounds the core would fail to contain the initial explosion long enough to channel its energy into igniting fusion for the secondary hydrogen detonation.

But many scientists and officials refute this so-called Morse effect, pointing to several successful tests of the weapons package in the 1980s. The "W76 is fine. It's gone through its annual assessment," says Hank O'Brien, RRW program leader at Lawrence Livermore National Laboratory.

The life-extension program itself could inadvertently cause reliability issues, however. Replacing aging parts changes the weapon incrementally. "I couldn't provide the fuse that was done in the 1980s if somebody put a gun to my head," notes J. Stephen Rottler, vice president for weapons engineering and product realization at Sandia National Laboratories. "The more you move away, the greater the uncertainties," Rottler continues. "Then you must either retire the weapon or test, and neither is an acceptable outcome." *—D.B.*

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sies and twosies," says Martin Schoenbauer, principal assistant deputy administrator for operations at the NNSA. The TA-55 "doesn't have the right capacity."

Aside from doubting the need for a new nuclear warhead, critics worry about the infrastructure investment required to support its construction in addition to the cost of currently scheduled refurbishments of the W76 and other weapons. "If you are going to life-extend weapons, you need to re-create the enterprise, the production complex of the 1970s, which is an enormous investment in infrastructure," Goodwin explains. "Do you want to reinvest in technologies that in many cases are extremely unpleasant? Or do you want to make the smallest possible enterprise to support a very different deterrent stockpile, a much smaller stockpile?"

Further complicating the issue is that no one knows how much the RRW1 or Complex 2030 will cost. A detailed bill for the entire RRW program should be available by the end of this year, after engineers compile their estimates. Until such estimates are available, there is no way to determine whether the RRW program presents a savings or an additional financial burden compared with the $6.5 billion requested to fund stockpile stewardship in 2008.

Production on the W76 replacement could begin by 2012, depending on how much money Congress provides, Sandia's Rottler says. In the bomb makers' preferred scenario, the RRW1 would replace some portion of the W76s that would otherwise be refurbished. This swap would likely take decades, according to AAAS experts, and would require a commitment of "significant new funds."

"In this year's budget, the NNSA requested $88 million for the first design and development stages of RRW1. Where did [the funding] come from? It came out of the life-extension program for the W80," another nuclear weapon, notes Robert Nelson, a senior scientist at the Union of Concerned Scientists, an independent scientific research and advocacy group. "We're worried about the long-term reliability of the stockpile, but to pay for [the RRW program] we are going to cut the very programs that maintain the reliability of the stockpiles." He adds that cutting the funding for the maintenance programs for existing weapons precludes other options: "It makes it impossible to reverse course."

LAND, AIR OR SEA: Weapons can be launched from ground silos (*not shown*), submarines (*top*) and aircraft (*bottom*) to ensure retaliation.

PAUL SHAMBROOM

The Ultimate Cost

Billions more will be needed to retool the production infrastructure if Congress decides to authorize the RRW program and Complex 2030, both proponents and opponents say. And members from both sides of the aisle on the House Appropriations Subcommittee on Energy and Water Development have expressed skepticism about the program and the strategy behind it, as laid out in July by the DOD and DOE. "Although a lot of time and energy went into determining the winning design for a new nuclear warhead, there appears to have been little thought given to the question of why the United States needs to build new nuclear warheads at this time," said panel chair Representative Pete Visclosky of Indiana in a written statement. "Without a comprehensive defense

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strategy that defines the future mission, the emerging threats and the specific U.S. nuclear stockpile necessary to achieve the strategic goals, it is impossible for Congress to appropriate funding for RRW in a responsible and efficient manner." And Livermore makes no claims that an RRW would last any longer in storage than existing weapons, raising the possibility of an RRW for the RRW in a few decades' time.

The planned replacement of the W76 with the RRW1 is also just the first of such substitutions. "If we're really going to have an impact as to a reduction in the stockpile, we have to address the whole stockpile," said Steve Henry, deputy assistant to the secretary of defense for nuclear matters, at a press conference announcing the design winner. And that will require different laboratory priorities and manufacturing capabilities. "It is a responsive infrastructure that you rely on to mitigate technical surprise and changes in the geopolitical environment. That responsiveness allows you to trade off numbers of weapons," Henry said.

The NNSA has already launched a feasibility study for a second RRW-produced weapon specifically designed for air delivery, according to Harvey. A likely candidate for replacement by an eventual RRW2 would be the W78 warhead that sits atop land-based intercontinental ballistic missiles, Kristensen says. It is nearly as old and also lacking insensitive high explosives and security features. Neither the DOD nor NNSA has any comment on how many RRWs might ultimately be necessary.

A Credible Deterrent

The biggest impact of the replacement weapons program might be on the global nuclear arms situation. The U.K., France, Russia and China have similar modernization efforts under way or planned, but construction of the RRW1 by the U.S. might send an inflammatory signal to the rest of the world. "If the United States, the strongest nation in the world, concludes that it cannot protect its vital interests without relying on new nuclear weapons for new military missions, it would be a clear signal to other nations that nuclear weapons are valuable, if not necessary, for their security purposes, too," said Sidney Drell, an arms-control expert and physicist at the Stanford Linear Accelerator Center, at the American Physical Society Conference in Denver in March.

As a result, former secretaries of state Henry Kissinger and George Shultz, former secretary of defense William Perry and former senator Sam Nunn of Georgia (a former chair of the Senate Committee on Armed Services) have argued for the elimination of such weapons. "We endorse setting the goal of a world free of nuclear weapons and working energetically on the actions required to achieve that goal," they wrote earlier this year in a *Wall Street Journal* editorial.

Ultimately, the RRW program may address a more fundamental concern: ensuring that the U.S. retains the capacity to build and field nuclear weapons well into the future, should they be needed once again. "We want to exercise the scientists and engineers," Harvey says. "The folks who did this back in the cold war are about to retire. We need the next generation to do this and do it now so that they can be mentored by that older generation."

Adds physicist Bob Civiak, former budget and policy analyst at the U.S. Office of Management and Budget: "We have existing warheads that can be maintained mostly by the production sites. That leaves the labs with nothing to do, and that is why we have an RRW program."

The true rationale for the RRW program, then, may be reliable replacement scientists, engineers and technicians—and the maintenance of the capacity to build new nuclear weapons. Whether they, in fact, need replacing is yet another subject of controversy. ■

David Biello is an associate editor, online, at SciAm.com

PAUL SHAMBROOM

NINE TYPES of active bombs and warheads exist in the U.S. arsenal, including these B83 gravity bombs, and all need routine maintenance.

MORE TO EXPLORE

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The Reliable Replacement Warhead Program: Background and Current Development. Congressional Research Service Report for Congress, 2007. Available at **www.fas.org/sgp/crs/nuke/RL32929.pdf**

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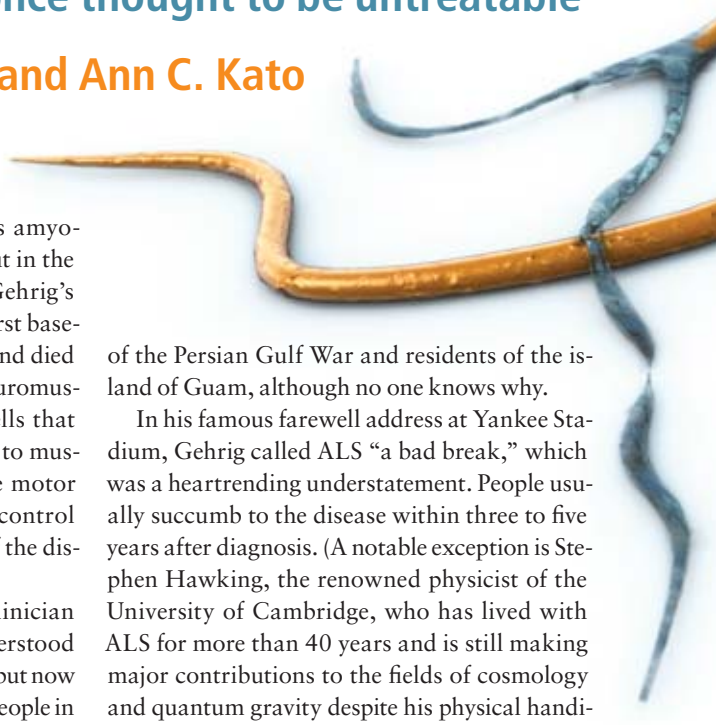
PLAYING DEFENSE AGAINST LOU GEHRIG'S DISEASE

Researchers have proposed potential therapies for a paralyzing disorder once thought to be untreatable

By Patrick Aebischer and Ann C. Kato



KEY CONCEPTS

- Amyotrophic lateral sclerosis (ALS) is a disease that kills motor neurons. Patients become paralyzed and usually die within three to five years of onset. The most famous victim is legendary New York Yankees player Lou Gehrig (*below*).
- ALS was once considered nearly impregnable to a scientific attack, but researchers have recently discovered treatments that can slow the progress of the disease in rodents by protecting the axons of motor neurons.
- Investigators are now preparing clinical trials to test the effectiveness of the proposed ALS treatments in humans.

—The Editors

AP PHOTO

The official name of the illness is amyotrophic lateral sclerosis (ALS), but in the U.S. it is better known as Lou Gehrig's disease. The great New York Yankees first baseman was diagnosed with ALS in 1939 and died two years later from the progressive neuromuscular disorder, which attacks nerve cells that lead from the brain and the spinal cord to muscles throughout the body. When these motor neurons die, the brain can no longer control muscle movements; in the later stages of the disease, patients become totally paralyzed.

First described in 1869 by French clinician Jean-Martin Charcot, ALS is a misunderstood illness. Doctors once thought it was rare but now consider it fairly common: about 5,000 people in the U.S. are diagnosed with ALS every year. In total there are about 30,000 ALS patients in the U.S. and approximately 5,000 in the U.K. ALS typically develops between the ages of 40 and 70, but the disease strikes younger and older patients as well. Other well-known people who suffered from ALS include British actor David Niven, Russian composer Dmitri Shostakovich and Chinese leader Mao Tse-tung. Researchers have found unusual clusters of patients with the disorder among Italian soccer players, veterans of the Persian Gulf War and residents of the island of Guam, although no one knows why.

In his famous farewell address at Yankee Stadium, Gehrig called ALS "a bad break," which was a heartrending understatement. People usually succumb to the disease within three to five years after diagnosis. (A notable exception is Stephen Hawking, the renowned physicist of the University of Cambridge, who has lived with ALS for more than 40 years and is still making major contributions to the fields of cosmology and quantum gravity despite his physical handicap.) Until recently, investigators had few practical ideas for fighting the disorder, but in the past several years researchers have made great progress in determining how motor neurons die in ALS patients. In the near future, scientists may develop therapies that could retard the progress of ALS and perhaps even prevent its onset.

A Devastating Disorder

You can glean a basic understanding of amyotrophic lateral sclerosis by parsing its name.

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BRYAN CHRISTIE DESIGN

DYING BACK: One of the key breakthroughs in the fight against ALS is the finding that the degeneration of the motor neurons begins at the ends of the axon—the nerve cell's main branch—and proceeds back to the cell body.

"Amyotrophic" is an amalgam of Greek terms: "a" for negative, "myo" for muscle and "trophic" for nourishment. Putting it all together, the word conveys that the muscles in an ALS patient have no nourishment, so they atrophy or wither away. "Lateral" signifies the area of the spinal cord where portions of the dying nerve cells are located. As this area degenerates, it becomes hardened or scarred. ("Sclerosis" means hardening.) Perhaps the most devastating aspect of the illness is that the higher functions of the brain remain undamaged and patients are obliged to watch the demise of their own bodies.

The most common form of the disease is called sporadic ALS because it appears to strike randomly, targeting anyone in any given place. Familial ALS is a particular form of the disease that is inherited, but only about 5 to 10 percent of all patients fall into this category. Although the early symptoms of the disorder vary from one individual to another, they usually include dropping objects, tripping, unusual fatigue in the arms or legs, difficulty in speaking, muscle cramps and twitches. The weakness that affects ALS patients makes it hard for them to walk or use their hands for daily activities such as washing and dressing. The disease eventually hampers swallowing, chewing and breathing as the weakening and paralysis spread to the muscles in the trunk. Once the muscles responsible for breathing are attacked, the patient must be put on a mechanical ventilator to survive.

Because ALS harms only motor neurons, the senses of sight, touch, hearing, taste and smell are not affected. For unknown reasons, the motor neurons responsible for movements of the eyes and bladder are spared for long periods. Hawking, for example, still has control of his eye muscles; at one time he communicated by raising an eyebrow as an assistant pointed to letters on a spelling card. (He can also move two fingers on his right hand and now uses a speech synthesizer controlled by a hand switch.) The U.S. Food and Drug Administration has so far approved only one treatment for ALS: riluzole, a molecule that can prolong survival by several months, most likely by curbing the release of harmful chemicals that damage motor neurons.

What do we know about the causes of this horrible disease? Investigators have put forward a vast number of theories to explain its origin, including infectious agents, a faulty immune system, hereditary sources, toxic substances, chemical imbalances in the body and poor nutrition. Although scientists have not yet determined what triggers the disorder in most patients, a breakthrough came in 1993, when a consortium of geneticists and clinicians discovered a gene that was responsible for one form of hereditary ALS that represents approximately 2 percent of all cases. This gene turned out to code for an enzyme called superoxide dismutase (SOD1) that protects cells from damage caused by free radicals (highly reactive molecules produced

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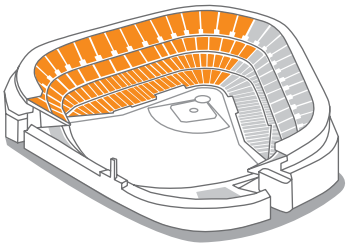
A CROWD OF PATIENTS

ALS was once thought to be rare, but about 30,000 Americans suffer from the disease—enough to fill more than half the seats in Yankee Stadium.



in the body by normal metabolic processes).

Researchers subsequently identified more than 100 different mutations in the SOD1 gene that cause ALS. It remains a mystery, though, how alterations in this ubiquitous enzyme can produce such specific damage to one type of cell in the nervous system. At first scientists thought that the toxicity was related to a loss of the cell's capacity to fight free radicals. Now, however, several lines of evidence suggest that the various mutations confer some destructive property to the mutated enzyme, a phenomenon that geneticists call a gain of function.

