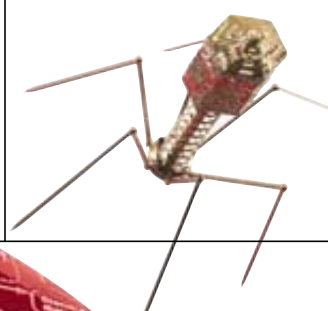
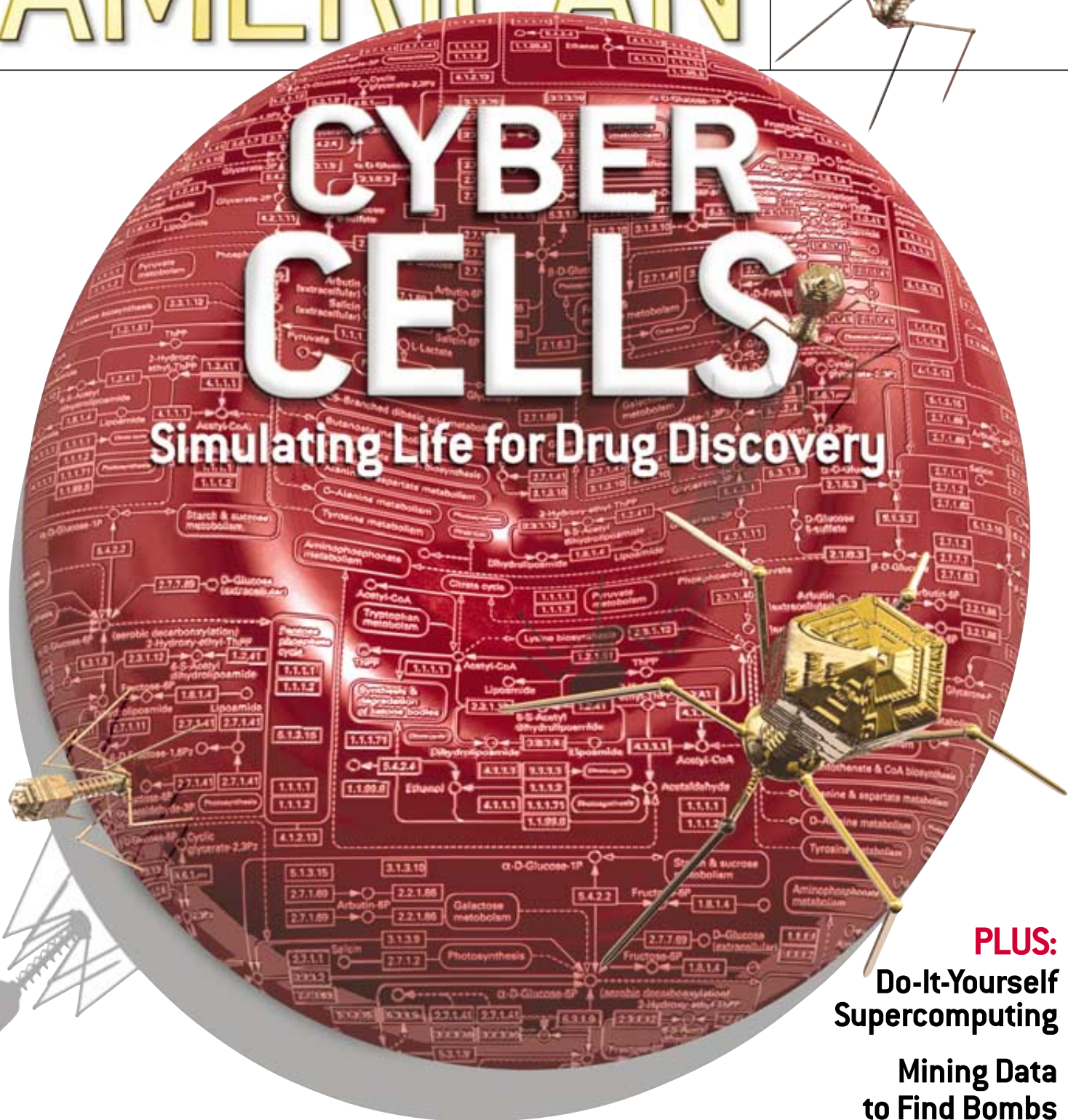


SCIENTIFIC AMERICAN



CYBER CELLS

Simulating Life for Drug Discovery



PLUS:
Do-It-Yourself
Supercomputing

Mining Data
to Find Bombs

august 2001

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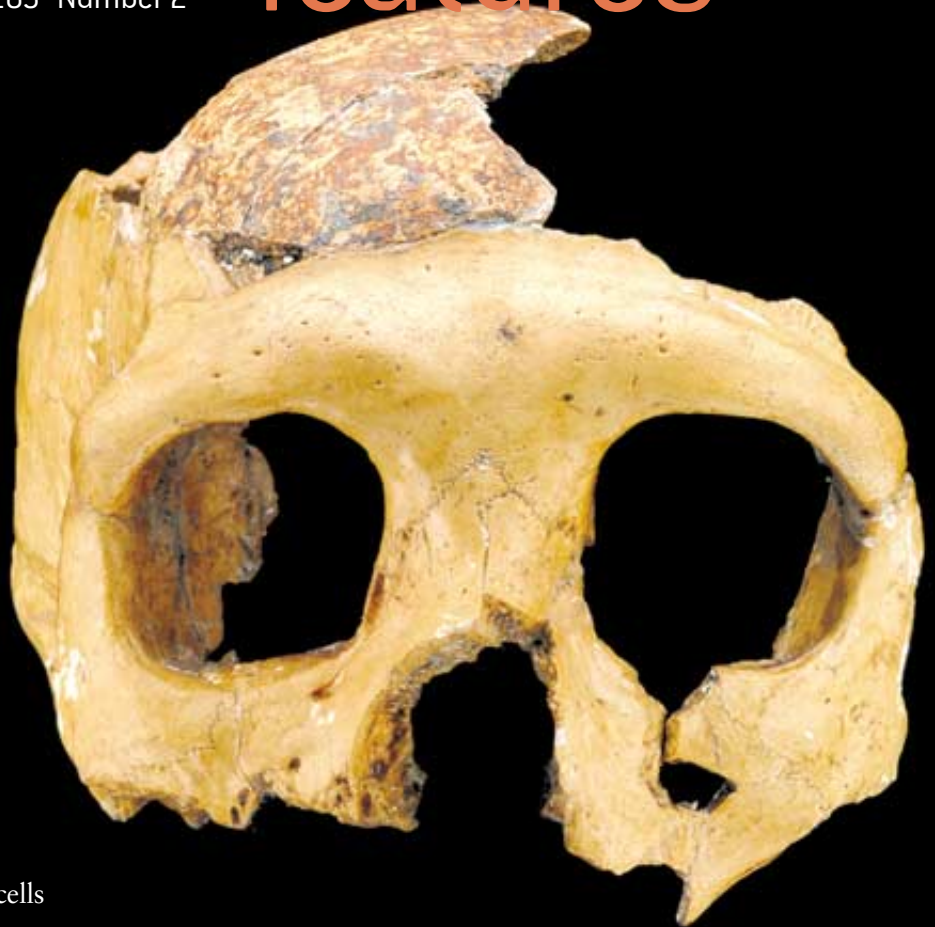
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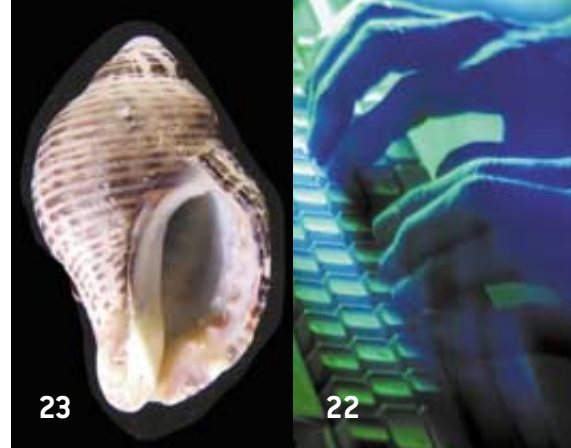
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Another Cup of CAFE, Please

Believe it or not, government regulation sometimes *can* lead to technological innovation. During the energy crisis of the 1970s, Congress passed a law that required automobile manufacturers to improve the fuel economy of their cars and light trucks. The automakers promptly adopted cheap, ingenious ways to comply with the Corporate Average Fuel Economy (CAFE) standards. Thanks largely to more advanced engines and computerized controls, the average gas mileage of new vehicles doubled over the next decade, reaching a high of 26.2 miles per gallon in 1987.

Since then, however, the average has slid to 24.5 mpg, even though automotive engineers are still brimming with ideas for enhancing fuel economy. The problem is that the CAFE standard for cars has been frozen at 27.5 mpg for the past 12 years, and the standard for light trucks is stuck at 20.7 mpg. Moreover, the phenomenal growth in the popularity

of sport utility vehicles—which are classified as light trucks—has changed the mix of new vehicles and thus lowered the overall average.

Improving fuel economy is a worthy national goal: it would reduce America's dependence on imported oil and cut the carbon emissions that contribute to global warming. Indeed, the Bush administration recently expressed support for crafting new fuel-economy standards based in part on the recommendations of a National Academy of Sciences panel. The Alliance of Automobile Manufacturers opposes higher standards, but some engineers in Detroit privately concede that they could increase the fuel economy of most vehicles without raising their cost unduly. Opponents of CAFE say higher standards would encourage manu-

facturers to make their vehicles lighter and hence less crashworthy. Trimming weight, however, need not threaten passenger safety, especially if automakers use more aluminum and other light but strong materials.

General Motors, Ford and DaimlerChrysler have already promised to boost the average gas mileage of their SUVs by 25 percent over the next five years. A report from the American Council for an Energy-Efficient Economy, a nonprofit organization based in Washington, D.C., estimates that manufacturers could upgrade the fuel economy of midsize cars by more than 50 percent at a cost of about \$1,000 per vehicle (which consumers would recoup at the gas pump in about three years). The most talked-about technology is the hybrid vehicle, which employs an electric motor to supplement a gas engine. But other innovations abound. The integrated starter generator, for example, replaces a conventional generator with a battery system, and the variable displacement engine shuts down some of its cylinders when they aren't needed.

Raising the CAFE standards is the surest way to promote these technologies. Market forces alone cannot do the job, because fuel economy ranks low among most car buyers' priorities. The beauty of CAFE is its flexibility. The standards apply to all automakers, foreign and domestic alike, allowing each to choose any approach for improving the average fuel economy of its fleet. In contrast, the recently proposed tax credit for the purchase of hybrid or fuel-cell vehicles would subsidize one technology that may not prove competitive.

The Sierra Club and other environmental groups support raising the CAFE standard to 40 mpg for all vehicles by 2012, but many automotive experts say this goal is unrealistic. Taking economic and technical considerations into account, a reasonable strategy would be to raise the standard for light trucks to 27 mpg by 2007 and to 32 mpg by 2012, while lifting the standard for cars to 32 and 37 mpg by the same dates.



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“JARON LANIER’S DESCRIPTION of the seven-camera tele-immersion project in ‘Virtually There’ [April] should have mentioned, for historical context, the traditional two-camera system that has a 20-millisecond latency: the system whose two cameras are called eyes and that uses a computer called a brain on which runs the ever popular Mind OS software that portrays external reality as a near-real-time, three-dimensional, internal representation viewed by ... the mysterious viewer called consciousness.” Okay, Robert Burruss of Chevy Chase, Md., consider it mentioned.

For discussions of other topics from the April issue, please direct your OS below.



CORD BLOOD: STAT

Ronald M. Kline [“Whose Blood Is It, Anyway?”] cites the odds that a newborn will need to use his or her own cord blood in the future as 1 in 200,000 and attributes this statistic to the National Institutes of Health. But the NIH provided the Cord Blood Registry with information estimating an individual’s need for such a transplant to be 1 in 2,703. To our knowledge, the 1-in-200,000 figure has never been explained or published in a peer-reviewed journal.

DAVID T. HARRIS

Scientific Director, Cord Blood Registry

KLING REPLIES: The 1-in-200,000 statistic came from an official at the National Heart, Lung and Blood Institute. Although several other researchers have made such estimates, determining the likelihood that an individual would ever need his or her own cord blood is an experiment in progress. My article cited a 20-fold range in probability that a newborn would need a cord blood transplant. This underscores how much still remains to be understood about the uses of cord blood transplantation in the treatment of disease.

We still do not fully comprehend why the cancers of some people who receive transplants recur. Until we answer this question, we will not know which patients will benefit most from cord blood transplants. It would be a great help if blood banks made available data on the total number of cord blood units they collect and the number of units that are used for transplantation. Only in this way will we know the probability that a person who has stored his or her cord blood will actually find a use for it.

[Editors’ note: The National Heart, Lung and Blood Institute—part of the NIH—informed SCIENTIFIC AMERICAN that it has a policy of not responding to letters to the editor.]

AMINO ACIDS THROUGH THE LOOKING GLASS

I cannot let Robert M. Hazen [“Life’s Rocky Start”] get away with pleading for pure chance as the reason why the amino acids in living organisms are predominantly “left-handed.” The left- and right-handed varieties of amino acids can be made in 50–50 quantities, as can mirror-image crystal faces. So the fact that all natural substances are predominantly left-handed must result not merely from chance. The other explanation is that somewhere in the mirror world of right-handed molecules, there is a combination that just does not work as well, and so natural selection ruled the right-handers out.

PETER ROSE

Knutsford, England

HAZEN REPLIES: I have two reasons for pleading pure chance. First, for every plausible mechanism that yields a significant excess of left over right, somewhere there exists the mirror mechanism. Second, even if the earth started with an excess of left- or right-handed molecules, amino acids gradually switch back and forth, yielding a 50–50 mix on a geologic timescale.

PRIDE AND PRAISE

Roy F. Baumeister’s ingenious research [“Violent Pride”] demonstrates that narcissists are aggressive. Narcissism, however, is a pathological view of oneself as

superior to others. It cannot be equated with self-esteem, and it has not been shown to result from children's receiving positive feedback.

On the contrary, many young people are in home and school environments with inadequate encouragement and structure. Research suggests that children from such environments are more likely to become alienated, to join gangs, to engage in behaviors that harm themselves and others and, quite possibly, to become narcissistic. The last thing our children need is less positive feedback.

SCOTT C. CARVAJAL
ANDREA J. ROMERO
University of Arizona

WHAT PRICE "Purer" AGRICULTURE?

Rebecca Goldberg of Environmental Defense ["Seeds of Concern," by Kathryn Brown] is quoted as saying that she prefers sustainable agriculture alternatives, such as crop rotation and organic farming, to conventional methods. But has a real comparison of the costs, loss of production, and disease inherent in those "alternative" methods ever been done? Organic farming is not "sustainable" if the nation's farmers go broke trying to do it. Environmentalists invoke nostalgia by recalling a simpler and thus supposedly cleaner era in agriculture prior to

chemical use. But has anyone ever looked at the past data on crop failure, weed invasions, famine, food spoilage and food-borne disease from prechemical days? The amounts are staggering.

JEFF FICEK
Former farmer and rancher
Dickinson, N.D.

NO GM RISKS? HMM, SOUNDS FAMILIAR

In "The Risks on the Table," by Karen Hopkin, Steve L. Taylor asks who else should shoulder the burden and the expense of performing safety tests for genetically engineered plants but the companies that produce these products. Come on! The rest of us learned a lesson from U.S. tobacco company executives, who found that their products were causing cancer but chose not to share this information with consumers.

VERONICA COLLIN
Denver

RESTRICTED ABORTION, DEADLY CONSEQUENCES

Marguerite Holloway's News Scan article "Aborted Thinking," on the "gag rule" order that U.S. aid cannot be used by organizations that promote or perform abortions, was powerfully argued but supported by questionable statistics. She lists six countries where abortion is legal and the average number of maternal deaths is 12 per 100,000 births, and six countries where it is illegal and the average is 148. Surely the more significant difference is economic. The "legal" countries are all in the developed world, whereas the "illegals" are all developing nations.

ELLIOTT MANLEY
Farnham, England

NEWS EDITOR PHILIP YAM REPLIES: *Certainly wealth matters, but legal codes also play a role. Romania is a case in point: according to the World Health Organization, maternal deaths resulting from abortion skyrocketed after the government there restricted abortions. Romania legalized abortion again in 1989, and by the next year the figure plummeted. Worldwide, unsafe abortions account for 13 percent of ma-*

ternal deaths; in eastern Europe and South America, they account for 24 percent. Poor countries in these regions stand to suffer the most from a cut in U.S. funds.

URSULA LeGUIN, WHERE ARE YOU?

In light of Joe Davis's embedding encoded messages into the nucleotides of living organisms ["Art as a Form of Life," by W. Wayt Gibbs], one wonders if the vast stretches of nonfunctional, or at least non-protein-encoding, DNA in our own genome might represent the music, poetry or imagery of some Davis of the distant past.

TOBIAS S. HALLER
Bronx, N.Y.

NOT A LIFESTYLE DISEASE

"Lifestyle Blues," by Rodger Doyle [News Scan], fails to distinguish between type 1 and type 2 diabetes. Type 1 diabetes is an autoimmune disease affecting roughly 10 percent of diabetics. It usually has its onset in juvenile years and totally destroys the body's ability to produce insulin, unlike the more common type 2 diabetes, which is associated with obesity and can frequently be managed solely by making "lifestyle" changes.

ALAN P. BURKE
Fremont, Calif.

ERRATA "At Your Fingertips," by Mark Fischetti [Working Knowledge], should have cited Sam Hurst of Oak Ridge National Laboratory as the primary developer of the first resistive touch screen, aided by Bill Gibson and John Talmage of Elo TouchSystems (then Elographics), and not just Bill Colwell.

"I, Robonaut," by Phil Scott [News Scan], attributed the development of a robot that incorporates the brain of the sea lamprey *Petromyzon marinus* to scientists in Somerset, England. In fact, Ferdinando Mussa-Ivaldi of Northwestern University leads the research team.

In "Seeds of Concern," Kathryn Brown stated that it is "unlikely that herbicide-tolerant or Bt crops [in the U.S.] will spread their biotech genes to weeds." Brown's comment actually applies only to Bt crops.



Warped Perception ■ Hostile Continent ■ Mad Scientist

AUGUST 1951

TRANSISTOR—“Even at the present very early stage of transistor development it seems certain that transistors will replace vacuum tubes in almost every application. What results can we expect from this major revolution in the techniques and capabilities of electronics? Since the revolution is just beginning, we can only speculate. A large part of the improvement in the performance of the device is due to the development of a new design called the ‘junction transistor.’ The early units consisted of a germanium crystal touched by two closely spaced fine wires—‘cat’s whiskers.’ In the junction transistor this point-contact arrangement has been replaced by a large-area contact. It therefore operates more efficiently and consumes far less power. —Louis N. Ridenour.”

THE EYE AND THE BRAIN—“Adelbert Ames, Jr., of the Institute for Associated Research in Hanover, N.H., has designed some new ways of studying visual perception. His theory suggests that the world each of us knows is a world created in large measure from our experience in dealing with the environment. In our illustration [right], figures are distorted when they are placed in a specially constructed room. The woman at left appears much smaller because the mind ‘bets’ that the opposite surfaces of the room are parallel.”

THE EXPANDING UNIVERSE—“The 200-inch Hale telescope on Palomar Mountain in California has given a tentative answer to one of the main questions it was built to explore: Does the universe continue to expand with increasing speed out beyond the seeing limits of earlier telescopes? The answer seems to be yes. At a distance of 360 million light-years, the limit of the 200-inch’s penetration so far, the nebulae apparently are receding from the earth with a velocity of 38,000 miles per second, at the rate predicted by the expanding-universe theory.”

AUGUST 1901

RADIATION BURNS—“Henri Becquerel has confirmed, by an unpleasant experience, the fact, first noted by Walkoff and Giesel, that the rays of radium have an energetic action on the skin. Having carried in his waistcoat pocket for about six hours a small sealed tube containing a few decigrammes of intensely active radiferous barium chloride, in ten days’ time a red mark corresponding to this tube was apparent on the skin; the skin peeled off and left a suppurating sore, which did

dition will set sail, HMS *Discovery*, was recently launched at Dundee (Scotland). The leader of the three-year expedition is Capt. R. F. Scott, Royal Naval Reserve.” [Editors’ note: This was Robert Falcon Scott’s first expedition to Antarctica.]

AUGUST 1851

ROCKS ON HIS MIND—“Mr. George Gibbs of Newport, R.I., who founded the magnificent cabinet of minerals at Yale College, was once collecting in the northern part of Vermont with the aid of three or



not heal for a month. Pierre Curie has had the same experience after exposing his arm for a longer period to a less active specimen.”

ANTARCTICA—“The present year will be a red letter one in the annals of Antarctic Exploration, as determined efforts are to be made by the British Geographical Society and the German Government in concert, to unravel a little of the *terra incognita*. The vessel in which the British expe-

four workmen. One day an acquaintance of Mr. Gibbs arrived by coach at the tavern where he was staying, shook hands with him, and mutual expressions of kindness were passed. Observing this, the landlord took the stranger aside and informed him that his friend was insane: he had been employing men for nearly a month in battering stones to bits, and if he had any friendship for the gentleman, he ought certainly to inform his family of his condition.”

Concorde's Comeback

FIXING THE SUPERSONIC TRANSPORT TO AVOID ANOTHER ACCIDENT BY STEVEN ASHLEY



NO TIRE BLOWOUTS is the goal for refitted Concordes.

NEED TO KNOW: WEIGHTY MATTERS

The safety alterations are expected to add about **400 kilograms** (about **880 pounds**) to each of the dozen serviceable Concordes, although new tires should reduce the overall weight gain somewhat. Other mass savings will be achieved through changes to the planes' interior. British Airways is spending about \$43 million to retrofit its seven-plane Concorde fleet.

LAST SUMMER, when Air France Flight 4590—Concorde service from Paris to New York—fell to earth, killing 113 people, shock waves reverberated throughout both Britain and France, as well as across the Atlantic. The first crash of the supersonic transport (SST), a symbol of Anglo-French technological achievement, was comparable in its effect to the explosion of the space shuttle *Challenger* in the U.S.

Ever since, the airframe builders—BAE Systems and the European Aeronautic Defence and Space Company (EADS)—and the airline operators—British Airways and Air

France—have been working feverishly to get the Concorde back into the air. This continuing effort involves retrofitting the SST with new safety systems designed to prevent a repeat disaster. During takeoff, the ill-fated airliner ran over a stray metal strip that had fallen off an earlier DC-10 flight, according to accident investigators. The strip cut into a tire on the plane's main landing gear, throwing debris up against the underside of the Concorde's delta wing, right at a fuel tank.

Although the impact did not perforate the skin, it deformed the tank wall enough to send intense pressure waves through the kerosene fuel, which eventually punched a hole the size of a sheet of notebook paper in the tank. Fuel spilled out of the ruptured reservoir as the plane became airborne. Whisked around the landing gear by the turbulent airflow, the leaking kerosene quickly became a long, roaring flame trail when it was set alight either by an electrical spark in the undercarriage or by hot gases from the front of the turbine engines. Soon afterward the supersonic airplane's close-mounted engines ingested tire debris or, more likely, leaked fuel or hot combustion gases; the engines failed in succession, leading to the subsequent crash.

When the flagship SST is fully retrofitted, it should be able to resist damage from tire blowouts, mishaps that have not been un-

common in the past. “The design is such that we can absolutely guarantee that a fire like the one that happened in Paris could never happen again,” states British Airways’s chief Concorde pilot, Mike Bannister.

Among the more significant modifications are new Kevlar aramid-rubber fuel tank liners. Manufactured by EADS, the liners, which are similar in appearance to gardeners’ seed trays, cost around \$2.1 million each to install. Technicians are laboriously fitting about 150 of the individually molded liner sections, jigsaw-fashion, into the tight spaces of the fuel reservoirs of each jet. In an approach already employed in military helicopters and Formula 1 racing cars, the cardboard-thin liners are designed to contain the flow of escaping fuel by being sucked into the breach should the wing skin be pierced. During the accident, kerosene gushed out at a rate of around 100 liters per second, which created a sufficiently rich fuel-air mixture to allow the fuel to burst into flames. “The liners will stem that kind of flow, limiting it to something like a liter per second, which would not ignite,” explains Peter Middleton, a British Airways spokesperson.

New puncture-resistant tires from Michelin should go a long way toward reducing the risks as well. The Concorde’s original nylon bias-ply tires—the standard aviation industry design in which woven reinforcing fabric plies are stacked with their weaves set at crisscrossing angles—could be replaced by special

radial tires, which have rim-to-rim reinforcement. In tests the new radials not only stand up better to incisions but when severely damaged are designed to break apart into pieces too tiny to rupture a fuel tank, says Jean Couratier, research-and-development director for Michelin Aviation Products. The tires are constructed using a proprietary high-strength reinforcement material in the belts and sidewalls that limits the expansion of the tires’ diameter under pressure. “This reduces the degree to which the rubber tread is elongated, which in turn improves its resistance to cuts and tears,” Couratier explains. The NZG (which stands for “near zero growth”) technology also halves the number of plies in the tire, thereby cutting tire weight by 20 percent, he notes, an attribute that will help offset the additional weight of the other safety modifications.

Once the refitting is complete, the modified Concorde will undergo a series of proving flights. Then civil aviation authorities will have to recertify the craft for airworthiness. If everything goes smoothly, supersonic service may resume sometime this fall. The Concorde’s main clientele—international bankers and business executives, transatlantic jet-setters and celebrities—will be relieved.



CHANGES FOR THE BETTER

Safety modifications under way are:

- Lining fuel tanks with a Kevlar-rubber compound to limit leaks (photograph above)
- Encasing electrical wiring in the undercarriage in steel braiding
- Arranging shutdown of power to the cooling fans for the landing-gear brakes during takeoff
- Installing improved fire-detection and warning systems
- Adopting puncture-resistant, lighter-weight tires

Road Map for the Mind

OLD MATHEMATICAL THEOREMS UNFOLD THE HUMAN BRAIN BY DIANE MARTINDALE

All those folds and fissures make life difficult for a neuroscientist: they bury two thirds of the brain’s surface, or cortex, where most of the information processing takes place. With so much of the brain hidden, researchers have a hard time seeing exactly which parts of the cortex are doing what and how they are related to one another. “People want to see what’s in the folds,” says Monica K. Hurdal, a computer scientist at Florida State University, who has created a computer program to flat-map the brain. Conventional imaging techniques usually display cross sections of the brain, making it difficult to view the entire surface. For example,

an MRI scan might show areas that look to be adjacent but are, if they have a deep fold between them, actually far apart.

“Converting a sphere into a plane is not so difficult,” Hurdal explains, “but it does require that certain compromises be made.” The Mercator projection of the earth, for instance, preserves shapes and angles at the expense of areas, so that the polar regions look far too large in relation to the equatorial ones. The mathematical basis for the Mercator projection is an 1851 law of geometry known as the Riemann mapping theorem (although the 16th-century cartographer himself wasn’t aware of it, of course). It says that a three-di-

ALTERNATIVE PROJECTION

In contrast to Mercator projections, a flat-mapping technique called CARET (computerized anatomical reconstruction and editing toolkit) preserves the area and length of objects, instead of their angles.

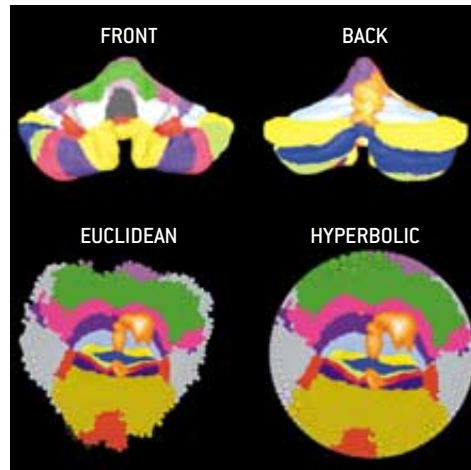
FLAT MAPS OF THE BRAIN

A Mercator-like flat map of the brain can be viewed in three ways:

- **Euclidean**, which is flat like a road map. Distance is measured or scaled as expected.
- **Hyperbolic**, which is disk-shaped and allows the map focus to be changed so that the chosen center is in sharp focus and the edges distorted, much like moving a magnifying glass over a piece of paper.
- **Spherical**, which wraps a flattened brain image around a sphere.

mensional curved surface can be flattened while preserving the angular information, thereby yielding a so-called conformal map.

To flatten the cortex, Hurdal takes anatomical information from a high-resolution, 3-D MRI scan and feeds it into her program. Within a few minutes, several algorithms convert the surface of the brain into a network of thousands or even millions of cortical points (the number depends on the size of the area to be flattened), each connected to



CEREBELLUM'S FRONT AND BACK can be combined into single flat maps (shown here in Euclidean and hyperbolic views) to reveal details that are normally hidden in the brain's folds.

its nearest neighbors by lines. The result is a triangulated mesh.

The key to flattening this landscape of convoluted triangles lies in a Greek theorem called circle packing. It says that three circles can always be drawn around the corners of a triangle so that each circle just touches the other two. Any two of these circles also belong to a neighboring triangle. Hence thousands of triangles in a flat plane can perfect-

ly pack that plane with thousands of circles.

Applying the theorem to the brain may sound easy enough, but there is one problem, Hurdal notes: the triangles that represent the surface of a brain are not lying flat, so the touching circles will stick out. To fix this, the program employs a contemporary version of circle packing. It extends the theorem to three dimensions, moving all the cortical points until they settle down with the circles into a well-packed plane. Because the resulting maps are not perfect conformal maps, Hurdal calls them quasi-conformal. She has already flat-mapped the cerebellum and various bits of the cortex. To match precise regions with brain activity, researchers can take images from subsequent scans, flatten them and overlay them on the initial MRI.

Surgeons may eventually rely on the maps in brain surgery, particularly in epilepsy operations in which cutting out chunks of the cortex is necessary to help stop seizures. Werner K. Doyle, a neurosurgeon who performs more than 200 such operations every year at New York University–Mount Sinai Comprehensive Epilepsy Center, says, “Which parts are removed is often an educated guess.”

The most commonly used method to locate malfunctioning regions is electroencephalography (EEG). It requires placing several electrodes directly on the surface of the brain and waiting for a seizure. Unfortunately, EEG readings don't always mark the right spot, and so too much cortex or the wrong region is sometimes removed. Flat maps turn the 3-D brain into a 2-D image, which, Doyle says, “will make it easier and safer for neurologists to navigate the mind.” Ideally, no one will get lost, because directions aren't included.

Diane Martindale is a science writer based in New York City.

COSMOLOGY

The Peak of Success

THE BIG BANG THEORY CLICKS TOGETHER BETTER THAN EVER BY GEORGE MUSSER

Whenever *Scientific American* runs an article on cosmology, we get letters complaining that cosmology isn't a science, just unconstrained speculation. But even if that used to be the case, it is certainly not true anymore. The past several months

alone have seen a remarkable outpouring of high-precision observations of the universe on its largest scales. Not only do they give the big bang theory a new quantitative rigor, they hint at secondary effects—perhaps the long-sought signatures of cosmic inflation and cold

dark matter. “Previously, cosmology had been independent strands of thought,” says cosmologist David Tytler of the University of California at San Diego. “It can now go on to address the next level of detail.”

Although the big bang theory has long been supported by three observational pillars—cosmic microwave background radiation, abundance of light elements, and outward velocity of distant galaxies—these pillars uphold different aspects of the theory. Only last year did observations of the first pillar reach the precision needed to cross-check the second one. Two balloon-borne telescopes, Boomerang and Maxima, measured the microwave background with a resolution of better than one degree, revealing small-scale fluctuations. Unlike the larger-scale fluctuations made famous by the COBE satellite a decade ago—which are scale-invariant, occurring with the same relative strength no matter their size—the small ones seem to be strongest on certain scales known as peaks.

The size and strength of these peaks allow cosmologists to get at the geometry of space and the density of matter. The thinking is that as the universe grew, density fluctuations that started off as scale-invariant developed into synchronized oscillations on ever increasing scales. The microwave background reveals how far this process had gotten when the cosmos was 400,000 years old. After that time, the oscillations started to subside as gravity pulled matter into bodies such as galaxies.

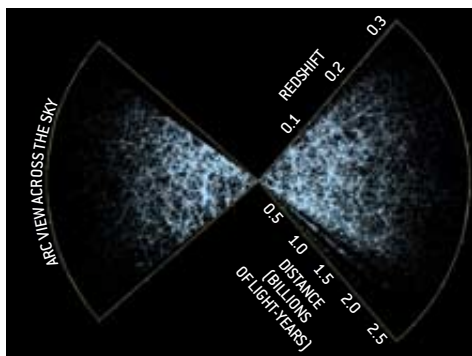
Boomerang’s and Maxima’s results were a case of good news and bad news. The instruments saw the largest of the expected peaks, demonstrating that the universe is geometrically flat, but they failed to see a second peak. That suggested the universe had much more ordinary matter than the element abundances could countenance.

To universal relief, the discrepancy has now disappeared. This past April a third telescope—the ground-based Degree Angular Scale Interferometer (DASI), run by John E. Carlstrom and his group at the University of Chicago—detected the second peak. Meanwhile the Boomerang team realized that it had overestimated the pointing accuracy of its instrument, which had the effect of smudging the fine details in the images. When the team undid this bias and incorporated new data, the second peak popped out. Maxima’s results for the second peak haven’t changed, but its error bars encompass the other experiments’ values anyway.

Boomerang’s revisions have left some cosmologists wondering what to believe, but observers respond that the agreement of independent techniques is grounds for confidence. In any case, certainty should soon arrive on the wings of NASA’s Microwave Anisotropy Probe and new ground-based instruments with still higher resolution.

Although some media accounts described the findings as “confirmation” of cosmic inflation and cold dark matter, that is not quite true. Geometric flatness and scale invariance were predicted long before inflation, based on very general principles. It is true that most alternatives to inflation are ruled out, having failed to foresee multiple peaks, but that is not the same as ruling inflation in. Similarly, it’s hard to be sure that dark matter is real stuff rather than a theoretical artifact.

Direct evidence may not be far off, though. Already there are hints of a slight “tilt”—a deviation from exact scale invariance, as inflationary models predict—in the microwave background and, according to



170,000 DOTS, each one a galaxy, spin a dense web through a slice of space. Such maps are now extensive enough to correlate cosmic structures with the primordial fluctuations that seeded them.

Rupert A. C. Croft of the Harvard-Smithsonian Center for Astrophysics, in the distribution of intergalactic gas clouds. As for dark matter, Arthur Kosowsky of Rutgers University says the relative strength of the peaks is the do-or-die test. Cold dark matter contributes to gravity but not to pressure, thereby accentuating the odd-numbered peaks (which represent the gravity-dominated part of the primordial oscillation cycle) at the expense of the even-numbered ones (the pressure-dominated part). If you squint at the current data, you might say that the third peak is indeed bigger. Fortunately, with observational precision improving at its present rate, squinting will soon be unnecessary.

THE BIG BANG'S FOUR PILLARS

Cosmic microwave background radiation Its spectrum indicates that hot plasma once filled the universe. Patchiness reveals that this primordial soup was slightly uneven.

Element abundances Historically the most precise of the pillars, it confirms that nuclear reactions took place in a hot, expanding universe.

Galaxy velocities The proportionality of distance and velocity shows that the cosmos is expanding. Slight deviations at large distances suggest that the expansion has accelerated. The most distant supernova ever seen, identified in April by the High-Z Supernova Search Team, strengthens the case.

Large-scale structure Studies of the arrangement and motion of galaxies and intergalactic clouds, such as the 2dF Galaxy Redshift Survey, have been erecting this new pillar. They typically look on scales of several hundred million light-years and smaller, neatly dovetailing with the work on the microwave background, which probes nascent structures 100 million light-years across and larger. Not only are both patterns broadly consistent, but traces of the microwave background fluctuations have appeared in the arrangement of galaxies.

The Post-Genome Project

WHETHER THE HUMAN PROTEOME WILL BE SUCCESSFULLY MAPPED IN THREE YEARS DEPENDS ON HOW YOU DEFINE "PROTEOME" BY KAREN HOPKIN

If the proof of the pudding is in the eating, then the proof that biology can be done on an industrial scale has been in the sequencing—the recent determination of the complete genome sequences of dozens of organisms, from viruses and bacteria to worms, flies, flowers and humans. Now biotech companies and their investors are betting that a similar souped-up, assembly-line approach can be applied to the new science of proteomics: an effort to catalogue which proteins our genes encode and to decipher how these proteins function to direct the behavior of a cell, an organ or a next-door neighbor.

The latest boast comes from researchers at Myriad Genetics in Salt Lake City, who in April announced that they plan to map the entire human proteome in less than three years. To do this, Myriad has spawned a subsidiary, called Myriad Proteomics, with Hitachi and Oracle, which will supply the hardware and the database software needed to handle the massive amount of information that will be generated by the project.

Their bold proclamation has raised a few eyebrows in the scientific community. "It's easy to say that you'll complete a comprehensive proteome map," notes Marc Vidal of the Dana-Farber Cancer Institute in Boston. "But none of us knows what that means." There may be only one genome, but when it comes to the proteome, different proteins can be more or less active in different cells at different times during development, under different physiological conditions or in different disease states. The proteome's nature "makes it hard to define what we're doing—not just Myriad, but all of us," remarks Joshua LaBaer, director of the Institute of Proteomics at Harvard Medical School. "There's no such thing as a human proteome," adds Keith L. Williams, CEO of Proteome Systems, headquartered in Sydney, Australia. Look at the liver, for example, he says: "After a glass of red wine, you'll have a different proteome."

"Proteomics" is a newly invented word, so it means different things to different people," notes Sudhir Sahasrabudhe, executive vice president of research at Myriad Genet-

ics. For its part, Myriad is narrowing its definition: it will zero in on "systematically uncovering all protein-protein interactions," Sahasrabudhe says. With a detailed inventory of which proteins touch one another inside cells, scientists can begin to place proteins within biochemical pathways and predict their intracellular operations.

To accomplish this feat, Myriad has been industrializing techniques that scientists have traditionally used to examine protein interactions one at a time. One such method is the yeast two-hybrid system. It uses a single bait protein to fish for binding partners in a sea of prey proteins produced artificially inside a yeast cell. The binding of bait to prey activates a reporter gene, allowing researchers to easily detect when an interaction occurs.

Myriad will adopt a "shotgun" approach, throwing together collections of bait and collections of prey to see what falls out. Repeat the analysis again and again, looking at tens of thousands of reactions a day, and the bulk of the interactions will reveal themselves, Sahasrabudhe says. If the human proteome contains 300,000 to 400,000 proteins, each of which interacts on average with an estimated five to 10 protein partners, it should take three years to generate a comprehensive map.

At that point, the problem becomes ascertaining which of these interactions are biologically meaningful. Two proteins may be physically able to interact but may never actually meet up in a cell. To filter out such false positives, Sahasrabudhe envisions follow-up studies to assess whether interactions in the primary map are physiologically relevant.

Time will tell how successful this large-scale approach will be. Even Myriad's official press announcement of its proteome plan includes a boilerplate disclaimer: "This news release includes forward-looking statements that are subject to risks and uncertainties, including statements regarding the ability of Myriad Proteomics to map the entire human proteome in less than three years." In any case, Williams says, "We wish them luck."

Karen Hopkin is a Boston-based writer who was relieved to learn that she isn't the only one who has trouble defining "proteome."



PROTEOME SAMPLER shows 1,458 yeast proteins (circles) and their 1,948 interactions (lines). Removing proteins has different effects on the yeast: lethal (red); nonlethal (green); slowed growth (orange); unknown (yellow). Hawoong Jeong and his colleagues at the University of Notre Dame generated this map.

A SEARCH FOR PROTEINS

Myriad Proteomics is not alone in its efforts to map proteins and their interactions. Large Scale Biology in Vacaville, Calif., announced in January that it has completed a proprietary, first version of the human proteome. CuraGen in New Haven, Conn., is mapping the yeast proteome using the same two-hybrid approach as Myriad. And academic labs are assembling similar protein interaction maps.

All are works in progress. Still, even incomplete data will be useful in helping biologists—but only if the information is publicly available. To start, Myriad plans to make its data commercially available only to collaborators and paying customers.

Computing with Light

CLASSICAL WAVES FOR PSEUDO QUANTUM COMPUTING BY GRAHAM P. COLLINS

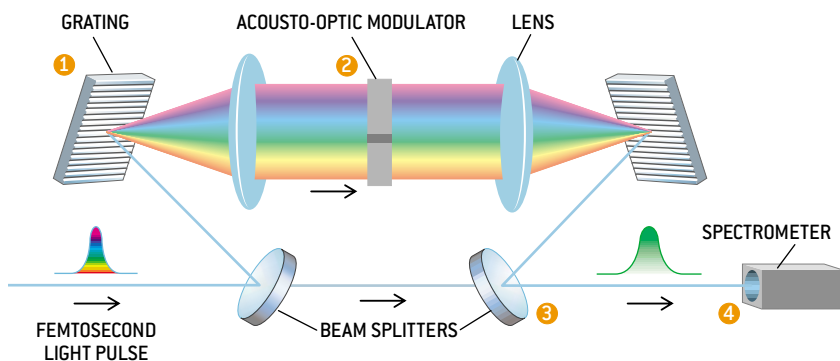
THE POWER OF THE QUANTUM

Three levels of computational ability are, from weakest to strongest:

- **Classical, bit-based computing of today's digital machines**
- **Classical light-wave computing, which uses limited aspects of quantum computing—namely, its wave nature**
- **Quantum computing, which uses entanglement of quantum states as well as their wave nature to speed processing exponentially for certain problems**

LIGHT WAVES AT WORK can search a database as efficiently as a quantum computer.

- 1 Diffraction grating spreads the pulse into its component spectrum, bands of which correspond to the 50 database elements.
- 2 The modulator shifts the phase of one band, that of the target database element.
- 3 Ordinary wave interference cancels the unshifted bands.
- 4 Spectrometer reads off the remaining light—the target element.



Large quantum computers could in principle handle some of the toughest computing problems, such as factoring numbers to break encrypted messages—answering those questions in seconds instead of the centuries that today’s computers would require. But quantum computers are extraordinarily difficult to build; they rely on exquisitely controlled interactions among fragile quantum states. Do they have to? Recently Ian A. Walmsley and his co-workers at the University of Rochester demonstrated that ordinary, classical light waves can perform as efficiently as one class of quantum computer.

The Rochester experiment searched a sorted 50-element database. An ordinary computer doing a binary search of such a database would need to query the database six times (enough to search 64 elements: $2^6 = 64$). In 1997 Lov K. Grover of Bell Laboratories proved that a quantum computer only has to query once, no matter how large the database.

Walmsley’s group used a light pulse in an interferometer, a device that gives light waves a choice of two paths to follow. Along one path, a diffraction grating splits the pulse apart into its broad range of frequencies, like white light through a prism. The 50 elements of the database correspond to 50 bands of that spectrum. The database itself is represented by an acousto-optic modulator through which the light passes. The modulator imprints a phase shift (that is, it moves the positions of the peaks and troughs of the light wave) on just one of the 50 bands. In essence, each band of the light “looks at” a different database entry (a different part of the modulator), and only one “finds” the target. When the pulse is recombined with light from the other arm of the in-

terferometer, the phase-shifted band alone shines brightly into a spectrometer, which reads off the result. Only the wave nature of light, not its quantum features, is used.

The experiment is similar to established methods of optical signal processing that, for example, pass beams through holograms. What’s new is that it directly exemplifies a general result that Walmsley and his colleagues demonstrated theoretically late last year. “For every machine that uses [only] quantum interference,” Walmsley explains, “there is an equivalent, equally efficient one that uses classical optical interference.” Reading out a result on a quantum computer necessarily involves detection of particles, and the extra device components and computational steps for that process eliminate the quantum computer’s advantage. According to Emanuel H. Knill of Los Alamos National Laboratory, that insight provides a new perspective “on the relationship between computing with waves and quantum computing.”

The most powerful quantum algorithms, such as fast factoring, however, require an additional quantum feature: so-called entanglement of the states of many particles. Classical waves cannot emulate those algorithms efficiently, but light turns out to be well suited to such true quantum computation in another way. In theory, a full-power quantum computer can be built by sending individual photons through simple linear optical elements, such as beam splitters and phase shifters. Such an approach was proposed in 1997, but those early designs needed exponentially more optical elements as the number of qubits increased—utterly impractical for any but the smallest devices.

In January, Knill, his colleague Raymond Laflamme and Gerard J. Milburn of the University of Queensland in Australia exhibited a design whose circuit complexity would increase in linear proportion, not exponentially. Unlike the Rochester experiment, this scheme relies on quantum effects of individual photons navigating paths through the device but avoids the need for nonlinear interactions between photons, something only readily achieved at very high intensities or with extraordinary equipment such as resonant cavities or light-slowing Bose-Einstein condensates.

An Environmental Solution

news

SCAN

IONIC LIQUIDS MAY REPLACE HAZARDOUS SOLVENTS BY REBECCA RENNER

Chemistry depends on solutions. Liquids are important because, once substances are dissolved, their molecules can readily come together to react. But many substances prove to be hard, if not impossible, to dissolve. Now a growing number of chemists believe they have discovered the correct solution—ionic liquids, peculiar combinations of salts that are liquid at room temperature. These new solvents can be tailor-made to dissolve a variety of substances, including coal, crude oil, inks, plastics, DNA and even some rocks.

Kenneth R. Seddon, chair of inorganic chemistry at Queen's University Belfast in Northern Ireland, estimates that there are, in theory, more than a trillion different ionic liquids, millions of which are extremely stable (they remain liquid over a range of about 300 degrees Celsius) and nonvolatile (they can be used over and over). They may replace toxic, flammable and polluting volatile organic solvents, such as toluene, hexane and dichloromethane, for which the worldwide annual market is about \$6 billion.

Chemists make ionic liquids by combining large organic positive ions—with unfriendly names such as 1-ethyl-3-methylimidazolium [emim]⁺—and smaller inorganic negative ions, like aluminum tetrachloride. This combination of large and small ions is very different from most ionic salts, such as table salt (NaCl).

Table salt is a solid at room temperature because positively charged sodium clings to negatively charged chlorine; thus stuck, the ions stack up to form a regular lattice. But in ionic liquids, the positive charge is less focused: because the positive ions are large, the total charge is smeared out across several atoms. In addition, the big, irregular shapes don't form crystal structures at room temperature. "It's like trying to stack bananas instead of oranges. Bananas just don't stack well," comments chemist James H. Davis, Jr., of the University of South Alabama. Unable to crystallize, the substance remains a liquid.

Serving as a new kind of solvent, however, may be just the start. "This feels like a revolution in the making," says Robert B. Morland, an organic chemist at BP Amoco Chemicals in Naperville, Ill. He predicts that ionic liquids will revolutionize the use of catalysts

in industrial chemistry. This is because, for a particular reaction, chemists can make an ionic liquid with the right positive and negative charge combination to dissolve the catalyst and the chemicals involved in a reaction; the liquid, however, does not affect the product of the reaction. The catalyst stays in the ionic liquid to be reused, and the product may even rise to the surface, where it can be skimmed off, he says. The French Petroleum Institute is getting ready to license for commercial use a dimer manufacturing process that exploits these very properties, according to Davis.

Despite chemists' enthusiasm, "for industry to adopt ionic liquids there will have to be a unique advantage. It's not enough to be a bit more green," cautions Robin D. Rogers, director of the Center for Green Manufacturing at the University of Alabama. Expense is a major hurdle: right now a pound of ionic liquid costs about \$4,000 to \$5,000. The amount could drop to about \$200 a pound, depending on composition and quantity, Morland says. But it is still pricey compared with organic solvents—per pound, acetone sells for about \$0.15 and toluene about \$0.10. Of course, because ionic liquids can be recycled, a few tons would replace many tons of organic solvent.

Toxicity and environmental tests also need to be conducted, Seddon says. Initial animal test results look good, but the generous bounty of possible ionic liquids creates a catch-22 situation, points out Albert Robertson, a senior chemist with specialty chemical maker Cytec Canada. Toxicity tests cost hundreds of thousands of dollars, so manufacturers are playing a waiting game, unwilling to start testing until they are certain they have the right ionic liquid. But proponents say the hurdles will just slow down the inevitable. Seddon and Rogers believe that major applications are some seven to 10 years away. A small-scale industrial application could emerge much sooner, in less than three years.

Rebecca Renner is a geologist turned science writer based in Williamsport, Pa.



IONIC CRYSTAL called 1-octadecyl-3-methylimidazolium tetrafluoroborate, as seen through polarizing filters. Textures result from the molecular formation of hydrocarbon- and ion-rich regions.

BREAKING SOLUTION RULES

Substances dissolve when their molecules are similar to the molecules of the solvent, a fact embodied in the chemist's rule of thumb that "like dissolves like." In other words, covalent molecules, which have no overall electric charge—substances that include fat, oil and many organic compounds—dissolve in covalent volatile organic solvents. But they don't dissolve in water, which is slightly charged. In contrast, ionic solids, which consist of positively and negatively charged ions, dissolve readily in water. Ionic liquids break the solution rules: they manage to dissolve organic covalent molecules. Chemists don't understand why.

Wireless Wonder

A DARK-HORSE STANDARD COULD WIN THE BROADBAND RACE BY WENDY M. GROSSMAN

LONDON—For the past couple of years, everyone has assumed that the next big technological thing would be wireless data services. WAP, the wireless application protocol put together by a huge group of companies, permits Web surfing over mobile phones. It's going to really come into its own, the firms insist, when third-generation, high-speed mobile telephony rolls out, perhaps as soon as year's end. Simultaneously, Bluetooth, a standard developed by a different huge set of companies, is expected to enable all kinds of personal networking—for instance, writing with a pen that can later transmit the data to your PC.

Yet neither WAP nor Bluetooth has taken over the world; in fact, there's a chance that neither will, considering the rise of a dark-horse challenger: the cryptically named 802.11b. The standard, developed by the Institute of Electrical and Electronic Engineers (IEEE), was embraced first by Apple Computer in 1999, in the form of its AirPort base station. The "b" indicates that this second version of 802.11, originally ratified in 1997, is faster than the first: 802.11b transmits data at up to 11 megabits per second. It is, in other words, wireless broadband, and it operates in a part of the spectrum (roughly, near microwaves) that, unlike third-generation, or 3G, mobile telephony, requires no license.

Many compatible products are available. Set up one of those flying-saucer-like AirPort devices and a card in your desktop or laptop, and you have a local-area network without all those wires. Stick the saucer in your window, and you can go work in a nearby café. This year's Computers, Freedom and Privacy conference placed an 802.11b access point in its Internet room. "What I love about it," says Dan O'Brien, editor of the U.K.'s satirical e-zine *Need to Know (Now)*, "is that it makes the Net into what it should be: something that's all around you all the time, and you can just tap into it."

Such enthusiasm is making 802.11b one of the fastest-growing wireless standards. Local scuttlebutt has it that the entire Massachusetts Institute of Technology campus will be outfitted with 802.11b within the next year. The

commercial service MobileStar is setting up wireless Internet access nodes in airports and hotel chains. For \$2.95 for the first 15 minutes and \$0.20 a minute thereafter, you can sit in the American Airlines terminal at JFK and browse the Net at broadband speeds on your laptop. Now. Today. No squinting at mobile-phone screens. The securities brokerage company Nomura stated in March that it views 802.11b as a serious threat to 3G mobile telephony's hopes to make serious money out of wireless data services.

The London-based hacker group *Consume.net* is trying to line up enough public-spirited folks to paint the town wireless. So far it's in just a few spots, but the dream is that if everyone sticks a base station in the window, anyone will be able to access the Net from anywhere in town. Moreover, 802.11b enables machines to communicate directly. "It puts control into the hands of the public," observes James Stevens, one of the group's leaders. "It's not just about wireless. It's the broader idea that you can share what you've got." If, he says, you're sending local e-mail, why not do it locally? On the Internet, e-mail for your next-door neighbor might go via Auckland and Singapore.

It's hard to tell how far 802.11b and its successors (with different letters and higher speeds, such as 802.11g) can go. Critics argue that such systems can't hand off connections the way mobile networks transfer calls. But that feature is pointless to many Web surfers: unlike talking, clicking on links and scrolling are hard to do while you're walking. Bluetooth may be a lot cheaper—manufacturers expect to embed the technology on a chip costing less than \$5—but at 722 kilobits per second, it moves data comparatively slowly.

What 802.11b has is momentum that these other standards can only dream of. Given a ubiquitous broadband wireless connection, anything, from voice calls to large chunks of data, can be transmitted. At the moment, 802.11b is still a geek thing, requiring fiddling, configuring and tolerance for imperfections. But in 1990, so was the Internet.

Wendy M. Grossman writes about information technology from London.



BORROWING BANDWIDTH

The 1980s witnessed the popularity of "war dialing"—the hacker term for the mass dialing of phone numbers in search of modems to co-opt. Now war dialing may have given way to "war driving." Security Labs director Mark Seiden's term for driving around scanning for open wireless networks. Some of the tales may be apocryphal, but it's possible: hackers have reported finding dozens of open 802.11b access points along several blocks near San Francisco's Moscone Center.

DATA POINTS:
YOUR TAXES AT WORK

In terms of science spending, President George W. Bush's fiscal year 2002 budget proposal rewards biomedicine; funds for other civilian R&D will fall. Despite an expected increase, NASA has no funds to develop a Pluto flyby because of projected cost overruns, including those anticipated for the International Space Station. Congress, however, will probably modify the budget before the fiscal year starts on October 1.



Proposed budget (billions) Change from FY2001

Defense	\$45.86	+8.5%
National Institutes of Health	\$23.1	+13.8%
NASA	\$9.97	+0.4%
Energy	\$7.44	-5.4%
National Science Foundation	\$3.23	-1.6%
Agriculture	\$1.83	-10.2%
Interior (includes U.S. Geological Survey)	\$0.59	-6.1%
Environmental Protection Agency	\$0.57	-6.5%

SOURCES: Office of Management and Budget; American Association for the Advancement of Science

NEUROLOGY

Wrist Watch

Common wisdom has it that the computer keyboard often leads to carpal tunnel syndrome. Mayo Clinic scientists, however, report that even seven hours daily on the computer does not increase the risk of developing the nerve disorder. The researchers used a handy study population—their own secretaries and other heavy computer users at the Mayo Clinic in Scottsdale, Ariz. Of the more than 250 employees surveyed about symptoms associated with carpal tunnel, such as tingling and numbness, only 10.5 percent met official clinical criteria for the syndrome, and nerve conduction tests confirmed the condition in only 3.5 percent. These numbers are consistent with previous data for the general population. The study, which appeared in the June 12 *Neurology*, suggests that symptoms assumed to indicate carpal tunnel syndrome may have numerous other explanations, such as pinched neck nerves.

—Steve Mirsky



NOT SO RISKY after all.

HEMATOLOGY

Sticky Situation

The great hope for curing sickle-cell disease—affecting one in about 650 African-Americans—remains gene therapy: it would correct the single mutation responsible for the misshapen red blood cells that adhere to blood vessels and impede proper blood flow. But research from the University of North Carolina at Chapel Hill has revealed another important aspect of the disease—a protein largely responsible for the cellular stickiness. The protein, called thrombospondin, binds to red blood cells and provokes them into releasing molecules that increase the cells' tendency to stick to blood vessel walls. The revelation, which appeared in the June 15 *Journal of Clinical Investigation*, brings up the possibility of treating sickle-cell disease by interfering with thrombospondin and its effects.

—Steve Mirsky

HEALTH

Fat Kills

Combating obesity in childhood could prevent up to four million cancer cases a year worldwide, said researchers at the 11th European Congress on Obesity, held in Vienna in May. About 30 to 40 percent of all cancer cases stem from excessive weight. Obesity, which

can also cause heart disease and diabetes, leads to 300,000 deaths annually in the U.S., second only to the 400,000 who die from tobacco use. It also accounts for 5.5 to 7 percent of U.S. health care costs, more than double that of other developed countries, such as Australia (2 percent), France (2 percent) and Canada (2.4 percent). One cause is the variety of foods available, which keeps the taste buds from getting tired of the same food and makes overeating more likely. In reviewing 39 dietary studies, scientists from the University of Buffalo found that people offered different choices in multicourse meals ate 44 percent more than those who ate the same food for each course. The review appears in the May *Psychological Bulletin*.

—Philip Yam



VARIETY may be the spice of life, but it's also fattening.

DENNIS GALANTE Stone (top); LAWRENCE MANNING Corbis (bottom); ILLUSTRATION BY WATT COLLINS

EVOLUTION

Faster Than a Snail's Pace

Animals are often driven from their native territories by habitat destruction or severe climate change. *Acanthinucella spirata*, a marine snail common along the California coast, was one of many species that survived the last ice age in the relatively warm, southernmost part of their ranges. The snail recolonized northern coastlines about 12,000 years ago as the ice released its grip on North America. But in a relatively short time, the snails' shells evolved into shapes that had never before existed, most likely in response to their new environments. The study's authors, writing in the June 1 *Science*, offer a caution to conservationists who relocate endangered species in efforts to save them: when you move a species around, you may quickly end up with a whole different beast.



QUICK, from evolution's point of view.

—Sarah Simpson

PHYSICS

Crystallizing Sound

Turning a liquid into a solid usually means tossing it into the freezer for a while. Researchers at the École Normale Supérieure in Paris, though, have effected that phase change with acoustic waves. They blasted liquid helium with a burst of one-megahertz ultrasound, producing intense pressure levels (about 200 decibels) in the liquid helium. Acoustic waves consist of alternating regions of high and low pressure—compression followed by rarefaction. The compression cycle started the crystallization, which spread through the helium at about 100 meters a second—nearly the speed of sound. During rarefaction, the solid melted even more quickly. The work, appearing in the June 11 *Physical Review Letters*, helps physicists understand the stability of supercooled or overpressurized liquids.



FROZEN HELIUM could be made with sound waves.

—Philip Yam

TOXICOLOGY

When Fish Is Not Brain Food

The Great Lakes harbor a variety of pollutants, including the particularly persistent polychlorinated biphenyls. Research has long associated exposure to PCBs with memory problems in infants and children, and a new study, headed by Susan Schantz of the University of Illinois, suggests that the compounds can also affect adults. In the June *Environmental Health Perspectives*, Schantz and her colleagues describe an experiment in which fish eaters older than 49 years and eating at least 24



pounds of fish from Lake Michigan every year were less able to recall a story after hearing it than people who ate less than six pounds of fish. The researchers also point out that workers at manufacturing plants (such as those making capacitors) may be exposed to 10 to 100 times as many PCBs as the fish eaters in this study and therefore may be at risk for PCB-related cognitive impairment.

—Alison McCook

MEMORY TROUBLES could develop from eating too much fish from Lake Michigan.

WWW.SCIAM.COM/NEWS
BRIEF BITS

- Near an ancient Egyptian coastline, paleontologists have unearthed the remains of the second-largest dinosaur yet discovered: *Paralititan stromeri*, or "tidal giant." /060101/1.html
- A review of past studies concludes that the placebo effect may be no effect at all: patients on placebos fared no better than those who had no treatment. /052501/1.html
- Even before they can speak, babies know where words begin and end—an ability that appears as young as eight and a half months. /060401/3.html
- Researchers have transferred the electron's spin between *n*- and *p*-type semiconductors, raising hopes that spintronics—electronics based on spin rather than charge—is possible. /061401/2.html

KAUSTUV ROY (top); SEBASTIEN BALIBAR ET AL. École Normale Supérieure (middle); ANDY SACKS Stone (bottom)

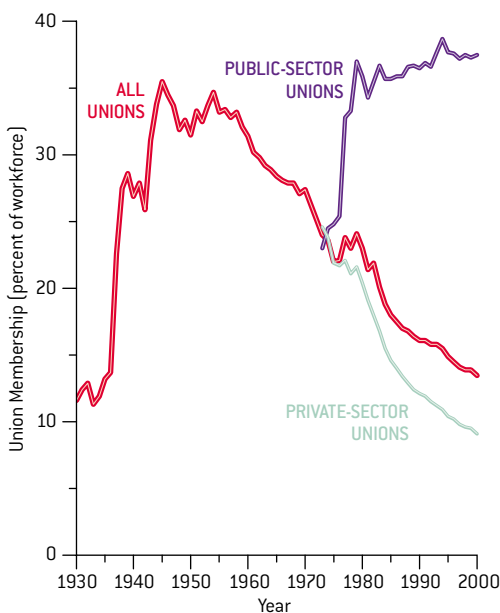
U.S. Workers and the Law

LABOR RIGHTS OF AMERICANS LAG BEHIND THOSE OF OTHER NATIONS BY RODGER DOYLE

LABORING WITH NO PROTECTION

Millions of U.S. workers are not covered by labor-rights legislation, such as the Labor-Management Relations Act of 1947. Among them:

- Managers and supervisors: **14 million**
(In some cases, employers may grant these titles simply to circumvent labor laws.)
- Independent contractors: **7 million**
(Many are not independent but are tied exclusively to a single employer.)
- Farmworkers: **3 million**
- Domestic workers: **1 million**
- Employees of religious institutions: **500,000**
- Native American casino employees: **100,000**



In the U.S., unions have the best songs, but for decades management has held the best cards. Even in the public sector, where unions have maintained their membership in recent times, they have relatively little power. Teachers, for example, are perhaps the best-organized government employees. Only 11 states grant them the right to strike; in 15 states they have no legal means to compel school boards to bargain. The other 24 states consider teacher strikes illegal but permit local governments to bargain with the boards.

In terms of labor rights, teachers fall midway between powerful industrial unions such as the United Auto Workers and certain groups not protected by federal labor regulations at all. Federal law, particularly the Labor-Management Relations Act of 1947 (also known as the Taft-Hartley Act), compels employers to bargain with unions in good faith and protects workers from arbitrary firing for union activity. The situation of unprotected groups—which include farm laborers, domestics, supervisors, managers and independent contractors—is documented in detail by Human Rights Watch in its recent report *Unfair Advantage*. These employees, who may number up to 20 million, have minimal protection when trying to form a union. Although they may have some legal safeguards

against arbitrary discharge under common law and antidiscrimination statutes, Human Rights Watch finds that an employer bent on discharging a worker for trying to form a union generally has the upper hand.

That also applies to jobs covered by labor laws. According to Human Rights Watch, the financial penalty for firing a worker for organizing is small and often is not paid until years of litigation go by. Another problem for workers, even those protected

by labor laws, is the employer's right under court decisions to replace them permanently if they strike for higher wages. Sympathy strikes are illegal. Employers have a virtually unlimited right to present their point of view in the workplace but can prevent union organizers from doing the same.

The U.S. has long been out of step with standards established by the International Labor Organization, an arm of the United Nations. The standards affirm workers' right to organize, to bargain collectively, to have a speedy resolution of grievances and, with certain limitations, to strike and conduct sympathy strikes. It disallows practices that would undermine the right to strike, such as the hiring of permanent replacement workers. Lance Compa, the author of *Unfair Advantage* and an expert on international labor law at Cornell University, notes that most other industrial countries follow the U.N. rules, which, among other things, allow teachers to strike.

Would granting American workers U.N. standard rights harm the U.S. economy? Compa thinks the economy would be enhanced, because workers would feel more respected and worry less about employer reprisal. Thomas I. Palley, an economist with the AFL-CIO, argues that the chief effect would be a lessening of income disparities in the U.S. and that there is no evidence it would diminish America's competitive edge abroad. Marvin H. Koster, an economist at the American Enterprise Institute, says any effect would be minor.

On the other hand, Randall Johnson, vice president for labor and employee benefits at the U.S. Chamber of Commerce, believes that the damage to the U.S. position would be substantial. Mark Wilson, an economist at the Heritage Foundation, says beefing up workers' rights would reduce the nation's competitive advantage with European trading partners and developing countries such as China and Mexico.

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SOURCES: U.S. Bureau of Labor Statistics (all unions); Bureau of National Affairs, Inc., of Washington, D.C. (private- and public-sector data). Data based on nonagricultural employment except those for all unions after 1973, which are based on total employment. Private- and public-sector data available only from 1973 onward. The graph lines are not strictly comparable but are believed to measure overall trends reliably.



The Company's Company

Venture capitalism becomes a new mission for the nation's spymasters By DANIEL G. DUPONT

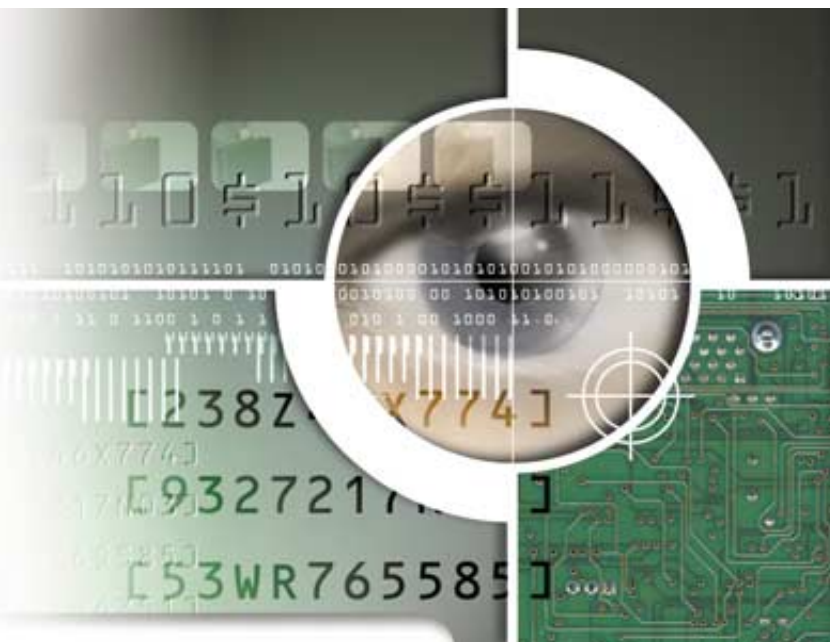
In 1998 Ruth A. David, then the Central Intelligence Agency's top science and technology official, came away impressed from a trip to the Massachusetts Institute of Technology's Media Lab. On the flight back to Washington, she remarked to her deputy, Joanne Isham, that the agency could benefit from a high-powered, in-house technology incubator.