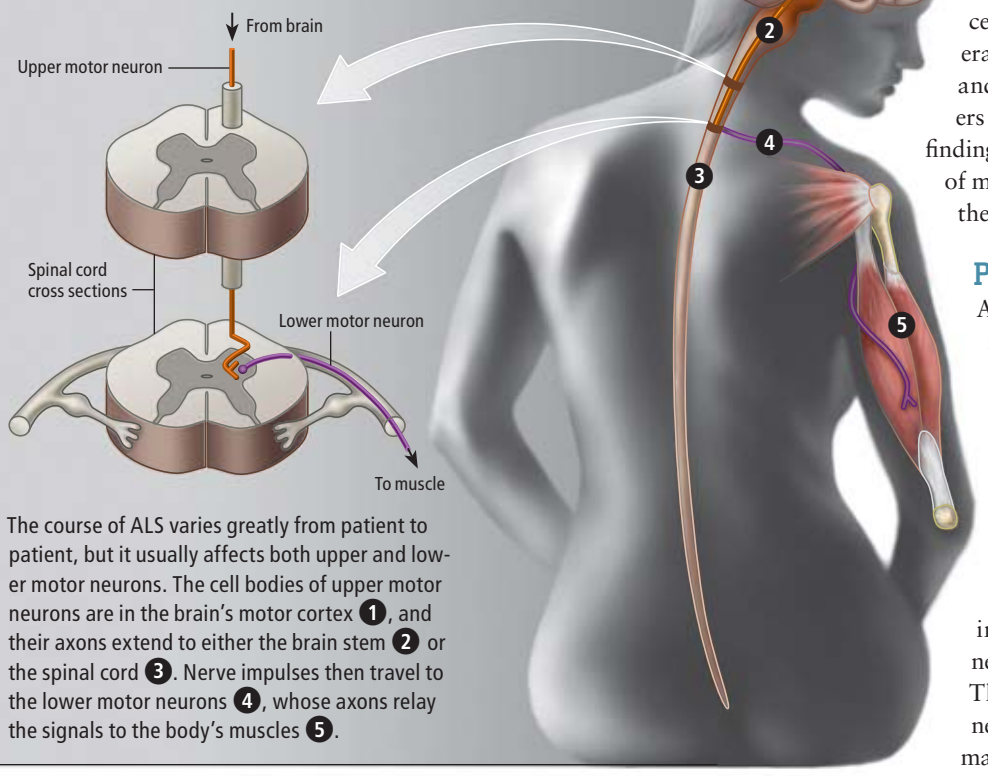
The identification of mutations in the SOD1 gene enabled scientists to insert the variant DNA into the genomes of laboratory animals, creating lines of rodents that would develop a motor neuron disorder that is very similar to ALS. Because investigators could now examine the course of the disorder in these animal models, there was a sudden explosion of research and publications on a disease that had previously been considered nearly impregnable to a scientific attack. Other animal models became available after the discovery of unrelated genes that also caused the death of motor neurons. At last, it was possible to challenge the assortment of hypotheses that had been proposed over the years to explain how ALS arises.

We are beginning to understand that the motor neuron may have a novel mechanism for degenerating. The motor neuron's axon—the main branch extending from the cell body—is unusually long, extending as much as one meter in a tall person [*see box below*]. At its terminal, the axon splits into a series of branches whose tips sit glued onto the muscle like the tines of a rake. Each connection between the nerve and the muscle is called a synapse. By releasing small molecules called neurotransmitters, the nerve stimulates the muscle to contract.

For many years, researchers believed that the motor neuron and its various parts die simultaneously. Scientists have now learned, however, that the different compartments of the motor neuron can die by different mechanisms. The cell body, which contains the nucleus of the neuron, usually dies by a process called apoptosis in which cells self-destruct by cutting themselves into pieces and packaging the fragments into small membrane bags that are easily removed. The axon dies by another mechanism, and, most likely, the synapse by yet another. If the nerve cell dies starting from the terminal region of the axon, the process is called "dying back." If it dies starting from the cell body, the process is called "dying forward." More and more evidence indicates that in ALS the nerve cells show their first signs of degeneration in the region of the synapse and the axon. As a result, researchers are concentrating their efforts on finding drugs that can protect the axons of motor neurons rather than simply the cell bodies.

[ANATOMY]

THE TARGETS OF ALS



The course of ALS varies greatly from patient to patient, but it usually affects both upper and lower motor neurons. The cell bodies of upper motor neurons are in the brain's motor cortex ❶, and their axons extend to either the brain stem ❷ or the spinal cord ❸. Nerve impulses then travel to the lower motor neurons ❹, whose axons relay the signals to the body's muscles ❺.

Paths of Destruction

As mentioned earlier, some motor neurons are more susceptible to ALS than others, but researchers are only beginning to understand why. Recently Pico Caroni and his colleagues at the Friedrich Miescher Institute in Basel, Switzerland, have addressed this issue by making a map that shows how nerve impulses travel from the motor neurons to the muscles of a mouse. The investigators genetically engineered the mice to have fluorescent markers in the axons of some of their

JEN CHRISTIANSEN

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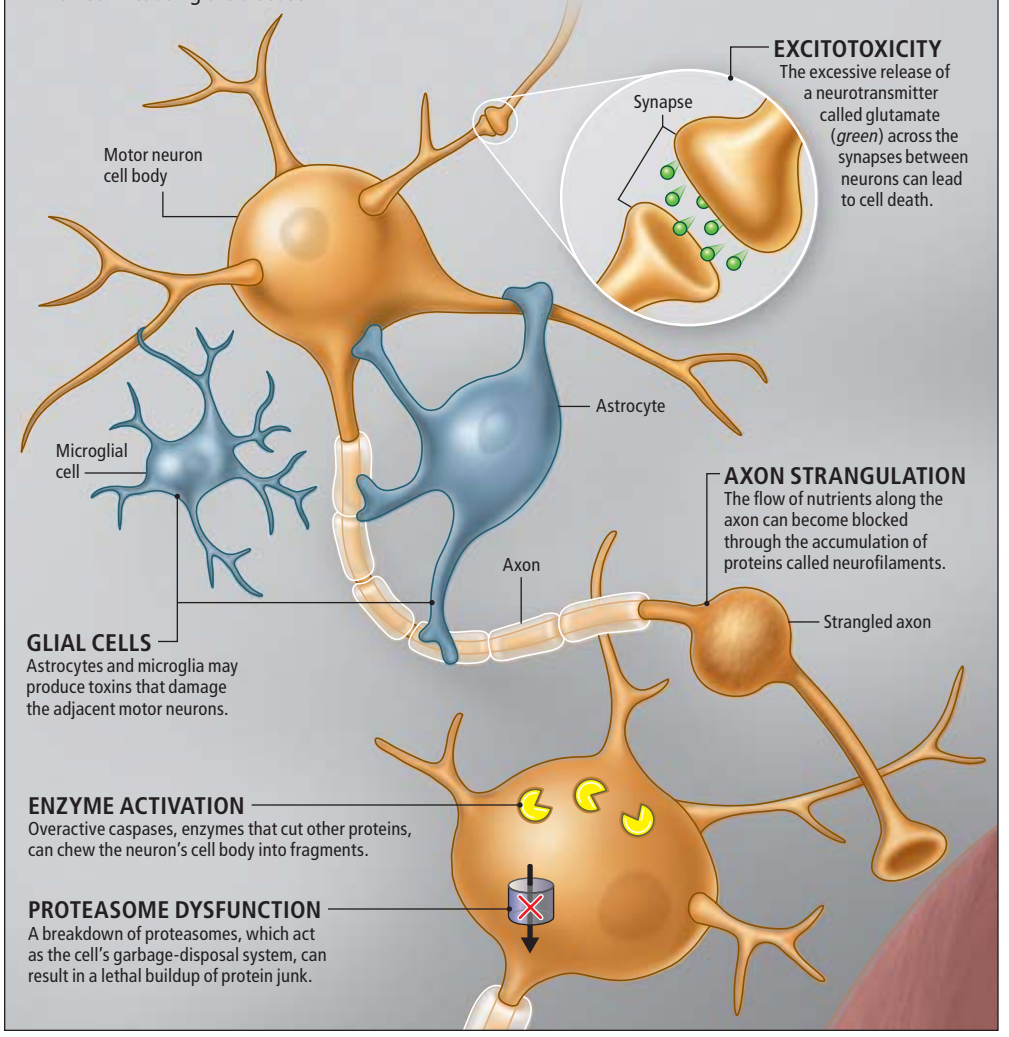
[UP CLOSE]

HOW ALS KILLS

Researchers have identified several mechanisms that may be responsible for the degeneration of motor neurons in ALS patients. Different parts of the neuron—the cell body, the axon, and so on—apparently die by different processes. The neighboring glial cells, which normally support the neurons, may also be involved in causing the disease.



COURTESY OF PATRICK AEBISCHER AND ANN C. KATO (*photographs*); JEN CHRISTIANSEN (*illustration*)

motor neurons. The neurons that connect to muscles in the limbs are divided into three types. The first type innervates fast-twitch and fast-fatigable (FF) muscle fibers that enable rapid, high-energy movements in the arms and legs. The second class of neurons controls fast-twitch and fatigue-resistant (FR) fibers that are common in the smaller muscles in the limbs, and the third group innervates slow-twitch (S) fibers that are in constant use, such as the ones in the torso that maintain posture.

When Caroni and his co-workers examined the fluorescent markers in the SOD1 mice that were genetically prone to ALS, they found that the neurons controlling FF fibers degenerated early in the course of the disease. The FR neurons failed during the intermediate period, and the S neurons stayed intact until the latter stages. This pattern closely matches the progression of symptoms in people with ALS, confirming the similarity between the animal and human forms of the disease.

Joshua Sanes and Jeff Lichtman, both now at Harvard University, have taken a similar approach, studying fluorescent axons with time-lapse imaging in living SOD1 mice. In this way, they were able to distinguish degenerating motor neurons from closely related nerve cells that are making an attempt to regenerate. Sanes and Lichtman concluded that two types of neurons exist within the same motor pathways in ALS mice: "losers" that become so fragmented that

[THE AUTHORS]

Patrick Aebischer and Ann C. Kato have been working together to study amyotrophic lateral sclerosis (ALS) using animal models since 1993. Aebischer has been president of the Swiss Federal Institute of Technology in Lausanne for the past seven years. His laboratory is located in the Brain Mind Institute of the same university. Kato, a professor of basic neuroscience at the University of Geneva, has been on the school's medical faculty for 29 years. Working with mice that have been engineered to be susceptible to ALS, Aebischer and Kato are currently investigating different ways to slow down or even stop this devastating condition.

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their connection with the muscle is broken and "compensators" that grow new axonal branches. If scientists can determine what factors are keeping the compensator neurons alive, they may be able to apply the results in future therapies.

Studies have shown that it is necessary to protect both the axon and the cell body to extend the life span of animals with ALS; protection of the cell body alone has no effect. These experiments reinforce the idea that different parts of the motor neuron are dying by different molecular processes. In the axon, the most abundant proteins responsible for maintaining its rigid shape are the neurofilaments. For unknown reasons, the more of these proteins there are in the axon, the larger its diameter and the greater its vulnerability to ALS. A group led by Jean-Pierre Julien at Laval University in Quebec has shown that when abnormally high amounts of neurofilaments accumulate in axons, they can block the flow of nutrients from the cell body to the synapse. This interference in the transport of material through the axon essentially strangles the motor neuron's cell body to death. About 1 percent of all ALS cases arise from mutations in the gene that codes for neurofilaments.

Because of the structural asymmetry of the motor neuron, the cell body has to furnish an enormous amount of energy to keep its long axon and synaptic terminal alive. Important cellular components, such as energy-generating mitochondria, must be fabricated in the cell body and then transported down the axon to the terminal; conversely, certain critical substances such as growth factors (proteins that can stimulate cell maturation and proliferation) must be transported from the terminal back to the cell body. All this intracellular movement requires molecular motors that are hooked up in a cogwheel fashion to minuscule tracks composed of microtubules. A breakdown in any of these processes can lead to the development of a motor neuron disease. Several research groups have shown that mutations in the molecular motors can kill motor neurons.

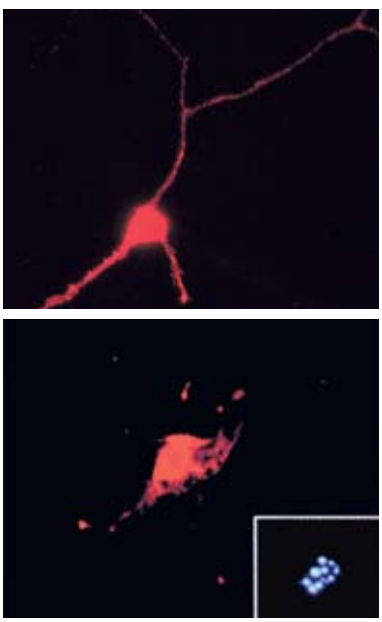
Researchers have made great progress in determining how motor neurons die in ALS patients.

Until recently, scientists had believed that the motor neurons in ALS patients caused their own destruction, but new evidence is beginning to reveal that neighboring glial cells, which normally provide physical support and nutrition for neurons, may also play a role in inflicting the damage. ALS does not develop in mice with one type of SOD1 mutation, for example, if the mutant enzyme is produced only in the motor neurons or neighboring glial cells. Furthermore, Don Cleveland's group at the University of California, San Diego, has shown that healthy glial cells can protect sick motor neurons and that, conversely, sick glial cells can induce degeneration in healthy motor neurons. Thus, it appears that both motor neurons and adjacent glial cells collaborate in causing the disease.

Hopes on the Horizon

Given all the recent advances in basic research on ALS, what are the prospects for discovering effective treatments for the disorder? Researchers have already identified certain molecules that can protect the axons of motor neurons. One of these is a protein called ciliary neurotrophic factor, which is crucial to the survival of both motor and sensory neurons. Other molecules, such as glial cell–derived neurotrophic factor, protect the neuron's cell body from self-destruction but do nothing for the axon.

In one study to find molecules that can protect axons, a group led by Jeffrey Milbrandt at Washington University in St. Louis decided to use a mouse mutant called Wld^S (which stands for slow Wallerian degeneration) that has a natural mechanism of axonal protection because the animal's DNA has an unusual fusion of two different genes. This genetic sequence codes for a chimeric protein that includes a peptide, or protein fragment, that is essential to the cellular garbage-disposal system, as well as the enzyme



NEURODEGENERATION: Whereas a healthy motor neuron in culture (*top left*) has distinct axonal branching, a dying motor neuron (*bottom left*) has a distorted shape and a withered axon. Furthermore, DNA in the neuron's nucleus forms clumps (*inset*). Although most ALS patients die within a few years, renowned physicist Stephen Hawking (*right*) has lived with the disease for more than four decades.

COURTESY OF CHRIS H. HENDERSON, REPRINTED FROM "MOTONEURON DEATH TRIGGERED BY A SPECIFIC PATHWAY DOWNSTREAM OF FAS: POTENTIATION BY ALS-LINKED SOD-1 MUTATIONS," BY RAOUL ET AL., IN *NEURON*, VOL. 35; 2002, WITH PERMISSION FROM ELSEVIER (*top*); COURTESY OF CHRIS H. HENDERSON, REPRINTED FROM *JOURNAL OF CELL BIOLOGY*, VOL. 147; 1999, © 1999 THE ROCKEFELLER UNIVERSITY PRESS (*bottom* and *inset*); DAVID SILVERMAN *Getty Images (Hawking)*

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Reading the Ailing Brain

With effective treatments for ALS still years away, researchers are developing devices that can receive signals from paralyzed patients' minds, enabling such patients to communicate, perform basic computer functions and, in some cases, operate prosthetic devices. Some of these so-called brain-computer interfaces (BCIs) require surgically implanted electrodes, which read the output of small clusters of neurons inside the brain's motor cortex, the brain's movement-control center.

Noninvasive BCIs, on the other hand, pick up the wavelike electrical activity emanating from millions of neurons through electrodes affixed to a patient's scalp. Neuroscientists Jonathan Wolpaw, Theresa Vaughan and Eric Sellers of the Wadsworth Center, part of the New York State Department of Health in Albany, and their colleagues have developed such a BCI—essentially, a brain-wave keyboard for ALS patients—that works by tapping into a brain signal that turns up when something attracts a person's attention. In the Wadsworth system (*photograph at right*), 17 rows and columns in a grid of 72 letters, numbers, punctuation marks and keyboard controls flash rapidly in sequence on a computer screen while an ALS patient watches for the symbol or function he wants. Each time the desired symbol or function flashes, the user's brain emits the characteristic wave, and a computer processes the wave's timing and other features to discern what the individual is trying to select.

So far five ALS patients have used the Wadsworth BCI to write and converse. One ALS-afflicted scientist uses it to run his research laboratory. Another depends on the technology to convey simple but important requests and information such as "Do not put sweaters on me" and "The dog peed on the floor."

—***Ingrid Wickelgren,***
Scientific American Mind *staff editor*

BRAIN-COMPUTER interface in action.

COURTESY OF THE WADSWORTH CENTER, *New York State Department of Health*

COMPARING NERVE DISEASES

Researchers hope that the study of ALS will yield insights for treating other neurological disorders as well. Below is a comparison of the characteristics of the diseases.

ALS
Age of onset:
typically between 40 and 60
Disease course:
usually three to five years
Genetically linked:
about 10 percent of cases
Neurons affected:
motor
Patients in the U.S.: **30,000**

HUNTINGTON'S
Age of onset:
usually about 40
Disease course:
about 14 years
Genetically linked:
100 percent
Neurons affected:
in the striatum (deep within each hemisphere of the brain)
Patients in the U.S.: **30,000**

PARKINSON'S
Age of onset:
typically between 60 and 70
Disease course:
about 10 to 20 years
Genetically linked:
about 10 percent
Neurons affected:
in the substantia nigra (part of the midbrain)
Patients in the U.S.: **1 million**

ALZHEIMER'S
Age of onset:
usually between 60 and 70
Disease course:
about five to 20 years
Genetically linked:
about 5 to 10 percent
Neurons affected:
in the brain's cortex and hippocampus
Patients in the U.S.: **5 million**

for synthesizing nicotinamide adenine dinucleotide (NAD), a small molecule that is required for many metabolic reactions. When a nerve cell is injured in a Wld^S mouse, the axon will degenerate much more slowly than it would in an ordinary mouse.

By studying mouse neurons in culture, Milbrandt's team showed that the Wallerian mutation enhances the activity of the NAD-synthesizing enzyme and that the resulting increases in NAD somehow protect the axons. The researchers extended their findings to show that higher levels of NAD were stimulating a biochemical pathway in the cell that appears to be responsible for prolonging longevity in roundworms and fruit flies [see "Unlocking the Secrets of Longevity Genes," by David A. Sinclair and Lenny Guarente; Scientific American, March 2006]. What is more, other small molecules such as resveratrol, which is found in the skin of red grapes, are active on this pathway and may also safeguard injured neurons. Several pharmaceutical companies are now trying to develop drugs that could fight ALS and other neurodegenerative diseases by invigorating the NAD pathway.

Another promising possibility comes from a group led by Peter Carmeliet at the Catholic University in Leuven, Belgium. In the course of studying a different research problem, the investigators created transgenic mice—carrying genes transferred from another species—that were defective in producing vascular endothelial growth factor (VEGF), a protein involved in controlling the growth and permeability of blood vessels. Unexpectedly, these mice developed motor neuron disease.

The scientists wanted to know whether they could slow the degeneration of the mice's neurons by delivering VEGF to the nerve cells. Administering therapeutic proteins to the brain and spinal cord is a formidable task, however, because the walls of the blood vessels in the central nervous system are impermeable to large molecules. A team led by Mimoun Azzouz and Nicholas Mazarakis at Oxford Biomedica, a British pharmaceutical company, tackled this challenge with a gene therapy approach, using a virus that could manufacture VEGF after it entered a nerve cell. The researchers injected the virus into various muscles in the VEGF-deficient mice; the terminals of the motor neurons captured the virus, which was then transported to the cell bodies in

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POTENTIAL THERAPIES

Scientists have identified several possible treatments that may be able to slow the progress of ALS.

NEUROTROPHIC FACTORS

Proteins such as vascular endothelial growth factor (VEGF) and insulinlike growth factor 1 (IGF-1) appear to protect motor neurons. These large molecules, however, cannot pass from the bloodstream to the central nervous system, so clinicians would have to use direct injections or viral delivery to administer the therapy.

SMALL MOLECULES

Compounds such as resveratrol, which is found in the skin of red grapes, may be able to protect neurons by stimulating the production of nicotinamide adenine dinucleotide (NAD). One advantage of small molecules is that they can pass through the blood-brain barrier.

STEM CELLS

Grafted stem cells can act as biological pumps for delivering vital growth factors to damaged neurons. Experiments in rodents have shown that the stem cells can actually migrate to the regions where the injured neurons are located.

RNA INTERFERENCE

Synthetic strands of RNA can interfere with the production of toxic proteins in neurons and glial cells. The RNA strands bind to certain messenger RNAs (mobile carriers of genetic information), preventing them from manufacturing their corresponding proteins.

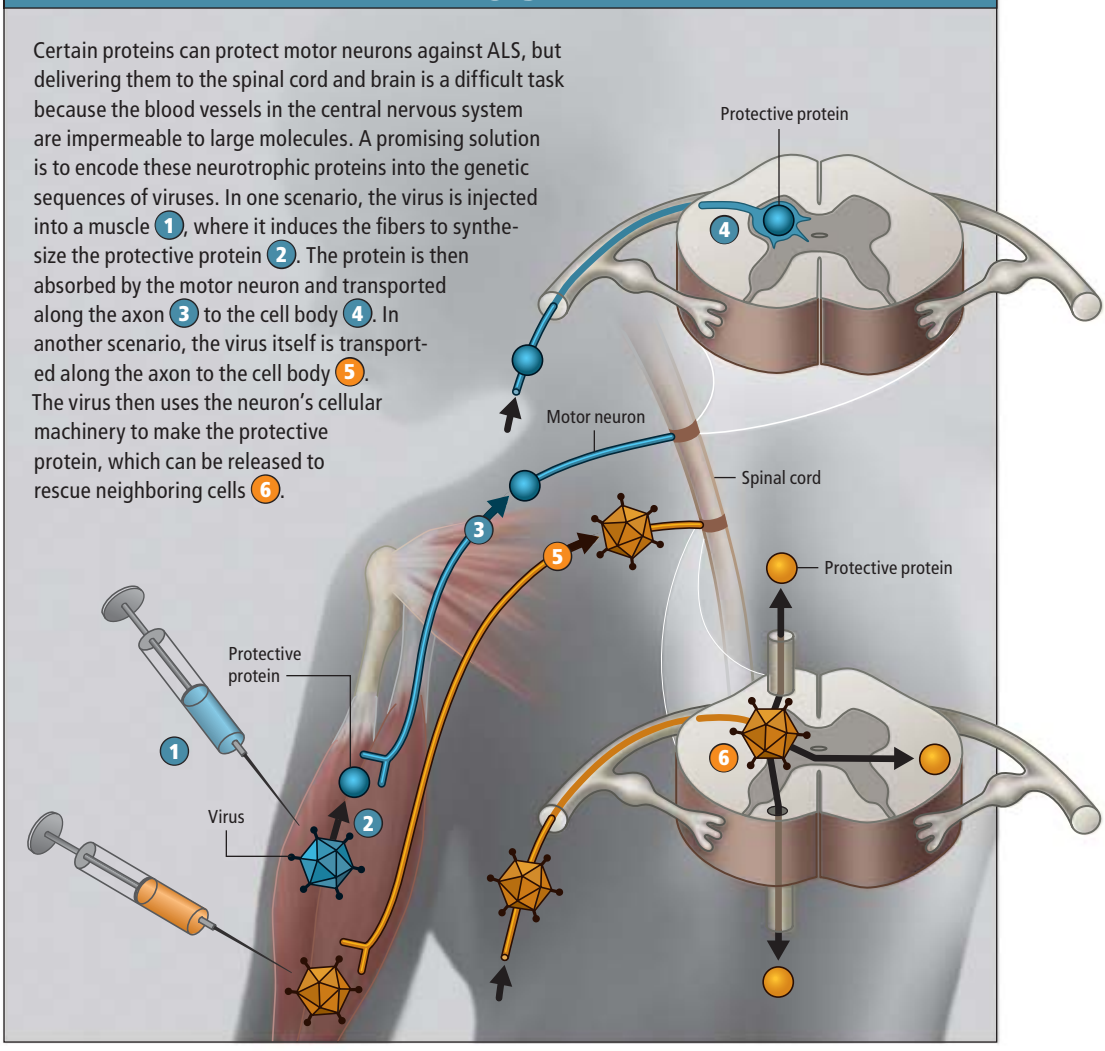
PHYSICAL EXERCISE

Studies have shown that putting mice on a regimen of exercise on running wheels can slow the progress of ALS. Combining the exercise with IGF-1 therapy has a synergistic effect that is more pronounced than that of either treatment alone.

[TREATMENTS]

DELIVERY BY VIRUS

Certain proteins can protect motor neurons against ALS, but delivering them to the spinal cord and brain is a difficult task because the blood vessels in the central nervous system are impermeable to large molecules. A promising solution is to encode these neurotrophic proteins into the genetic sequences of viruses. In one scenario, the virus is injected into a muscle (1), where it induces the fibers to synthesize the protective protein (2). The protein is then absorbed by the motor neuron and transported along the axon (3) to the cell body (4). In another scenario, the virus itself is transported along the axon to the cell body (5). The virus then uses the neuron's cellular machinery to make the protective protein, which can be released to rescue neighboring cells (6).



the spinal cord [*see box above*]. Once inside the motor neurons, the virus produced VEGF in sufficient quantities to delay the onset, and slow the progression, of ALS in the mice.

Employing a different drug-delivery technique, Carmeliet's research group used a small pump to convey VEGF into the cerebrospinal fluid of the brains of rats with ALS. Again the degeneration of motor neurons was slowed, demonstrating that the direct administration of the growth factor could protect the nervous system from the disease. What is more, the team found that human subjects with ALS had significantly lower levels of VEGF in their blood. Carmeliet's group is now working with NeuroNova, a Swedish pharmaceutical company, to develop clinical trials for the VEGF therapy.

Another nerve-protecting protein that holds promise for the treatment of ALS is insulinlike growth factor 1 (IGF-1), which has shown powerful effects on motor neurons both in cultured cells and in animal models. Fred Gage of the Salk Institute for Biological Studies in San Diego and his colleagues engineered a virus that produces IGF-1, then injected the infectious material into mice that had developed an ALS-like disease because they carried SOD1 mutations. From the injection sites in the muscles, the virus traveled to the motor neuron terminals and then to the cell bodies, where it began to produce IGF-1. The treatment resulted in a 30 percent increase in the life span of the mice, probably by acting directly on their motor neurons and the neighboring cells. Researchers are currently laying the groundwork for clinical trials that would test the effectiveness of viral delivery of IGF-1 in humans with ALS.

One of the most surprising discoveries in the past few years is that regular physical exercise can stimulate the growth of new neurons, improve learning and increase the level of growth

JEN CHRISTIANSEN

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factors in the nervous system. Furthermore, animal studies have shown that physical exercise can protect neurons following trauma or disease. Gage and his co-workers, for example, found that putting their ALS-SOD1 mice on a regimen of exercise on running wheels boosted their average life span from 120 to 150 days. The researchers hypothesized that exercise may somehow stimulate the production of IGF-1 in the mice, improving their motor responses and even rescuing damaged neurons. In view of these results, Gage's team decided to examine the consequences of combining physical exercise with IGF-1 treatment. Remarkably, the combination had a synergistic effect that was much more pronounced than that of either treatment alone: the mice that exercised and received IGF-1 injections lived an average of 202 days.

Recent breakthroughs in stem cell research have also opened up new avenues for treating ALS and other neurological disorders. At first scientists focused on the idea of using stem cells—precursor cells that can differentiate into specialized cells such as neurons—to replace the nerve cells harmed by neurodegenerative diseases. Over the past few years, however, several studies have indicated that grafted stem cells can act as a biological pump that delivers vital growth factors to damaged neurons. In this way, it may be possible not only to protect the injured nerve cells but also to promote regeneration in the spinal cord. Surprisingly, experiments in rodent models of motor neuron disease have shown that grafted stem cells can actually migrate to the region where the damaged neurons are located. The tissue at the injury site apparently emits some molecular signal to tell the stem cells to move into that area. Because new evidence suggests that both motor neurons and neighboring cells are responsible for motor neuron disease, it may be necessary to graft stem cells that can produce a variety of cell types and not just motor neurons.

Yet another intriguing possibility for treatment has come from the revolutionary discovery of RNA interference (RNAi). This process occurs when short strands of RNA specifically bind to certain messenger RNAs (mobile carriers of genetic information that serve as templates for making proteins); the binding prevents the messenger RNAs from synthesizing their corresponding proteins. Investigators can take advantage of this phenomenon by infecting target cells with viruses that encode RNAi strands, which can then stop the cells from manufacturing toxic proteins. Research groups headed by one of us (Aebischer) and Oxford Biomedica's Azzouz have shown that this technique can slow disease progression in ALS-SOD1 mice by using RNAi to shut down the faulty SOD1 gene.

Turning any of these novel approaches into an effective therapy will be challenging.

The success of these experiments has encouraged researchers and physicians to plan a clinical trial for the treatment of patients that have the familial form of ALS caused by a mutated SOD1 gene. (Cleveland of U.C.S.D. is spearheading this effort.) In the initial trials, a mechanical pump will deliver a synthetic segment of interfering RNA (called an oligonucleotide) directly into the cerebrospinal fluid of the patients. These molecules are designed to interact with messenger RNAs before they can assemble amino acids to manufacture the toxic SOD1 protein in neurons and glial cells. If this new technology produces promising results in ALS patients, it could possibly be used in other neurodegenerative diseases triggered by flawed genes.

Turning any of these novel approaches into an effective therapy will be challenging. Before doctors can deliver growth factors or RNAi strands by viruses, for example, they must ensure that the procedure can be performed safely. (Viral delivery of genes has had a checkered history in humans.) Furthermore, clinicians must calculate how many muscles in an ALS patient would need to be injected to cause a functional improvement. Ideally, researchers will be able to devise treatments incorporating combinations of proteins and RNAi strands that would confer much greater survival benefits than any one factor alone would. In the meantime, a nonprofit group called the ALS Association is already conducting clinical trials of a drug combination that has prolonged survival in animals: celecoxib (an anti-inflammatory drug that can curb the cellular destruction caused by overactive glial cells) plus creatine (an amino acid). Because these substances are small molecules, they can easily reach motor neurons in the central nervous system.

Of course, the best outcome would be for researchers to discover a way to prevent ALS from developing instead of just a method to treat the symptoms once they appear. The secret to this goal may well depend as much on lifestyle as it does on genes. Researchers know that regular exercise can offer some protection against neurodegenerative diseases, and they are beginning to explore the effects of eating habits as well. Once scientists determine which physical activities and foods provide the best defense against ALS, we may be able to combat this horrible disease before it has time to strike the nervous system. ■

MORE TO EXPLORE

Unraveling the Mechanisms Involved in Motor Neuron Degeneration in ALS. Lucie Bruijn et al. in *Annual Review of Neuroscience,* Vol. 27, pages 723–749; July 2004.