The CIA was having a tough time tapping into the information technology revolution, yet it had a pressing need to implement more advanced software tools for tasks such as Internet security to prevent hacker incursions. The agency could no longer rely solely on its traditional contractor base and government labs for the cutting-edge information technologies that would allow it to keep spying on the world. It had unsuccessfully tried a number of internal efforts to take advantage of new technologies. But it often had trouble reaching out beyond the confines of the agency. Security concerns frequently hindered it from detailing its needs to outside suppliers.

George J. Tenet, the agency's director, convinced of the importance of adopting new information technology, gave the green light to David and other agency employees who wanted to try a wholly new approach. Using outside consultants and legal experts, the team began putting together an infrastructure for linking the CIA with the network of investment bankers, venture capitalists and information technology entrepreneurs who turn new ideas into useful products. After much refinement, the CIA created In-Q-Tel, a private not-for-profit venture-capital firm whose funding comes from taxpayer dollars.

The CIA has set up companies before, but they have been primarily undisclosed fronts for secret agency operations, such as Air America, the airline the CIA ran for many years in Southeast Asia. In-Q-Tel is different: the agency acknowledges and promotes its relationship with In-Q-Tel. Company officials like to call the publicly funded CIA creation a "venture catalyst" because it does more than seed start-ups and new technologies. It does, of course, shell out much needed funding. "No one comes to us *not* looking for our money," says Christopher Tucker, the company's chief strategist. But In-Q-Tel also acts as a buffer between the agency and the information technology community. It offers the expertise of a group of people who have spent a great deal of time thinking through the particular problems the agency confronts.

The CIA requires a series of target technologies: software for Internet security—threat detection and eradication of hackers who pry into its databases—as well as information management, network security access, and the searching and indexing of open-source documents, just to name a few. But the agency's insular culture keeps it from acknowledging that existing systems may be deficient. And security is always paramount. Just getting a list of technology-related needs on paper was difficult. Doing so, Tucker says, "was a real watershed event, and then having it articulated at



a level of abstraction that allowed for making it unclassified was another watershed event, because all of a sudden you can actually talk to industry.”

The CIA has In-Q-Tel working largely in the public realm, a strategy that has kept security issues to a minimum; very few of its 36 employees have security clearance. An in-house CIA office called the In-Q-Tel Interface Center provides guidance on agency needs and candidate technologies. “Without the interface center,” Tucker notes, “it’s hard to imagine that we’d be able to know anything about [the CIA’s] real needs unless we essentially turned ourselves into an element of the agency.”

To find new ideas and technologies that might be quickly developed and adapted for agency use, In-Q-Tel, with offices in the Washington, D.C., area and Silicon Valley, spends a lot of time doing “terrain mapping”—reviewing open-source information on the Internet or in trade literature. “It’s amazing what you can learn by just doing that,” Tucker says. “It’s also amazing what you don’t get.” In-Q-Tel fills the gap by tracking less visible technologies, doing for the CIA what the agency can’t do for itself. It monitors what it calls “deal flow.” “There’s an enormous undercurrent of companies that haven’t disclosed themselves to the marketplace either to maintain their trade secrets or to maintain their competitive edge until they get bigger,” Tucker explains. “There are huge amounts of ingenuity out there in that section of the economy.”

For this reason, In-Q-Tel keeps close tabs on a network of other venture capitalists and investment bankers. It supports an outreach program involving traditional investors as well as universities and commercial laboratories. When it comes across a technology that shows promise, it makes sure the company has solid credentials before agreeing to invest. Then, once it signs up a new company, it serves as a conduit between the agency and the technology developers, providing direction but, in many cases, shielding the agency’s plans. As a result, no one talks much about the applications themselves. Tucker says three In-Q-Tel projects have gone into the agency so far, meaning they have been implemented inside the wall of secrecy.

Projects in early stages of development are more aboveboard. A company called SafeWeb is adapting its product, PrivacyMatrix, a 128-bit Internet encryption system, for the agency’s use. SafeWeb entered into a licensing and venture arrangement with In-Q-Tel last year. In exchange for financing, SafeWeb gives the CIA warrants that it can convert to equity later. In the meantime, In-Q-Tel will evaluate PrivacyMatrix, pro-

vide the company with advice, and hope that the support will lead to a system that can benefit the CIA.

No one at SafeWeb has security clearance. In fact, says Stephen Hsu, the company’s co-founder and chief executive, the CIA would prefer that SafeWeb know “as little as possible” about how it uses PrivacyMatrix. So far, Tucker says, this kind of arrangement has not caused a problem. Although In-Q-Tel has provided funds to major government contractors, including SAIC, officials have focused from the beginning on technologies and ideas promoted by smaller companies that, like SafeWeb, usually would not do business with a government entity such as the CIA.

Most small entrepreneurial companies, which are not part of the traditional government contractor base, don’t want security clearance or the headaches associated with government accounting and acquisition regulations. With In-Q-Tel, they avoid the red tape that

In-Q-Tel helps entrepreneurial companies avoid the welter of red tape they would confront as government contractors.

they would otherwise face if they dealt directly with the agency. “We provide them an opportunity to come and play without having to be a government contractor,” Tucker notes.

While Congress keeps its eye on In-Q-Tel, receiving periodic progress reports, the few critics of the company are outnumbered by the many supporters that have emerged. Other government agencies are paying close attention, and some frequently ask for information and advice. NASA, Tucker says, “has been all over us,” probing how a similar arrangement might work for the space agency. The army has gone further than that: in January the service asked its Science Board, a group of outside experts, to look into prospects for a venture-capital firm of its own.

In-Q-Tel isn’t having any difficulty finding companies to work with either. According to Tucker, it has evaluated more than 750 companies, about 600 of which have contacted the agency through an Internet Web site. “You’ve got to out the cattle ranchers and the people trying to sell you nuclear bombs and things like that,” he adds. “But then, you get a nontrivial amount of stuff. Some of our more interesting things have just kind of wandered through the door.” ■

Daniel G. Dupont edits InsideDefense.com, an independent online news service.

Talking Gene Patents

JOHN J. DOLL, director of biotechnology for the U.S. Patent and Trademark Office, tells SCIENTIFIC AMERICAN about granting exclusive rights to make, sell and use a gene

The idea of patents on genes is still inherently counterintuitive to some people. Would you explain briefly why genes are patentable?

Genes are complex organic molecules, and when you isolate and purify them from the chromosomes where they reside, they are eligible to be patented as chemical compounds. And that is the extent of the patent protection that is given. We're not giving patents on whole chromosomes, and we certainly don't give patents on anything as it exists in nature.

How many genes have been patented in the U.S., and how many applications for patents are still outstanding?

The only number that I have is a guesstimate: since 1980 we have granted more than 20,000 patents on genes or other gene-related molecules [for humans and other organisms]. And we also know that

we have more than 25,000 applications outstanding that actually claim genes or related molecules.

Can you describe why you recently tightened the rules for gene patent applications?

The four main criteria for getting a patent are that the invention must have a utility; it must have an adequate written description; it must be nonobvious to one of ordinary skill in that particular field; and it must not have been done exactly before. The biggest hurdle that genomic inventions face is the utility standard.

In 1995 we issued guidelines, and we very clearly stated that if you had a secreted protein from a gene and you didn't know what role it played in disease or the diagnostics of disease, but the protein was secreted in a

diseased cell line [breast cancer cells, for instance], you could use that protein as an additive in a shampoo. You could have done that, and we would have allowed you to cross the utility hurdle for getting a patent. So that if anybody else wanted to make, use, sell or import into the United States this protein, your patent rights could be used to stop any of those actions.

That is the major change instituted by the new utility guidelines. We've gotten rid of proteins being used as shampoo additives or proteins being used as animal food or nutritional supplements. We've gotten rid of transgenic mice being used as snake food. And that is exactly what the utility bar has been raised to do—to exclude throwaway utilities and to make sure that when you have a genomic-type invention that you have a real-world and specific utility that is credible.

One of the major findings of the Human Genome Project was just how common it is for a gene to code for multiple proteins. What if someone applies for a patent for a gene that expresses a particular protein and someone else applies for a patent for the same gene coding for another protein? Does the owner of a gene patent have rights to all the proteins expressed by a gene?

When you have a patent on a particular gene, it's made up of a series of nucleotide sequences called exons that code for a particular protein. Let's say you have six blocks of exons that came together to express a particular protein. Under a different condition in that cell line, maybe all six of the exons don't function. So now there are maybe four blocks of exons that come together to express a totally different protein. That new set of exon blocks would be a separate patentable invention, and the people who had the patent to the first six would not gain exclusive rights to the protein expressed by the four new blocks of exons. ■

Please let us know about interesting or unusual patents. Send suggestions to: patents@sciam.com





Deconstructing the Dead

“Crossing over” to expose the tricks of popular spirit mediums By MICHAEL SHERMER

Like all other animals, we humans evolved to connect the dots between events so as to discern patterns meaningful for our survival. Like no other animals, we tell stories about the patterns we find. Sometimes the patterns are real; sometimes they are illusions.

A well-known illusion of a meaningful pattern is the alleged ability of mediums to talk to the dead. The hottest medium today is former ballroom-dance instructor John Edward, star of the cable television series *Crossing Over* and author of the *New York Times* best-selling book *One Last Time*. His show is so popular that he is about to be syndicated nationally on many broadcast stations.

The hottest medium today is a former ballroom-dance instructor.

How does Edward appear to talk to the dead? What he does seems indistinguishable from tricks practiced by magicians. He starts by selecting a section of the studio audience, saying something like “I’m getting a George over here. George could be someone who passed over, he could be someone here, he could be someone you know,” and so on. Of course, such generalizations lead to a “hit.” Once he has targeted his subject, the “reading” begins, seemingly using three techniques:

1. Cold reading, in which he reads someone without initially knowing anything about them. He throws out lots of questions and statements and sees what sticks. “I’m getting a ‘P’ name. Who is this, please?” “He’s showing me something red. What is this, please?” And so on. Most statements are wrong. If subjects have time, they visibly shake their heads “no.” But Edward is so fast they usually have time to acknowledge only the hits. And as behaviorist B. F. Skinner showed in his experiments on superstitious behavior, subjects need only occasional reinforcement or reward to be convinced. In an exposé I did for WABC-TV in New York City, I counted about one statement a second in the opening minute of Edward’s show, as he riffled through names, dates, colors, diseases, conditions, situations, relatives and the like. He goes from one to the next so quickly

you have to stop the tape and go back to catch them all.

2. Warm reading, which exploits nearly universal principles of psychology. Many grieving people wear a piece of jewelry that has a connection to a loved one. Mediums know this and will say something like “Do you have a ring or a piece of jewelry on you, please?” Edward is also facile at determining the cause of death by focusing on either the chest or the head area and then working rapid-fire through the half a dozen major causes of death. “He’s telling me there was a pain in the chest.” If he gets a positive nod, he continues. “Did he have cancer, please? Because I’m seeing a slow death here.” If the subject hesitates, Edward will immediately shift to heart attack.

3. Hot reading, in which the medium obtains information ahead of time. One man who got a reading on Edward’s show reports that “once in the studio, we had to wait around for almost two hours before the show began. Throughout that time everybody was talking about what dead relative of theirs might pop up. Remember that all this occurred under microphones and with cameras already set up.”

Whether or not Edward gathers information in this way, mediums generally needn’t. They are successful because they are dealing with the tragedy and finality of death. Sooner or later we all will confront this inevitability, and when we do, we may be at our most vulnerable.

This is why mediums are unethical and dangerous: they prey on the emotions of the grieving. As grief counselors know, death is best faced head-on as a part of life. Pretending that the dead are gathering in a television studio in New York to talk twaddle with a former ballroom-dance instructor is an insult to the intelligence and humanity of the living. ■

*Michael Shermer is the founding publisher of Skeptic magazine (www.skeptic.com) and the author of *How We Believe* and *The Borderlands of Science*.*

Dissident or Don Quixote?

Challenging the HIV theory got virologist Peter H. Duesberg all but excommunicated from the scientific orthodoxy. Now he claims that science has got cancer all wrong **By W. WAYT GIBBS**

SENAGO, ITALY—Three centuries ago cardinals seeking refuge from a plague in nearby Milan stayed here at the Villa San Carlo Borromeo, a grand estate surveying the village from its highest hill. The villa and its inhabitants have fallen on harder times since. The cracked plaster and faded paint on its high walls are covered with modern art of dubious quality. Now it is the private museum of Armando Verdiglione, a once promi-

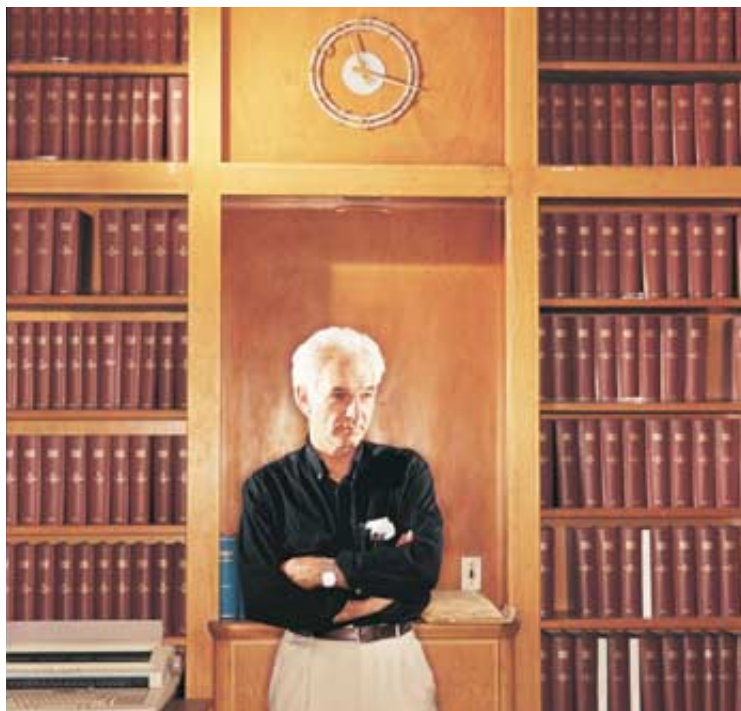
nent psychoanalyst whose reputation was stained when he was convicted in 1986 of swindling wealthy patients. Today the villa is hosting refugees of a different sort: scientific dissidents flown in by Verdiglione from around the world to address an eclectic conference of 100-odd listeners.

At the other end of the dais from Verdiglione is Sam Mhlongo, a former guerrilla fighter and prison-mate of Nelson Mandela and now head of the department of family medicine and primary health care at the Medical University of Southern Africa near Pretoria. Mhlongo has urged President Thabo Mbeki to question the near universal belief that AIDS is epidemic in South Africa and that HIV is its cause.

Between them sits Peter H. Duesberg, an American virologist who has also challenged that belief. Duesberg is now tilting at a different windmill, however. In a reedy voice clipped by a German accent, he explains why he believes the scientific establishment has spent two decades perfecting an utterly incorrect theory of how cancer arises.

It is an odd speaking engagement for a scientist who isolated the first cancer-causing gene from a virus at age 33, earned tenure at the University of California at Berkeley at 36 and was invited into the exclusive National Academy of Sciences at 49. Today many of his colleagues from those early efforts to map the genetic structure of retroviruses occupy the top of the field. Robert A. Weinberg has a huge lab at the Whitehead Institute for Biology in Cambridge, Mass., with 20 research assistants, a multimillion-dollar budget and a National Medal of Science to hang in his office. David Baltimore got a Nobel Prize and now presides over the California Institute of Technology.

“I could have played the game and basked in the glory” of early success, Duesberg says, and he is probably right. But instead he broke ranks and bruised egos. And so, 10 days before attending this eccentric symposium, Duesberg had to dash off a desperate letter to



PETER H. DUESBERG: SHUNNED SCIENTIST

- His theory that HIV does not cause AIDS, outlined at duesberg.com, is rebutted at www.niaid.nih.gov/spotlight/hiv00/
- Twice married, he has one five-year-old son and three grown daughters. When not in the lab, he likes to roller-skate.
- “Surely 5 percent of the funds for science could be set aside for work on fringe theories that could be revolutionary.”

Abraham Katz, one of the handful of rich philanthropists who have been his sole source of funding since he was cut off from all the normal channels five years ago.

"We're down to our last \$45,000," the 64-year-old Duesberg confides glumly as we stand in the dark courtyard of the villa. Katz, whose wife suffers from leukemia, is his final hope; if this grant doesn't come through, Duesberg will have to cut loose his two assistants, close his lab at Berkeley and move to Germany. That is where he was born to two doctors, where he worked through a Ph.D. in chemistry and where he says he still has an open invitation to teach at the University of Heidelberg.

Leaving the U.S., if it comes to that, would thus close the loop on a roller coaster of a career. Although his ascendance is clear enough, it is hard to say exactly when his fall from grace began. Several weeks later as we talk in his small lab—one fifth the size of the facilities he once had—he hands me a paper he published in 1983. "This is the one that started it all," he says.

The paper is not, as I expect, his now infamous 1988 article in *Science* provocatively entitled "HIV Is Not the Cause of AIDS." Nor is it any of the several dozen articles and letters he published in peer-reviewed journals over the next 10 years arguing that the link between HIV and AIDS is a mirage, an artifact of sloppy epidemiology that has lumped together different diseases with disparate causes just because the sufferers have all been exposed to what he calls "a harmless passenger virus."

Although these dissenting theories of AIDS did not originate with Duesberg, he soon became their champion—and thus the target of derision for those who feared that disagreement among scientists could confuse the public and endanger its health. When Mbeki, after consulting with Duesberg and other AIDS experts, told the International AIDS Conference last year that he felt "we could not blame everything on a single virus," more than 5,000 scientists and physicians felt it necessary to sign the Durban Declaration, devoutly affirming their belief that HIV is the one true cause of AIDS.

Duesberg's arguments ultimately converted no more than a tiny minority of scientists to his view that "the various AIDS diseases are brought on by the long-term consumption of recreational drugs and anti-HIV drugs, such as the DNA chain terminator AZT, which is prescribed to prevent or treat AIDS." Or, as he puts it more bluntly in Milan, in rich countries it is the toxicity of the very drugs that are prescribed to save HIV-infected people that kills them.

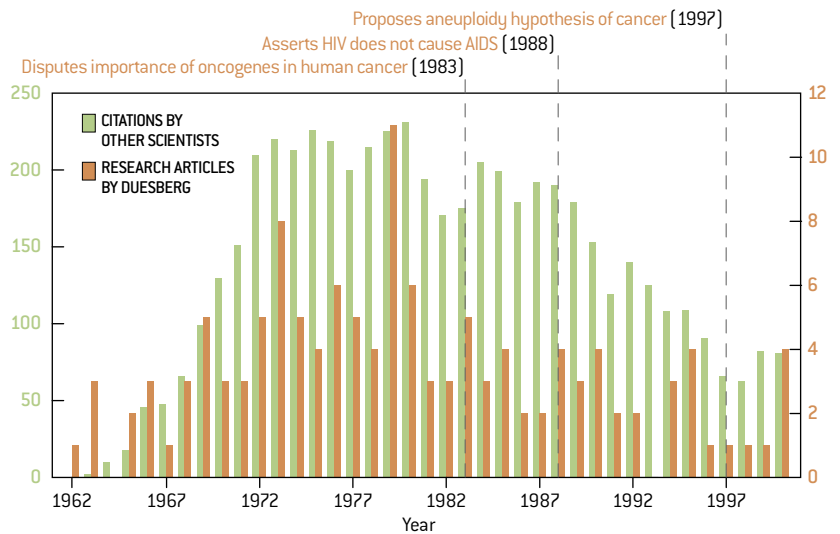
The hypothesis has never been tested directly, although Duesberg claims it could be done ethically by comparing 3,000 HIV-positive army recruits with 3,000 HIV-negative recruits matched for disease and drug use. And so his idea has died as most failed

theories do, never fully disproved but convincingly rebutted—in this case by a 40-page treatise from the National Institute for Allergic and Immune Disease—and ultimately ignored by nearly everyone working in the field.

But Duesberg didn't even know AIDS existed in 1983, when he wrote the paper that he says first marked him as a troublemaker. The title seems innocuous: "Retroviral Transforming Genes in Normal Cells?" But in Duesberg papers the question mark often signals that he is about to yank on the loose threads of a popular theory. This time the theory concerned cancer.

He and others had shown that when certain retroviruses insinuate their genes into the cells of mice, the cells turn malignant. Weinberg, Baltimore and others in the field speculated that perhaps similar genes, which they called "proto-oncogenes," lie dormant in the human genome, like time bombs that turn on only if a random mutation flips some sort of genetic switch. This hypothesis spawned a cottage industry to search for oncogenes, so-called tumor suppressor genes and, most recently, cancer "predisposition" genes.

As two decades passed, human genes with sequences similar to the viral oncogenes were found, and support for this story of cancer's origin solidified. "If you were to poll researchers,



ROLLER-COASTER CAREER of Peter H. Duesberg is traced by the rate at which he has published research articles and the rate at which other scientists have cited his work.

I'd guess 95 percent would say that the accumulation of mutations [to key genes] causes cancer," says Cristoph Lengauer, an oncologist at Johns Hopkins University.

But the story also grew steadily more complicated—and, to Duesberg, less convincing. Scientists expected to find some combination of oncogenes and tumor suppressor genes that are always mutated, at least in certain forms of cancer. They did not. Instead the number of putative cancer genes has leaped into the dozens, experiments have shown that different cells in the same

malignancy often contain different mutations, and no clear pattern perfectly matches the supposed cause to actual human disease. Cells taken from patients' tumors typically translate their mutant genes into a mere trickle of protein, in contrast to the flood of mutated protein churning in cells transformed by a virus.

Beginning with his 1983 paper, Duesberg has also picked at theoretical weak spots in the orthodox view. Some tumors are caused by asbestos and other carcinogens that are chemically incapable of mutating specific genes, he points out. Mice genetically engineered to lack tumor suppressor genes and to overexpress oncogenes should all develop cancer in infancy—but they don't. Given the measured rate of spontaneous mutations and the number of cells in the human body, the average person should harbor 100,000 cancer cells if even one dominant oncogene existed in the genome, Duesberg calculated in a paper last year. But if simultaneous mutations to three genes were required,



ANEUPLOIDY, seen in the aberrant chromosomes of this breast tumor cell analyzed by Robert A. Weinberg's group at the Whitehead Institute, is so common in cancer that it must be a cause, Duesberg argues. A normal female cell has two copies of each chromosome (except Y), for a total of 23 pairs. The cancerous cell contained three or more copies, as well as chromosomes with transposed pieces (such as 1, 6 and 22) or missing segments (1, 3 and 13).

then only one in 100 billion people would ever acquire cancer.

In 1997 Duesberg published what he thought was a better hypothesis. There is one characteristic common to almost every malignant tumor ever studied: nearly all the cancerous cells in it have abnormal chromosomes. In advanced cancers the cells often have two or three times the normal complement of 46 chromosomes. In new tumors the gross number may be normal, but closer examination usually reveals that parts of the chromosomes are duplicated and misplaced.

German biologist Theodor Boveri noted this so-called aneuploidy of tumor cells almost a century ago and suggested that it could be the cause of cancer. But that idea lost traction when no one could find a particular pattern of aneuploidy that correlated with malignancy, except in chronic myelogenous leukemia, which is not a true cancer because it doesn't spread from the blood to other parts of the body.

Recently, however, Duesberg and a few other scientists analyzed aneuploidy more closely and argued that it can explain

many of the mysteries of cancer better than the current dogma can. Their alternative story begins when a carcinogen interferes with a dividing cell, causing it to produce daughter cells with unbalanced chromosomes. These aneuploid cells usually die of their deformities. If the damage is minor, however, they may survive yet become genetically unstable, so that the chromosomes are altered further in the next cell division. The cells in tumors thus show a variety of mutations to the genes and the chromosomes.

Because each chromosome hosts thousands of genes, aneuploidy creates massive genetic chaos inside the cell. "The cell becomes essentially a whole new species unto itself," Duesberg says. Any new "species" of cell is extremely unlikely to do better in the body than a native human cell—and that may explain why tumors take so long to develop even after intense exposure to a carcinogen, he argues. The aneuploid cells must go through many divisions, evolving at each one, before they hit on a combination that can grow more or less uncontrollably anywhere in the body.

So far Duesberg has only a scattering of experimental evidence to support his hypothesis. In 1998 he showed that there is a roughly 50-50 chance that a highly aneuploid human cancer cell will gain or lose a chromosome each time it divides. Last December he reported that aneuploid hamster cells quickly developed resistance to multiple drugs—a hallmark of cancer—whereas normal cells from the same culture did not.

But it isn't easy to do experiments when every one of his last 22 grant proposals to nonprivate funding agencies was rejected, he says. Although Duesberg maintained a facade of defiance in Milan, he acknowledged in a moment of fatigue that "it is depressing that even private foundations are unwilling to fund research that has high risk but high potential payoff."

His mood had lifted somewhat by May, when I visited his lab. A letter from Abraham Katz tacked to the door stated that his request was approved: he would be getting \$100,000, enough to keep the lab running for another nine months.

It seems unlikely that nine months will be enough to persuade other researchers to take his aneuploidy hypothesis seriously. But it is possible. Numerous papers in major journals this year have pointed out the importance of "chromosome instability," a synonymous phrase, in cancer formation. Lengauer and Bert Vogelstein, also at Johns Hopkins, have been particularly active in promoting the idea that aneuploidy—which Lengauer insists must be a consequence of gene mutations—may be a necessary step for any tumor to progress.

Is Duesberg now willing to lay down his lance and play within the rules of polite scientific society? He recognizes that his combative stance in the HIV debate came across as arrogant. "With AIDS, I was asking for it a bit," he concedes. "At the time, I thought I was invulnerable." The experience may have tempered his ego, although he still mentions the Nobel Prize four times in a three-hour interview. Duesberg himself is pessimistic that he will ever be welcomed back into the club. "When you are out of the orthodoxy," he says softly, "they don't recall you." ■



Go Forth and Replicate

Birds do it, bees do it,
but could machines do it?
New computer simulations
suggest that the answer is yes

Apples beget apples, but can machines beget machines? Today it takes an elaborate manufacturing apparatus to build even a simple machine. Could we endow an artificial device with the ability to multiply on its own? Self-replication has long been considered one of the fundamental properties separating the living from the nonliving. Historically our limited understanding of how biological reproduction works has given it an aura of mystery and made it seem unlikely that it would ever be done by a man-made object. It is reported that when René Descartes averred to Queen Christina of Sweden that animals were just another form of mechanical automata, Her Majesty pointed to a clock and said, “See to it that it produces offspring.”

The problem of machine self-replication moved from philosophy into the realm of science and engineering in the late 1940s with the work of eminent mathematician and physicist John von Neumann. Some researchers have actually constructed physical replicators. Forty years ago, for example, geneticist Lionel Penrose and his son, Roger (the famous physicist), built small assemblies of plywood that exhibited a simple form of self-replication [see “Self-Reproducing Machines,” by Lionel

Penrose; *SCIENTIFIC AMERICAN*, June 1959]. But self-replication has proved to be so difficult that most researchers study it with the conceptual tool that von Neumann developed: two-dimensional cellular automata.

Implemented on a computer, cellular automata can simulate a huge variety of self-replicators in what amount to austere universes with different laws of physics from our own. Such models free researchers from having to worry about logistical issues such as energy and physical construction so that they can focus on the fundamental questions of information flow. How is a living being able to replicate unaided, whereas mechanical objects must be constructed by humans? How does replication at the level of an organism emerge from the numerous interactions in tissues, cells and molecules? How did Darwinian evolution give rise to self-replicating organisms?

The emerging answers have inspired the development of self-repairing silicon chips [see *box on page 40*] and autocatalyzing molecules [see “Synthetic Self-Replicating Molecules,” by Julius Rebek, Jr.; *SCIENTIFIC AMERICAN*, July 1994]. And this may be just the beginning. Researchers in the field of nanotechnology have long proposed that self-replication will be crucial to manu-

By Moshe Sipper and James A. Reggia

Photoillustrations by David Emmite

facturing molecular-scale machines, and proponents of space exploration see a macroscopic version of the process as a way to colonize planets using in situ materials. Recent advances have given credence to these futuristic-sounding ideas. As with other scientific disciplines, including genetics, nuclear energy and chemistry, those of us who study self-replication face the twofold challenge of creating replicating machines and avoiding dystopian pre-

scription could be used in two distinct ways: first, as the instructions whose interpretation leads to the construction of an identical copy of the device; next, as data to be copied, uninterpreted, and attached to the newly created child so that it too possesses the ability to self-replicate. With this two-step process, the self-description need not contain a description of itself. In the architectural analogy, the blueprint would include a plan for building a pho-

the cellular-automata world. All decisions and actions take place locally; cells do not know directly what is happening outside their immediate neighborhood.

The apparent simplicity of cellular automata is deceptive; it does not imply ease of design or poverty of behavior. The most famous automata, John Horton Conway's Game of Life, produces amazingly intricate patterns. Many questions about the dynamic behavior of cellular

Her Majesty pointed to a clock and said, "See to it that it produces offspring."

dictions of devices running amok. The knowledge we gain will help us separate good technologies from destructive ones.

Playing Life

SCIENCE-FICTION STORIES often depict cybernetic self-replication as a natural development of current technology, but they gloss over the profound problem it poses: how to avoid an infinite regress. A system might try to build a clone using a blueprint—that is, a self-description. Yet the self-description is part of the machine, is it not? If so, what describes the description? And what describes the description of the description? Self-replication in this case would be like asking an architect to make a perfect blueprint of his or her own studio. The blueprint would have to contain a miniature version of the blueprint, which would contain a miniature version of the blueprint and so on. Without this information, a construction crew would be unable to re-create the studio fully; there would be a blank space where the blueprint had been.

Von Neumann's great insight was an explanation of how to break out of the infinite regress. He realized that the self-de-

scription machine. Once the new studio and the photocopier were built, the construction crew would simply run off a copy of the blueprint and put it into the new studio.

Living cells use their self-description, which biologists call the genotype, in exactly these two ways: transcription (DNA is copied mostly uninterpreted to form mRNA) and translation (mRNA is interpreted to build proteins). Von Neumann made this transcription-translation distinction several years before molecular biologists did, and his work has been crucial in understanding self-replication in nature.

To prove these ideas, von Neumann and mathematician Stanislaw M. Ulam came up with the idea of cellular automata. A cellular-automata simulation involves a chessboardlike grid of squares, or cells, each of which is either empty or occupied by one of several possible components. At discrete intervals of time, each cell looks at itself and its neighbors and decides whether to metamorphose into a different component. In making this decision, the cell follows relatively simple rules, which are the same for all cells. These rules constitute the basic physics of

automata are formally unsolvable. To see how a pattern will unfold, you need to simulate it fully [see *Mathematical Games*, by Martin Gardner; *SCIENTIFIC AMERICAN*, October 1970 and February 1971; and "The Ultimate in Anty-Particles," by Ian Stewart, July 1994]. In its own way, a cellular-automata model can be just as complex as the real world.

Copy Machines

WITHIN CELLULAR AUTOMATA, self-replication occurs when a group of components—a "machine"—goes through a sequence of steps to construct a nearby duplicate of itself. Von Neumann's machine was based on a universal constructor, a machine that, given the appropriate instructions, could create any pattern. The constructor consisted of numerous types of components spread over tens of thousands of cells and required a book-length manuscript to be specified. It has still not been simulated in its entirety, let alone actually built, on account of its complexity. A constructor would be even more complicated in the Game of Life because the functions performed by single cells in von Neumann's model—such as transmission of signals and generation of new components—have to be performed by composite structures in Life.

Going to the other extreme, it is easy to find trivial examples of self-replication. For example, suppose a cellular automata has only one type of component, labeled +, and that each cell follows only a single rule: if exactly one of the four neighboring

MOSHE SIPPER and JAMES A. REGGIA share a long-standing interest in how complex systems can self-organize. Sipper is a senior lecturer in the department of computer science at Ben-Gurion University in Israel and a visiting researcher at the Logic Systems Laboratory of the Swiss Federal Institute of Technology in Lausanne. He is interested mainly in bio-inspired computational paradigms such as evolutionary computation, self-replicating systems and cellular computing. Reggia is a professor of computer science and neurology, working in the Institute for Advanced Computer Studies at the University of Maryland. In addition to studying self-replication, he conducts research on computational models of the brain and its disorders, such as stroke.

cells contains a +, then the cell becomes a +; otherwise it becomes vacant. With this rule, a single + grows into four more +'s, each of which grows likewise, and so forth.