Lentiviral-Mediated Silencing of SOD1 through RNA Interference Retards Disease Onset and Progression in a Mouse Model of ALS. Cédric Raoul et al. in *Nature Medicine,* Vol. 11, No. 4, pages 423–428; April 2005.

Silencing Mutant SOD1 Using RNAi Protects against Neurodegeneration and Extends Survival in an ALS Model. G. Scott Ralph et al. in *Nature Medicine,* Vol. 11, No. 4, pages 429–433; April 2005.

Axon Degeneration Mechanisms: Commonality amid Diversity. Michael Coleman in *Nature Reviews Neuroscience,* Vol. 6, No. 11, pages 889–898; November 2005.

More information about ALS research can be found online at **www.alsa.org**

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Brilliant Displays

A new technology that mimics the way nature gives bright color to butterfly wings can make cell phone displays clearly legible, even in the sun's glare

By M. Mitchell Waldrop

KEY CONCEPTS

- Interferometric modulator (IMOD) displays can produce brilliant colors by exploiting the physical effect of interference while using little of the limited battery power in mobile devices such as cell phones. They are also readily seen in bright daylight.
- The basic unit of an IMOD display is a tiny mechanism that consists of two mirrored surfaces with a gap between them. The gap determines the color that reflects back when light strikes the display.
- Qualcomm, a large wireless electronics firm, hopes that IMOD technology can make inroads in a mobile electronics market dominated by liquid-crystal displays (LCDs). —*The Editors*

The next time you buy a cell phone, take a close look at the display panel. If things go the way Qualcomm hopes, that colorful little rectangle could give a whole new meaning to the expression "butterfly effect." True, the interferometric modulator (IMOD) displays recently introduced by the San Diego–based firm have nothing to do with the unexpectedly strong effect a wing beat can theoretically have on the weather. But the devices do use an array of artificial microstructures to produce the same kind of iridescent colors as are seen on the wings of tropical butterflies. And Qualcomm is betting that its approach will give IMODs several advantages over today's dominant liquid-crystal-display (LCD) technology.

Most important is that an IMOD display is much easier on a handset's battery—a characteristic that will matter more and more as people increasingly use cell phones for Web browsing, text messaging, and playing games, videos and music. Such intensified use poses a severe power-management challenge for LCDs, most of which cannot be read at all unless they have a backlight shining up through them. But an IMOD display simply reflects ambient light the way paper (or a butterfly wing) does.

"So an IMOD consumes as little as 6 percent of the handset's battery power, versus nearly 50 percent for an LCD," says James Cathey, Qualcomm's vice president of business development. And that means that an IMOD-equipped handset should run a lot longer on a single charge—even allowing for the supplementary illumination it would need for low-light situations. "In a typical usage scenario, we estimate that an IMOD-equipped phone would give you 140-plus minutes of video time, versus 50-plus minutes with an LCD display," he notes.

Being reflective, IMOD displays are also far easier to read in bright daylight: rather than turning black, as most LCD displays effectively do, they actually get clearer and more vivid. "If you're using your phone for video, text, pictures, you want the same viewing quality in many environments," Cathey says.

IMOD displays can also switch their basic unit cells on and off within about 10 microseconds, roughly 1,000 times faster than LCD displays can, a feature that makes them considerably better suited to video. And IMOD displays are at least as rugged as LCDs. Qualcomm has tested the IMOD unit cells through at least 12 billion on-off cycles, the equivalent of more than seven years of continuous operation, without a failure.

Of course, there are many other alternatives to LCDs, ranging from OLEDs (organic light-emitting-diode) displays to electrophoretic "e-paper"

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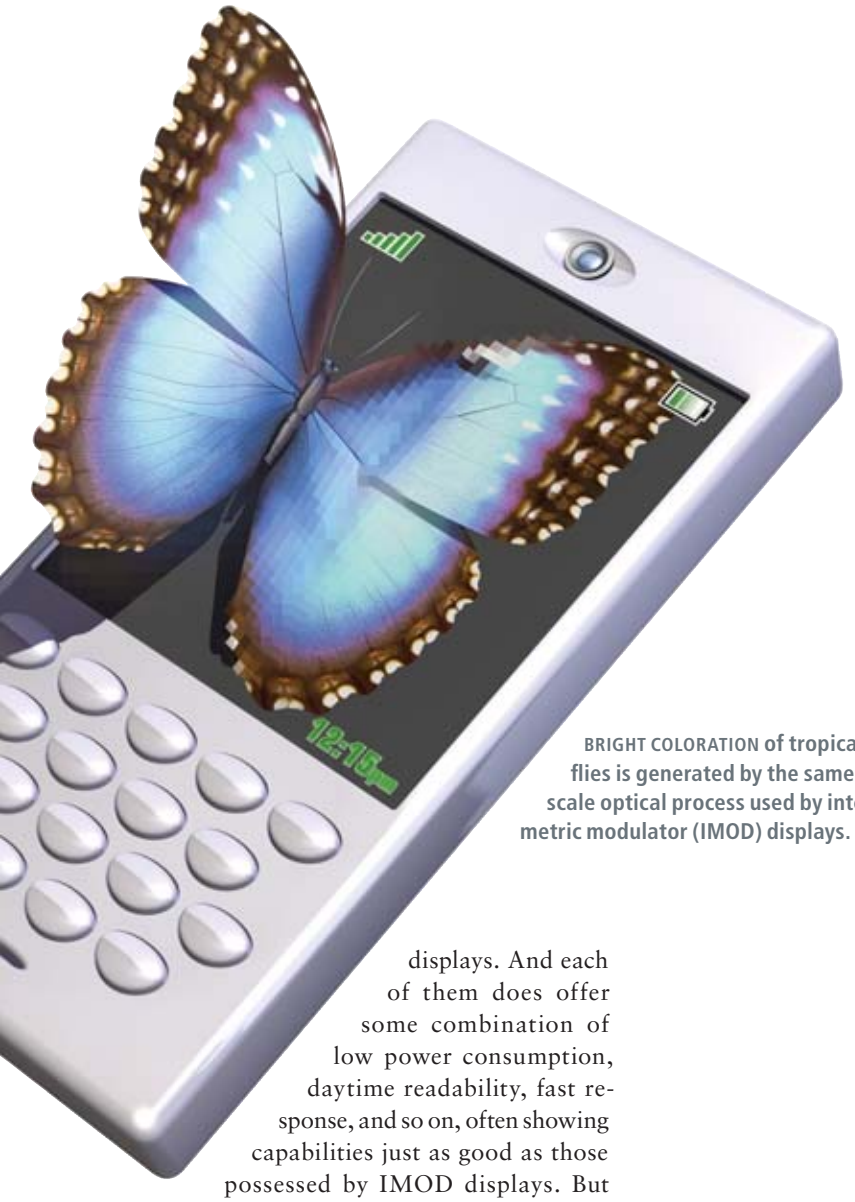

BRIGHT COLORATION of tropical butterflies is generated by the same nanoscale optical process used by interferometric modulator (IMOD) displays.

displays. And each of them does offer some combination of low power consumption, daytime readability, fast response, and so on, often showing capabilities just as good as those possessed by IMOD displays. But none of them can deliver all such features at once, which is why Qualcomm is so hopeful.

A Multidecade Odyssey

The idea that became IMOD first occurred to Mark Miles, then a Massachusetts Institute of Technology electrical engineering major, in 1984, when he was working at a summer job with Hughes Aircraft in Los Angeles.

"I happened to read an article that discussed how you might use arrays of submicroscopic antennas to convert sunlight directly into electricity," Miles recalls, "and I was fascinated." He was familiar with the large-scale antennas used for radar, television and broadcast radio. And he had learned that radio waves are basically the same as ordinary visible light waves: both are intertwining electric and magnetic fields, rippling through space at 300,000 kilometers a second. The only difference is that radio waves are measured from crest to crest in centimeters, meters or even kilometers, whereas light waves are roughly a million times as short. The visible range extends from about 700 nanometers (red) to about 400 nanometers (violet) from crest to crest, with all the other colors of the rainbow in between.

Despite knowing all that, Miles had never put those two concepts together to imagine a microscopic device able to manipulate light waves. "Then it occurred to me," he recalls. "If you could somehow control the characteristics of these microstructures—change their absorption and reflection as needed—you could make an incredible display." It would be just a flat panel, far more compact than the bulky cathode-ray tubes (CRTs) that were standard in televisions in those days.

True, Miles did not have the slightest idea how to build such a display, but no matter. After he finished his studies, he worked as a programmer in the computer printer industry and, in his spare time, researched the problem and discussed it with professors at M.I.T.

From one of those professors he learned about an optical device that would do exactly what he wanted. The Fabry-Pérot interferometer, or etalon, is basically a cavity formed by two reflective surfaces aligned in parallel. When light passes into the cavity through the top surface, which is translucent, it reflects from the bottom surface—and then bounces back and forth between the surfaces ad infinitum, with a little bit leaking out of the top each time. Thanks to a phenomenon called interference, all this bouncing causes most wavelengths of light to cancel themselves out. But the rebounding waves actually reinforce the reflection of wavelengths that just happen to fit precisely in the gap between the surfaces [*see box on next page*]. So, in effect, the etalon as a whole functions as a mirror that reflects only one specific color, which you can choose simply by changing the spacing between the surfaces.

The technique was perfect for Miles's purpose—except for one thing. Etalons were certainly an invaluable laboratory tool for measuring and controlling light, but for a high-resolution display, he needed to shrink them down to a microscopic scale and then array them across a screen surface by the millions, with small groups of them forming a single pixel (picture element). As it turned out, nature had already accomplished that feat: the iridescent colors on the wings of tropical butterflies, such as the blue morpho, are caused by nanoscale structures that function very much like tiny etalons. But how

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GEORGE RETSECK (*PDA*); BEN ZWEIG (*Waldrop*)

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was Miles going to make such minute structures? And, not incidentally, how was he going to turn the pixels on and off?

The question stymied him until he learned of microelectromechanical systems (MEMS)—tiny silicon-based machines. The basic idea of MEMS, which date back to the 1970s, is to carve microscopic mechanical structures into the surface of a silicon wafer by applying the same techniques used to create microprocessors. MEMS researchers had already learned to produce all manner of gears, springs, cantilevers, channels and the like, some of which were starting to reach the market.

"MEMS opened another path for me," he says. "Creating actual devices." Having no experience in MEMS fabrication, Miles continued to write software by day to support himself and spent his evenings taking an M.I.T. extension course on MEMS. Once that was completed, he wrangled permission to use the university's MEMS fabrication facilities. Eventually he arrived at a workable concept: the first version of IMOD. In essence, it was a microscopic etalon in which the parallel reflecting surfaces were thin-film layers created using MEMS techniques. During the fabrication process, the spacing between the films could be set to reflect a specific wavelength, or color. In this configuration the etalon would correspond to a unit cell in the on state.

Because the bottom layer was flexible, however, changing the unit cell to off was easy: one just had to apply a very brief voltage between the surfaces. The resulting electrostatic attraction would make the bottom layer bulge upward, thus narrowing the gap and shifting the reflected wavelength down into the invisible ultraviolet part of the spectrum, which appears black. Moreover, the unit cell would *stay* black, without consuming any further power, until the time came to flip it back to colored. And that was simple, too: one just had to apply another voltage pulse.

These first IMOD devices were crude and ugly, Miles admits. But they worked well enough that he could begin to see a path toward commercialization. By the mid-1990s he had quit his job and joined with his former M.I.T. classmate Erik J. Larson to found Iridigm in Cambridge. Cash was very hard to come by as they slowly refined the technology, but within a few years one of the firm's investors—Qualcomm—decided that it was time to acquire the company outright. Iridigm became the Qualcomm MEMS Technologies unit in October 2004.

A Tough Market

To succeed, IMOD is going to need all the help it can get. Competition in the handheld-display market is fierce, says Chris Chinnock, managing director of Insight Media, which specializes in news and analysis about the display industry. "LCDs are the gorilla here," he says. With a multidecade head start on technological develop-

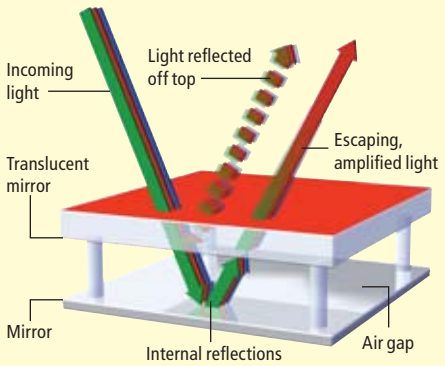
[THE BASICS]

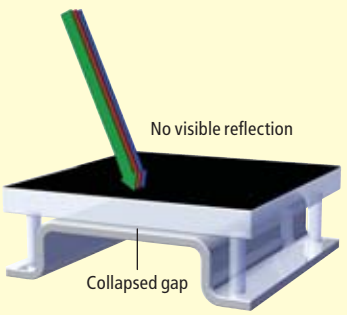
HOW IMOD WORKS

Interferometric modulator (IMOD) displays use interfering light waves to create bright colors on demand. Each basic unit cell produces either a single color (*top*) or black (*middle*). Placing many unit cells into arrays forms pixels, or picture elements (*bottom*). Qualcomm currently produces bichrome displays composed of single-color cells, but it says full-color displays, as depicted, are on the way.

COLORED UNIT CELL

The IMOD unit cell consists of two parallel, mirrored surfaces. When light hits the structure, some reflects off the top and some passes through the translucent top mirror into the gap, where it reflects internally. A little light, however, leaks out with each upward bounce. Many of the escaping light waves (*green and blue in this example*) will be slightly out of phase with those rebounding off the top as well as with other escaping waves. These waves will cancel one another out via destructive interference. But other reflecting light waves that are in phase (*here, red*) will add (constructively interfere) and so will be visible to the eye.



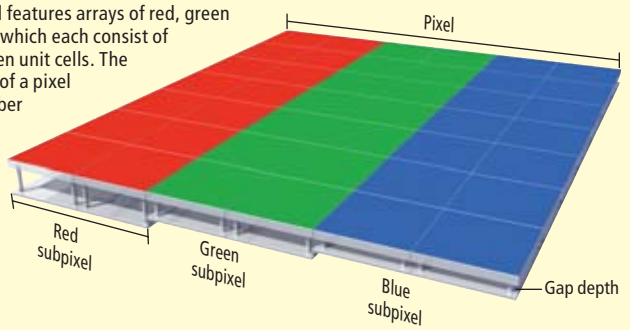


UNIT CELL IN BLACK STATE

A colored unit cell turns black when an applied voltage produces an electrostatic attraction between the mirrors, thereby collapsing the air gap. The black color appears because the shrunken gap shifts the reflected light into the invisible, ultraviolet range. Another voltage pulse reverses the cell back to color.

FULL-COLOR PIXEL

An IMOD color pixel features arrays of red, green and blue subpixels, which each consist of two columns of seven unit cells. The hue and brightness of a pixel depend on the number and color of activated cells. Gap depth determines if the cells are colored red, green or blue.



GEORGE RETSECK

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ment and manufacturing infrastructure, LCDs have been systematically conquering every segment of the flat-screen market, from handhelds to computer monitors to wall-mounted TVs. "So going up against them head-to-head is like a death wish," Chinnock warns. And then there are all those other LCD alternatives—OLEDs, e-paper and the like, not to mention the many variations on basic LCD technology itself.

Still, the market is huge. "The leading cell phone manufacturer, Nokia, makes 350 million handsets a year—almost a million per day," Chinnock says. The annual worldwide output is in the billions. And that is not even counting all the digital music players, personal digital assistants, GPS receivers and other handheld electronics. "So it doesn't take much market penetration to have significant sales," he concludes.

Qualcomm's challenge has been to get the company's IMOD devices out there. It is one thing to make a display work in the laboratory, Qualcomm's Cathey says, but quite something else to create a robust consumer product. He asks, for example, "Can you adapt it for mass production?" The answer to that question turns out to be yes: the individual IMOD unit cells are much simpler than their LCD counterparts but similar enough that IMOD displays can be made in existing flat-panel fabrication facilities. That is a huge advantage, Cathey says, because building a completely new fab facility is a billion-dollar proposition. But then you have to work on manufacturing yields: What fraction of the displays coming off the assembly line actually work? Likewise, quality control: "A display is right out there in front," he says. "If there are dead pixels, or areas of nonuniformity, people see them." And cost control is paramount, Cathey adds. "In this market we *have* to be price-competitive."

Finally, there is the issue of color. Just as in any other display, LCDs included, a color display requires that each of its pixels actually consist of three subpixels: one for each of the three primary colors. And each of those subpixels has to have several unit cells, or sub-subpixels, that can be turned on or off independently, so as to produce a range of color and brightness. In this case, Cathey says, individual IMOD unit cells will need to be less than 100 microns across to produce a good-quality display.

Given this steep learning curve, Cathey says, the company's strategy has been to start small and build, gaining experience and working out the production bugs as it goes. Qualcomm's initial products are only bichrome—black lettering on a background of, say, gold. But full-color IMOD displays are on the way, he reports. "We haven't released the upper-end resolution. But we will be able to compete with other technologies on that score—and maybe even exceed them."

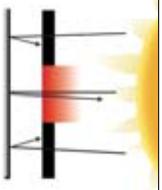
Qualcomm's first publicly announced licensing agreement, this past May, was with the Korean electronics firm Ubixon, which will market a line of IMOD-equipped Bluetooth headsets that provide the user with a wireless connection to cell phones and digital music players. The bichrome IMOD screens will display text messages and song titles.

Obviously, Qualcomm is hoping that IMOD technology will catch on quickly. Although Cathey cannot discuss the research in detail, he says the company is in the meantime investigating a variety of nondisplay applications. As Miles points out, "IMOD is a very powerful photonic device and can be integrated with many other kinds of devices that are involved in manipulation of light." Still, Cathey says, displays are where IMOD should ultimately shine the brightest—from handsets and camcorders to electronic books, computer monitors, wall-mounted TVs and beyond. "We can scale to that," he says, "but give us some time!" ■

[THE BIGGER PICTURE]

COMPETING TECHNOLOGIES

IMOD technology is entering the tough, multibillion-dollar mobile-display market, which already includes several other approaches. Liquid-crystal displays (LCDs) currently dominate, but organic light-emitting-diode displays (OLEDs) are finding application niches.

DISPLAY TECHNOLOGY	ADVANTAGES	DISADVANTAGES
LCD Optically active material modulates an artificial light source, such as a backlight	Inexpensive, widely available, technically simple	High power consumption, poor legibility in sunlight, low resistance to temperature extremes, limited viewing angles, thick mechanism
OLED Organic substances generate light when exposed to electric current	Should be inexpensive after fabrication plants are built, rapid electrical response	High power consumption, poor legibility in sunlight, relatively short life span, susceptible to water and oxygen contamination, technically complex
IMOD Reflective materials modulate ambient light and bounce it back off a mirrorlike surface 	Inexpensive, low power usage, always on, rapid electrical response, good readability in bright sunlight, wide viewing angle, technically simple	New, unfamiliar technology, not yet available as full-color displays

MORE TO EXPLORE

Description of a Fabry-Pérot interferometer: **hyperphysics.phy-astr.gsu.edu/hbase/phyopt/fabry.html**

Qualcomm's IMOD Web site: **www.qualcomm.com/technology/imod/**

ANN SANDERSON

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THE SCIENCE OF DOING GOOD

By Sheri Fink

Information technology, satellite imaging and research carried out in disaster-relief areas have begun to transform humanitarian aid into a more efficient and less haphazard endeavor

SVEN TORFINN *Panos*

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◀ **REFUGEE in Chad who fled the conflict in Darfur, Sudan, stands by a satellite dish used by aid workers.**

In the span of a few days in the spring of 1999, hundreds of thousands of ethnic Albanians fled their homes in Kosovo as Serbian forces drove them into neighboring countries. At the time, I was a new medical school graduate put in charge of triaging sick and injured refugees who showed up in a constant stream at an improvised medical aid station in the cold, muddy no-man's-land between Kosovo and Macedonia. As I stood there, I could see thousands of men, women and children who had trudged across the border or arrived in trucks, cars, horse-drawn carts or the arms of fellow refugees. Their numbers taxed the ability of overstretched United Nations refugee officials to track them. Many families had been abruptly separated during the chaos of expulsion. Once inside the border in refugee camps, desperate mothers and fathers posted paper notes with names and descriptions of their missing children.

Soon after I began working, a new way to help that did not involve scraps of paper became available. Employees at Microsoft's European headquarters in Paris, aware of the tragedy unfolding nearby, offered their services to the U.N. A few weeks after my arrival, I walked into a tent and found a Microsoft team photographing refugees and presenting them with computer-generated ID cards. The Microsoft workers hoped to register the refugees for food and shelter assistance and, through cross-checks made in these newly created databanks, to help locate lost family members.

It was odd to see the modern information age materialize in a teeming refugee camp packed with people stripped to their bare essentials. Why did computers look so foreign there? Perhaps it was because, before Kosovo, most refugee camps were situated in poorer, less developed places, where computers were a rarity. Perhaps it was because computers and other modern technologies demonstrate humankind's progress, and forced migration reflects its regression. Ultimately, the precision of a computer database seemed incongruous when set against the chaos of relief work, with its rapidly changing environment and unpredictable donations discharged by well-intentioned but often poorly organized do-gooders.

As humanitarian workers try to save lives and relieve suffering, they are increasingly taking advantage not only of information and communications technologies but also of remote sensing operations perfected by the military, forensic identification techniques reminiscent of *CSI*, and quantitative methods applied routinely by epidemiologists (who track the causes of disease outbreaks and devise public health strategies for limiting their toll). Workers are also employing more systematic approaches to planning and delivering aid, enabling the field of humanitarian assistance to evolve into an applied social science. Now the challenge for aid workers and policymakers is to ensure that these advances help the people who need such assistance the most and to prevent the tools from becoming mere high-tech window dressing framing human catastrophes.

An Eye on High

The desire to find quick and accurate ways to come to grips with the scale of a crisis was one of the early spurs to applying new technologies to relief work. Recognition of that need dates back to one of the deadliest recorded natural disasters in history. In the summer of 1931, after weeks of heavy rain and flooding, a typhoon stalled over China and sent water from rivers, lakes and canals crashing through levees and flood walls. The massive inundation made it difficult for Chinese authorities to locate survivors. Charles A. and Anne Morrow Lindbergh, arriving in Nanjing on what was to be a vacation tour, used their long-distance Lockheed Sirius airplane to conduct aerial surveys that identified millions of additional victims and thousands more square miles of flooding. Their work helped to guide the Chinese government's response. It also drew

KEY CONCEPTS

- The chaos that ensues in a humanitarian crisis often complicates the efforts of aid workers trying to provide food, shelter and medical assistance to those who most need it.
- Judicious deployment of computer and communications technology, DNA analysis and social science survey techniques can assist the multitude of aid organizations that arrive on the scene in locating people who need help, in avoiding duplication of effort and in assessing whether their labors really make a difference.
- Aid workers still struggle in the midst of a crisis to find the best ways to use technology and to ensure that the poor, and not only the affluent, benefit from high-tech measures.

—The Editors

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[TIMELINE]

Science and Technology Transform the Practice of Humanitarian Aid

1859 Battle of Solferino: Thousands of injured soldiers lay strewn across the battlefield with no organized efforts to provide relief. Having witnessed this tragedy, Swiss businessman Jean Henri Dunant wrote a book about the need for organized relief, which inspired the founding of the Red Cross four years later.

1931 Disaster appraisal from the air: Charles A. and Anne Morrow Lindbergh conduct aerial surveys of the Chinese flood disaster, now recognized as the deadliest recorded nonfamine disaster in history.

1945 Founding of the U.N.: The new organization evolves to become a focal point for coordination of relief efforts. Various U.N. agencies lead humanitarian assistance campaigns that bring together local and international nongovernmental organizations (NGOs), private citizens, government agencies, companies and armies, among others.

1980s Tools targeted at aid work: Equipment specifically for humanitarian assistance becomes available. In the health sector, aid workers from Doctors Without Borders develop the first standardized drug kits and manuals for medical treatment of refugees.

1990s Quantitative assessments: The use of epidemiological methods and computerized systems to track the health problems of refugees leads to recognition of the priority of measures such as measles vaccination and reproductive health care (emergency obstetrics and treating victims of sexual violence).

international relief aid to the affected regions and evoked a prescient opinion from the *New York Times:* "This broad sky-survey … [of] woes is [a] significant [example] of the aid that wings will give in this new age by telling matters that are seen from above the surface of the earth to … inhabitants far and wide."

Today's "sky-surveys" harness satellite and information technology to offer a far broader and more comprehensive picture of disasters. Satellite imagery can be combined with computer-based tools known as geographic information systems (GIS) that integrate data from various sources with digital maps. In a humanitarian crisis, a GIS might superimpose data regarding the whereabouts of victims, their health status and other information onto a map or satellite images.

The devastating earthquake and tsunami that struck South Asia in December 2004, which together killed more than a quarter of a million people spread throughout 12 countries, demonstrated the worth of techno-do-goodism, along with the inevitable entanglements that accompany any crisis. The immediate aftermath in the hardest-hit area, the Indonesian province of Aceh, began in disarray. Political sensitivities related to a decades-long conflict between government forces and a rebel insurgency reportedly delayed the public release of some imaging data of the island, barring access to information that could have helped workers locate survivors in the critical first days.

The Indonesian government also took two days to invite international relief workers to enter the area, which it had recently closed to foreigners during an upsurge in the conflict. Soon, however, hundreds of aid groups began arriving by plane, helicopter and boat. Their services were supplemented by logistical help provided by military forces from multiple nations that delivered thousands of tons of supplies and equipment.

The initial relief effort was chaotic. Too many aid workers showed up in some areas, while other places remained underserved. But when I arrived a month later as a health team leader for the International Rescue Committee (IRC), after having worked in tsunami-affected areas of Thailand, the aid effort had already become more organized—in part because of the use of technology. In Banda Aceh, the province's capital city, I went immediately to a Humanitarian Information Center (HIC), set up by the U.N.'s Office for Coordination of Humanitarian Assistance.

There I collected GIS maps that depicted the disaster zone at different scales, from the regional down to the village level. The maps were accompanied by various spreadsheets that compiled the number of displaced, injured, dead and missing persons; coverage areas for various aid groups; the location of hospitals, clinics and pharmacies; and the most common potential disease outbreaks in each area. This data packet served as a useful guide when I traveled along Aceh's northern coastline to coordinate a vaccination campaign aimed at halting the spread of a small measles outbreak among displaced children and the families that hosted them. (Having studied medicine, I deal primarily with the

[THE AUTHOR]

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SUZI CAMARATA (*Fink*); CHARLES LINDBERGH.COM (*top left*)

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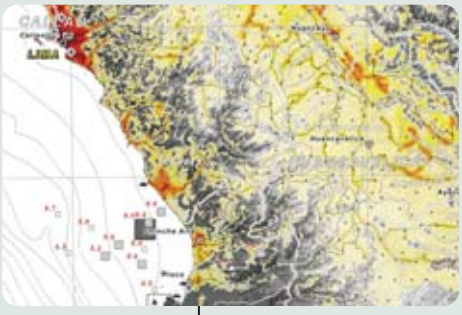

1994 Wake-up call: A large number of groups converge in Rwanda and the Democratic Republic of the Congo (then known as Zaire). Poor coordination and insufficient training of some aid workers plague assistance efforts. The death rate among refugees was the highest in decades, highlighting the need for improved practices.

1997–1998 Standards: The Sphere Project establishes minimum standards for services provided by aid groups in five areas (water supply and sanitation, nutrition, food aid, shelter and health services), partly in a response to events in Rwanda.

2000 Satellite surveillance: Major space agencies agree to allow countries affected by disasters to gain access to satellite data free of charge under provisions of the International Charter on Space and Major Disasters. Also, relief efforts make increasing use of the Global Positioning System and geographic information systems (GIS).

2005 Reforms: The U.N. Office for Coordination of Humanitarian Assistance (OCHA) leads an effort to improve effectiveness in the field, including the establishment of a Central Emergency Response Fund to quickly dispense cash based on need.

2007 Gauging effectiveness: Various aid organizations launch efforts to appraise the success of relief interventions and to better allocate resources and guide field operations. A "humanitarian tracking service" is started to monitor disease, malnutrition and deaths.

health issues that arise from large crises, but aid workers providing food, water, sanitation and shelter and working on mine detection and removal also use GIS to support their efforts.)

A humanitarian information infrastructure has begun to emerge. Space agencies now collaborate to release satellite imagery free of charge during a disaster, and several new nonprofit organizations specialize in providing crisis-related mapping and geographic data to aid workers. Supplementing the presence of HICs in major crises, the Internet-based ReliefWeb assembles maps, reports and consolidated funding appeals from dozens of international aid agencies. In 2004 a partnership of relief and development agencies led by the Inter-Agency Standing Committee launched the Humanitarian Early Warning Service (HEWS), a Web site that provides continually updated information on existing and predicted droughts, floods, storms, locust invasions, and so on, in the hope that interventions can begin before a nascent crisis worsens.

Promoting Justice and Human Rights

Beyond improving the delivery of help during a crisis, technologies such as remote sensing, GIS and DNA testing, along with the use of systematic research methods common in epidemiology and the social sciences, have facilitated the documentation of refugee and civilian casualties resulting from violent conflicts. For discerning the scale of atrocities, survey methods from the social sciences are more powerful tools than anecdotal accounts of killing, torture, rape and indefinite detention.

In 1999, during the war in Kosovo, several of my colleagues and I worked with Physicians for Human Rights on a comprehensive, randomized survey of ethnic Albanian refugees to determine the pattern and distribution of human-rights abuses perpetrated against them, the first such inquiry conducted on victims of atrocities during an ongoing humanitarian crisis. We found that abuses were widespread and that the vast majority of refugees fled their homes as a result of Serbian police or military forces. Our results, published in the *American Journal of Public Health,* in conjunction with two studies of killings and refugee flows by other researchers, contributed to international war crimes prosecutions against then Yugoslav president Slobodan Milošević and other officials.

Evidence of war crimes has also come from forensic technologies. In Bosnia-Herzegovina in the 1990s, the U.S. military captured satellite and aerial photographs of hundreds of mass graves. Despite the presence of international forces, the images failed to prompt an immediate halt to the slaughter, although they did lead investigators to where the killings took place. Scientists with the International Commission on Missing Persons (ICMP) in Bosnia then developed a computer system capable of matching DNA profiles from thousands of remains with DNA from living relatives.