Such weedlike proliferation does not shed much light on the principles of replication, because there is no significant machine. Of course, that invites the question of how you would tell a “significant” machine from a trivially prolific automata. No one has yet devised a satisfactory answer. What is clear, however, is that the replicating structure must in some sense be complex. For example, it must consist of multiple, diverse components whose interactions collectively bring about replication—the proverbial “whole must be greater than the sum of the parts.” The existence of multiple distinct components permits a self-description to be stored within the replicating structure.

In the years since von Neumann’s seminal work, many researchers have probed the domain between the complex and the trivial, developing replicators that require fewer components, less space or simpler rules. A major step forward was taken in 1984 when Christopher G. Langton, then at the University of Michigan, observed that looplike storage devices—which had formed modules of earlier self-replicating machines—could be programmed to replicate on their own. These devices typically consist of two pieces: the loop itself, which is a string of components that circulate around a rectangle, and a construction arm, which protrudes from a corner of the rectangle into the surrounding space. The circulating components constitute a recipe for the loop—for example, “go three squares ahead, then turn left.” When this recipe reaches the construction arm, the automata rules make a copy of it. One copy continues around the loop; the other goes down the arm, where it is interpreted as instructions.

By giving up the requirement of universal construction, which was central to von Neumann’s approach, Langton showed that a replicator could be constructed from just seven unique components occupying only 86 cells. Even smaller and simpler self-replicating loops have been devised by one of us (Reggia) and our colleagues [see box on next page]. Be-

cause they have multiple interacting components and include a self-description, they are not trivial. Intriguingly, asymmetry plays an unexpected role: the rules governing replication are often simpler when the components are not rotational-ly symmetric than when they are.

Emergent Replication

ALL THESE SELF-REPLICATING structures have been designed through ingenuity and much trial and error. This process is arduous and often frustrating; a small change to one of the rules results in an entirely different global behavior, most likely the disintegration of the structure in question. But recent work has gone beyond the direct-design approach. Instead of tailoring the rules to suit a par-

ticular type of structure, researchers have experimented with various sets of rules, filled the cellular-automata grid with a “primordial soup” of randomly selected components and checked whether self-replicators emerged spontaneously.

In 1997 Hui-Hsien Chou, now at Iowa State University, and Reggia noticed that as long as the initial density of the free-floating components was above a certain threshold, small self-replicating loops reliably appeared. Loops that collided underwent annihilation, so there was an ongoing process of death as well as birth. Over time, loops proliferated, grew in size and evolved through mutations triggered by debris from past collisions. Although the automata rules were deterministic, these mutations were effectively random,



because the system was complex and the components started in random locations.

Such loops are intended as abstract machines and not as simulacra of anything biological, but it is interesting to compare them with biomolecular structures. A loop loosely resembles circular DNA in bacteria, and the construction arm acts as the enzyme that catalyzes DNA replication. More important, replicating loops illustrate how complex global behaviors can arise from simple local in-

teractions. For example, components move around a loop even though the rules say nothing about movement; what is actually happening is that individual cells are coming alive, dying or metamorphosing in such a way that a pattern is eliminated from one position and reconstructed elsewhere—a process that we perceive as motion. In short, cellular automata act locally but appear to think globally. Much the same is true of molecular biology.

In a recent computational experiment,

Jason Lohn, now at the NASA Ames Research Center, and Reggia experimented not with different structures but with different sets of rules. Starting with an arbitrary block of four components, they found they could determine a set of rules that made the block self-replicate. They discovered these rules via a genetic algorithm, an automated process that simulates Darwinian evolution.

The most challenging aspect of this work was the definition of the so-called

BUILD YOUR OWN REPLICATOR

SIMULATING A SMALL self-replicating loop using an ordinary chess set is a good way to get an intuitive sense of how these systems work. This particular cellular-automata model has four different types of components: pawns, knights, bishops and rooks. The machine initially comprises four pawns, a knight and a bishop. It has two parts: the loop itself, which consists of a two-by-two square, and a construction arm, which sticks out to the right.

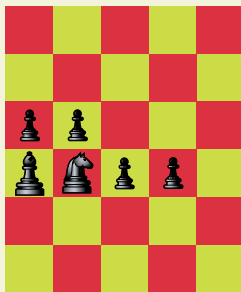
The knight and bishop represent the self-description: the knight, whose orientation is significant, determines which direction to grow, while the bishop tags along and determines how long the side of the loop should be. The pawns are fillers that define the rest of the shape of the loop, and the rook is a transient signal to guide the growth of a new construction arm.

As time progresses, the knight and bishop circulate counterclockwise around the loop. Whenever they encounter the arm, one copy goes out the arm while the original continues around the loop.

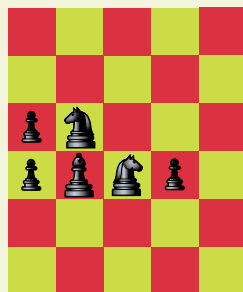
HOW TO PLAY: You will need two chessboards: one to represent the current configuration, the other to show the next configuration. For each round, look at each square of the current configuration, consult the rules and place the appropriate piece in the corresponding square on the other board. Each piece metamorphoses depending on its identity and that of the four squares immediately to the left, to the right, above and below. When you have reviewed each square and set up the next configuration, the round is over. Clear the first board and repeat. Because the rules are complicated, it takes a bit of patience at first. You can also view the simulation at www.epfl.ch/chess

The direction in which a knight faces is significant. In the drawings here, we use standard chess conventions to indicate the orientation of the knight: the horse's muzzle points forward. If no rule explicitly applies, the contents of the square stay the same. Squares on the edge should be treated as if they have adjacent empty squares off the board. —M.S. and J.A.R.

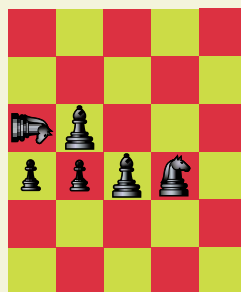
STAGES OF REPLICATION



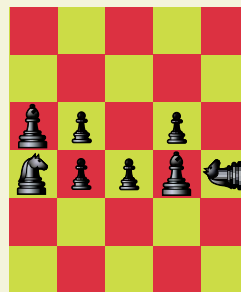
INITIALLY, the self-description, or "genome"—a knight followed by a bishop—is poised at the start of the construction arm.



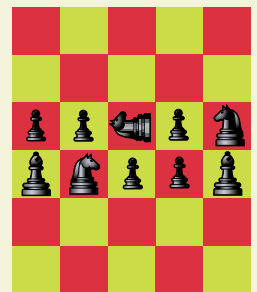
1 The knight and bishop move counterclockwise around the loop. A clone of the knight heads out the arm.



2 The original knight-bishop pair continues to circulate. The bishop is cloned and follows the new knight out the arm.



3 The knight triggers the formation of two corners of the child loop. The bishop tags along, completing the gene transfer.



4 The knight forges the remaining corner of the child loop. The loops are connected by the construction arm and a knight-errant.

fitness function—the criteria by which sets of rules were judged, thus separating good solutions from bad ones and driving the evolutionary process toward rule sets that facilitated replication. You cannot simply assign high fitness to those sets of rules that cause a structure to replicate, because none of the initial rule sets is likely to allow for replication. The solution was to devise a fitness function composed of a weighted sum of three measures: a growth measure (the extent to which

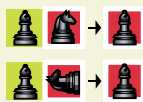
each component type generates an increasing supply of that component), a relative position measure (the extent to which neighboring components stay together) and a replicant measure (a function of the number of actual replicators present). With the right fitness function, evolution can turn rule sets that are sterile into ones that are fecund; the process usually takes 150 or so generations.

Self-replicating structures discovered in this fashion work in a fundamentally

different way than self-replicating loops do. For example, they move and deposit copies along the way—unlike replicating loops, which are essentially static. And although these newly discovered replicators consist of multiple, locally interacting components, they do not have an identifiable self-description—there is no obvious genome. The ability to replicate without a self-description may be relevant to questions about how the earliest biological

Continued on page 43

KNIGHT



IF THERE is a bishop just behind or to the left of the knight, replace the knight with another bishop.



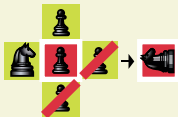
OTHERWISE, if at least one of the neighboring squares is occupied, remove the knight and leave the square empty.

PAWN

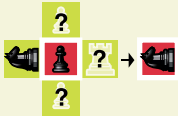
IF THERE is a neighboring knight, replace the pawn with a knight with a certain orientation, as follows:



IF A NEIGHBORING knight is facing away from the pawn, the new knight faces the opposite way.



OTHERWISE, if there is exactly one neighboring pawn, the new knight faces that pawn.



OTHERWISE the new knight faces in the same direction as the neighboring knight.

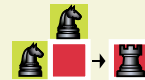
BISHOP OR ROOK



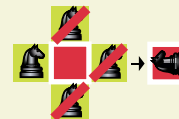
REPLACE IT with a pawn.



EMPTY SQUARE



IF THERE are two neighboring knights and either faces the empty square, fill the square with a rook.



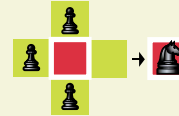
IF THERE is only one neighboring knight and it faces the square, fill the square with a knight rotated 90 degrees counterclockwise.



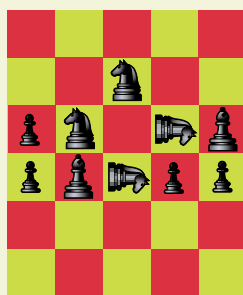
IF THERE is a neighboring knight and its left side faces the square, and the other neighbors are empty, fill the square with a pawn.



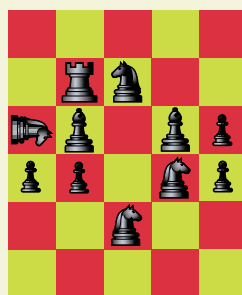
IF THERE is a neighboring rook, and the other neighbors are empty, fill the square with a pawn.



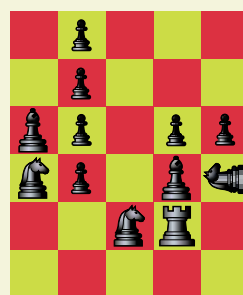
IF THERE are three neighboring pawns, fill the square with a knight facing the fourth, empty neighbor.



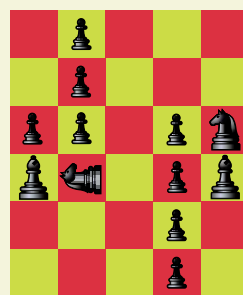
5 The knight-errant moves up to endow the parent with a new arm. A similar process, one step delayed, begins for the child loop.



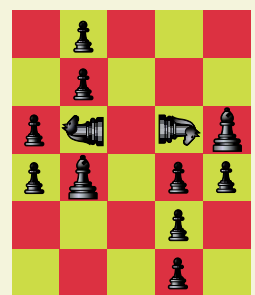
6 The knight-errant, together with the original knight-bishop pair, conjures up a rook. Meanwhile the old arm is erased.



7 The rook kills the knight and generates the new, upward arm. Another rook prepares to do the same for the child.



8 At least the two loops are separate and whole. The self-descriptions continue to circulate, but otherwise all is calm.



9 The parent prepares to give birth again. In the following step, the child too will begin to replicate.

ROBOT, HEAL THYSELF

Computers that fix themselves are the first application of artificial self-replication

LAUSANNE, SWITZERLAND—Not many researchers encourage the wanton destruction of equipment in their labs. Daniel Mange, however, likes it when visitors walk up to one of his inventions and press the button marked KILL. The lights on the panel go out; a small box full of circuitry is toast. Early in May his team unveiled its latest contraption at a science festival here—a wall-size digital clock whose components you can zap at will—and told the public: Give it your best shot. See if you can crash the system.

The goal of Mange and his team is to instill electronic circuits with the ability to take a lickin' and keep on tickin'—just like living things. Flesh-and-blood creatures might not be so good at calculating π to the millionth digit, but they can get through the day without someone pressing Ctrl-Alt-Del. Combining the precision of digital hardware with the resilience of biological wetware is a leading challenge for modern electronics.

Electronics engineers have been working on fault-tolerant circuits ever since there were electronics engineers [see "Redundancy in Computers," by William H. Pierce; *SCIENTIFIC AMERICAN*, February 1964]. Computer modems would still be dribbling data at 1200 baud if it weren't for error detection and correction. In many applications, simple quality-control checks, such as extra data bits, suffice. More complex systems provide entire backup computers. The space shuttle, for example, has five processors. Four of them perform the same calculations; the fifth checks whether they agree and pulls the plug on any dissenter.

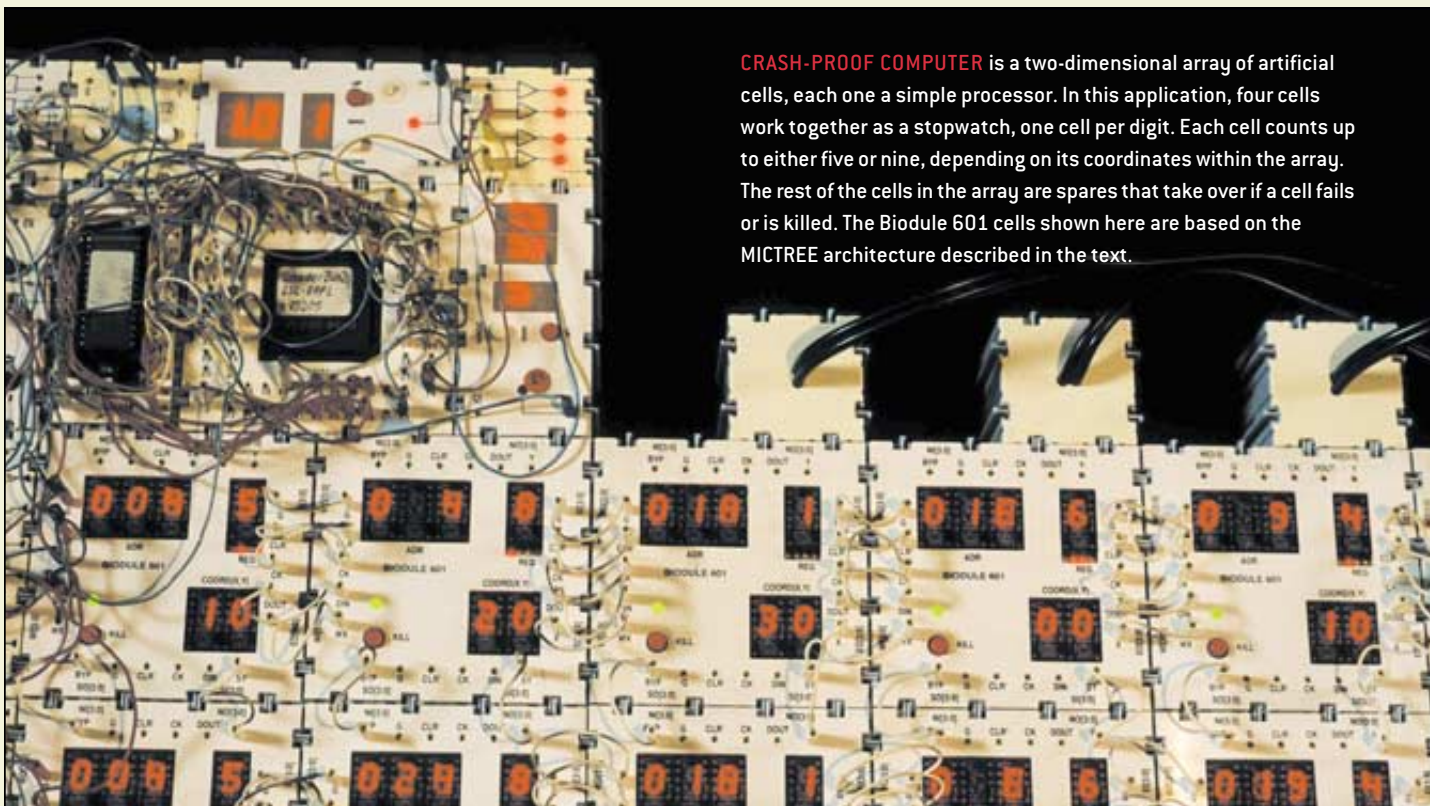
The problem with these systems, though, is that they rely on centralized control. What if that control unit goes bad?

Nature has solved that problem through radical decentralization. Cells in the body are all basically identical; each takes on a specialized task, performs it autonomously and, in the event of infection or failure, commits hara-kiri so that its tasks can be taken up by new cells. These are the attributes that Mange, a professor at the Swiss Federal Institute of Technology here, and others have sought since 1993 to emulate in circuitry, as part of the "Embryonics" (embryonic electronics) project.

One of their earlier inventions, the MICTREE (microinstruction tree) artificial cell, consisted of a simple processor and four bits of data storage. The cell is contained in a plastic box roughly the size of a pack of Post-its. Electrical contacts run along the sides so that cells can be snapped together like Legos. As in cellular automata, the models used to study the theory of self-replication, the MICTREE cells are connected only to their immediate neighbors. The communication burden on each cell is thus independent of the total number of cells. The system, in other words, is easily scalable—unlike many parallel-computing architectures.

Cells follow the instructions in their "genome," a program written in a subset of the Pascal computer language. Like their biological antecedents, the cells all contain the exact same genome and execute part of it based on their position within the array, which each cell calculates relative to its neighbors. Waste-

CRASH-PROOF COMPUTER is a two-dimensional array of artificial cells, each one a simple processor. In this application, four cells work together as a stopwatch, one cell per digit. Each cell counts up to either five or nine, depending on its coordinates within the array. The rest of the cells in the array are spares that take over if a cell fails or is killed. The Biodule 601 cells shown here are based on the MICTREE architecture described in the text.



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ful though it may seem, this redundancy allows the array to withstand the loss of any cell. Whenever someone presses the KILL button on a cell, that cell shuts down, and its left and right neighbors become directly connected. The right neighbor recalculates its position and starts executing the deceased's program. Its tasks, in turn, are taken up by the next cell to the right, and so on, until a cell designated as a spare is pressed into service.

Writing programs for any parallel processor is tricky, but the MICTREE array requires an especially unconventional approach. Instead of giving explicit instructions, the programmer must devise simple rules out of which the desired function will emerge. Being Swiss, Mange demonstrates by building a superreliable stopwatch. Displaying minutes and seconds requires four cells in a row, one for each digit. The genome allows for two cell types: a counter from zero to nine and a counter from zero to five. An oscillator feeds one pulse per second into the rightmost cell. After 10 pulses, this cell cycles back to zero and sends a pulse to the cell on its left, and so on down the line. The watch takes up part of an array of 12 cells; when you kill one, the clock transplants itself one cell over and carries on. Obviously, though, there is a limit to its resilience: the whole thing will fail after, at most, eight kills.

The prototype MICTREE cells are hardwired, so their processing power cannot be tailored to a specific application. In a finished product, cells would instead be implemented on a field-programmable gate array, a grid of electronic components that can be reconfigured on the fly [see "Configurable Computing," by John Villasenor and William H. Mangione-Smith; SCIENTIFIC AMERICAN, June 1997]. Mange's team is now custom-designing a gate array,

known as MUXTREE (multiplexer tree), that is optimized for artificial cells. In the biological metaphor, the components of this array are the "molecules" that constitute a cell. Each consists of a logic gate, a data bit and a string of configuration bits that determines the function of this gate.

Building a cell out of such molecules offers not only flexibility but also extra endurance. Each molecule contains two copies of the gate and three of the storage bit. If the two gates ever give different results, the molecule kills itself for the greater good of the cell. As a last gasp, the molecule sends its data bit (preserved by the triplicate storage) and configuration to its right neighbor, which does the same, and the process continues until the rightmost molecule transfers its data to a spare. This second level of fault tolerance prevents a single error from wiping out an entire cell.

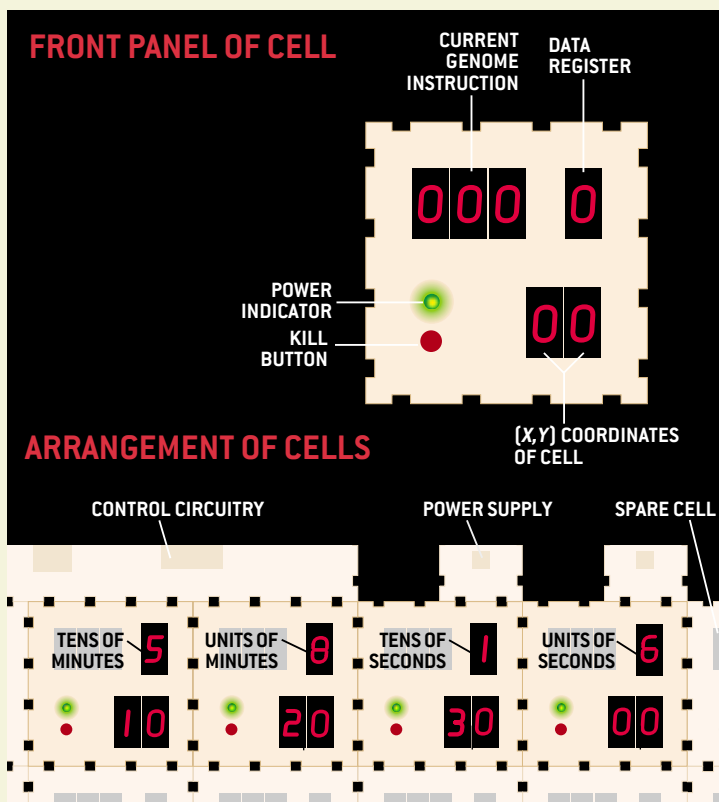
A total of 2,000 molecules, divided into four 20-by-25 cells, make up the BioWall—the giant digital clock that Mange's team has just put on display. Each molecule is enclosed in a small box and includes a KILL button and an LED display. Some molecules are configured to perform computations; others serve as pixels in the clock display. Making liberal use of the KILL buttons, I did my utmost to crash the system, something I'm usually quite good at. But the plucky clock just wouldn't submit. The clock display did start to look funny—numerals bent over as their pixels shifted to the right—but at least it was still legible, unlike most faulty electronic signs.

That said, the system did suffer from display glitches, which Mange attributed mainly to timing problems. Although the processing power is decentralized, the cells still rely on a central oscillator to coordinate their communications; sometimes they fall out of sync. Another Embryonics team, led by Andy Tyrrell of the University of York in England, has been studying making the cells asynchronous, like their biological counterparts. Cells would generate handshaking signals to orchestrate data transfers. The present system is also unable to catch certain types of error, including damaged configuration strings. Tyrrell's team has proposed adding watchdog molecules—an immune system—that would monitor the configurations (and one another) for defects.

Although these systems demand an awful lot of overhead, so do other fault-tolerance technologies. "While Embryonics appears to be heavy on redundancy, it actually is not that bad when compared to other systems," Tyrrell argues. Moreover, MUXTREE should be easier to scale down to the nano level; the "molecules" are simple enough to really be molecules. Says Mange, "We are preparing for the situation where electronics will be at the same scale as biology."

On a philosophical level, Embryonics comes very close to the dream of building a self-replicating machine. It may not be quite as dramatic as a robot that can go down to Radio Shack, pull parts off the racks, and take them home to resolder a connection or build a loving mate. But the effect is much the same. Letting machines determine their own destiny—whether reconfiguring themselves on a silicon chip or reprogramming themselves using a neural network or genetic algorithm—sounds scary, but perhaps we should be gratified that machines are becoming more like us: imperfect, fallible but stubbornly resourceful.

—George Musser, *imperfect but resourceful* staff editor and writer





Continued from page 39

replicators originated. In a sense, researchers are seeing a continuum between nonliving and living structures.

Many researchers have tried other computational models besides the traditional cellular automata. In asynchronous cellular automata, cells are not updated in concert; in nonuniform cellular automata, the rules can vary from cell to cell. Another approach altogether is Core War [see *Computer Recreations*, by A. K. Dewdney; *SCIENTIFIC AMERICAN*, May 1984] and its successors, such as ecologist Thomas S. Ray's *Tierra* system. In these

simulations the "organisms" are computer programs that vie for processor time and memory. Ray has observed the emergence of "parasites" that co-opt the self-replication code of other organisms.

ments, one for the program and the other for data. The loops can execute an arbitrary program in addition to self-replicating. In a sense, they are as complex as the computer that simulates them. Their main limitation is that the program is copied unchanged from parent to child, so that all loops carry out the same set of instructions.

In 1998 Chou and Reggia swept away this limitation. They showed how self-replicating loops carrying distinct information, rather than a cloned program, can be used to solve a problem known as satisfiability. The loops can be used to determine whether the variables in a logical ex-

pression can be assigned values such that the entire expression evaluates to "true." This problem is NP-complete—in other words, it belongs to the family of nasty puzzles, including the famous traveling-salesman problem, for which there is no known efficient solution. In Chou and Reggia's cellular-automata universe, each replicator received a different partial solution. During replication, the solutions mutated, and replicators with promising solutions were allowed to proliferate while those with failed solutions died out.

Although various teams have created cellular automata in electronic hardware, such systems are probably too wasteful for practical applications; automata were never really intended to be implemented directly. Their purpose is to illuminate the underlying principles of replication and, by doing so, inspire more concrete efforts. The loops provide a new paradigm for designing a parallel computer from either transistors or chemicals [see "Computing with DNA," by Leonard M. Adleman; *SCIENTIFIC AMERICAN*, August 1998].

In 1980 a NASA team led by Robert Freitas, Jr., proposed planting a factory on the moon that would replicate itself, using local lunar materials, to populate a large area exponentially. Indeed, a similar probe could colonize the entire galaxy, as physicist Frank J. Tipler of Tulane University has argued. In the nearer term, computer scientists and engineers have experimented with the automated design of robots [see "Dawn of a New Species?" by George

In a sense, researchers are seeing a continuum between nonliving and living structures.

simulations the "organisms" are computer programs that vie for processor time and memory. Ray has observed the emergence of "parasites" that co-opt the self-replication code of other organisms.

Getting Real

SO WHAT GOOD are these machines? Von Neumann's universal constructor can compute in addition to replicating, but it is an impractical beast. A major advance has been the development of simple yet useful replicators. In 1995 Gianluca Tempesti of the Swiss Federal Institute of Technology in Lausanne simplified the loop self-description so it could be interlaced with a small program—in this case, one that would spell the acronym of his lab, "LSL." His insight was to create automata rules that allow loops to replicate in two stages. First the loop, like Langton's loop, makes a copy of itself. Once finished, the daughter loop sends a signal back to its parent, at which point the parent sends the instructions for writing out the letters.

Drawing letters was just a demonstration. The following year Jean-Yves Perrier, Jacques Zahnd and one of us (Sipper) designed a self-replicating loop with universal computational capabilities—that is, with the computational power of a universal Turing machine, a highly simplified but fully capable computer. This loop has two "tapes," or long strings of compo-

pression can be assigned values such that the entire expression evaluates to "true." This problem is NP-complete—in other words, it belongs to the family of nasty puzzles, including the famous traveling-salesman problem, for which there is no known efficient solution. In Chou and Reggia's cellular-automata universe, each replicator received a different partial solution. During replication, the solutions mutated, and replicators with promising solutions were allowed to proliferate while those with failed solutions died out.

Although various teams have created cellular automata in electronic hardware, such systems are probably too wasteful for practical applications; automata were never really intended to be implemented directly. Their purpose is to illuminate the underlying principles of replication and, by doing so, inspire more concrete efforts. The loops provide a new paradigm for de-

Musser; *SCIENTIFIC AMERICAN*, November 2000]. Although these systems are not truly self-replicating—the offspring are much simpler than the parent—they are a first step toward fulfilling the queen of Sweden's request.

Should physical self-replicating machines become practical, they and related technologies will raise difficult issues, including the *Terminator* film scenario in which artificial creatures outcompete natural ones. We prefer the more optimistic, and more probable, scenario that replicators will be harnessed to the benefit of humanity [see "Will Robots Inherit the Earth?" by Marvin Minsky; *SCIENTIFIC AMERICAN*, October 1994]. The key will be taking the advice of 14th-century English philosopher William of Ockham: *entia non sunt multiplicanda praeter necessitatem*—entities are not to be multiplied beyond necessity. SA

MORE TO EXPLORE

Simple Systems That Exhibit Self-Directed Replication. J. Reggia, S. Armentrout, H. Chou and Y. Peng in *Science*, Vol. 259, No. 5099, pages 1282–1287; February 26, 1993.

Emergence of Self-Replicating Structures in a Cellular Automata Space. H. Chou and J. Reggia in *Physica D*, Vol. 110, Nos. 3–4, pages 252–272; December 15, 1997.

Special Issue: Von Neumann's Legacy: On Self-Replication. Edited by M. Sipper, G. Tempesti, D. Mange and E. Sanchez in *Artificial Life*, Vol. 4, No. 3; Summer 1998.

Towards Robust Integrated Circuits: The Embryonics Approach. D. Mange, M. Sipper, A. Stauffer and G. Tempesti in *Proceedings of the IEEE*, Vol. 88, No. 4, pages 516–541; April 2000.

Moshe Sipper's Web page on artificial self-replication is at islwww.epfl.ch/~moshes/selfrep/

Animations of self-replicating loops can be found at necsi.org/postdocs/sayama/sdsr/java/

For John von Neumann's universal constructor, see alife.santafe.edu/alife/topics/jvn/jvn.html

Ice in its earthly guise is hostile to living things. But an exotic form of space ice can actually promote the creation of organic molecules—and may have seeded life on Earth



THE ICE OF LIFE

by David F. Blake and Peter Jenniskens

AS VOYAGER 1 RACED OUT OF THE SOLAR SYSTEM

11 years ago, NASA engineers turned the spacecraft's camera arm around to take a parting snapshot of Earth. The planet appeared as a single pale-blue pixel, its color arising from the scattering of sunlight in its vast oceans. Earth is a water planet. And no matter how far researchers travel around the globe, no matter how high or deep they send their probes, if they find liquid water, they find some form of life that manages to survive.

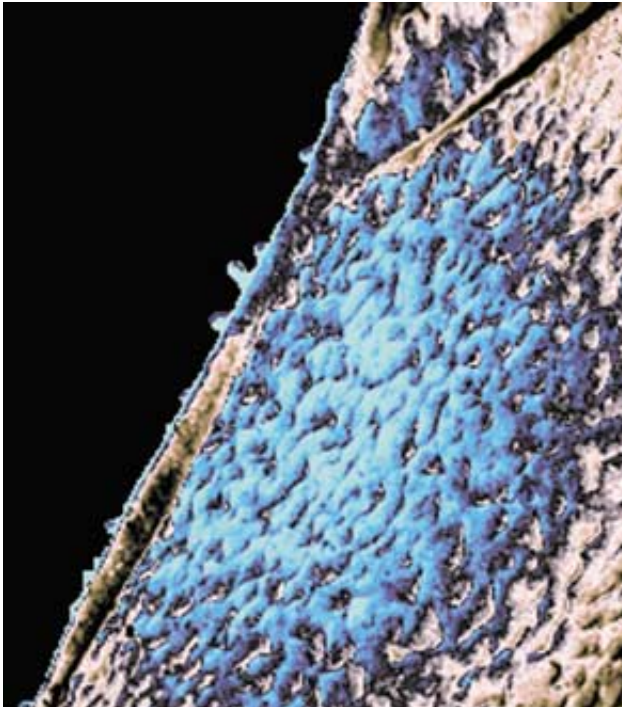
And yet there is a cruel dichotomy about water's nature. Liquid water cradles life, but water in its solid crystalline form destroys it. Organisms can roost in geysers, wallow in brine and gulp down acid, but they recoil from ice. The rigid ordering of water molecules in ice crystals expels impurities and tears organic tissue beyond repair. Such is the nature of ice on Earth. Yet recent discoveries about an unusual kind of frozen water that is absent from Earth but ubiquitous in interstellar space have inspired scientists to revise their assumptions about ice. In its interstellar form, water ice (as distinct from icy forms of carbon dioxide or other compounds) can harbor the kind of simple organic compounds from which life arose—and may even encourage their formation. As a result, this interstellar ice may actually have played an intrinsic role in the origins of life.

Uncovering the source of the organic materials that may have been the precursors to life has long been one of the most passion-inspiring quests in origins-of-life research. For more than a decade, scientists have known that organic compounds thrive in interstellar clouds and comets. They have also concluded that a frost rich in water ice exists everywhere in space where dust and gas become cold enough to condense into solids—primarily in cold molecular clouds [see “Life's Far-Flung Raw Materials,” by Max P. Bernstein, Scott A. Sandford and Louis J. Allamandola; *SCIENTIFIC AMERICAN*, July 1999].