To date, the system has identified more than 12,000 victims from the former Yugoslavia, re-

ASAP FOR SOS

As Web access expands even to the poorest areas, endangered remote villages may one day gain early warning of impending attacks, enabling evacuations or expediting calls for help. Several examples demonstrate the potential for the technology. Amnesty International's Eyes on Darfur project already monitors villages at risk of attack in war-torn Sudan. Also, the U.S. Holocaust Memorial Museum helped to produce "Crisis in Darfur," high-resolution satellite imagery available through Google Earth that allows anyone with a Web connection to zoom in on the destruction that has to date ravaged more than 1,600 rural hamlets.

left to right above: JOCKEL FINCK *AP Photo;* UNOSAT; REUTERS/MUHAMMAD KHALID/IFRC HANDOUT

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[CASE STUDY: ASIAN TSUNAMI]

TECHNOLOGY EXTENDS A LIFELINE

TSUNAMI FOLLOWS EARTHQUAKE
A massive earthquake strikes off the coast of Sumatra, Indonesia, on December 26, 2004, triggering a devastating tsunami that kills people in more than a dozen countries. A U.S. soldier on a relief flight surveys the damage off the coast of the province of Aceh.

SATELLITE IMAGES REVEAL DAMAGE
In Banda Aceh, the capital of Aceh province, the tsunami simply washes away miles of the city. Before and after satellite images document the extent of the destruction.

GIS HELPS SET PRIORITIES
Aid workers feed data, such as the locations of damaged health clinics or the sites of disease outbreaks, into a GIS able to create maps and help visualize the conditions at locations in the disaster zone. U.N. workers and the private sector help to disseminate GIS-derived data at Humanitarian Information Centers (HICs) and on the Internet.

Beyond improving the delivery of help during a disaster, new technologies have facilitated the documentation of refugee and civilian casualties resulting from violent conflicts.

vealing which groups were targeted. This evidence helped to convince Bosnian Serb authorities, after years of denial, to acknowledge the war crimes their forces committed against Bosnian Muslims in the town of Srebrenica. Forensic experts in the U.S. adapted the DNA-matching system for similar use following the World Trade Center attack, and the ICMP helped to identify more than 900 victims of the Indian Ocean tsunami in Thailand.

Rapid-Response Epidemiology

A desire to document both the impact of a natural disaster or local conflict and the effectiveness of relief work has drawn the attention of public health professionals, enabling development of what might be called "emergency epidemiology." For many years, the public health establishment doubted that epidemiological research, a labor-intensive endeavor involving surveys of individual households, could be accomplished in the midst of an emergency or even that it should be. "Carrying out epidemiological investigations in the muddle of disaster can be viewed as a squalid preoccupation while so many people need help," observed the editors of the *International Journal of Epidemiology* in 1975, who then went on to encourage their colleagues to embrace the "almost untouched field." Epidemiologists now study health in disasters by employing simplified disease surveillance methods and population-sampling techniques known as cluster sample surveys, often used in international vaccine research.

Striking the right balance between assessment and action remains a challenge: time, skilled personnel and funding are often in short supply. Emergency epidemiology has more than proved its worth, though, by demonstrating that a small set of infectious diseases accounts for the vast majority of deaths and illnesses in displaced populations. In particular, measles—rare and rarely fatal in well-nourished and immunized populations—has often become the leading cause of death among young children in refugee camps. In a four-month period at a single Sudanese camp in 1985, measles killed an estimated 2,000 children. Such findings have alerted aid workers to the importance of preventing the disease, and vaccinations now tend to begin as soon as aid workers arriving on the scene can organize them.

Epidemiological findings provide important baseline data for a GIS. They also have led to the development of more effective, though still imperfectly executed, methods to quickly vaccinate large numbers of children against measles. For common refugee ailments, Doctors Without Borders volunteers designed treatment guidelines and standardized drug and equipment kits. Beginning in 1990, the World Health Organization began stockpiling and distributing versions of the kits, packed with oral rehydration sachets (to treat diarrhea) and antibiotics. The latest ad-

left to right above: ANDY AMES *AP Photo;* GEOEYE/PHOTO RESEARCHERS, INC.; HUMANITARIAN EARLY WARNING SERVICE/WFP EMERGENCY PREPAREDNESS AND RESPONSE BRANCH (ODAP)

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VACCINATIONS PREVENT DISEASE
Because epidemiological studies from previous relief efforts have shown that measles are one of the biggest threats to children, aid workers use databases to track the spread of the disease and then fan out to vaccinate as many children as possible in the tsunami-affected zones.

DNA MATCHING OF VICTIMS
The International Commission on Missing Persons (ICMP) assists in identifying more than 900 unclaimed bodies found in Thailand. The ICMP uses a DNA-profiling database originally developed to match the remains of thousands of massacre victims from mass graves in the former Yugoslavia with living relatives.

ASSESSING THE AFTERMATH
Large-scale surveys of nutrition and disease in Aceh show that acute illnesses such as diarrhea and measles drop over the early post-tsunami months, indicating that aid efforts may have been effective. Social science researchers also survey the affected populations to identify areas where national and international relief efforts need improvement.

dition to the kits is a rapid diagnostic test for malaria that is nearly as simple to use as an at-home pregnancy test. It allows health workers to diagnose the most lethal form of the disease in minutes without a microscope so treatment can begin promptly.

Recent work in the Democratic Republic of the Congo gives insight into how formal survey methods can be carried out in the hostile conditions of regional conflicts and can help set an agenda not only for aid workers but also for policymakers. Five times over the past decade, researchers from the IRC have set out to investigate how warfare involving the Congolese government, rebel factions and forces from other countries was affecting the health of civilians.

To conduct accurate studies in harsh and sometimes insecure working environments, the researchers often used GIS and the Global Positioning System to help locate representative samples of households to survey—after pinpointing the samples, they launched a grueling marathon, visiting huts and houses and inquiring about recent deaths. Workers calculated the crude mortality rate and compared it with baseline statistics compiled by the U.N. for sub-Saharan Africa. The shocking and unexpected results testify to how warfare undermines a civilian population's public health defenses. According to an article authored by scientists from the IRC, the Australian National University and the Burnet Institute that appeared in the *Lancet* in January 2006, an estimated 3.9 million more people died between 1998 and 2004 than would have been expected had the country not been in conflict. Yet fewer than 10 percent of the fatalities resulted from direct violence. Preventable and treatable illnesses, including malaria, diarrhea, respiratory infections, measles and malnutrition, heightened the number of deaths in areas where livelihoods, transportation and health services had been disrupted by the conflict.

The results were sobering to humanitarians; clearly, their relief efforts had been insufficient to prevent widespread death and suffering. The scientific evidence of massive humanitarian need in the Democratic Republic of the Congo attracted media attention, helping to convince policymakers in the U.S. and elsewhere to increase pitifully low levels of relief funding for the country. Still, evidence does not always lead to action or even acceptance. Per capita aid for the Democratic Republic of the Congo still lags far behind that provided to other crisis-torn areas, including Darfur and northern Uganda.

A Fog of Uncertainty

Scientific and technological advances have greatly facilitated aid work, but much remains to be learned about applying these new methods, which often still founder in a fast-paced refugee crisis. Microsoft's efforts to register the roughly

A POLL UNDER FIRE

Surveys conducted in the midst of a war or in a disaster zone can provide a picture of a crisis not available in other ways—although not everyone appreciates having such information. When researchers used a statistical method called cluster sampling to conduct two mortality studies of representative households in Iraq and found death rates that far exceeded official statistics, President George W. Bush and other politicians quickly rejected the findings. Emergency epidemiological methods were subjected, as were the scientists themselves, to unusual scrutiny and criticism.

left to right above: JOHN VINK *Magnum Photos;* AMEL EMRIC *AP Photo;* ELHAM MONSEF

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STANDARDS OF CARE

When massive human displacement followed the Rwanda genocide in 1994, cholera and dysentery, both highly preventable and treatable ailments, were the biggest killers. Roughly 80,000 Rwandans died in refugee and displaced-persons camps. An estimated 20,000 more perished in areas where aid workers did not reach them. The death rate among refugees was the highest in decades, despite the presence of the Red Cross, the U.N., military forces, civil defense organizations and at least 200 nongovernmental agencies.

The tragedy taught aid workers a crucial lesson. They needed to do a better job of applying their knowledge and tools through improved coordination and training of their staff members. Dozens of aid organizations have voluntarily accepted that the people they serve have a right to quality assistance and have committed to a Humanitarian Charter and to minimum standards (*far right*) for disaster response, created by what is known as the Sphere Project.

Now aid workers faced with a population in need can refer to expert guidelines that tell them, for example, how much water they should provide daily, the minimum number of latrines they need to dig (and how far to locate them from water supplies), and the amount of calories, vitamins and minerals adults and children require. —*S.F.*

RWANDAN receives aid at a refugee camp.

▶ WATER
Minimum of 15 liters a day per person for drinking, cooking, personal hygiene

▶ SANITATION
Hand washing encouraged for aid recipients before food handling. At least one latrine for every 20 persons

▶ NUTRITION
At least 2,100 kilocalories per person, with 10 to 20 percent energy from protein and 17 percent from fat, plus vitamin and mineral supplements. Nutrition exclusively from breast-feeding for infants younger than six months

▶ HEALTH CARE
Measles vaccination unless 90 percent of children (aged nine months to 15 years) have already been vaccinated. Bed nets to prevent malaria. Establishment of a disease surveillance network

Aid officials who fail to use communications equipment in the way it was intended may only exacerbate the inherent chaos of a crisis.

one million refugees who fled Kosovo in 1999 were well intentioned and the first of their kind in an emergency. But the program was just getting under way when, thankfully, those displaced were able to return home. Only a small fraction of the population had received ID cards by June when NATO bombing routed Serbian forces, leading the Yugoslav government to accept a peace plan and allowing refugees to pour back across the borders. We aid workers are often humbled by circumstances—for good or ill, political, diplomatic and military interventions often exert a greater impact on refugee well-being than we do, as the Microsoft registration team soon discovered.

Refugee registration still tends to lag behind escalating crises. The numerous agencies involved have yet to adopt a common format for storing information, despite the obvious benefits of computer-assisted identification. Technology can also fail. A kit or computer may simply stop functioning in the heat or dust. Humanitarian assistance does not represent a large market for equipment providers; hence, aid workers often make do with, say, portable water-purification devices or geographic databases that were first developed for other purposes and that may not be up to the task at hand. Conversely, long delays persist in developing and implementing truly needed technologies, such as effective malaria medications and better emergency shelters. And a technician putting together a GIS may experience frustration in producing an accurate picture of refugees' true needs if aid workers fail to share their assessments—poor data can lead to impressive-appearing but ultimately unusable maps.

Aid officials who fail to use communications equipment in the way it was intended may only exacerbate the chaos. After the 2004 tsunami hit, the WHO worked with the government in

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Aceh to establish a text-messaging system that would allow health workers to rapidly report diseases that could result in an epidemic. Using satellite and cell phones, members of our IRC medical team working in a remote area of the province diligently sent a text message every time we discovered a child with measles. Unfortunately, whichever health official was supposed to receive the messages did not record them, or perhaps the mobile phone networks failed to deliver them. For several weeks clusters of measles in our district were not registered in the official public health statistics.

Technology can also be abused or remain beyond the reach of those who most need it. Some human-rights activists have warned that electronic refugee data banks may be commandeered by repressive governments or by armed forces trying to track down opponents. In poor countries, the rich may receive the first benefits of expensive new technologies. The Indian Ocean tsunami affected a massive region, but large-scale forensic identification was attempted only in coastal Thailand, in a resort area in and around Phuket. Although more than half of the people reported missing were Thai, disaster-victim-identification teams from more than two dozen countries first tried to identify Caucasian vacationers. I visited the sophisticated, tented forensics facility and found, just feet away, Thai scientists laboring under a tree to identify native victims.

Too often international workers sideline local relief efforts, to the detriment of everyone. The creation of separate computer databases for Thais and foreigners ultimately slowed the entire identification process. A lesson to be drawn from the experience was that new technologies bring with them the need for new ethical guidelines. Making technology available to affected communities is critical.

Making a Measurable Difference

With all its advances, humanitarian action should be much more effective now than ever before. But is it? No single system measures the effectiveness of aid. Aid workers have historically been sloppy about monitoring and evaluating their programs; often they are too busy just trying to help. And when a militia or another outside force deliberately disrupts aid activities, it becomes difficult to assess performance. Still, donors are beginning to demand proof of the value of their funding, and the U.N. has started to reform the way that international aid is financed, staffed and coordinated. Aid organizations now collaborate with academic institutions and researchers on developing ways to assess their work. Aid groups and their donors are also launching a humanitarian tracking service that aims to provide information about nutrition, health and deaths during a crisis to help improve relief programs based on these data.

Humanitarian assistance, despite its heroic aura, is at its base a poultice, not a prophylactic or a cure. No matter how solid its scientific basis, outside aid always signifies failure. In the case of human-generated disasters, it is the failure of countries to prevent conflicts or to protect their populations from war crimes and crimes against humanity. In a natural disaster, it is the failure of communities to protect their populations from potential hazards through better preparation and prediction. Improving the world's will and capacity to forestall calamity and safeguard civilians through political measures, infrastructure renovation and other steps should remain as the most important objective.

Unfortunately, though, humanitarian aid will likely be needed more and more often. Roughly a billion people have settled in developing-world slums, where they often inhabit poorly constructed dwellings in disaster-prone areas. Global warming and rising sea levels also raise the specter of future hazards. Wars, sadly, are not going away. Science and technology have provided us with the tools needed to save many more lives and reduce more suffering and disease than ever before in disasters and complex emergencies. The international public, the private sector, governments and militaries have all shown a willingness to help. All the elements are there. What is needed is a willingness to transcend vested interests so that scientifically rigorous information about vulnerable populations and how to help them is used to direct resources impartially and efficiently to where they are needed.

Some longtime aid workers worry that technology and growing professionalism in their own ranks will rob humanitarian assistance of the heart and spirit that have led generations to brave danger and physical discomfort to provide aid. But when Jean Henri Dunant published *A Memory of Solferino* in 1862, setting out his vision for the seminal humanitarian organization the Red Cross, he called for aid workers that were "zealous, devoted and thoroughly qualified." Because aid so often spells the difference between life and death for those trapped in tragic circumstances, it should be delivered with the utmost competence as well as humanity. ■

New technologies bring with them the need for new ethical guidelines.

MORE TO EXPLORE

War Hospital: A True Story of Surgery and Survival. Sheri Fink. PublicAffairs, 2003.

Paul Currion, a consultant specializing in information management for humanitarian operations, writes a blog on how information technology can help with humanitarian assistance: **www.humanitarian.info**

A comprehensive information hub on humanitarian emergencies and disasters can be accessed at ReliefWeb: **www.reliefweb.int**

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Blood Cells for Sale

There's more to blood banking than just bagging blood

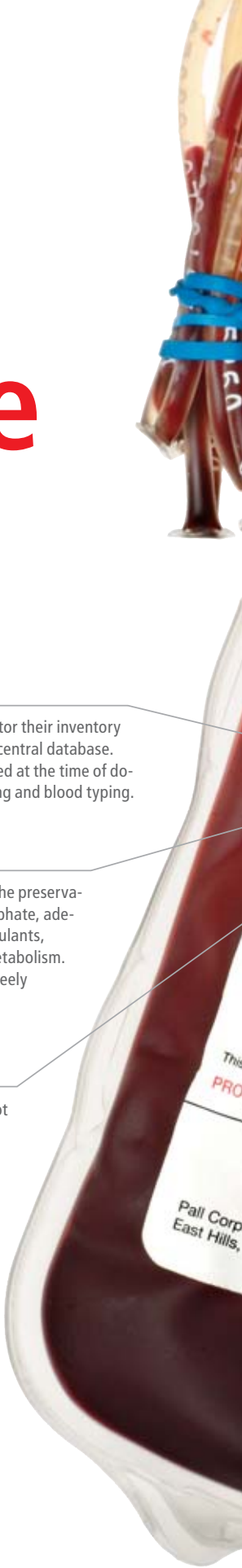
BY EMILY HARRISON // *Photograph by Cary Wolinsky*

THIS IS NOT A BAG OF BLOOD. Granted, it did begin as a blood donation, drawn from the arm of a volunteer donor in Massachusetts. Within hours of collection, though, that precursory pint of warm whole blood had been centrifuged, fractionated and decanted into a red blood cell concentrate laced with a cocktail of chemical buffers and nutrients. The ruddy yield, shown here, is one chilled unit of processed blood product, suitable for a patient desperately in need of red cells. Such units—screened, packaged and tracked through their life cycles in keeping with the dictates of the U.S. Food and Drug Administration—are manufactured with assembly-line efficiency to optimize the safety and utility of a precious, limited resource.

A half-liter unit of whole blood, when spun, separates into layers. The 275-milliliter top layer of lemon-yellow plasma is rich in platelet cells, which are principal to blood clotting. The 225-ml bottom layer of red cells (erythrocytes), which shuttle oxygen and carbon dioxide around the body, is skimmed with a slick of the immune system's white cells (leukocytes). Because different patients need varying boosts for different blood functions, packaging these layers separately lets each whole blood donation help several people. And reducing unnecessary biological material, such as the leukocytes in the red cell concentrate, lowers the risk that a patient's immune system will reject a transfusion.

Synthetic blood replacements, which would carry no disease risk and could be manufactured in surplus, have an enormous potential market. Although several are in development, nothing can yet take the place of genuine blood cells grown by the human body. ■

Emily Harrison is photography editor at Scientific American.



KEEPING TABS
A unique bar code on each package lets blood banks monitor their inventory and anonymously link each unit to donor information in a central database. The same bar code labels four small tubes of blood collected at the time of donation and sent to testing laboratories for disease screening and blood typing.

SUSTAINABLE ENVELOPMENT
Living red cells have needs, even in refrigerated storage. The preservative AS-3 provides them with sodium citrate, sodium phosphate, adenine, sodium chloride and dextrose, which act as anticoagulants, maintain the cells' structural integrity and sustain their metabolism. AS-3 also dilutes the red cell concentrate so that it flows freely through tubes and needles into blood vessels.

CLOT STOPPER
Once outside the body, blood has a natural tendency to clot and dry. To counter that, an anticlotting solution called CP2D is added to the whole blood at the time of donation.

COST OF LIVING
The product of 24 hours of processing, this unit of leukocyte-reduced AS-3 red cells costs $220. A typical kidney transplant surgery requires one to two units; a heart transplant requires four to six. Car accident victims consume as many as 20 units.

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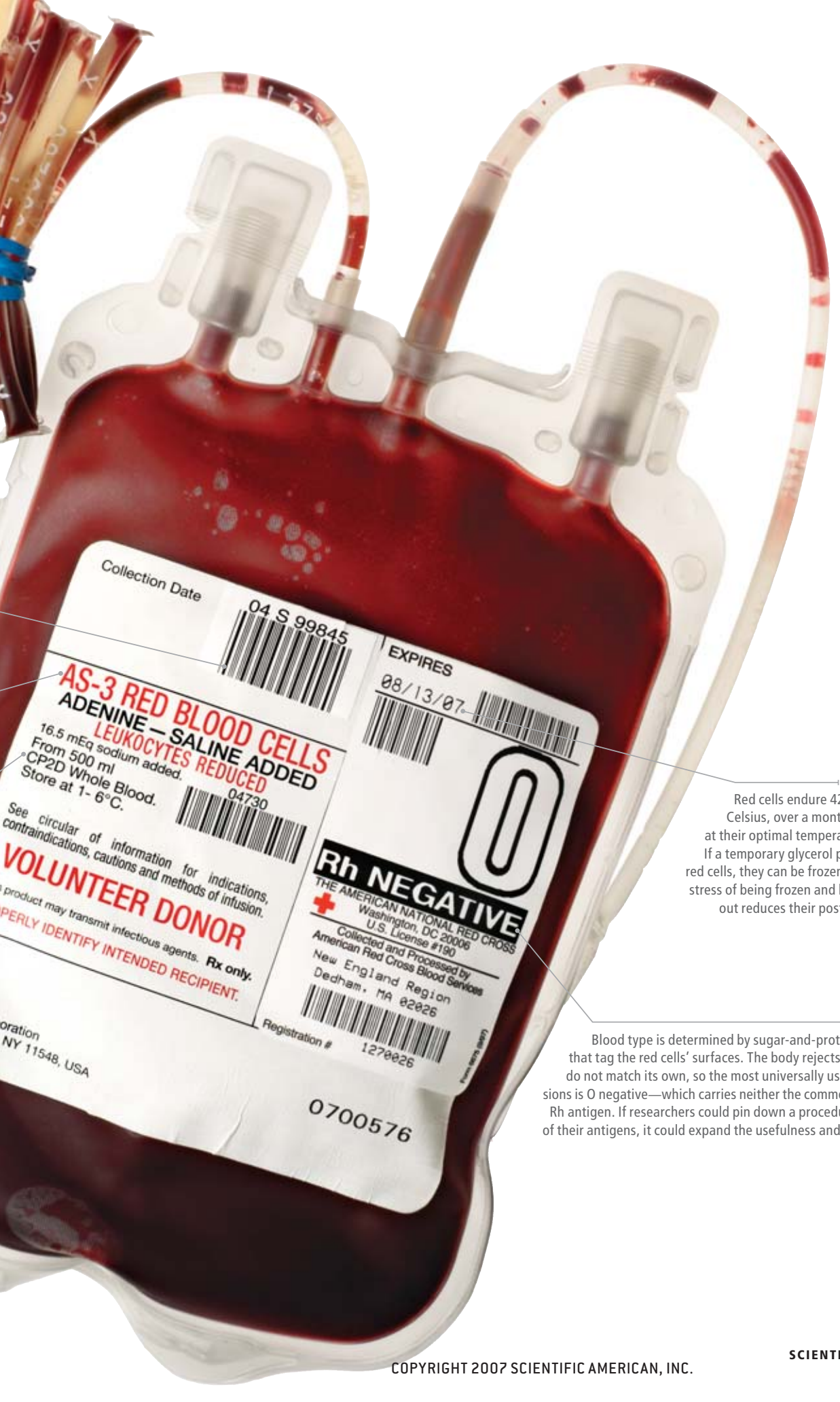

SANGUINE EXPIRATION

Red cells endure 42 days at one to six degrees Celsius, over a month longer than platelets last at their optimal temperature of 20 to 24 degrees C. If a temporary glycerol preservative is added to the red cells, they can be frozen for up to one year, but the stress of being frozen and having the glycerol washed out reduces their post-thaw shelf life to one day.

TYPE TREATMENT

Blood type is determined by sugar-and-protein chains, called antigens, that tag the red cells' surfaces. The body rejects cells bearing antigens that do not match its own, so the most universally useful blood type for transfusions is O negative—which carries neither the common A and B antigens nor the Rh antigen. If researchers could pin down a procedure for stripping blood cells of their antigens, it could expand the usefulness and safety of the blood supply.

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Two Technologies Shine

By Mark Fischetti

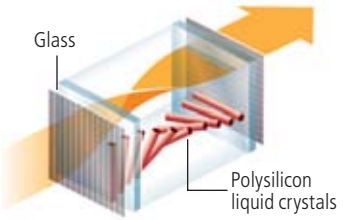
As prices drop, consumers are increasingly buying digital projectors to cast big images in company conference rooms, home living rooms and backyard "drive-ins." Two technologies—micromirrors and liquid-crystal displays (LCDs)—have been vying for these markets, but they are doing equally well in today's home and business arenas, says Art Feierman, editor of ProjectorReviews.com.

Both varieties can project sharp images from DVDs, digital cameras and presentation software such as PowerPoint. The choice depends on what buyers value most. In the inexpensive range (below $1,200 or so), micromirror machines may be slightly smaller and lighter and may project higher-contrast images. LCD machines may have better color accuracy, however, and run quieter and cooler. More expensive models of both types often compensate for any inherent technological weaknesses.

Micromirror units are usually called DLP projectors because they harness the Digital Light Processing chip pioneered by Texas Instruments. Home and business units create imagery with a single DLP chip and a color wheel [*see illustration below*]. Commercial movie theaters that have gone digital use a more sophisticated system comprising three DLP chips that can generate much larger images [*see illustration at far right*]. Cinema systems cost $50,000 or more and are installed in front of a 3,000- to 10,000-watt xenon lamp that can project at far greater distances than the 200- to 400-watt lamps inside consumer models.

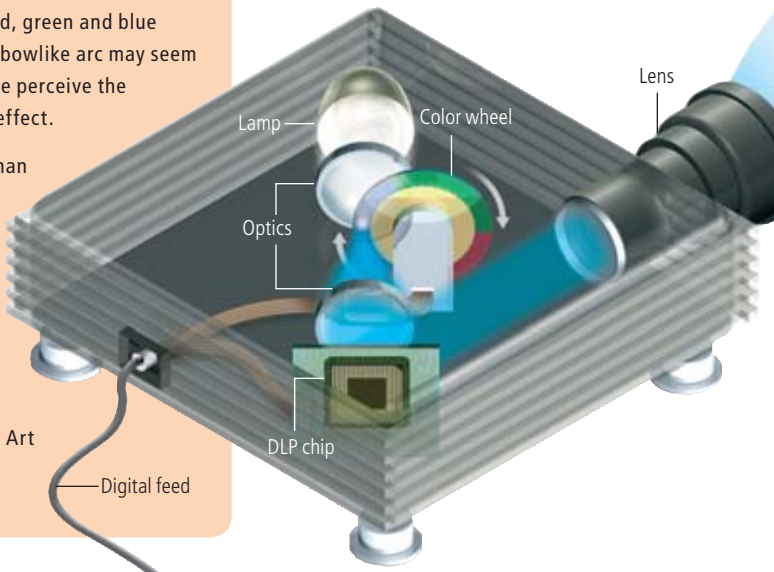
Early projectors created images at SVGA resolution (800 lines by 600 pixels per line), but today most run at XGA resolution (1,024 by 768) or higher, in part because almost all notebook computers now output images at XGA or greater. And although standard DVDs look fine at SVGA, the Blu-ray and HD DVD disks now capturing the video market require a widescreen version of XGA or better, often referred to as 720p or 1,080p. Projectors with higher resolutions are also available. "The best decision is to match the resolution of the projector with the resolution of the source you intend to use," says Steve Stark, vice president of R&D at InFocus in Wilsonville, Ore., one of only a few companies that make both DLP and LCD machines.

LCD PROJECTOR
Dichroic mirrors (*right*) send red, green and blue beams to individual liquid-crystal displays. Pixels in each display allow color to pass or not as needed to form the image, coordinated by a digital feed.



LIQUID CRYSTAL inside a pixel (*above*) blocks light when oriented orthogonally to the light source. A voltage twists them into alignment, allowing light to pass. Twisting them to various degrees creates shades of color.

SINGLE-CHIP MICROMIRROR PROJECTOR
A steadily spinning wheel fitted with color filters allows only a single color of light to transmit at regular intervals. These rays strike a DLP chip covered with micromirrors that reflect the colors as needed through a lens. A digital feed turns the mirrors on and off, timed with the wheel to reflect the required color.



DID YOU KNOW ...

RAINBOW EFFECT: Because the color wheel in DLP machines combines red, green and blue filters rotating past the light source to create color images, a fleeting rainbowlike arc may seem to trail bright, fast-moving objects in a scene. Only a few percent of people perceive the artifact. Certain models spin the wheel at higher speeds to eliminate the effect.

SCREEN DOOR: The pixels on LCD chips have wider gaps between them than the mirrors on DLP chips. If a low-resolution LCD machine is casting a large image, viewers may perceive a grid pattern: the screen-door effect. Manufacturers are making pixels smaller and packing them tighter to eliminate it—a design attribute more common in higher-end models.

HIT THE WALL: Many executives and homeowners seem content to shine their big visuals on a blank wall, but screens optimized for projectors can improve image quality significantly. For $100 to $150 at the low end, says Art Feierman of ProjectorReviews.com, "it seems silly not to use them."

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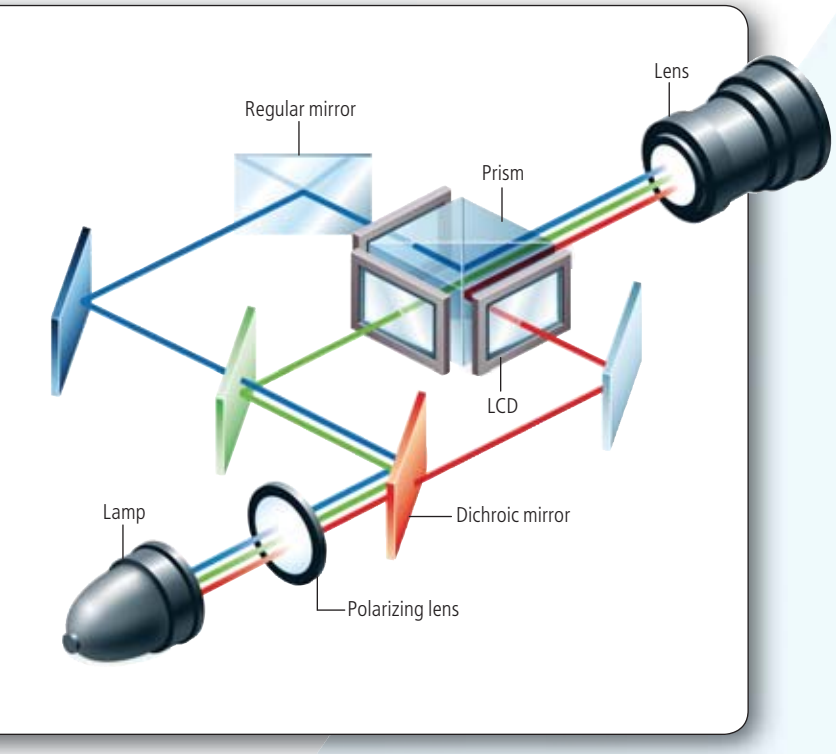
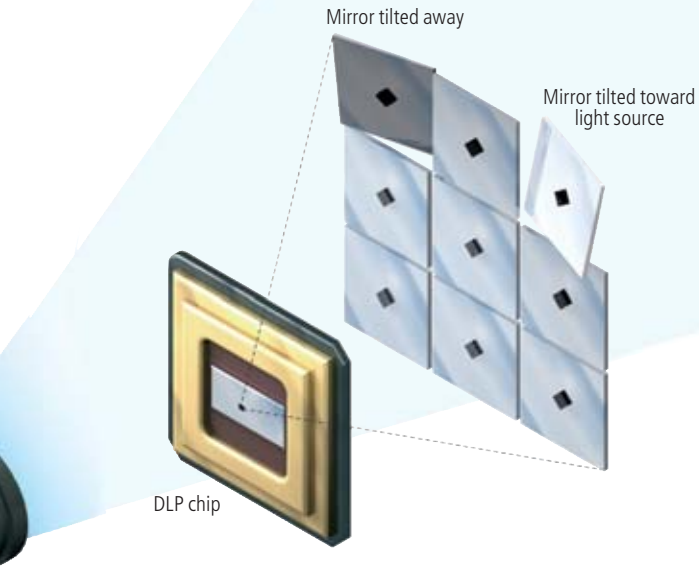
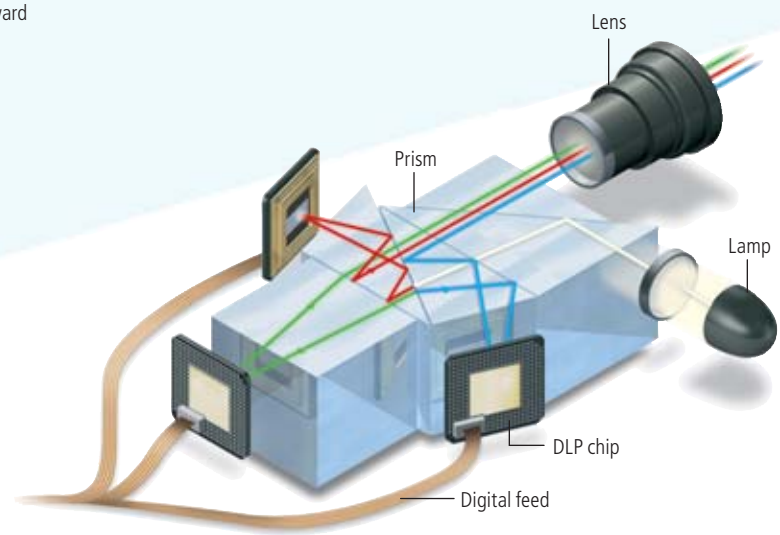