Many planetary scientists have gone further, arguing that the ice-bound organics could have hitched a ride to Earth. When a cold molecular cloud collapsed to form our solar system 4.5 billion years ago, as the theory goes, some of the cloud's ice would have coalesced into comets. These balls of ice and rock could then have carried the organic compounds on a collision course with the young Earth. After reaching this planet, the organics could have participated in the chemical reactions from which the first living organisms arose.

This scenario has offered a compelling explanation for how organic compounds could have been delivered to Earth, but until recently no one

DARK CLOUDS of gas and dust in nebulae such as NGC 1999 (located in the constellation Orion) are the largest reservoirs of ice in space.



DAVID F. BLAKE AND PETER JENNISKENS; COURTESY OF SCIENCE, VOL. 265, 1994, ©AAS

MICROSCOPIC LAYER of amorphous and cubic ice (blue) formed when researchers warmed an icy film a few hundred molecules thick to 183 kelvins inside a cryogenic microscope.

knew how they first formed in interstellar space. Now scrutiny of water's behavior at temperatures near absolute zero (where all molecular motion ceases) has revealed that subtle changes in the structure of the ice sparked the first association of carbon, nitrogen and other biologically crucial elements.

Spaced Out

AS OUR RESEARCH TEAM at the NASA Ames Research Center probed the mysterious and surprising properties of interstellar ice, one of the first things we confirmed is that it has no crystalline structure. In other words, it is amorphous. It has no appreciable molecular or atomic order and no crystal surfaces, and it would be as transparent as window glass to an interstellar traveler.

Most solids exist naturally in crystalline form, with their molecules arrayed in a well-ordered structure. When some liquids are cooled rapidly, however, the transition to the crystalline state is suppressed and the liquid solidifies in an amor-

phous state. This process is best known from the manufacturing of glass, which is an amorphous form of silica. Although rapid cooling works for making amorphous silica, it does not work for liquid water. Water droplets tend to crystallize even when cooled rapidly. As a result, amorphous ice was discovered only when, in 1935, scientists investigated the behavior of water vapor deposited slowly in a vacuum.

This discovery was of special interest to astronomers, because they knew that water behaves differently in the vacuum of space than it does on Earth. Most people know that a water molecule consists of one oxygen atom chemically bonded to two atoms of hydrogen. But what makes water such a mutable substance is that the oxygen atom has two negatively charged, paired electrons that can form weak bonds with the positively charged hydrogen atoms of a nearby water molecule. At temperatures below freezing, the water molecules move into their most stable configurations, thus strengthening the so-called hydrogen bonds, and the resulting ice becomes neatly organized over many hundreds of molecules.

The particular stacking pattern that develops as water freezes depends on pressure. The pattern forms one of 12 known phases of crystalline water ice, but only one—hexagonal ice—occurs naturally on Earth. The oxygen atoms form a sixfold pattern, which we see in the shape of snowflakes. At temperatures well below freezing, the oxygen atoms can stack in a cubic pattern or, as in the case of amorphous ice, can even be prevented from forming any noticeable order at all.

Much of the bonding network that is characteristic of crystalline ice also binds molecules of liquid water. The essential difference—and the one that is critical for life—is that the hydrogen bonds in liquid water redistribute rapidly and constantly. Liquid water is thus capable of adjusting its structure to accommodate the physical and chemical requirements of living things. Just as an air bubble can rise through water but not through solid ice, organic molecules must be able to travel between water molecules if they are going to recombine into more complex compounds.

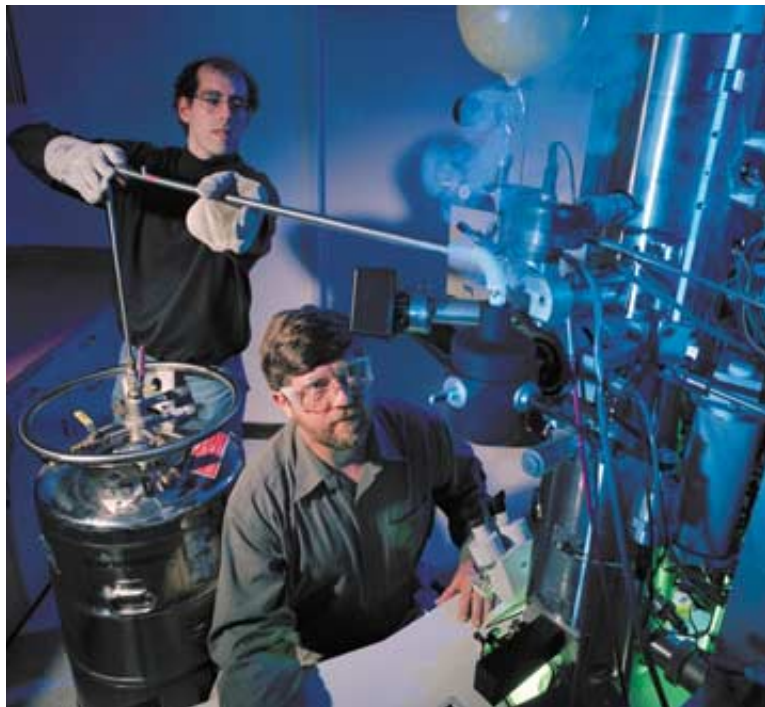
Perhaps the most exciting property of interstellar amorphous ice is that when exposed to radiation such as that found in deep space, it too can flow—even though its temperature is a scant few degrees above absolute zero (which is equivalent to -273 degrees Celsius). Indeed, the similarity of this ice to liquid water allows it to participate in the creation of organic compounds. Researchers first began to suspect this similarity in the early 1970s, as they investigated the chemistry of ice in the heart of cold molecular clouds in interstellar space. Early experiments of that era by the pioneering laboratory scientists J. Mayo Greenberg of Leiden University in the Netherlands and Louis J. Allamandola of the Ames research center demonstrated that as much as 10 percent of the volume of interstellar ice grains is composed of simple molecules such as carbon dioxide, carbon monoxide, methanol and ammonia.

Since then, specialized telescopes that observe infrared and submillimeter radiation—which can penetrate larger amounts

Continued on page 47

Overview/Shifting Bonds

- Water comes in a variety of forms because of the special bonds that H_2O molecules form with their neighbors.
- These hydrogen bonds remain rigid in the crystalline ice that occurs naturally on Earth, but they tend to rearrange themselves when exposed to the ultraviolet radiation common in deep space.
- This disruption of hydrogen bonds makes amorphous space ice much more similar to liquid water than to the frozen water of snowflakes and ice cubes.



DOMINIC HART; COURTESY OF NASA AMES RESEARCH CENTER

LIQUID HELIUM escapes a specialized cryogenic electron microscope as the authors, Peter Jenniskens (*left*) and David F. Blake, prepare a sample of amorphous ice.

of dust and gas than visible light can—have enabled astronomers to detect more than 100 different organic compounds in cold molecular clouds. By comparing the infrared spectra of clouds in space with similar measurements of interstellar ice made in the laboratory, scientists came to suspect that many of the organic compounds originated in interstellar ice grains frozen on cores of silicate or carbon. In dense molecular clouds, these dust cores are no larger than one thousandth of a millimeter.

Despite these painstaking observations, researchers still had no explanation for how the organic molecules could endure and react within the ice. The importance of ice's anomalous material properties to organic synthesis became apparent only in 1993 when we began studying its low-pressure forms at the Space Science Microscopy Laboratory at Ames. We made films of ice just a few hundred molecules thick by freezing water vapor inside a specially modified cryogenic transmission electron microscope [see *photograph above*]. To monitor changes in the ice's shape and structure, we record-

THE AUTHORS

DAVID F. BLAKE and **PETER JENNISKENS** have worked together at the NASA Ames Research Center since 1993. That year Jenniskens won a National Research Council award to study unusual ice forms with Blake at the center's Space Science Microscopy Laboratory, which Blake founded in 1990. Blake also serves as chief of the Exobiology Branch at Ames. His other research interests include searching for signs of life in extraterrestrial rocks and designing spacecraft instruments that can analyze minerals on other planets. Jenniskens also led NASA's first astrobiology mission to explore how comet matter impacted Earth during the recent Leonid meteor showers.

ed high-magnification images and electron-diffraction patterns as the ice warmed or cooled.

When the temperature in our cryogenic microscope was low enough (below 30 kelvins) and when the water molecules were deposited slowly enough (fewer than 100 microns an hour), we created an amorphous solid very similar to the structures of interstellar ice that are interpreted from infrared spectra. Our experiments showed that this ice was in a special high-density form, known until then only from one unconfirmed x-ray-diffraction experiment conducted in 1976. We confirmed that water vapor deposited at about 14 degrees above absolute zero had a different amorphous structure than a similar deposit formed at a warmer temperature of 77 K. Indeed, we could follow the transition from the low-temperature form into the higher-temperature form as we gradually warmed the ice. We could best explain the diffraction patterns of the low-temperature form if we assumed that some water molecules were frozen inside the partially formed cages of neighboring molecules. This overpacking of oxygen atoms yields high-density amorphous ice, which at 1.1 grams per cubic centimeter is about 15 percent denser than ordinary ice.

We also confirmed the 1984 findings of H. G. Heide, then at the Fritz Haber Institute of the Max Planck Society in Berlin, who bombarded high-density amorphous ice with high-energy electrons. When he conducted this experiment at temperatures below 30 K, the ice restructured rapidly; in fact, it flowed. The discovery that amorphous ice is more like liquid water than it is like crystalline ice came as a huge surprise. Most scientists had previously assumed that all forms of water ice, when cooled below a few tens of kelvins, would remain unchanged nearly indefinitely. Heide had found that, irrespective of its initial structure, the ice would transform into the high-density amorphous form once it was irradiated. Other researchers have since discovered that ultraviolet photons, which frequently irradiate cold molecular clouds, can also change the ice's structure in this manner.

Drawing on our experiments at Ames, we reasoned that this radiation converts most interstellar ice into the high-density amorphous form. We now understand that overpacked water molecules in this ice, and the defects that exist within the molecular stacking pattern, facilitate molecular mobility within the structure. As a result, it is within interstellar ice that the biologically important elements carbon, oxygen and nitrogen joined together for the first time to form organic compounds. Studies show that exposing high-density amorphous ice to energetic particles or photons breaks impurities such as carbon monoxide and ammonia into radicals that can migrate within the ice until they combine with other reactive species.

Once we had established a reasonable mechanism for the origin of organic compounds within interstellar ice, we wondered how such materials could have been preserved over the times and distances necessary to reach Earth. The best candidates for this duty are comets—relicts of the icy planetesimals that coalesced during the gravitational collapse of a cold

Continued on page 50

molecular cloud during the formation of our solar system. During that process, temperatures near the protosun were high enough to convert all but the most heat-resistant elements and compounds into gas. In the cooler regions of the solar nebula outside the orbit of Jupiter, however, amorphous ice and the organic compounds that were generated within it could have been preserved as the dust coalesced into comets and other planetesimals.

Earthbound

BY STUDYING THE TAILS OF COMETS as they pass through the inner solar system, researchers have inferred that most water ice in comets must still be in an amorphous form. As comets approach the sun, they begin to release gases such as carbon monoxide and methane into their tails. But this release happens at much higher temperatures than would be expected if the compounds had solidified in deposits separate from the ice. (If these highly volatile compounds were frozen

Below this critical temperature range, called the glass transition, the material resists deformation and behaves like a solid; above this range, it can be molded and shaped. The viscosity of the liquid just above the glass transition temperature, though, is more like cold molasses than ordinary liquid water. A motion that would take one second in liquid water would require 100,000 years in the viscous variety. Still, that is not a long time in the life of a comet.

Until our discovery, this unusual form of liquid water was thought to be rare in space. Most researchers had assumed that water at this temperature would crystallize rapidly into cubic ice, but we found that between 150 and 200 K the viscous liquid can coexist indefinitely with the cubic ice. This liquid is therefore a potentially important component of the surfaces of comets and the icy moons of neighboring planets, all of which lie within this temperature range. As for comets, the mix of viscous liquid and crystalline ice could trap gas molecules below the surface, helping to preserve key organic com-

It is within **interstellar ice** that the biologically important elements carbon, oxygen and nitrogen joined together for the first time to form **organic compounds**.

in comets as discrete components, the comets would have released them at much lower temperatures—long before reaching the inner solar system.) The gases must instead have been trapped within the structure of the ice, but how?


During comet formation, the ice warms and is therefore not likely to retain its high-density amorphous structure. Rather the slight warming will transform the structure into the low-density amorphous form. In our cryogenic experiments we learned that the transition occurs gradually between 35 and 65 K. Hydrogen bonds break and re-form during this process, allowing for the movement and chemical recombination of molecular fragments within the ice. Not until the ice warms enough to crystallize are volatile molecules excluded from the water structure and expelled into space.

When studying how crystallization depends on time and temperature, we found that the first stage of true crystallization begins at about 135 K and forces water molecules to become stacked in a cubic pattern [see box on page 51]. Organic molecules would not survive in this cubic ice, but we also discovered that a distinct amorphous component remains even when the ice warms. Only about one third of the total volume of ice ever crystallizes; the balance remains in a disordered structure that differs very little from the high- and low-density amorphous varieties.

Before we conducted our experiments, researchers were aware that amorphous ice turns into a viscous liquid between 125 and 136 K. Within this range the warming rate of the ice changes abruptly—a phenomenon well known from the study of other amorphous materials such as window glass.

pounds over time—perhaps even until the comet reached Earth's orbit.

And that brings us back to the more familiar form of water ice on Earth. Further warming of the mixture of cubic ice and viscous liquid water to about 200 K (still a bone-chilling -73 degrees C) will lead to a complete restructuring of the ice into its earthly hexagonal form. During this recrystallization, all remaining impurities—including organic compounds—are excluded from the solid. From this point on, ice is much as we know it: the ice of snowflakes, glaciers and ice cubes. But fortunately, the organics now have a new place to find shelter: in the liquid water found nearly everywhere on Earth.

Water, it seems, was present at every step in the creation and processing of molecules necessary for life. It endured the long journey from its origin as frost on interstellar dust grains to its ultimate fate as liquid water on Earth—and perhaps in other habitable zones in the universe. These exotic ice forms, with physical properties and chemistries that we are just beginning to appreciate, may eventually explain more about the history of the universe than scientists ever expected. 

MORE TO EXPLORE

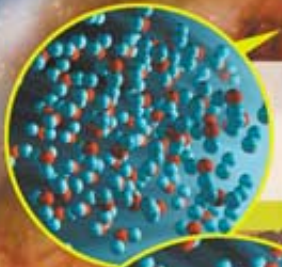
Solar System Ices. B. Schmitt, C. DeBergh and M. Festou. Kluwer Academic Publishers, 1998.

Organic Molecules in the Interstellar Medium, Comets and Meteorites: A Voyage from Dark Clouds to the Early Earth. P. Ehrenfreund and S. Charnley in *Annual Review of Astronomy and Astrophysics*, Vol. 38, pages 427–483; 2000.

Ice at the NASA Ames Research Center:
<http://exobiology.arc.nasa.gov/ice>

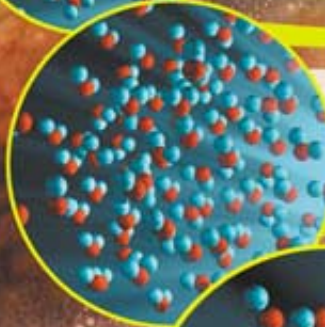
AMORPHOUS JOURNEY

The rigid structure of earthy ice expels organic molecules, but new experiments have revealed that most ice in space more closely resembles the ever changing structure of liquid water. This so-called amorphous ice can foster the formation of organic compounds and preserve them even as it warms. When an ancient molecular cloud collapsed to form our own hot sun, for instance, some of the cloud's organic-laden ice coalesced into comets, which could have later collided with the young Earth.



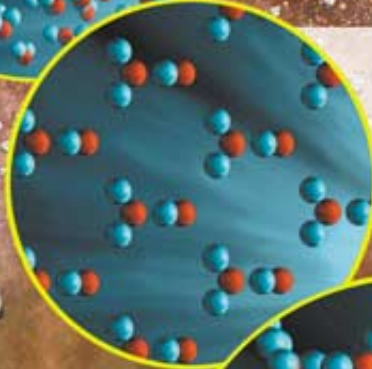
High-Density Amorphous Ice
Ultraviolet radiation causes the ice to flow like water, which enables the formation of organic molecules within it.

Temperature: 10 to 65 K



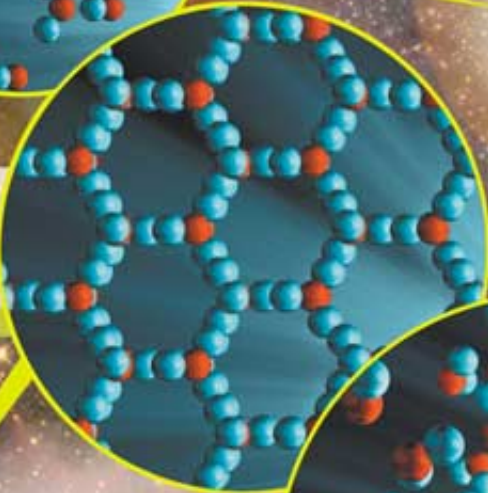
Low-Density Amorphous Ice
As ice warms and becomes less dense, hydrogen bonds break and re-form, allowing for recombination of organic compounds.

Temperature: 65 to 125 K



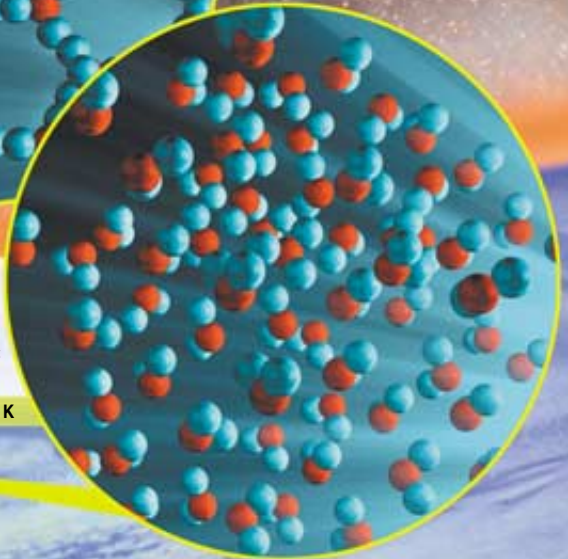
Cubic Ice
About one third of comet ice crystallizes into cubic form. The rest stays amorphous and can preserve organic materials until they reach Earth.

Temperature: 135 to 200 K



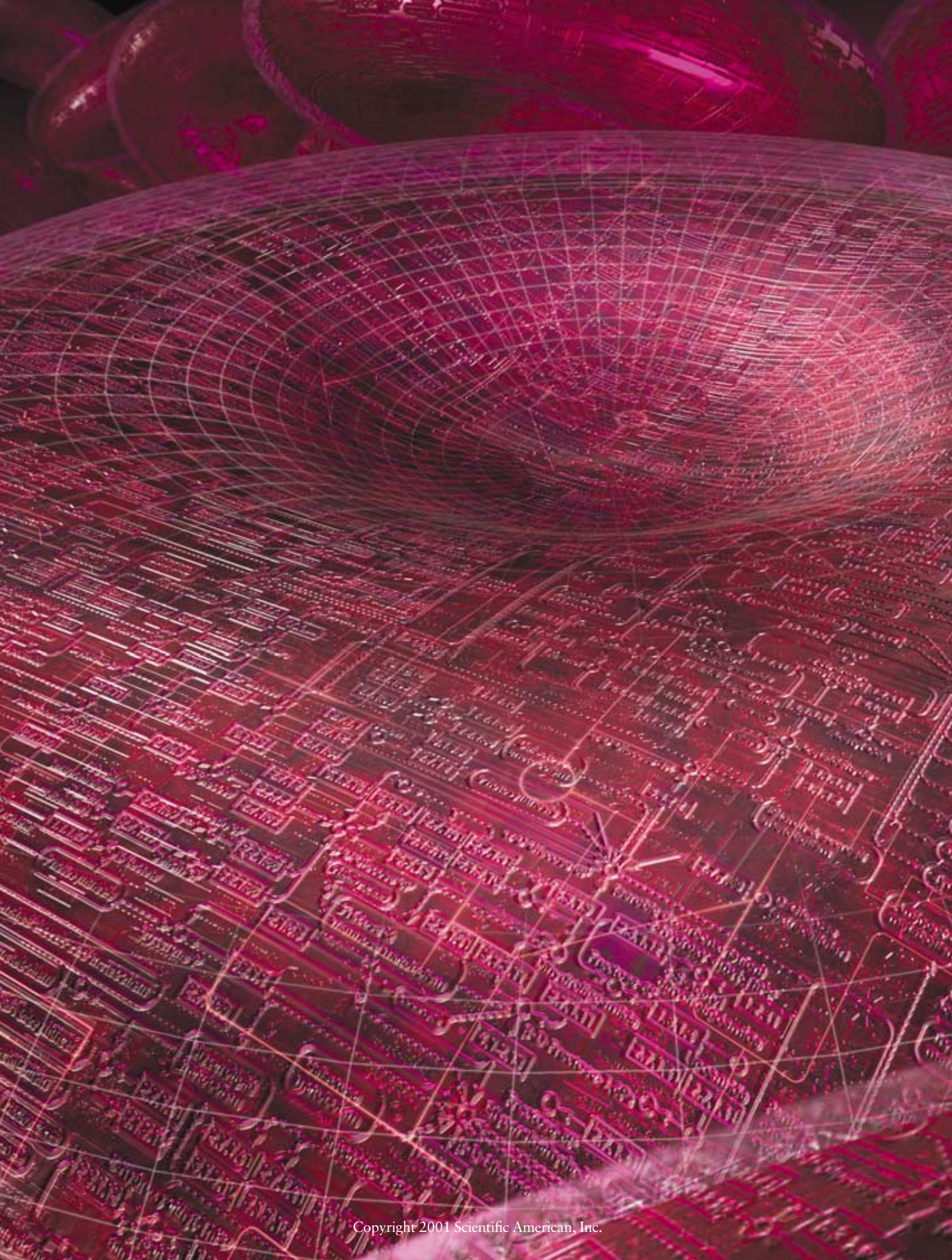
Hexagonal Ice
Highly ordered stacking of water molecules—manifest in the shape of snowflakes—expels organic compounds from the crystal structure.


Temperature: 200 to 273 K



Liquid Water
Hydrogen bonds are rapidly redistributed. This ever changing structure can accommodate organic molecules, as does amorphous ice.

Temperature: 273 to 373 K





CYBERNETIC CELLS

BY W. WAYT GIBBS

Illustrations by Slim Films

THE SIMPLEST LIVING CELL IS SO COMPLEX THAT SUPERCOMPUTER MODELS MAY NEVER SIMULATE ITS BEHAVIOR PERFECTLY. BUT EVEN IMPERFECT MODELS COULD SHAKE THE FOUNDATIONS OF BIOLOGY

RED BLOOD CELLS were the first human cells to be modeled with computers.

THREE CENTURIES OF REDUCTIONISM IN BIOLOGY RECENTLY CULMINATED IN ITS ultimate triumph. Dissecting life into ever smaller pieces—organisms to organs, tissues to cells, chromosomes to DNA to genes—scientists at last hit the limit. They identified each molecular rung on the chemical ladders of the majority of the human genome. Even before the draft sequence was in hand this past February, some researchers with a philosophical bent began looking ahead to the next major phase of biology—the era of integrationism. It is clear that computer models

will be the main tools with which all the biochemical pieces will be placed into a complete theory. But if the variety of “virtual cells” under development is any indication, there is no consensus yet on how best to use those tools.

“People are imagining that this is the final step,” observes Drew Endy of the Molecular Sciences Institute at the University of California at Berkeley. “We have the complete parts list for a human being. Now it seems just a matter of assembling the parts in a computer and flipping the switch” to untie all the knotted mysteries of medicine. In fact, he says, “Nothing could be further from the truth.”

Endy speaks as one who learned the hard way. In 1994 he and John Yin of the University of Wisconsin–Madison began programming a computer model that would incorporate virtually everything known about the way that a certain virus, T7 bacteriophage, infects *Escherichia coli* bacteria that live in the human gut. The virus looks like a lunar lander. It uses clawlike appendages to grasp the outer wall of a bacterium as the phage injects its DNA into the cell. The genetic material hijacks the cell’s own reproductive apparatus, forcing it to churn out bacteriophage clones until it bursts.

Endy and Yin’s model simulated

mathematically how all 56 of the virus’s genes were translated into 59 proteins, how those proteins subverted the host cell and even how the viruses would evolve resistance to various RNA-based drugs. That seems impressive. But peek inside the equations, Endy says, and you’ll find that despite including measurements from 15 years of laborious experiments, “there are still a tremendous number of degrees of freedom.” The equations can be tweaked to produce almost any behavior. “A useful model must suggest a hypothesis that forces the model builder to do an experiment,” Endy says. This one didn’t.

Many early attempts to re-create life in silico suffered the same problem. And so most biologists still use computers as little more than receptacles for the surge of data gushing from their robotic sequencers and gene chip analyzers. The “models” they publish in their journal articles are sketchy caricatures based on the best theory they have: the central dogma that a gene in DNA is converted to an RNA that is translated to a protein that performs a particular biochemical function.

But the past few years have seen a growing movement among mathematically minded biologists to challenge the central dogma as simplistic and to use computer simulation to search for a more

Overview/*Virtual Cells*

- Biologists have sequenced the genomes of many simple microorganisms—including germs that sicken humans. Yet they still cannot accurately predict how such cells will react to drugs or external stimuli.
- Microbiologists are now using computer models to simulate the biochemistry of cells. Some try to build models that calculate all important reactions that occur inside a bacterium. Others take an engineering approach, estimating the behavior of the cell by figuring out the basic chemical, physical and biological laws that it must obey.
- The ultimate goal is to find a way to perform virtual experiments that can speed up the discovery of new medical treatments and reduce their cost. A few companies have already begun offering such services, but the accuracy of their models has not been verified by scientific peer review.

powerful theory. “We’re witnessing a grand-scale Kuhnian revolution in biology,” avers Bernhard Ø. Palsson, head of the genetic circuits research group at the University of California at San Diego. Two years ago Palsson co-founded Genomatica, one of several companies that are creating computer models of cells to try to avoid some of the mistakes that make drug development so costly and slow.

Indeed, reports James E. Bailey of the Institute of Biotechnology at the Swiss Federal Institute of Technology in Zurich, “the cost to discover drugs is actually going up,” despite billions of dollars invested in monoclonal antibodies, cloning, sequencing, combinatorial chemistry and robotics. One reason those technologies haven’t paid off as hoped, he says, is that they are “based on the naive idea that you can redirect the cell in a way that you want it to go by sending in a drug that inhibits only one protein.” The central dogma says that that should usually work. But nine times out of 10 it doesn’t.

Consider, too, Bailey urges, that geneticists have engineered hundreds of “knockout” strains of bacteria and mice to disable a particular gene. And yet in many of those mutants, the broken gene causes no apparent abnormality. The central dogma also cannot readily explain how the complex behavior of myriad human cell types emerges from a mere 30,000 or so genes.

“I could draw you a map of all the components in a cell and put all the proper arrows connecting them,” says Alfred G. Gilman, a Nobel Prize-winning biochemist at the University of Texas Southwestern Medical Center at Dallas. But for even the simplest single-celled microorganism, “I or anybody else would look at that map and have absolutely no ability to predict anything.”

Bailey compares the confused state of microbiology with astronomy in the 16th century. “The astronomers had large archives detailing the movement and positions of celestial objects,” he says. “But they couldn’t predict the planetary motions with accuracy. They would never have believed that all the orbits are elliptic and described by a simple equation. Nevertheless, Kepler proved it. Now, I

Cybernetic Cell Projects



Genetic Circuits Research Group, led by Bernhard Ø. Palsson (above) of the University of California at San Diego, is building genome-based models of *Escherichia coli*, *Hemophilus influenzae*, *Helicobacter pylori* and other bacteria that cause human illness.

E-Cell is a mathematical microbe built at the Laboratory for Bioinformatics at Keio University in Japan from the genes of *Mycoplasma genitalium*.

The Virtual Cell is a general cell-simulation package built by the National Resource for Cell Analysis and Modeling at the University of Connecticut Health Center.

MCell is a supercomputer simulation of the synapse between a nerve cell and a muscle cell developed at the Salk Institute and the Pittsburgh Supercomputing Center.

In Silico Cell, constructed by Physiome Sciences in Princeton, N.J., is written in CellML, a programming language that the company is promoting as a lingua franca through which scientists can share and combine their cell models.

Microbial Cell Project, a 10-year program sponsored by the U.S. Department of Energy, plans to spend \$15 million a year analyzing single-celled organisms at the molecular level and constructing models of their biochemistry. —W.W.G.

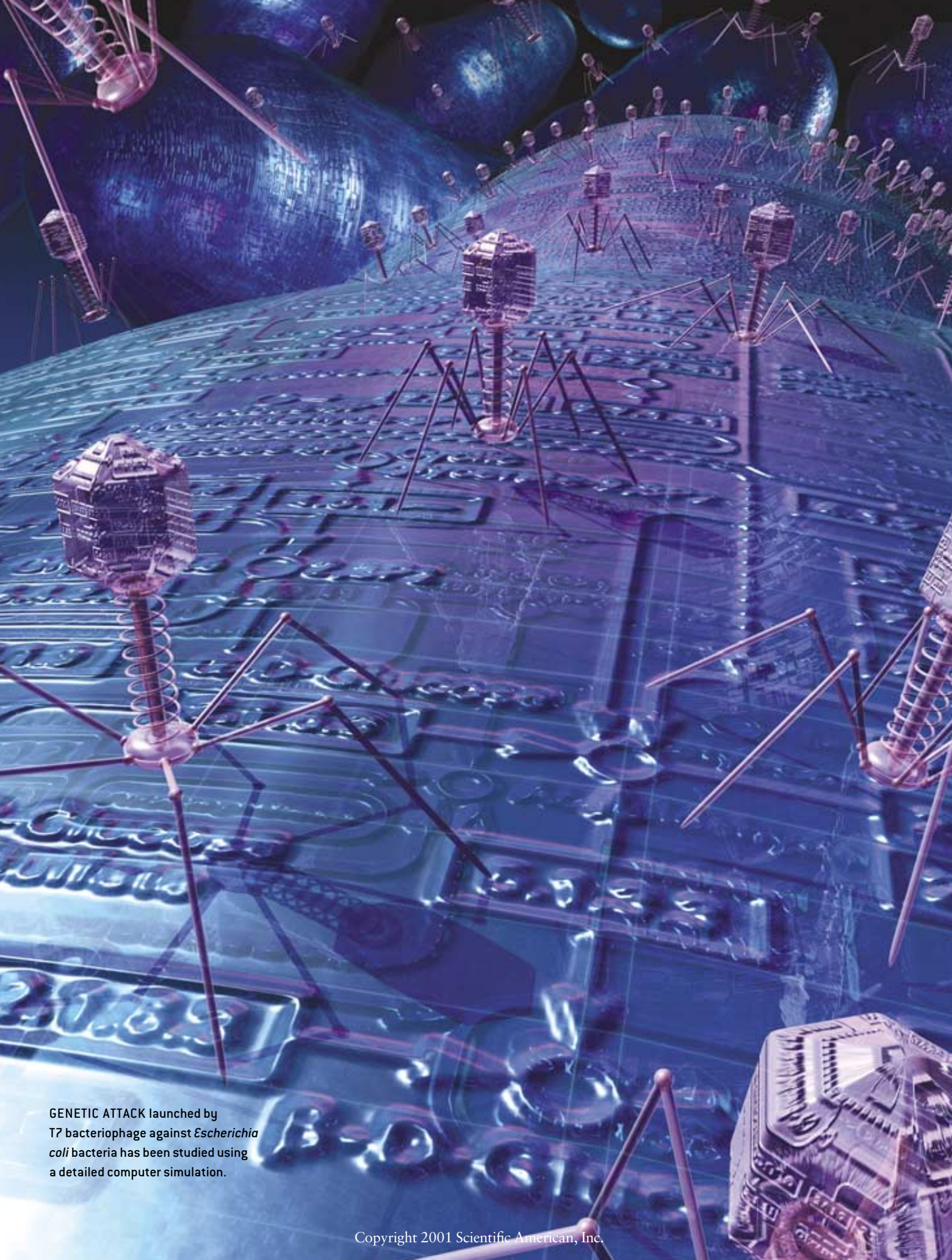
don’t pretend there is any simple equation for the biology of a cell. But we should be looking for unifying principles that will order our facts into some understanding.”

One early candidate to emerge from the more sophisticated cell simulations now under construction is the principle of robustness. Life of every kind has to cope with dramatic swings in temperature, changes in food supply, assaults by toxic chemicals, and attacks from without and within. To survive and prosper, cells must have backup systems and biological networks that tolerate interference.