DIGITAL LIGHT PROCESSOR CHIP has millions of tiny, hinged mirrors. Each reflects one pixel of color to the screen. When a mirror is tilted by an electrode toward the light source, the pixel is lit (on); when tilted away, the pixel is dark (off). Tipping the mirror thousands of times a second creates shades of color.



THREE-CHIP MICROMIRROR PROJECTOR White light passes through a prism that splits red, green and blue components to their own DLP chips. Mirrors on the chips reflect colors as needed to form an image.

5W INFOGRAPHICS (*illustrations*); ANJA NIEDRINGHAUS *AP Photo* (*soccer players*)

SEND IDEAS *to workingknowledge@SciAm.com*

Topic suggested by readers Duane Rueb, Daniel Escoté and Harold Diamond, Jr.

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Peking Man ▪ Posthuman Man ▪ Polar Plight

BY MICHELLE PRESS

THE CASE AGAINST PERFECTION: ETHICS IN THE AGE OF GENETIC ENGINEERING
by Michael J. Sandel. Belknap Press of Harvard University Press, 2007 ($18.95)

ENHANCING EVOLUTION: THE ETHICAL CASE FOR MAKING BETTER PEOPLE
by John Harris. Princeton University Press, 2007 ($27.95)

NOTABLE BOOKS MARKING THE INTERNATIONAL POLAR YEAR

Vanishing World: The Endangered Arctic
photography by Mireille de la Lez; text by Fredrik Granath. 130 full-color photographs. Abrams, 2007 ($40)

The Ends of the Earth: An Anthology of the Finest Writing on the Arctic and the Antarctic
edited by Elizabeth Kolbert and Francis Spufford. With contributions from Jon Krakauer, Jack London, Diane Ackerman, Barry Lopez, Ursula K. LeGuin and others. Bloomsbury USA, 2007 ($29.95)

FROM *VANISHING WORLD*. Photograph by Mireille de la Lez.

Few books could present more implacably opposed views, and few could raise more provocative questions. Michael J. Sandel, a professor of government at Harvard University and a former member of the President's Council on Bioethics, assumes that many people find the more extreme forms of genetic engineering (cloning and designer children, for example) disquieting, and he attempts to explain why this unease makes moral sense. John Harris, a professor of bioethics at the University of Manchester School of Law and a member of Britain's Human Genetics Commission, assumes not only that biotechnological enhancement is going to happen but that we have a moral obligation to make it happen. "I propose," Harris writes, "both the wisdom and the necessity of intervening in what has been called the natural lottery of life, to improve things by taking control of evolution and our future development to the point, and indeed beyond the point, where we humans will have changed, perhaps into a new and certainly into a better species altogether."

Sandel argues that the drive to enhance human nature through genetic technologies is objectionable because it represents a bid for mastery that fails to acknowledge that human powers are a gift (whether from nature, God or fortune). If biotechnology dissolved our sense of giftedness, he continues, we would lose three key features of our moral landscape—humility, responsibility and solidarity. "Rather than employ our new genetic powers to straighten 'the crooked timber of humanity,' " he writes, "we should do what we can to create social and political arrangements more hospitable to the gifts and limitations of imperfect human beings."

One is the more eloquent—and even at times uplifting—argument. The other is no doubt the way the world is going to go.

For further commentary on the ethics of bioengineering, see Daniel Kevles's review of Francis Fukuyama's *Our Posthuman Future* (from May 2002) at **www.SciAm.com/ontheweb**

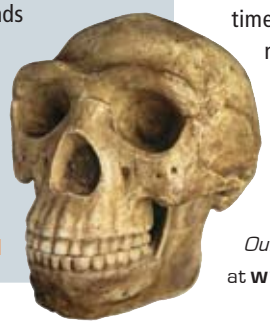
EXCERPT

THE JESUIT AND THE SKULL: TEILHARD DE CHARDIN, EVOLUTION, AND THE SEARCH FOR PEKING MAN
by Amir D. Aczel. Riverhead Books/Penguin, 2007 ($24.95)

Two stories in one, The Jesuit and the Skull *recounts the search for the "missing link" between apes and humans and the dramatic life of one of the principal participants in this search, a charismatic and mysterious Jesuit who cared passionately about science:*

"In 1923, Father Pierre Teilhard de Chardin arrived in China as an exile, by the order of his superiors at the Jesuit headquarters in Rome. His transgressions included questioning the doctrine of original sin and supporting Darwin's theory of evolution.... And as fate would have it, in 1929, in China ... Teilhard became a crucial player in one of the most important discoveries in modern anthropology, and one that provided us with invaluable evidence for the theory that Charles Darwin had published exactly seventy years earlier. This great discovery was the unearthing of the skeletal remains of Peking man [*Homo erectus*].

And then, seemingly overnight, everything was lost.... [In 1941] the finds were clandestinely packed in two crates, and readied for shipment by sea to the American Museum of Natural History in New York, to be kept there until the end of the war. But when the crates left Peking Union Medical College to be brought to the ship that was to take them to America, they vanished without a trace. Not a shred of evidence has surfaced over the intervening six and a half decades to point to what actually happened to this collection."



CAST OF Peking man (*Homo erectus*) skull

REPRINTED FROM *THE JESUIT AND THE SKULL* BY AMIR D. ACZEL BY ARRANGEMENT WITH RIVERHEAD BOOKS, A MEMBER OF PENGUIN GROUP (USA), INC., COPYRIGHT © 2007 BY AMIR D. ACZEL; NATURAL HISTORY MUSEUM/ALAMY (*skull*)

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Q *Could the International Space Station (ISS) serve as a* ***repair hangar for satellites*** *or a way station for craft headed beyond its orbit?*

Jack Bacon of the Mission Analysis and Integration Group at NASA's ISS Program Integration Office explains:

Repairing satellites onboard the ISS may prove impractical, but chances are better for the way-station option. The main issue with repair is that a service platform must start in the same orbital plane as the satellite, and the chances are slim that any particular satellite would meet that condition. Even a one-degree orbital plane change to meet a satellite would cost the station nearly 12 metric tons of propellant, and most satellites are much farther inclined to the ISS's orbit than just one degree. Similarly, most satellites do not have the propellant available to change their own orbital plane, so they cannot come to the station.

Working on a spacecraft inside the ISS also presents real problems. Every craft deploys instruments and valves using pyrotechnic mechanisms once it reaches orbit, but it is unwise to have unexploded pyrotechnics in a so-called shirt-sleeve environment, and, conversely, it is difficult to fit a fully deployed spacecraft inside. Astronauts do not have the same unlimited supply of fresh air that workers on the ground enjoy, so any toxic risk (such as propellant) is potentially catastrophic.

Even if we chose to accept the risks, we would face the final hurdle of how to build a chamber wide enough or a doorway strong enough to accommodate a large spacecraft. The aerodynamics of launch vehicles limits the diameter of the payload (or chamber) to about five meters. Even assuming we worked with only a few centimeters of clearance between the spacecraft and the walls, we would still have the problem of getting the spacecraft in and out of the chamber. A five-meter hatch must withstand nearly 200 tons of force, requiring some massive framing and hardware that would further complicate the design, building and launch processes.

The prospects are much more favorable for using the station as a staging base for further deployment of spacecraft that leave Earth's orbital environment, such as the James Webb Space Telescope and missions to the moon or Mars. But such outfitting would need to be done in the vacuum of space with the spacecraft docked to the station. In any case, the launch window to the moon, Mars or other points would occur far less often from the station than the ground.

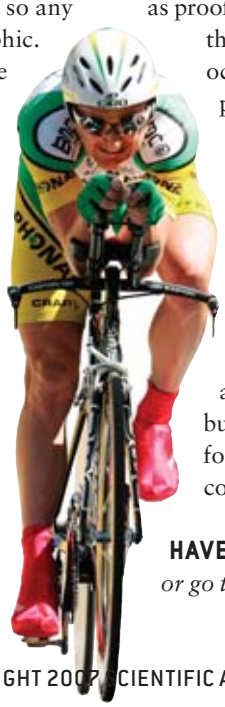
Q *Can a dose of* ***testosterone*** *produce an improvement as immediate and profound as that which Floyd Landis showed in the 2006* ***Tour de France****?*

—R. Abt, Meadowbrook, Pa.

Michael S. Bahrke, co-editor of the 2002 book *Performance-Enhancing Substances in Sport and Exercise* (Human Kinetics Publishers), replies:

A single dose of testosterone most likely would not produce a quick recuperative effect resulting in a sensational turnaround in performance.

During the Tour de France race, Landis's ratio of testosterone to epitestosterone (an inactive steroid usually found in roughly equal abundance to testosterone), the so-called T/E ratio, tested higher than 4 to 1, the limit considered by the World Anti-Doping Agency as proof of steroid use. Because Landis previously tested within the acceptable bounds, speculation as to why a sudden spike occurred centered on his possible use of a testosterone patch or gel. (This past September, Landis lost his appeal of the result and was stripped of the 2006 Tour title.)



Research indicates that large doses of testosterone can significantly increase muscular strength within six to 12 weeks of administration, and one recent study found significant effects after just three weeks of use; further testing is needed to determine what, if any, shorter-term effects testosterone provides. In other words, testosterone would not be used for recovery and increased work output during a single Tour stage, but if taken early and long enough, it would be beneficial for maintenance and improved performance over the course of the entire 22-day race. ■

HAVE A QUESTION?... *Send it to experts@SciAm.com or go to* **www.SciAm.com/asktheexperts**

NASA (*spacecraft*); FRANCK ROBICHON *epa/Corbis* (*Landis*)

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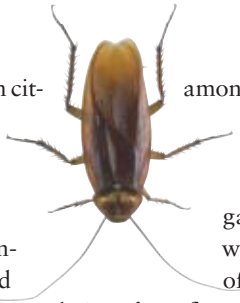
Can a Cockroach Live without Its Head?

BY CHARLES Q. CHOI



Cockroaches, infamous for their tenacity, are often cited as the most likely survivors of a nuclear war. Some pundits even claim the critters can live without their heads. It turns out that this assertion is fact: at times headless roaches can live for weeks.

To understand why cockroaches—and many other insects—can survive decapitation, it helps to understand why humans cannot, says physiologist and biochemist Joseph G. Kunkel of the University of Massachusetts Amherst, who studies cockroach development. First, decapitation in humans results in blood loss and a drop in blood pressure, hampering transport of oxygen and nutrition to vital tissues. "You'd bleed to death," Kunkel states.

In addition, humans breathe through their mouth or nose, and the brain controls that critical function, so breathing would stop. Moreover, the human body cannot eat without the head, ensuring certain death from starvation should one survive the other ill effects of head loss.

Cockroaches do not have the same kind of circulatory system as people. For blood to make its way through the vast network of human blood vessels, and especially through the tiny capillaries, a fair amount of pressure must be maintained. The roach vascular system is much less extensive and lacks tiny capillaries, Kunkel notes, so pressure can be significantly lower. "After you cut their heads off, very often their necks will seal off just by clotting," he adds. "There's no uncontrolled bleeding."

Moreover, the hardy vermin breathe through spiracles, or little holes in each body segment. The roach brain does not control this breathing, and blood does not carry oxygen throughout the body. Rather the spiracles pipe air directly to tissues through a set of tubes called tracheae.

Cockroaches are also poikilothermic, or cold-blooded. Consequently, they do not expend energy to heat themselves up and so can get by on much less food than humans need. They can survive for weeks after just one meal, Kunkel says. "As long as some predator doesn't eat them, they'll just stay quiet and sit around."

Entomologist Christopher Tipping of Delaware Valley College has actually decapitated American cockroaches (*Periplaneta americana*)—"very carefully under microscopes," he observes—to study what happens, among other things. "We sealed the wound with dental wax to prevent them from drying out. A couple lasted for several weeks in a jar."

Roaches and many other insects have clumps of ganglia—nerve tissue agglomerations—distributed within each body segment, and the clumps are capable of performing the basic nervous functions responsible for reflexes, "so without the brain, the body can still function in terms of very simple reactions," Tipping says. "They can stand, react to touch and move."

And it is not just the body that can survive decapitation; the lonely head can keep on functioning, too, waving its antennae back and forth for several hours until it runs out of steam, Kunkel says. If given nutrients and refrigerated, a roach head can last even longer.

Still, in roaches "the body provides a huge amount of sensory information to the head, and the brain cannot function normally when denied these inputs," explains neuroscientist Nicholas J. Strausfeld of the University of Arizona, who specializes in arthropod learning, memory and brain evolution. For instance, although cockroaches have a fantastic memory, he says, trying to teach them is futile when they have bits of their body missing. "We have to keep their bodies completely intact."

Cockroach decapitation may seem macabre, but scientists have conducted many experiments with headless roach bodies and bodiless roach heads to answer serious questions. Loss of the noggin deprives roach bodies of hormones from glands in their heads that control maturation, a finding that is helping researchers investigate metamorphosis and reproduction in insects. And studies of bodiless roach heads elucidate how insect neurons work. Ultimately, though, the results provide one more testament to the cockroach's enviable endurance. A headless roach may not be the smartest of its kind, but it can certainly survive. ■

Charles Q. Choi is a freelance science writer based in New York City.

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