Masaru Tomita saw this property emerge in virtual experiments he ran on his E-Cell model. With teammates at the Laboratory for Bioinformatics at Keio

University in Fujisawa, Japan, Tomita built the virtual cell from 127 genes, most borrowed from *Mycoplasma genitalium*, a single-celled microbe that has the smallest genome yet discovered in a self-reproducing life-form. The team’s ultimate goal is to find the minimal number of genes needed to create a self-sufficient organism and then synthesize it—an eminently reductionist strategy. But Tomita was surprised when he changed by several orders of magnitude the strength at which various genes in the model were expressed: the E-Cell’s behavior hardly budged at all.

“That was an interesting revelation for us as well,” says Jeff K. Trimmer, a life scientist at Entelos. The Menlo Park,



GENETIC ATTACK launched by T7 bacteriophage against *Escherichia coli* bacteria has been studied using a detailed computer simulation.

Calif.-based firm has built a functional model of a human fat cell, as well as whole-body models that attempt to mimic the physiological response of obese and diabetic patients to diet and drug treatments. Pharmaceutical firms such as Eli Lilly, Bristol-Myers Squibb, and Johnson & Johnson have hired Entelos to help them prioritize their drug candidates. But when Entelos scientists adjust the virtual cell to reflect the activity of the drug, “we’re often quite surprised at how little efficacy a dramatic change in cellular state has on the disease condition,” Trimmer says.

Several model-building biologists suspect that what most strongly affects how a cell behaves in response to a drug or

culated on a commercial circuit simulator. The biological “circuits” that most closely matched the input-output patterns of E-Cell were retained for further evolution; the rest were killed.

After a day, Koza’s 1,000-processor custom-made Beowulf supercomputer [see “The Do-It-Yourself Supercomputer,” by William W. Hargrove et al., on page 72] spit out a program that matched the actual reaction network. It had four enzymes, five intermediate chemicals and all the right feedback loops. It even found the correct reaction rates for each enzyme. There was a definite “right” answer; no alternative arrangements worked nearly as well.

Koza believes genetic programming

in Palsson’s lab, says the goal is not perfect prediction but reliable approximation: “Engineers can design an airplane in a computer and test it virtually without ever building a prototype, even though they can’t compute exactly how the air will flow.” In February, Palsson’s team reported that their simulation successfully predicted that *E. coli* is optimized for growth, not energy production.

This top-down approach to simulating cells has caught on. Gilman notes that an academic consortium called the Alliance for Cellular Signaling, which he chairs, has secured federal funding to build such models of the internal lives of heart muscle cells and B cells, key players in the im-

“When we have these sorts of models, it will be the most incredible DRUG DISCOVERY ENGINE there ever was.”

—ALFRED G. GILMAN, UNIVERSITY OF TEXAS SOUTHWESTERN MEDICAL CENTER, DALLAS

disease is not whether any particular gene is turned up or down, and not whether any single protein is blocked, but how all the genes and proteins interact dynamically. Like a connect-the-dots flip book, the story emerges from the links, which shift over time. If that is so, modelers could face a big problem: for most biochemical systems, scientists don’t know what reacts with what, and when.

John R. Koza, a computer scientist at Stanford University, recently conducted an experiment that may help biologists connect their genetic dots. Koza is a pioneer in genetic programming, a technique for evolving software by instructing the computer to generate random programs, mutate them repeatedly and then screen them to identify the ones that perform the desired task best. Nicely closing a circle of metaphor, Koza used genetic programming to re-create a small but complicated part of the E-Cell model, itself built from software to mimic genes.

Koza rigged his system to evolve programs that piece together known enzymes into chemical machinery that can convert fatty acid and glycerol to diacylglycerol. Each variant program was converted, for the sake of convenience, to an equivalent electrical circuit, whose behavior was cal-

culated on a commercial circuit simulator. The biological “circuits” that most closely matched the input-output patterns of E-Cell were retained for further evolution; the rest were killed.

can handle larger problems, perhaps one day even deducing the convoluted paths by which cells turn food into energy, growth and waste—but only in cases where biochemists have measured how cells process chemicals over time. Such data are still scarce.

The observation that many biochemical problems most likely have an optimal answer is exploited by Palsson and his colleagues in the models they have built of *E. coli*, *Hemophilus influenzae* and *Helicobacter pylori*, the germ found in stomach ulcers. They comb the literature to reconstruct as much of the biochemical networks as they can. “Then we subject them to constraints that they must abide,” Palsson explains. Mass must be conserved, for example. Electrical charges must balance. Thermodynamics makes many reactions irreversible. “We try to home in on the range of solutions that are physically possible.”

Markus W. Covert, a graduate student

mune system. He figures the effort will take a decade to complete, at \$10 million a year. “But when we have these sorts of models,” Gilman predicts, “it will be the most incredible drug discovery engine there ever was. You could model disease in that cell and then see what drug manipulation could do. Ultimately—though maybe not in 10 years—I have no doubt that there will be quantitative models of cell function, organ function and eventually whole-animal function.”

“I would approach such a goal with a fair amount of humility,” Bailey cautions. “History teaches us that simulations can help explore particular questions, but there won’t be any master model that answers all questions. Eventually the models will become as complicated as the cell itself and as difficult to understand.” Unless, perhaps, the next Kepler happens to be a computer wizard. SA

W. Wayt Gibbs is senior writer.

MORE TO EXPLORE

Modelling Cellular Behaviour. Drew Endy and Roger Brent in *Nature*, Vol. 409, pages 391–395; January 18, 2001.

Whole-Cell Simulation: A Grand Challenge of the 21st Century. Masaru Tomita in *Trends in Biotechnology*, Vol. 19, No. 6, pages 205–210; June 2001.

Details of John R. Koza’s genetic programming approach can be found in the proceedings of the 2001 Pacific Symposium on Biocomputing at psb.stanford.edu/psb-online/#PATH



Clear evidence of cannibalism in the human fossil record has been rare, but it is now becoming apparent that the practice is deeply rooted in our history

BY TIM D. WHITE

Once Were CAN



NEANDERTAL CRANIUM from the Krapina rockshelter in Croatia. Physical anthropologists and archaeologists have recently determined that this specimen and hundreds of other skeletal remains at this site attest to cannibalism. This cranium was smashed so the brain could be removed and consumed.

NIBALS

It can shock, disgust and fascinate in equal

measure, whether through tales of starved pioneers and airplane crash survivors eating the deceased among them or accounts of rituals in Papua New Guinea. It is the stuff of headlines and horror films, drawing people in and mesmerizing them despite their aversion. Cannibalism represents the ultimate taboo for many in Western societies—something to relegate to other cultures, other times, other places. Yet the understanding of cannibalism derived from the past few centuries of anthropological investigation has been too unclear and incomplete to allow either a categorical rejection of the practice or a fuller appreciation of when, where and why it might have taken place.

New scientific evidence is now bringing to light the truth about cannibalism. It has become obvious that long before the invention of metals, before Egypt's pyramids were built, before the origins of agriculture, before the explosion of Upper Paleolithic cave art, cannibalism could be found among many different peoples—as well as among many of our ancestors. Broken and scattered human bones, in some cases thousands of them, have been discovered from the prehistoric pueblos of the American Southwest to the islands of the Pacific. The osteologists and archaeologists studying these ancient occurrences are using increasingly sophisticated analytical tools and methods. In the past several years, the re-

sults of their studies have finally provided convincing evidence of prehistoric cannibalism.

Human cannibalism has long intrigued anthropologists, and they have worked for decades to classify the phenomenon. Some divide the behavior according to the affiliation of the consumed. Thus, endocannibalism refers to the consumption of individuals within a group, exocannibalism indicates the consumption of outsiders, and autocannibalism covers everything from nail biting to torture-induced self-consumption. In addition, anthropologists have come up with classifications to describe perceived or known motivations. Survival cannibalism is driven by starvation. Historically documented cases include the Donner Party—whose members were trapped during the harsh winter of 1846–47 in the Sierra Nevada—and people marooned in the Andes or the Arctic with no other food. In contrast, ritual cannibalism occurs when members of a family or community consume their dead during funerary rites in order to inherit their qualities or honor their memory. And pathological

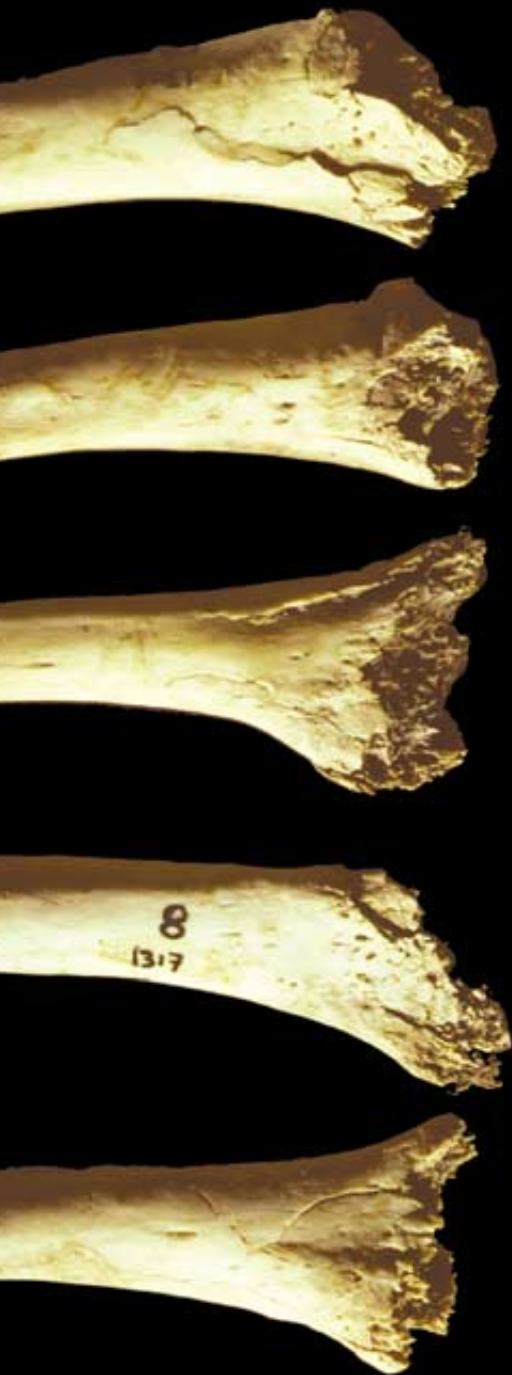
cannibalism is generally reserved for criminals who consume their victims or, more often, for fictional characters such as Hannibal Lecter in *The Silence of the Lambs*.

Despite these distinctions, however, most anthropologists simply equate the term “cannibalism” with the regular, culturally encouraged consumption of human flesh. This dietary, customary, gourmet, gustatory or gastronomic cannibalism, as it is variously called, is the phenomenon on which ethnographers have focused much of their attention. In the age of ethnographic exploration—which lasted from the time of Greek historian Herodotus in about 400 B.C. to the early 20th century—the non-Western world and its inhabitants were scrutinized by travelers, missionaries, military personnel and anthropologists. These observers told tales of gastronomic human cannibalism in different places, from Mesoamerica to the Pacific islands to central Africa.

Controversy has often accompanied these claims. Professional anthropologists participated in only the last few waves of

THE AUTHOR

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CRUSHING

Many different types of damage can be seen on bones left by human cannibals. When this damage is identical to that seen on animal bones at the same sites, archaeologists infer that the human remains were processed in the same manner and for the same reason: for consumption. In these metatarsal [foot] bones from Mancos Canyon in Colorado, the spongy tissues at the ends were crushed so that fat could be removed. [All subsequent photographs of bones are from the same Anasazi site in Mancos.]

these cultural contacts—those that began in the late 1800s. As a result, many of the historical accounts of cannibalism have come to be viewed skeptically. In 1937 anthropologist Ashley Montagu stated that cannibalism was “pure traveler’s myth.”

In 1979 anthropologist William Arens of the State University of New York at Stony Brook extended this argument by reviewing the ethnographic record of cannibalism in his book *The Man-Eating Myth*. Arens concluded that accounts of cannibalism among people from the Aztec to the Maori to the Zulu were either false or inadequately documented. His skeptical assertion has subsequently been seriously questioned, yet he nonetheless succeeded in identifying a significant gulf between these stories and evidence of cannibalism: “Anthropology has not maintained the usual standards of documentation and intellectual rigor expected when other topics are being considered. Instead, it has chosen uncritically to lend its support to the collective representations and thinly disguised prejudices of western culture about others.”

The anthropologists whom Arens and Montagu were criticizing had not limited themselves to commenting solely on contemporary peoples. Some had projected their prejudices even more deeply—into the archaeological record. Interpretations of cannibalism inevitably followed many discoveries of prehistoric remains. Archaeological findings in Europe and elsewhere led to rampant speculation about cannibalism. And by 1871 American author Mark Twain had weighed in on the subject in an essay later published in *Life as I Find It*: “Here is a pile of bones of primeval man and beast all mixed together, with no more damning evidence that the man ate the bears than that the bears ate the man—yet paleontology holds a coroner’s inquest in the fifth geologic period on an ‘unpleasantness’ which transpired in the quaternary, and calmly lays it on the MAN, and then adds to it what purports to be evidence of CANNIBALISM. I ask the candid reader, Does not this look like taking advantage of a gentleman who has been dead two million years....”

In the century after Twain’s remarks, archaeologists and physical anthropologists described the hominids *Australopithecus africanus*, *Homo erectus* and *H. neanderthalensis* as cannibalistic. According to some views, human prehistory from about three million years ago until very recently was rife with cannibalism.

In the early 1980s, however, an important critical assessment of these conclusions appeared. Archaeologist Lewis Binford’s book *Bones: Ancient Men and Modern Myths* argued that claims for early hominid cannibalism were unsound. He built on the work of other prehistorians concerned with the composition, context and modifications of Paleolithic bone assemblages. Binford emphasized the need to draw accurate inferences about past behaviors by grounding knowledge of the past on experiment and observation in the present. His influential work coupled skepticism with a plea for methodological rigor in studies of prehistoric cannibalism.

Higher Standards of Evidence

IT WOULD BE HELPFUL if we could turn to modern-day cannibals with our questions, but such opportunities have largely disappeared. So today’s study of this intriguing behavior must be accomplished through a historical science. Archaeology has therefore become the primary means of investigating the existence and extent of human cannibalism.

One of the challenges facing archaeologists, however, is the amazing variety of ways in which people dispose of their dead. Bodies may be buried, burned, placed on scaffolding, set adrift, put in tree trunks or fed to scavengers. Bones may be disinterred, washed, painted, buried in bundles or scattered on stones. In parts of Tibet, future archaeologists will have difficulty recognizing any mortuary practice at all. There most corpses are dismembered and fed to vultures and other carnivores. The bones are then collected, ground into powder, mixed with barley and flour and again fed to vultures. Given the various fates of bones and bodies, distinguishing cannibalism from other mortuary practices can be quite tricky.

Consequently, scientists have set the standard for recognizing ancient cannibalism very high. They confirm the activity when the processing patterns seen on human remains match those seen on the bones of other animals consumed for food. Archaeologists have long argued for such a comparison between human and faunal remains at a site. They reason that damage to *animal* bones and their arrangement can clearly show that the animals had been slaughtered and eaten for food. And when *human* remains are unearthed in similar cultural contexts, with similar patterns of damage, discard and preservation, they may reasonably be interpreted as evidence of cannibalism.

When one mammal eats another, it usually leaves a record of its activities in the form of modifications to the consumed animal's skeleton. During life, varying amounts of soft tissue, much of it with nutritive value, cover mammalian bones. When the tissue is removed and prepared, the bones often retain a record of this processing in the form of gnawing marks and fractures. When humans eat

ence of cannibalism is strengthened. Judging which patterns are consistent with dietary butchery can be based on the associated archaeological record—particularly the nonhuman food-animal remains discovered in sites formed by the same culture—and checked against predictions embedded in ethnohistorical accounts.

This comparative system of determining cannibalism emphasizes multiple lines of osteological damage and contextual evidence. And, as noted earlier, it sets the standard for recognizing cannibalism very high. With this approach, for instance, the presence of cut marks on bones would not by themselves be considered evidence of cannibalism. For example, an American Civil War cemetery would contain skeletal remains with cut marks made by bayonets and swords, but this would not constitute evidence of cannibalism. Medical school cadavers are dissected, their bones cut-marked, but cannibalism is not part of this ritual.

With the threshold set so conservatively, most instances of past cannibalism will necessarily go unrecognized. A prac-

tice from Papua New Guinea, where cannibalism was recorded ethnographically, illustrates this point. There skulls of the deceased were carefully cleaned and the brains removed. The dry, mostly intact skulls were then handled extensively, often creating a polish on their projecting parts. They were sometimes painted and even mounted on poles for display and worship. Soft tissue, including brain matter, was eaten at the beginning of this process; thus, the practice would be identified as ritual cannibalism. If such skulls were encountered in an archaeological context without modern informants describing the cannibalism, they would not constitute direct evidence for cannibalism under the stringent criteria that my colleagues and I advocate.

Nevertheless, adoption of these standards of evidence has led us to some clear determinations in other, older situations. The best indication of prehistoric cannibalism now comes from the archaeological record of the American Southwest, where archaeologists have interpreted dozens of assemblages of human remains

One of the challenges facing archaeologists is the amazing variety of ways in which people dispose of their dead.

other animals, however, they mark bones with more than just their teeth. They process carcasses with tools of stone or metal. In so doing, they leave imprints of their presence and actions in the form of scars on the bones. These same imprints can be seen on butchered human skeletal remains.

The key to recognizing human cannibalism is to identify the patterns of processing—that is, the cut marks, hammering damage, fractures or burns seen on the remains—as well as the survival of different bones and parts of bones. Nutritionally valuable tissues, such as brains and marrow, reside within the bones and can be removed only with forceful hammering—and such forced entry leaves revealing patterns of bone damage. When human bones from archaeological sites show patterns of damage uniquely linked to butchery by other humans, the infer-

CHOPPING

Hack marks visible on the left side of this fragment of a human tibia are testament to the removal of muscle and tendon. Tools were also used to make finer slices, to remove tissue or to sever heads from bodies. Archaeologists have to be careful in their interpretations, however, because humans process their dead in many ways; not all slice or hack marks indicate cannibalism.



as providing evidence of cannibalism. Compelling evidence has also been found in Neolithic and Bronze Age Europe. Even Europe's earliest hominid site has yielded convincing evidence of cannibalism.

Early European Cannibals

THE MOST IMPORTANT paleoanthropological site in Europe lies in northern Spain, in the foothills of the Sierra de Atapuerca. Prehistoric habitation of the caves in these hills created myriad sites, but the oldest known so far is the Gran Dolina, currently under excavation. The team working there has recovered evidence of occupation some 800,000 years ago by what may prove to be a new species of human ancestor, *H. antecessor*. The hominid bones were discovered in one horizon of the cave's sediment, intermingled with stone tools and the remains of prehistoric game animals such as deer, bison and rhinoceros. The hominid remains consist of 92 fragments from six individuals. They bear unmistakable traces of butchery with stone tools, including skinning and removal of flesh, as well as processing of the braincase and the long bones for marrow. This pattern of butchery matches that seen on the nearby animal bones. This is the earliest evidence of hominid cannibalism.

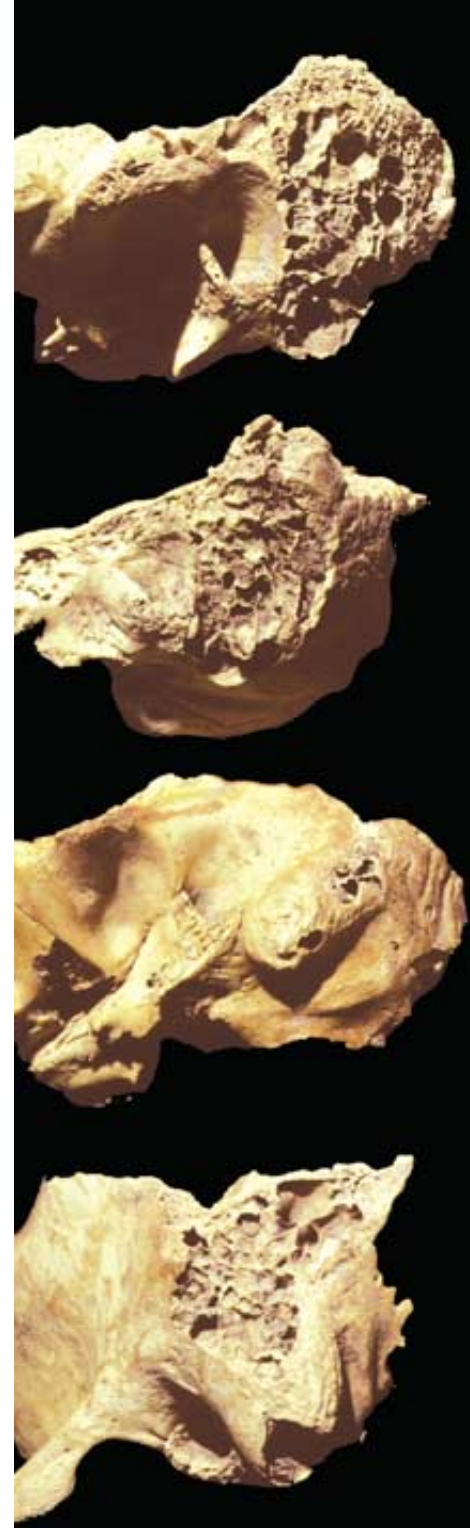
Cannibalism among Europe's much younger Neandertals—who lived between 35,000 and 150,000 years ago—has been debated since the late 1800s, when the great Croatian paleoanthropologist Dragutin Gorjanovič-Kramberger found the broken, cut-marked and scattered remains of more than 20 Neandertals entombed in the sands of the Krapina rockshelter. Unfortunately, these soft fossil bones were roughly extracted by today's standards and then covered with thick layers of preservative, which obscured evidence of processing by stone tools and made interpretation of the remains exceedingly difficult. Some workers believe the Krapina Neandertal bones show clear signs of cannibalism; others have attributed the patterns of bone damage to falling rocks from the cave's ceiling, to carnivore chewing or to some form of Neandertal burial. But recent analysis of the Krapina bones as well as those

from another Croatian cave, Vindija—which has younger Neandertal and animal remains—indicates that cannibalism was practiced at both sites.

In the past few years, yet another Neandertal site has offered support for the idea that some of these hominids practiced cannibalism. On the banks of the Rhône River in southeastern France, Alban Defleur of the University of the Mediterranean at Marseilles has been excavating the cave of Moula-Guercy for the past nine years. Neandertals occupied this small cave approximately 100,000 years ago. In one layer the team unearthed the remains of at least six Neandertals, ranging in age from six years to adult. Defleur's meticulous excavation and recovery standards have yielded data every bit the equivalent of a modern forensic crime scene investigation. Each fragment of fauna and Neandertal bone, each macrobotanical clue, each stone tool has been precisely plotted three-dimensionally. This care has allowed an understanding of how the bones were spread around a hearth that has been cold for 1,000 centuries.

Microscopic analysis of the Neandertal bone fragments and the faunal remains has led to the same conclusion that Spanish workers at the older Gran Dolina site have drawn: cannibalism was practiced by some Paleolithic Europeans. But determining how often it was practiced and under what conditions represents a far more difficult challenge. Nevertheless, the frequency of cannibalism is striking. We know of just one very early European site with hominid remains, and those were cannibalized. The two Croatian Neandertal sites are separated by hundreds of generations, yet analyses suggest that cannibalism was practiced at both. And now a Neandertal site in France has supported the same interpretation. These findings are built on exacting standards of evidence. Because of this, most paleoanthropologists these days are asking "Why cannibalism?" rather than "Was this cannibalism?"

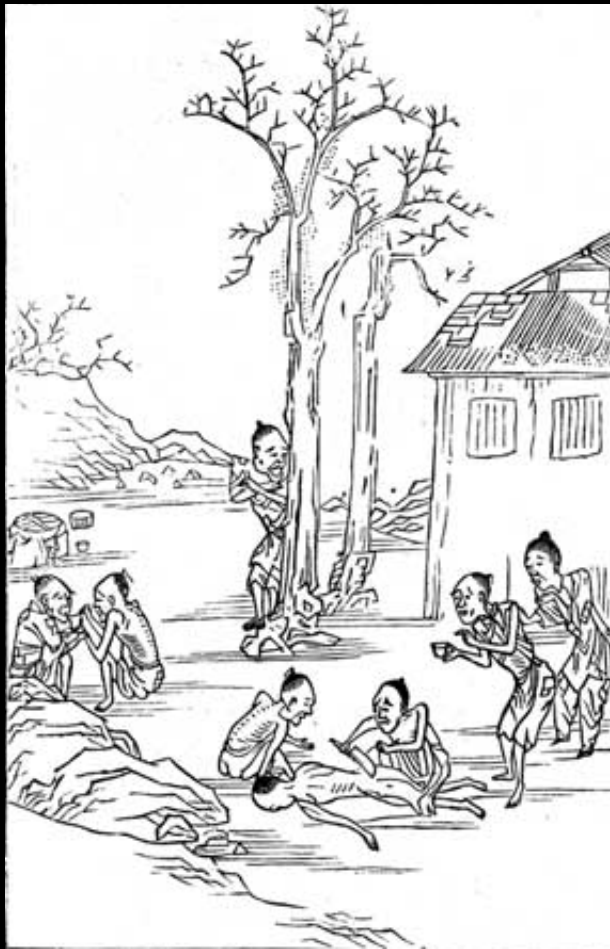
Similarly, recent discoveries at much younger sites in the American Southwest have altered the way anthropologists think of Anasazi culture in this area.



BURNING

The dark and damaged areas on these four mastoid regions—that is, the hard bump behind each ear—indicate that these human skulls were roasted. Because the mastoid region is not covered by much muscle or other tissue, damage from burning was often more intense in this area than on other parts of cranial bone. Burning patterns therefore provide clues about culinary practices.

HISTORICAL ACCOUNTS



ETHNOHISTORICAL REPORTS of cannibalism have been recorded for centuries in many corners of the globe. Although some involve well-documented accounts by eyewitnesses—such as the Donner Party expedition—other accounts by explorers, missionaries, travelers and soldiers often lack credibility. For example, these two artists' portraits depict cannibalism catalyzed by starvation in China in the late 1800s and a European view of cannibalism in the New World (based on a woodcut from 1497). Such ethnohistorical accounts do not carry the weight of archaeological and forensic evidence. They may, however, serve as rich sources of testable hypotheses, guiding future archaeological excavations.



Corn agriculturists have inhabited the Four Corners region of the American Southwest for centuries, building their pueblos and spectacular cliff dwellings and leaving one of the richest and most fine-grained archaeological records anywhere on earth. Christy G. Turner II of Arizona State University conducted pioneering work on unusual sets of broken and burned human skeletal remains from Anasazi sites in Arizona, New Mexico and Colorado in the 1960s and 1970s. He saw a pattern suggestive of cannibalism: site after site containing human remains with the telltale signs. Yet little in the history of the area's more recent Puebloan peoples suggested that cannibalism was a widespread practice, and some modern tribes who claim descent from the Anasazi have found claims of cannibalism among their ancestors disturbing.

The vast majority of Anasazi burials involve whole, articulated skeletons frequently accompanied by decorated ceramic vessels that have become a favorite target of pot hunters in this area. But, as Turner recorded, several dozen sites had fragmented, often burned human remains, and a larger pattern began to emerge. Over the past three decades the total number of human bone specimens from these sites has grown to tens of thousands, representing dozens of individuals spread across 800 years of prehistory and tens of thousands of square kilometers of the American Southwest. The assemblage that I analyzed 10 years ago from an Anasazi site in the Mancos Canyon of southwestern Colorado, for instance, contained 2,106 pieces of bone from at least 29 Native American men, women and children.

These assemblages have been found in settlements ranging from small pueblos to large towns and were often contemporaneous with the abandonment of the dwellings. The bones frequently show evidence of roasting before the flesh was removed. They invariably indicate that people extracted the brain and cracked the limb bones for marrow after removing the muscle tissue. And some of the long bone splinters even show end-polishing, a phenomenon associated with cooking in

HULTON-DEUTSCH COLLECTION Corbis (top); LEONARD DE SELVA Corbis (bottom)

ceramic vessels. The bone fragments from Mancos revealed modifications that matched the marks left by Anasazi processing of game animals such as deer and bighorn sheep. The osteological evidence clearly demonstrated that humans were skinned and roasted, their muscles cut away, their joints severed, their long bones broken on anvils with hammerstones, their spongy bones crushed and the fragments circulated in ceramic vessels. But articles outlining the results have proved controversial. Opposition to interpretations of cannibalism has sometimes seemed motivated more by politics than by science. Many practicing anthropologists believe that scientific findings should defer to social sensitivities. For such anthropologists, cannibalism is so culturally delicate, so politically incorrect, that they find any evidence for it impossible to swallow.

The most compelling evidence in sup-

HAMMERING

It is clear from the archaeological record that meat—fat or muscle or other tissue—on the bone was not the only part of the body that was consumed. Braincases were broken open, and marrow was often removed from long bones. In these two examples, stone hammers split the upper arm bones lengthwise, exposing the marrow.



It remains much more difficult to establish why cannibalism took place than to establish that it did.

port of human cannibalism at Anasazi sites in the American Southwest was published last fall by Richard A. Marlar of the University of Colorado School of Medicine and his colleagues. The workers excavated three Anasazi pit dwellings dating to approximately A.D. 1150 at a site called Cowboy Wash near Mesa Verde in southwestern Colorado. The same pattern that had been documented at other sites such as Mancos was present: disarticulated, broken, scattered human bones in nonburial contexts. Excellent preservation, careful excavation and thoughtful sampling provided a chemical dimension to the analysis and, finally, direct evidence of human cannibalism.

Marlar and his colleagues discovered residues of human myoglobin—a protein present in heart and skeletal muscle—on a ceramic vessel, suggesting that human flesh had been cooked in the pot. An unburned human coprolite, or ancient feces, found in the fireplace of one of the abandoned dwellings also tested positive for human myoglobin. Thus, osteological, ar-

chaeological and biochemical data indicate that prehistoric cannibalism occurred at Cowboy Wash. The biochemical data for processing and consumption of human tissue offer strong additional support for numerous osteological and archaeological findings across the Southwest.

Understanding Cannibalism

IT REMAINS MUCH more challenging to establish why cannibalism took place than to establish that it did. People usually eat because they are hungry, and most prehistoric cannibals were therefore probably hungry. But discerning more

than that—such as whether the taste of human flesh was pleasing or whether cannibalism presented a way to get through the lean times or a satisfying way to get rid of outsiders—requires knowledge not yet available to archaeologists. Even in the case of the Anasazi, who have been well studied, it is impossible to determine whether cannibalism resulted from starvation, religious beliefs or some combination of these and other things. What is becoming clear through the refinement of the science of archaeology, however, is that cannibalism is part of our collective past. SA

MORE TO EXPLORE

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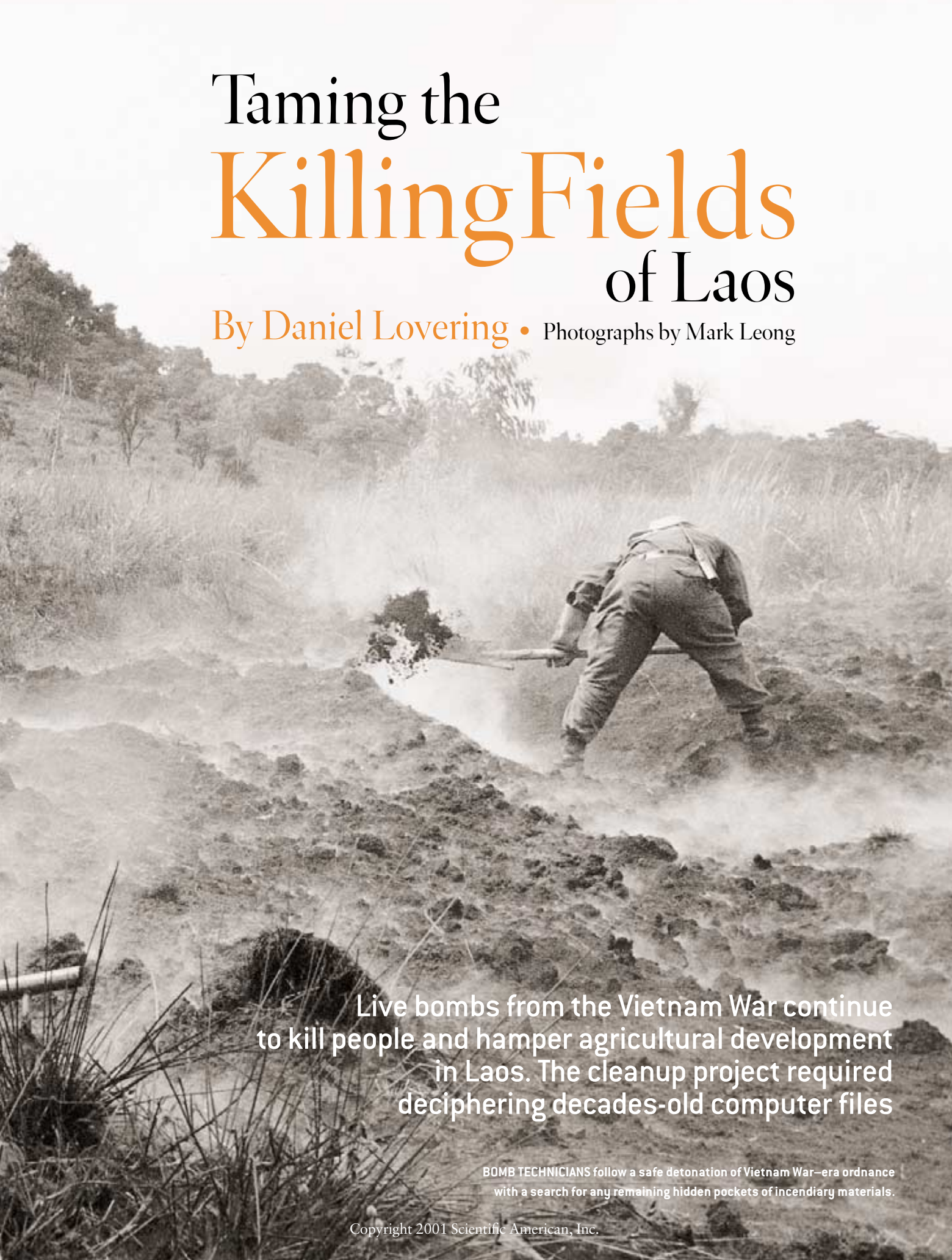
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Taming the Killing Fields of Laos

By Daniel Lovering • Photographs by Mark Leong



Live bombs from the Vietnam War continue to kill people and hamper agricultural development in Laos. The cleanup project required deciphering decades-old computer files

BOMB TECHNICIANS follow a safe detonation of Vietnam War-era ordnance with a search for any remaining hidden pockets of incendiary materials.

IN AN OFFICE ABOVE THE dusty streets of Vientiane, the tranquil capital city of Laos, Michael Sheinkman watches accidents waiting to happen. With finger poised on computer mouse, he gazes at a monitor revealing a grainy black-and-white digital map of Laos. He clicks, and suddenly a constellation of tiny pink dots appears like a pox on the countryside. Each dot marks the likely site of an unexploded bomb.

The dots represent the legacy of one of the world's most extensive bombing campaigns: they are U.S. bomb target coordinates from the Vietnam War era. U.S. forces dropped more than two million tons of bombs on the Ho Chi Minh Trail, the North Vietnamese supply route that snaked through the jungles of eastern Laos.

"The patterns show very clearly the targeting was on flat land and lines of communication," says Sheinkman, an

maimed more than 10,000 people. In addition to their effect on public health, unexploded bombs greatly hamper the small and fragile Lao economy, especially by impeding agricultural development.

After the war ended in 1975, bomb disposal groups tried to clear swaths of land with marginal success. But it wasn't until the mid-1990s that a more sophisticated, countrywide program called UXO Lao (the national office of which is in Vientiane) was launched by the Lao government with the support of international aid agencies. Finding and disposing of unexploded ordnance, or UXO, is the slow and exacting work of the program's 628 bomb technicians and 23 foreign advisers.

For the past two years, Sheinkman, employed first by a government contractor called Management Support Technology and now by Federal Resource Corporation, both based in Fairfax, Va., has as-

records. He and his colleagues at Bolling Air Force Base's History Support Office planned to write a history of air combat operations during the Vietnam War. He was browsing the office library and found an index of U.S. bombing records. "It had pages and pages of databases from the Vietnam War era," Stanley marvels. "I thought, 'This is just incredible.'"

The index, from a Rand Corporation study published in 1976, inspired Stanley to seek the actual magnetic tapes embedded with streams of arcane numerical codes used by the U.S. military during the war. Stanley realized that those tapes—if they still existed—should denote bomb and aircraft types, target coordinates and other information about U.S. bombing missions in Southeast Asia. Military analysts knew nothing of the antiquated records.

Stanley next checked closer to home, at the National Archives, in Maryland.

Bomb specialists and manufacturers estimate that up to **30 percent of bombs** dropped by the U.S. on the Ho Chi Minh Trail in eastern Laos **failed to explode.**

American geographer working on the extensive effort to locate and neutralize the unexploded ordnance. "The downside for the people of Laos some 30 years later is that flat land is at a premium."

Land mines, perhaps more familiar as a threat, represent a mere 4 percent of the unexploded bombs in Laos. U.S.-made aerial bombs account for the majority of ordnance lurking in topsoil and bamboo thickets, although artillery shells, antitank rockets, hand grenades and other types of ordnance from China, France, Russia and elsewhere emerge regularly from hiding.

The human cost of these unexploded bombs is considerable: they have killed or

sisted the group in using U.S. bombing records and digital mapping technology to identify areas most likely to be strewn with unexploded bombs. His work is an outgrowth of U.S. funding that began three years ago, when the U.S. Department of Defense's Humanitarian Demining Office began assisting UXO Lao with training and equipment. In late 1998 Sheinkman and his Lao advisees began charting old bombing runs that may have left unexploded ordnance in their wake.

Bomb Sniffing

THE DIGITAL MAPS splashed across Sheinkman's office incorporate bombing data that had to be painstakingly culled from electronic records kept by the U.S. military during the war. Roy Stanley, a U.S. Air Force reserve officer and statistician at the U.S. Department of Energy, began the project eight years ago, after a serendipitous discovery.

A part-time air force historian in Washington, D.C., Stanley had just finished archiving World War II combat



NINE-TRACK TAPES such as these contained code-within-code information about bombing during the Vietnam War—a planeload of bombs every eight minutes for nine years. Interpreting the data required years of detective work on military records as well as clever computer-system archaeology.

DANIEL LOVERING is a Bangkok-based correspondent for the French news service Agence France-Presse. He recently completed a Pew Fellowship in International Journalism at the School for Advanced International Studies at Johns Hopkins University. Lovering is a graduate of the Columbia University Graduate School of Journalism and Oberlin College.



LABEL from a bomb dispenser container was found in a Lao field, where it presumably spent the past three decades.

He found open-reel tapes, some of them disintegrating, as well as correspondence confirming that many of the databases he sought had been erased during and after the war, as officials saw no reason to keep them. Thomas E. Brown, manager of archival services at the Electronic and Special Media Records Services Division of the National Archives, says some Vietnam air combat databases were never transferred to the National Archives from the Department of Defense. "I am certain that some databases related to air missions were destroyed," Brown adds. Although the National Archives had informal policies aimed at preserving electronic records as early as 1968, they were not officially enforced until years later.

Despite these setbacks, Stanley did find two useful tape databases at the National Archives that had been listed in the Rand index: the Combat Activities File had details about missions flown in Southeast Asia from October 1965 through December 1970, and the Southeast Asia Data-

base documented missions flown between January 1970 and August 1975. These intact databases were created on IBM System 360 and System 370 mainframe computers using software called the National Military Command System Information Processing System 360 Formatted File System, or NIPS. Developed for the government by IBM in the 1960s, NIPS did what database software does: it created, structured, maintained and revised data files. But the details of missions over Laos—on average, a planeload of bombs every eight minutes for nine years—were coded to save space because of the limited storage capacity of mainframes at the time. "What you have is nested data," Brown explains. "You would have a fixed field with information about sorties and additional fields identifying each leg of the mission."

Further hindering Stanley's attempt to understand the databases was the scant documentation of changes in database codes. "Sometimes codes were reused and the data processors just assigned new val-

ues to the codes," Brown says. "These changes were not always incorporated into the systems manuals, and early versions of the manuals were not always saved." In the Southeast Asia Database, for example, the National Archives has a manual dated 1975, but it is uncertain whether the information applies to earlier years. So simple coded data included nested information, and the codes themselves may have variable meanings.

In 1994 Stanley landed a \$10,000 grant from the Department of Defense to complete a feasibility study of the data, still unaware that it would eventually help UXO Lao save lives. He enlisted the aid of Management Support Technology, the government contractor that eventually employed Sheinkman in Laos, to decipher the databases. The contractor then sought the help of a former IBM programmer who worked on the original database. The programmer created software to convert the NIPS data to a plain-text file readable by a modern personal computer. These ef-

Days of Destruction

Finding the bombs makes it possible to detonate them safely

CHANTHAVONG INTHAVONGSY can easily identify her prey on this day. In Champassak, a quiet province in southern Laos, Inthavongsy shines a flashlight into the tail section of what she recognizes to be a U.S. MK-81 aerial bomb sitting broadside in a bed of dead leaves. She peruses the bomb, then declares it safe to transport. Of course, not all unexploded bombs are so easy to handle. Some bombs have sensitive mechanical fuses and must be destroyed where they are found. Such diagnoses are easy for the 22-year-old, who leads a team of four technicians that frequently find the 250-pound bombs nosed into the ground or sitting in full view on the jungle floor. U.S. bombing data and reports from villagers help to guide teams such as Inthavongsy's



CLEARANCE TEAM carefully examines an uncovered bomb to determine whether it still poses a danger.

that are taking part in UXO (for “unexploded ordnance”) Lao, a countrywide program.

UXO Lao finds scores of different types of U.S. aerial bombs, some of which weigh a hulking 2,000 pounds. The millions of unexploded antipersonnel cluster bombs, locally nicknamed “bombies,” in Laos can be particularly nettlesome because of centrifugal fuses that were designed to arm the bomb as it fell through the air. Technicians need to examine such fuses closely to determine whether the bomb is armed. Although UXO Lao is familiar with most U.S. bomb designs, some are still classified by the U.S. government. Bomb technicians have also discovered several large aerial bombs that they have not been able to identify.

Inthavongsy's colleagues hoist the rusted bomb into the back of a GPS-equipped Toyota pickup truck and head for a demolition site a few miles away. At the site, a remote jungle grove with a nearby protective log bunker, the crew follows a routine procedure to destroy the battered MK-81 bomb. Its goal is to avoid a so-called high-order detonation, in which the bomb explodes at full force. Instead the team will attempt to set off a low-order

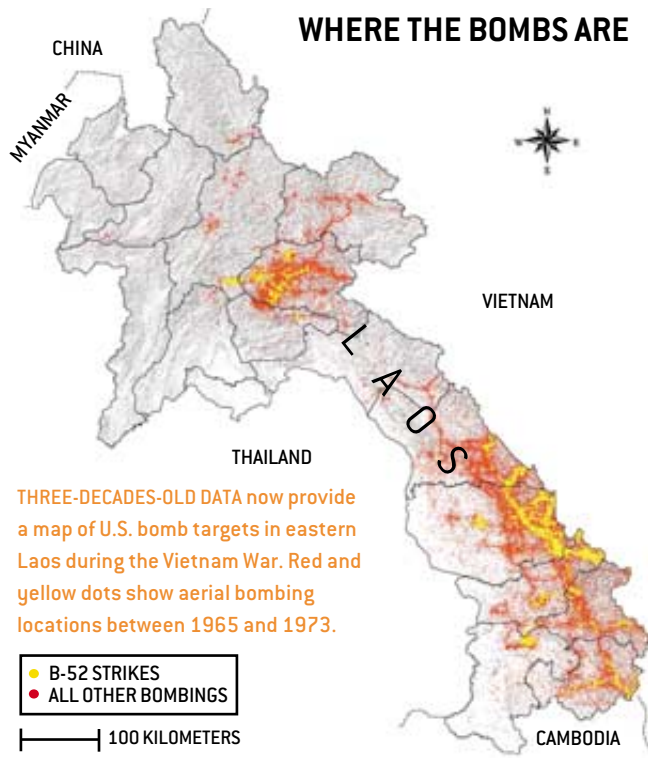
detonation that will quickly burn the bomb's contents and produce only a relatively small blast.

As a precaution, Inthavongsy clears the area of villagers and takes cover in a bunker in preparation for a bone-rattling blast that could still blow a five-foot hole in the ground.

To elicit a low-order explosion, the bomb technicians use a device dubbed a baldrick (named for a character on the British television program *Black Adder*, whose “cunning plan” for almost any problem involved a small explosive). The baldrick, a small aluminum tube crammed with 80 grams of plastic explosive and capped with a thin sheet of copper, pierces the outer casing of a bomb and ignites the plasterlike mixture of TNT and other explosive material inside. This action splits the bomb's casing and burns away its contents almost instantaneously, doing relatively little harm to the surrounding area. “The munition is usually attacked explosively from the outside using a charge sufficiently violent to cause a chemical reaction but not hard enough to cause [a high-order] detonation,” says Sidney Alford, a British explosives engineer who develops bomb disposal techniques used in Laos.

A member of Inthavongsy's team places the baldrick 80 millimeters from the bomb and inserts a blasting cap wired to an electrical switchbox in a faraway bunker. After a countdown by Inthavongsy, a zipping sound rings out from a hand-cranked switchbox as an electrical charge shoots down the wire and unleashes a thunderous boom. Pieces of shrapnel shriek through the air. Moments later Inthavongsy and her colleagues emerge from the bunker and return to the site. The demolition is successful. The ground is charred, and the grass flickers with small fires, but the area is largely intact.

—D.L.



MAP COURTESY OF MICHAEL SHEINKMAN

forts revealed another stratum to be excavated. “Once we got the data out, the data itself was encoded,” says Skip Jacobs, a government contractor who assisted Stanley in building the new database.

In 1996, almost four years after his search began, Stanley unearthed his Rosetta stone. In a vault at Hickam Air Force Base in Hawaii, where archival material from the war was stored, he found computer printouts with codes for Vietnam-era databases. “That helped us solve 85 to 90 percent of all the codes,” Stanley says. He and his colleagues funneled the data into a modern, searchable database.

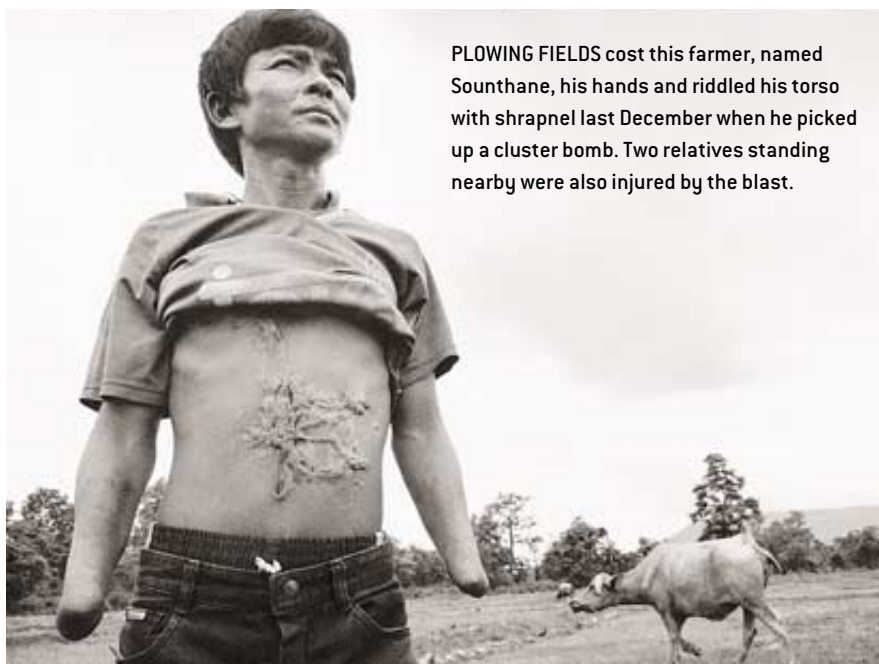
In the course of converting data, Stanley found what he calls “typos, hiccups and some plain wrong” information that may have made its way into the command chain during the war. For instance, the



“BOMBIE” is the most dangerous unexploded ordnance because of its small size and innocuous appearance. Millions landed on Laos.

AIM-4 Falcon, a 140-pound air-to-air missile, was mounted on U.S. aircraft, including the F-102 and F-4D/E, but the Combat Activities File database reports it was used on the F-100 and F-105, among others. Some errors may have been the result of poor data-entry techniques and inconsistent codes. “You’re still talking punch cards,” Jacobs says. “You’re talking key error or key entry errors that are in there.”

(An unexpected by-product of this research was a partial explanation for the 1998 reports by CNN and *Time* that contained erroneous information about a secret U.S. mission in Laos during the Vietnam War called Tailwind. The news agencies alleged that U.S. forces used deadly nerve-gas bombs against defectors in Laos. Stanley says the bomb code used in the report, CBU-15, temporarily stood for a standard cluster bomb but was also used



PLOWING FIELDS cost this farmer, named Souththane, his hands and riddled his torso with shrapnel last December when he picked up a cluster bomb. Two relatives standing nearby were also injured by the blast.

to denote an experimental gas bomb, the testing of which was halted in 1970.)

Stanley’s work attracted the attention of U.S. military officers in 1995, and the U.S. Humanitarian Demining Office went on to commission Management Support Technology to prepare the ongoing, large-scale study for use in Laos.

Deploying the Data

AT THE UXO LAO National Office in Vientiane, Sheinkman enters Stanley’s data into a geographic information system. The program plots as pink dots the target coordinates linked to the bombing database. The resulting maps are printed and used by bomb technicians equipped with handheld GPS units, which are capable of pinpointing coordinates on the ground via navigational satellites. The maps, which also include empirical data collected in the field, show bomb technicians what they might find as they scour villages and rice paddies. But they cannot determine

precisely what remains from the war. “We have no idea what exploded and what did not,” Sheinkman admits. And areas that look clear on the map could nonetheless be ridden with other types of explosives. Encouragingly, the data used so far have been accurate. “We’re finding [the bombs] pretty much where [the coordinates] say they are,” Jacobs says.

Although the bombing database has been used only in Laos—the country hit hardest by U.S. air strikes—data exist for Cambodia and Vietnam as well. A Vietnamese delegation visited the U.S. last year to discuss using the database.

Some commentators say it could take a century to clear Laos of its unexploded bombs. One UXO Lao adviser cites clearance projects in Europe, where bomb technicians still find unexploded ordnance from World War I. With Stanley’s historical detective work as a start, however, perhaps Laos may more swiftly end its fight against the ghosts of war. SA

MORE TO EXPLORE

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The Do-It-Yourself Supercomputer

By William W. Hargrove,
Forrest M. Hoffman and
Thomas Sterling

Photographs by Kay Chernush

CLUSTER OF PCs at the
Oak Ridge National
Laboratory in Tennessee
has been dubbed the
Stone SouperComputer.

FOCUS | NEXT-GENERATION SUPERCOMPUTERS

*This article is the second in a two-part series.
The first part, "How to Build a Hypercomputer," by
Thomas Sterling, appeared in the July 2001 issue.*

Computer

Scientists have found a cheaper way to solve tremendously difficult computational problems: connect ordinary PCs so that they can work together

IN THE WELL-KNOWN STONE SOUP FABLE, a wandering soldier stops at a poor village and says he will make soup by boiling a cauldron of water containing only a shiny stone. The townspeople are skeptical at first but soon bring small offerings: a head of cabbage, a bunch of carrots, a bit of beef. In the end, the cauldron is filled with enough hearty soup to feed everyone. The moral: cooperation can produce significant achievements, even from meager, seemingly insignificant contributions.

Researchers are now using a similar cooperative strategy to build supercomputers, the powerful machines that can perform billions of calculations in a second. Most conventional supercomputers employ parallel processing: they contain arrays of ultrafast microprocessors that work in tandem to solve complex problems such as forecasting the weather or simulating a nuclear explosion. Made by IBM, Cray and other computer vendors, the machines typically cost tens of millions of dollars—far too much for a research team with a modest budget. So over the past few years, scientists at national laboratories and universities have learned how to construct their own supercomputers by linking inexpensive PCs and writing software that allows these ordinary computers to tackle extraordinary problems.

In 1996 two of us (Hargrove and Hoffman) encountered such a problem in our work at Oak Ridge National Laboratory (ORNL) in Tennessee. We were trying to draw a national map of ecoregions, which are defined by environmental conditions: all areas with the same climate, landforms and soil characteristics fall into the same ecoregion. To create a high-resolution map of the continental U.S., we divided the country into 7.8 million square cells, each with an area of one square kilometer. For each cell we had to consider as many as 25 variables, ranging from average monthly precipitation to the nitrogen content of the soil. A single PC or workstation could not accomplish the task. We needed a parallel-processing supercomputer—and one that we could afford!

Our solution was to construct a com-

puting cluster using obsolete PCs that ORNL would have otherwise discarded. Dubbed the Stone SouperComputer because it was built essentially at no cost, our cluster of PCs was powerful enough to produce ecoregion maps of unprecedented detail. Other research groups have devised even more capable clusters that rival the performance of the world's best supercomputers at a mere fraction of their cost. This advantageous price-to-performance ratio has already attracted the attention of some corporations, which plan to use the clusters for such complex tasks as deciphering the human genome. In fact, the cluster concept

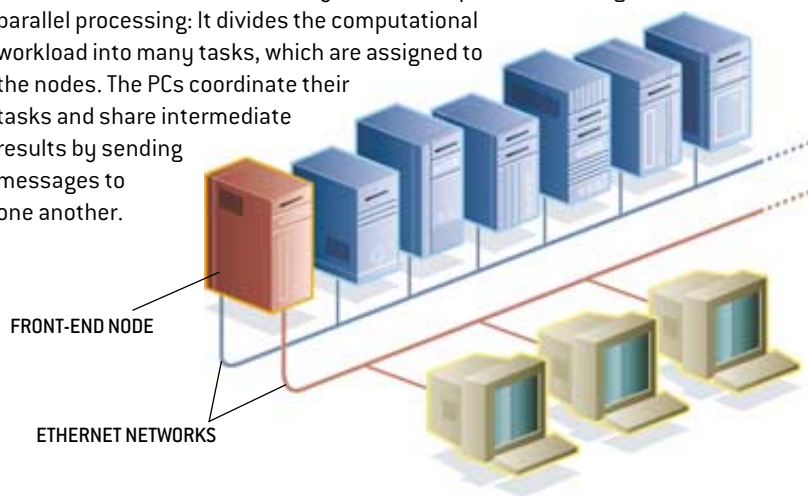
promises to revolutionize the computing field by offering tremendous processing power to any research group, school or business that wants it.

Beowulf and Grendel

THE NOTION OF LINKING computers together is not new. In the 1950s and 1960s the U.S. Air Force established a network of vacuum-tube computers called SAGE to guard against a Soviet nuclear attack. In the mid-1980s Digital Equipment Corporation coined the term “cluster” when it integrated its mid-range VAX minicomputers into larger systems. Networks of workstations—generally

A COMPUTING CLUSTER

The Stone SouperComputer at Oak Ridge National Laboratory consists of more than 130 PCs linked in a computing cluster. One of the machines serves as the front-end node for the cluster; it has two Ethernet cards, one for communicating with users and outside networks, and the other for talking with the rest of the nodes in the cluster. The system solves problems through parallel processing: It divides the computational workload into many tasks, which are assigned to the nodes. The PCs coordinate their tasks and share intermediate results by sending messages to one another.





less powerful than minicomputers but faster than PCs—soon became common at research institutions. By the early 1990s scientists began to consider building clusters of PCs, partly because their mass-produced microprocessors had become so inexpensive. What made the idea even more appealing was the falling cost of Ethernet, the dominant technology for connecting computers in local-area networks.

Advances in software also paved the way for PC clusters. In the 1980s Unix emerged as the dominant operating system for scientific and technical computing. Unfortunately, the operating systems for PCs lacked the power and flexibility of Unix. But in 1991 Finnish college student Linus Torvalds created Linux, a Unix-like operating system that ran on a PC. Torvalds made Linux available free of charge on the Internet, and soon hundreds of programmers began contributing improvements. Now wildly popular as an operating system for stand-alone computers, Linux is also ideal for clustered PCs.

The first PC cluster was born in 1994 at the NASA Goddard Space Flight Center. NASA had been searching for a cheaper way to solve the knotty computational problems typically encountered in earth and space science. The space agency needed a machine that could achieve one gigaflops—that is, perform a billion floating-

"CRASH CART" with a monitor and keyboard diagnoses problems with the Stone SouperComputer.

point operations per second. (A floating-point operation is equivalent to a simple calculation such as addition or multiplication.) At the time, however, commercial supercomputers with that level of performance cost about \$1 million, which was too expensive to be dedicated to a single group of researchers.

One of us (Sterling) decided to pursue the then radical concept of building a computing cluster from PCs. Sterling and his Goddard colleague Donald J. Becker connected 16 PCs, each containing an Intel 486 microprocessor, using Linux and a standard Ethernet network. For scientific applications, the PC cluster delivered sustained performance of 70 megaflops—that is, 70 million floating-point operations per second. Though modest by today's standards, this speed was not much lower than that of some smaller commercial supercomputers available at the time. And the cluster was built for only \$40,000, or about one tenth the price of a comparable commercial machine in 1994.

NASA researchers named their cluster Beowulf, after the lean, mean hero of medieval legend who defeated the giant monster Grendel by ripping off one of the creature's arms. Since then, the name has been widely adopted to refer to any low-cost cluster constructed from commercially available PCs. In 1996 two successors to the original Beowulf cluster appeared: Hyglac (built by researchers at the California Institute of Technology and the Jet Propulsion Laboratory) and Loki (constructed at Los Alamos National Laboratory). Each cluster integrated 16 Intel Pentium Pro microprocessors and showed sustained performance of over one gigaflops at a cost of less than \$50,000, thus satisfying NASA's original goal.

The Beowulf approach seemed to be the perfect computational solution to our problem of mapping the ecoregions of the U.S. A single workstation could handle the data for only a few states at most, and we couldn't assign different regions of the country to separate workstations—the en-

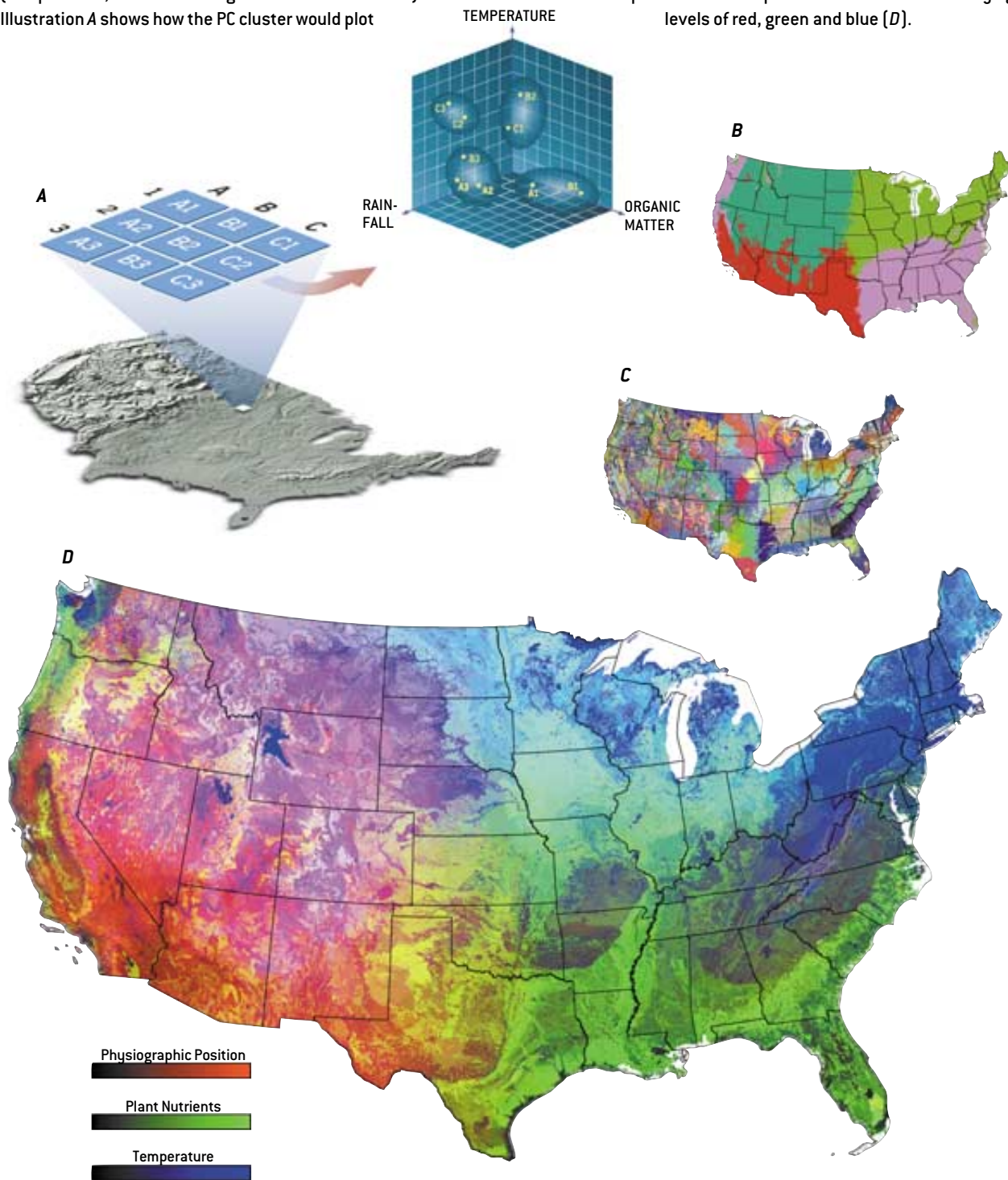
THE AUTHORS

WILLIAM W. HARGROVE, **FORREST M. HOFFMAN** and **THOMAS STERLING** are pioneers of Beowulf computing. Hargrove, who works in the computational physics and engineering division at Oak Ridge National Laboratory in Tennessee, is a landscape ecologist with big problems and too much data. Hoffman, a computer specialist in the environmental sciences division at ORNL, spends his spare time building supercomputers in his basement. Sterling, who created the first Beowulf cluster while at the NASA Goddard Space Flight Center, is at the California Institute of Technology's Center for Advanced Computing Research and is a principal scientist at the Jet Propulsion Laboratory.

MAKING MAPS WITH THE STONE SOUPERCOMPUTER

TO DRAW A MAP of the ecoregions in the continental U.S., the Stone SouperComputer compared 25 environmental characteristics of 7.8 million one-square-kilometer cells. As a simple example, consider the classification of nine cells based on only three characteristics (temperature, rainfall and organic matter in the soil). Illustration A shows how the PC cluster would plot

the cells in a three-dimensional data space and group them into four ecoregions. The four-region map divides the U.S. into recognizable zones (illustration B); a map dividing the country into 1,000 ecoregions provides far more detail (C). Another approach is to represent three composite characteristics with varying levels of red, green and blue (D).



ECOREGION MAPS COURTESY OF OAK RIDGE NATIONAL LABORATORY; SAMUEL VELASCO (illustrations)

vironmental data for every section of the country had to be compared and processed simultaneously. In other words, we needed a parallel-processing system. So in 1996 we wrote a proposal to buy 64 new PCs containing Pentium II microprocessors and construct a Beowulf-class supercomputer. Alas, this idea sounded implausible to the reviewers at ORNL, who turned down our proposal.

Undeterred, we devised an alternative plan. We knew that obsolete PCs at the U.S. Department of Energy complex at Oak Ridge were frequently replaced with newer models. The old PCs were advertised on an internal Web site and auctioned off as surplus equipment. A quick check revealed hundreds of outdated computers waiting to be discarded this way.

cation among the nodes and therefore can be solved very quickly by parallel-processing systems.

Anyone building a Beowulf cluster must make several decisions in designing the system. To connect the PCs, researchers can use either standard Ethernet networks or faster, specialized networks, such as Myrinet. Our lack of a budget dictated that we use Ethernet, which is free. We chose one PC to be the front-end node of the cluster and installed two Ethernet cards into the machine. One card was for communicating with outside users, and the other was for talking with the rest of the nodes, which would be linked in their own private network. The PCs coordinate their tasks by sending messages to one another. The two

disk, lots of memory or (best of all) an upgraded motherboard donated to us by accident? Often all we found was a tired old veteran with a fan choked with dust.

Our room at Oak Ridge turned into a morgue filled with the picked-over carcasses of dead PCs. Once we opened a machine, we recorded its contents on a “toe tag” to facilitate the extraction of its parts later on. We developed favorite and least favorite brands, models and cases and became adept at thwarting passwords left by previous owners. On average, we had to collect and process about five PCs to make one good node.

As each new node joined the cluster, we loaded the Linux operating system onto the machine. We soon figured out how to eliminate the need to install a key-

Our room at Oak Ridge **TURNED INTO A MORGUE** filled with the picked-over carcasses of dead PCs.

Perhaps we could build our Beowulf cluster from machines that we could collect and recycle free of charge. We commandeered a room at ORNL that had previously housed an ancient mainframe computer. Then we began collecting surplus PCs to create the Stone SouperComputer.

A Digital Chop Shop

THE STRATEGY BEHIND parallel computing is “divide and conquer.” A parallel-processing system divides a complex problem into smaller component tasks. The tasks are then assigned to the system’s nodes—for example, the PCs in a Beowulf cluster—which tackle the components simultaneously. The efficiency of parallel processing depends largely on the nature of the problem. An important consideration is how often the nodes must communicate to coordinate their work and to share intermediate results. Some problems must be divided into myriad minuscule tasks; because these fine-grained problems require frequent internode communication, they are not well suited for parallel processing. Coarse-grained problems, in contrast, can be divided into relatively large chunks. These problems do not require much communi-

most popular message-passing libraries are message-passing interface (MPI) and parallel virtual machine (PVM), which are both available at no cost on the Internet. We use both systems in the Stone SouperComputer.

Many Beowulf clusters are homogeneous, with all the PCs containing identical components and microprocessors. This uniformity simplifies the management and use of the cluster but is not an absolute requirement. Our Stone SouperComputer would have a mix of processor types and speeds because we intended to use whatever surplus equipment we could find. We began with PCs containing Intel 486 processors but later added only Pentium-based machines with at least 32 megabytes of RAM and 200 megabytes of hard-disk storage.

It was rare that machines met our minimum criteria on arrival; usually we had to combine the best components from several PCs. We set up the digital equivalent of an automobile thief’s chop shop for our cluster. Whenever we opened a machine, we felt the same anticipation that a child feels when opening a birthday present: Would the computer have a big

board or monitor for each node. We created mobile “crash carts” that could be wheeled over and plugged into an ailing node to determine what was wrong with it. Eventually someone who wanted space in our room bought us shelves to consolidate our collection of hardware. The Stone SouperComputer ran its first code in early 1997, and by May 2001 it contained 133 nodes, including 75 PCs with Intel 486 microprocessors, 53 faster Pentium-based machines and five still faster Alpha workstations, made by Compaq.

Upgrades to the Stone SouperComputer are straightforward: we replace the slowest nodes first. Each node runs a simple speed test every hour as part of the cluster’s routine housekeeping tasks. The ranking of the nodes by speed helps us to fine-tune our cluster. Unlike commercial machines, the performance of the Stone SouperComputer continually improves, because we have an endless supply of free upgrades.

Parallel Problem Solving

PARALLEL PROGRAMMING requires skill and creativity and may be more challenging than assembling the hardware of a Beowulf system. The most common



model for programming Beowulf clusters is a master-slave arrangement. In this model, one node acts as the master, directing the computations performed by one or more tiers of slave nodes. We run the same software on all the machines in the Stone SouperComputer, with separate sections of code devoted to the master and slave nodes. Each microprocessor in the cluster executes only the appropriate section. Programming errors can have dramatic effects, resulting in a digital train wreck as the crash of one node derails the others. Sorting through the wreckage to find the error can be difficult.

Another challenge is balancing the processing workload among the cluster's PCs. Because the Stone SouperComputer contains a variety of microprocessors with very different speeds, we cannot divide the workload evenly among the nodes: if we did so, the faster machines would sit idle for long periods as they waited for the slower machines to finish processing. Instead we developed a programming algorithm that allows the master node to send more data to the faster slave nodes as they complete their tasks. In this load-balancing arrangement, the faster PCs do most of the work, but the slower machines still contribute to the system's performance.

Our first step in solving the ecoregion mapping problem was to organize the

COMPUTING CLUSTER at the American Museum of Natural History in New York City contains 560 Pentium III microprocessors. Researchers use the system to study evolution and star formation.

enormous amount of data—the 25 environmental characteristics of the 7.8 million cells of the continental U.S. We created a 25-dimensional data space in which each dimension represented one of the variables (average temperature, precipitation, soil characteristics and so on). Then we identified each cell with the appropriate point in the data space [see *illustration A on page 76*]. Two points close to each other in this data space have, by definition, similar characteristics and thus are classified in the same ecoregion. Geographic proximity is not a factor in this kind of classification; for example, if two mountaintops have very similar environments, their points in the data space are very close to each other, even if the mountaintops are actually thousands of miles apart.

Once we organized the data, we had to specify the number of ecoregions that would be shown on the national map. The cluster of PCs gives each ecoregion an initial “seed position” in the data space. For each of the 7.8 million data points, the system determines the closest seed position and assigns the point to the corresponding ecoregion. Then the cluster finds the centroid for each ecoregion—the average position of all the points assigned to

the region. This centroid replaces the seed position as the defining point for the ecoregion. The cluster then repeats the procedure, reassigning the data points to ecoregions depending on their distances from the centroids. At the end of each iteration, new centroid positions are calculated for each ecoregion. The process continues until fewer than a specified number of data points change their ecoregion assignments. Then the classification is complete.

The mapping task is well suited for parallel processing because different nodes in the cluster can work independently on subsets of the 7.8 million data points. After each iteration the slave nodes send the results of their calculations to the master node, which averages the numbers from all the subsets to determine the new centroid positions for each ecoregion. The master node then sends this information back to the slave nodes for the next round of calculations. Parallel processing is also useful for selecting the best seed positions for the ecoregions at the very beginning of the procedure. We devised an algorithm that allows the nodes in the Stone SouperComputer to determine collectively the most widely dispersed data points, which are then chosen as the seed positions. If the cluster starts with well-dispersed seed

Above all, the Beowulf concept is an **EMPOWERING FORCE**.

positions, fewer iterations are needed to map the ecoregions.

The result of all our work was a series of maps of the continental U.S. showing each ecoregion in a different color [see illustrations B and C on page 76]. We produced maps showing the country divided into as few as four ecoregions and as many as 5,000. The maps with fewer ecoregions divided the country into recognizable zones—for example, the Rocky Mountain states and the desert Southwest. In contrast, the maps with thousands of ecoregions are far more complex than any previous classification of the country's environments. Because many plants and animals live in only one or two ecoregions, our maps may be useful to ecologists who study endangered species.

In our first maps the colors of the ecoregions were randomly assigned, but we later produced maps in which the colors of the ecoregions reflect the similarity of their respective environments. We statistically combined nine of the environmental variables into three composite characteristics, which we represented on the map with varying levels of red, green and blue. When the map is drawn this way, it shows gradations of color instead of sharp borders: the lush Southeast is mostly green, the cold Northeast is mainly blue, and the arid West is primarily red [see illustration D on page 76].

MORE TO EXPLORE

Cluster Computing: Linux Taken to the Extreme. F. M. Hoffman and W. W. Hargrove in *Linux Magazine*, Vol. 1, No. 1, pages 56–59; Spring 1999.

Using Multivariate Clustering to Characterize Ecoregion Borders. W. W. Hargrove and F. M. Hoffman in *Computers in Science and Engineering*, Vol. 1, No. 4, pages 18–25; July/August 1999.

How to Build a Beowulf: A Guide to the Implementation and Application of PC Clusters. Edited by T. Sterling, J. Salmon, D. J. Becker and D. F. Savarese. MIT Press, 1999.

More information about Beowulf computing can be found at the following Web sites:

stonesoup.esd.ornl.gov/
extremelinux.esd.ornl.gov/
www.beowulf.org/
www.cacr.caltech.edu/research/beowulf/
beowulf-underground.org/

Moreover, the Stone SouperComputer was able to show how the ecoregions in the U.S. would shift if there were nationwide changes in environmental conditions as a result of global warming. Using two projected climate scenarios developed by other research groups, we compared the current ecoregion map with the maps predicted for the year 2099. According to these projections, by the end of this century the environment in Pittsburgh will be more like that of present-day Atlanta, and conditions in Minneapolis will resemble those in present-day St. Louis.

The Future of Clusters

THE TRADITIONAL MEASURE of supercomputer performance is benchmark speed: how fast the system runs a standard program. As scientists, however, we prefer to focus on how well the system can handle practical applications. To evaluate the Stone SouperComputer, we fed the same ecoregion mapping problem to ORNL's Intel Paragon supercomputer shortly before it was retired. At one time, this machine was the laboratory's fastest, with a peak performance of 150 gigaflops. On a per-processor basis, the run time on the Paragon was essentially the same as that on the Stone SouperComputer. We have never officially clocked our cluster (we are loath to steal computing cycles from real work), but the system has a theoretical peak performance of about 1.2 gigaflops. Ingenuity in parallel algorithm design is more important than raw speed or capacity: in this young science, David and Goliath (or Beowulf and Grendel!) still compete on a level playing field.

The Beowulf trend has accelerated since we built the Stone SouperComputer. New clusters with exotic names—Grendel, Naegling, Megalon, Brahma, Avalon, Medusa and theHive, to mention just a few—have steadily raised the performance curve by delivering higher speeds at lower costs. As of last November, 28 clusters of PCs, workstations or servers were on the list of the world's 500 fastest computers. The LosLobos cluster at the University of New Mexico has 512 Intel Pen-

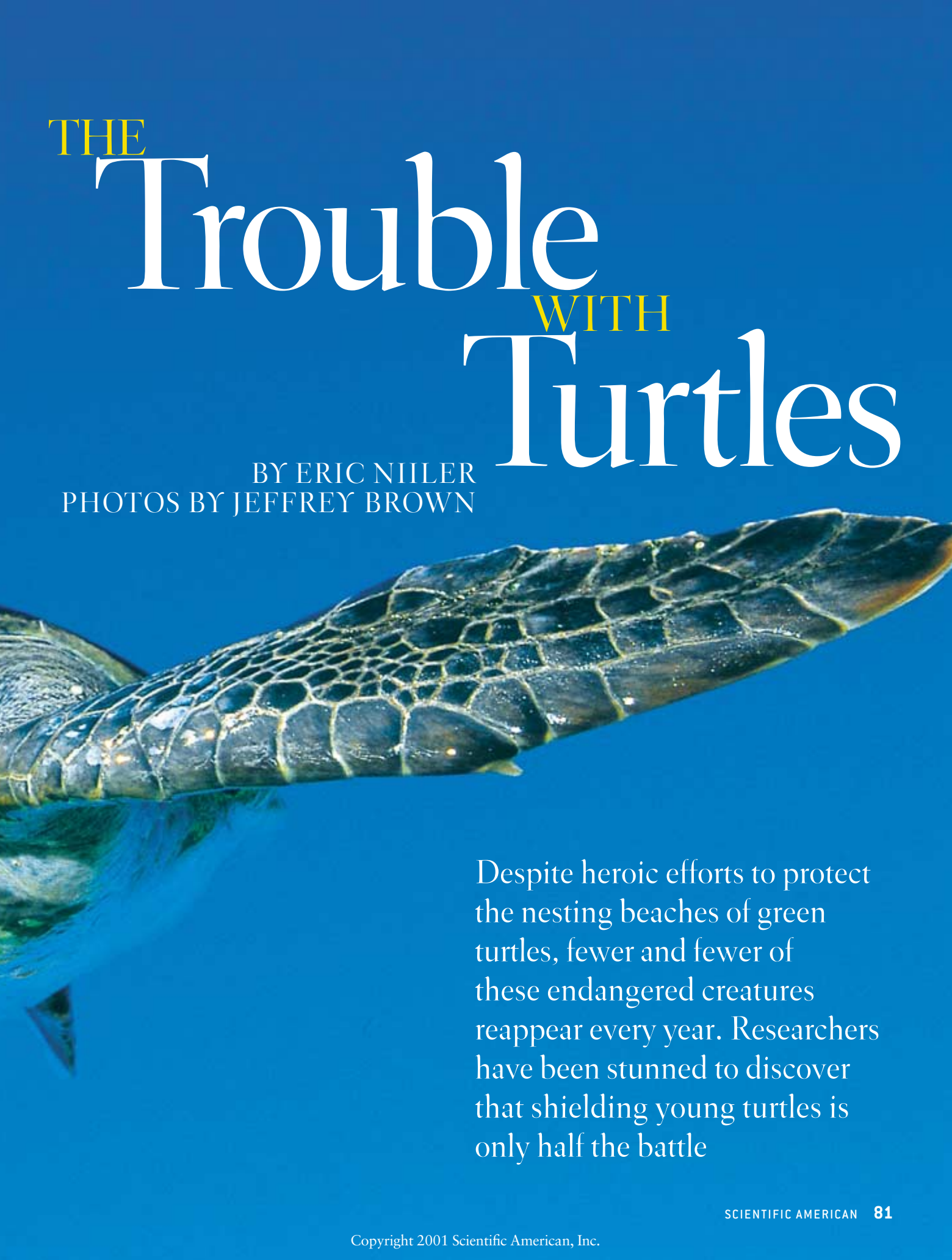
tium III processors and is the 80th-fastest system in the world, with a performance of 237 gigaflops. The Cplant cluster at Sandia National Laboratories has 580 Compaq Alpha processors and is ranked 84th. The National Science Foundation and the U.S. Department of Energy are planning to build even more advanced clusters that could operate in the teraflops range (one trillion floating-point operations per second), rivaling the speed of the fastest supercomputers on the planet.

Beowulf systems are also muscling their way into the corporate world. Major computer vendors are now selling clusters to businesses with large computational needs. IBM, for instance, is building a cluster of 1,250 servers for NuTec Sciences, a biotechnology firm that plans to use the system to identify disease-causing genes. An equally important trend is the development of networks of PCs that contribute their processing power to a collective task. An example is SETI@home, a project launched by researchers at the University of California at Berkeley who are analyzing deep-space radio signals for signs of intelligent life. SETI@home sends chunks of data over the Internet to more than three million PCs, which process the radio-signal data in their idle time. Some experts in the computer industry predict that researchers will eventually be able to tap into a "computational grid" that will work like a power grid: users will be able to obtain processing power just as easily as they now get electricity.

Above all, the Beowulf concept is an empowering force. It wrests high-level computing away from the privileged few and makes low-cost parallel-processing systems available to those with modest resources. Research groups, high schools, colleges or small businesses can build or buy their own Beowulf clusters, realizing the promise of a supercomputer in every basement. Should you decide to join the parallel-processing proletariat, please contact us through our Web site (<http://extremelinux.esd.ornl.gov/>) and tell us about your Beowulf-building experiences. We have found the Stone Soup to be hearty indeed. ■

EAST PACIFIC green turtle (*Chelonia mydas*) is one of five sea turtles that frequent the warm coastal lagoons of Mexico's Baja California. Biologist Wallace J. Nichols hoists a 55-pound green that will be tagged and released for further study.





THE
Trouble
WITH
Turtles

BY ERIC NIILER
PHOTOS BY JEFFREY BROWN

Despite heroic efforts to protect the nesting beaches of green turtles, fewer and fewer of these endangered creatures reappear every year. Researchers have been stunned to discover that shielding young turtles is only half the battle

PUERTO SAN CARLOS, MEXICO—

Here along the Pacific coast of Mexico's Baja California peninsula, a celebration—Easter, a birthday, the arrival of important guests—calls for a meal of *caguama*, or turtle. Locals also covet the animal's medicinal properties. The best-tasting, according to most, is the East Pacific green turtle (*Chelonia mydas*). But the green, one of five marine turtles in Pacific Mexico, is theoretically off limits. Killing them has been strictly prohibited by the U.S. Endangered Species Act since 1978 and by Mexican law since 1990.

Not relying solely on the law, every year scientists, volunteers and even army units camp out along green turtle nesting beaches in southern Mexico to block poachers and predators from snatching the eggs needed to produce new generations of the animals. Even so, the number of mature females returning to the green's primary nesting beach has plummeted from 1,280 in 1990 to 145 in 2000. Why are the turtles missing?

Researchers have known for decades that people in fishing communities occasionally eat the green turtle, but new research has only now revealed that this tradition is colluding with egg poaching to bring about the animal's devastating decline. Scientists at the Autonomous University of Baja California estimate that poachers kill as many as 30,000 green turtles every year in Baja. The study indicates that most of the demand for the turtles comes from the government sector—politicians, teachers and the military—those with cash to pay for the delicacy and positions of power to escape legal repercussions.

For some experts, the recent findings call into question the decades-old assumption that protection of turtle eggs and hatchlings is the best way to assure the animals' survival. Clearly, they say, the adults need better defending as well. Biologist Wallace J. Nichols, director of Wildcoast, a California-based conservation group, knows of poachers who have caught dozens of turtles and have been let go with a warning and confiscated catch. The last time a poacher went to jail was two years ago for only 12 days.



New research estimates
that as many as 30,000
green turtles are killed every year
by poachers in Baja.

AT ONE RESTAURANT in Puerto San Carlos, turtle is a specialty. The animal is butchered (*large photograph*), cleaned (*small photograph*), then cooked slowly for several hours to form a spicy stew. The final product can earn the restaurant owner a profit of more than \$400 for each turtle.



SOME OF THE INHABITANTS of Puerto San Carlos are trying to save the green turtle. Nichols and two fishermen helpers, Victor Meza and Juan Ramirez (*large photograph*), pull in a green turtle that was captured in a gill net (*small photograph*).

“I took life from the turtle,”
says a former fishing guide
turned conservationist.

“Now I want to give back.”





Nichols documents his findings in part by searching for turtle shells in town dumps and behind seafood restaurants. “The law is good,” he says, “but there’s no enforcement.”

And there is plenty of reason to hunt the animals. In the bustling community of Puerto San Carlos, a mature turtle is worth \$50 to \$200. That’s a powerful incentive to catch turtles instead of the seasonal harvest of yellowtail, snapper, corbinas, clams and crabs, which garner a fisherman a modest living for long hours of labor.

Some local residents are trying to change the situation. Adán Hernandez took the turtle cure when he was 14 years old: a glass of fresh blood collected directly from a turtle’s lopped-off flipper. He believes the concoction helped him grow from a scrawny, sickly kid into a healthy 25-year-old.

“I took life from the turtle,” says Hernandez, a former fishing guide now working with Nichols to spread the gospel of marine conservation in a town that often sees the marine reptiles as a reliable source of protein. “Now I want to give back. When I see a *caguama* in someone’s boat, I just go up to them and throw it back in the water. I know who is dangerous and who won’t do anything.”

Nichols, Hernandez and a few leaders of the fishing community are trying to establish a marine sanctuary in a nearby estuary, but the plan faces opposition from some political leaders—and is hardly likely to be endorsed by the poachers.

Given the cultural and political obstacles to stopping turtle harvesting, Nichols says his goals are modest. He tries to convince people to eat fewer turtles—say, five a year instead of 10—or perhaps to let the big reproductive females go free.

“It’s impossible to stop it,” Nichols says. “But you talk to people and agree that we both want turtles to be around in the future.”

San Diego-based freelance writer Eric Nüiler often reports on environmental issues in Baja California. For more information, see www.baja-tortugas.org

WORKING KNOWLEDGE

HUMAN-POWERED ELECTRONICS

Crank It Up!

Just shake the flashlight, and it shines. Crank the radio's handle, and it plays. Unlike earlier generations of human-powered electronics, which quit the instant you did, a new breed stores your muscle energy in springs, batteries and capacitors that provide lasting returns.

Freeplay Energy in London has sold more than 2.5 million hand-cranked radios and flashlights since 1995. In its original products, turning a crank wound a tight 33-foot steel ribbon, which slowly uncoiled. In its new line, the crank turns a mini transmission that drives an alternator to charge onboard batteries. Thirty seconds of human effort will yield 40 minutes of play or eight minutes of light, and the products will be one fifth the size and weight, addressing a primary consumer complaint: human-powered electronics tend to be big and heavy.

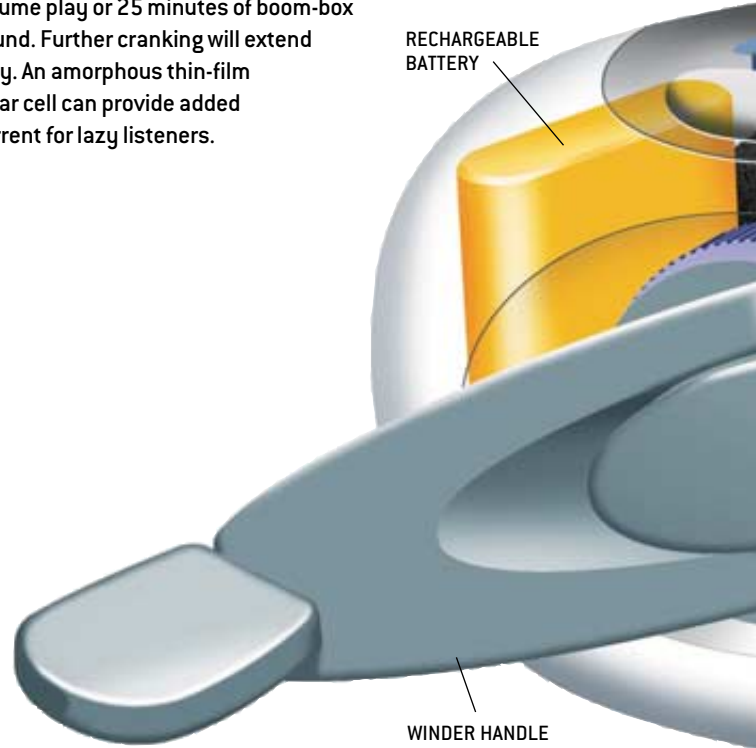
People buy human-powered electronics, which typically cost \$50 to \$80, because they're tired of spending money on batteries or because they want surety during storms or just because the gizmos are cool. But a mass market won't open "until prices drop to the \$29 range," says Vaughan Wiles, Freeplay's marketing director. New deals may help. This fall, outdoor-gear giant Coleman will sell a Freeplay flashlight under its brand name, as well as the radio. Freeplay also plans a hand-powered generator laden with electronics that can recharge certain popular cell phones. AladdinPower in Tampa markets a Step-charger that works like a foot pump to recharge cell-phone, laptop-computer and video-camera batteries.

Designing practical devices requires "very small, very strong, very efficient components that can produce power when an elderly woman turns the crank and yet can handle a tough guy cranking the thing like crazy," says Freeplay technical director John Hutchinson. Minimizing mechanical wear is also paramount. A number of start-up companies have jumped on the bandwagon, but some products simply don't work well. Ultimately, success depends on maximizing a user's reward. "If someone is stranded at sea, he'll crank all day" to keep his two-way radio working so he can be rescued, Hutchinson says. "But for the average guy in his garage, 60 seconds of effort is all he's willing to give."

—Mark Fischetti

TURNING THE CRANK

on Freeplay's Bravo AM/FM radio spins gears in a tiny transmission that drives an alternator. It sends current to a 3.6-volt nickel-metal hydride rechargeable battery. A 30-second wind of sufficient torque will provide 45 minutes of low-volume play or 25 minutes of boom-box sound. Further cranking will extend play. An amorphous thin-film solar cell can provide added current for lazy listeners.



WEARING

a Seiko Kinetic watch during daily activity provides enough motion to power its mechanism. When the watch is still, memory cells can keep time for four years.

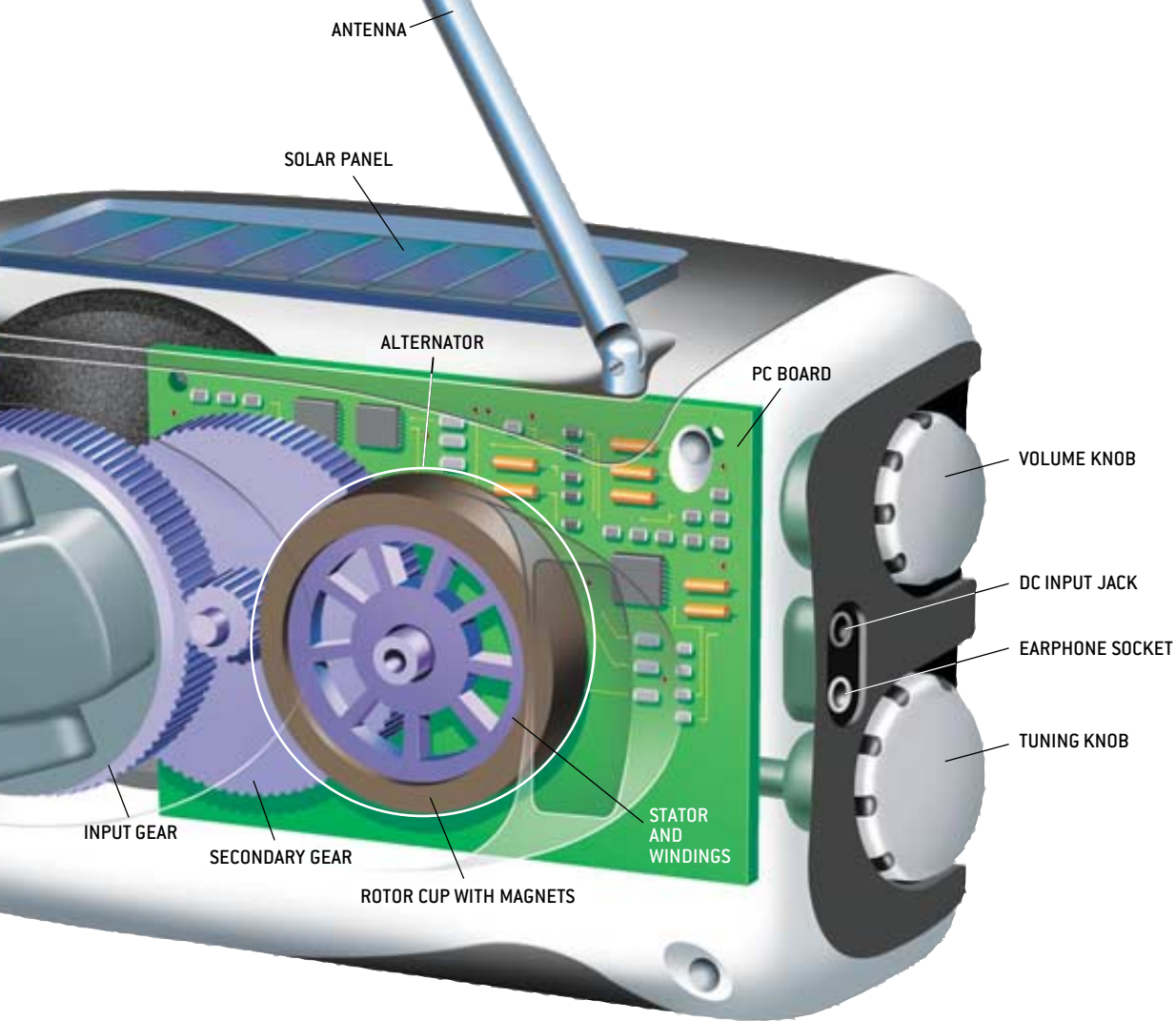


ILLUSTRATIONS BY GEORGE RETSECK

- > **KICK START** The Electric Shoe Company in Leicester, England, is investigating ways to charge small batteries during walking. One shoe under development has piezoelectric material in the sole, which generates a voltage every time it is compressed. Another shoe has a dynamo in the heel that creates current with every heel strike.
- > **HOT WATCH** Seiko's Thermic watch is powered by body heat. Your arm warms the back of the stainless-steel case, while the steel upper section assumes the temperature of the surrounding air. A polyarylate midsection insulates the layers and siphons tiny amounts of ener-

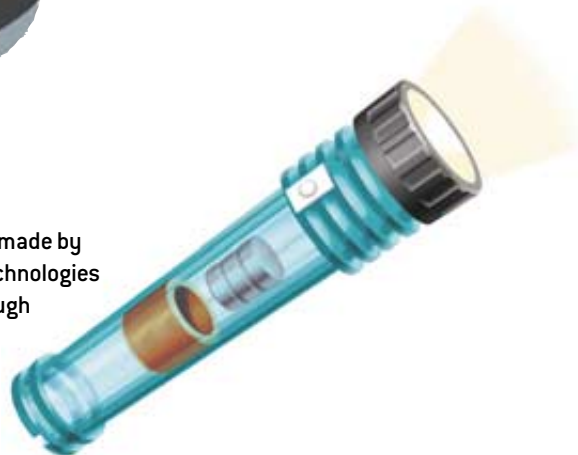
gy from the temperature gap, driving the timepiece.

- > **RELIEF** The Defense Advanced Research Projects Agency is studying many schemes to convert mechanical, thermal and chemical gradients into electrical energy that can lighten a soldier's battery load or power robotic vehicles and place-and-forget sensors. It is tinkering with everything from a boot's heel strike to chemical differences in ocean sediments. Then there's the urine-powered fuel cell: it would hydrolyze urea into carbon dioxide and ammonia and oxidize ammonia into nitrogen and water, providing the chemicals to create current.



SHAKING

a NightStar flashlight made by Applied Innovative Technologies moves a magnet through a wire coil, generating electrical energy stored in a capacitor.



Touchy-Feely Computing

A NEW MOUSE PICKS UP GOOD VIBRATIONS BY STEVE DITLEA

Imagine living with just two of your five senses: vision and hearing. That's the sensory-deprived state of personal computing today. PCs communicate with their users almost exclusively via images and sounds, ignoring all the other cues that humans rely on to perceive the world. Admittedly, interacting with your computer through the senses of smell and taste may not be absolutely essential. But now PC users can try the iFeel mouse, a device from peripherals manufacturer Logitech that adds the all-important sense of touch to desktop computing.

The human brain is exquisitely hardwired for touch. Anatomy textbooks often include a grotesque-looking diagram known as the homunculus, which distorts the human figure to show how much of the brain's sensory processing is devoted to each body part. Because large areas of the cortex interpret signals from the palms and fingers, the hands of the homunculus are enormous. This generous neural capacity allows us to sense minute variations in pressure and to detect barely perceptible vibrations, contributing to our remarkable dexterity.

Over the past two decades, computer scientists have struggled to build electro-mechanical contraptions that could provide the same kind of tactile feedback. The task has proved difficult: a touch-feedback peripheral must be small enough to fit in a hand, yet it must also offer substantial resistance to the hand's motion. In fact, accurately synthesizing tactile sensations in real time became possible only after recent advances in miniaturization and the introduction of faster microprocessors.



TOUCH-FEEDBACK MOUSE allows PC users to feel a virtual surface. As the user moves the cursor across the screen, a small motor in the mouse responds to software signals embedded in the program or Web page.

The first tactile devices to hit the market were designed for medical training. Doctors-to-be use the instruments to virtually feel the right way to perform a catheterization or a spinal injection. Engineers and architects employ similar devices for computer-assisted design, allowing them to “touch” the contours of their three-dimensional models. And for a few years now, computer gamers have been playing with force-feedback joysticks that can simulate a machine gun’s recoil or the stresses on an airplane’s controls. But no touch-feedback device for general-purpose computing was available until the introduction of the iFeel mouse last year.

The iFeel looks like an ordinary mouse (albeit one attractively finished in iridescent teal blue). And its retail price is modest—only \$10 more than a comparable mouse without touch feedback. There are two models available: a simple symmetrical design that sells for \$39 and a \$59 premium version that has a contoured shape intended to fit the hand more comfortably. Both are optical devices that detect movement with reflected light rather than with a less precise trackball.

At the pulsating heart of the new mouse is technology licensed from Immersion Corporation, which pioneered the development of touch-feedback sys-

tems in the 1990s. Louis Rosenberg, the company's chairman, says the key hardware component is a 25-gram motor that can move up and down, imparting about 150 grams of force against the user's hand. The mouse can also vibrate up to 300 times a second, enabling the device to reproduce a wide range of sensations. For example, Immersion's special-effects software library allows Web site developers to enhance pages with simulated textures such as corduroy or sandpaper. When the iFeel user drags the cursor across such a page, the mouse rapidly jiggles up and down, as if it were traveling over a rough surface.

Trying out the iFeel mouse for the first time can be disconcerting. The installation is straightforward: just plug this USB device into an appropriate computer port and load the driver software from a CD-ROM. (Mac users are out of luck; so far the mouse works only with Windows.) Once connected, the iFeel fundamentally alters one's perception of Windows' familiar screens. If you slide the cursor across one of the desktop program icons, the mouse shakes like dice in a cup. If you glide the mouse over the selections in a menu bar, it feels like a set of chattering false teeth. Push the iFeel back and forth over the options in a pull-down menu, and it hums like an electric shaver. The mouse also shakes up Web pages (iFeel works with either Explorer or Netscape, but Explorer must be installed on the computer even if you use only Netscape). The most noticeable sensation is the bump that occurs when the cursor crosses a hot link or menu choice.

For anyone accustomed to an inert mouse, such physical cues may be distracting. Because people have different thresholds for sensing force, Immersion's software developers have provided access to an onscreen control for adjusting the strength of the feedback. Another control allows you to choose a different set of sensations. In addition to the default setting (which simulates the feeling of tapping a wooden surface), the iFeel offers six oth-

er options: crisp, metallic, spongy, rubbery, steel drum and sonic vibe.

With continued use, something unexpected happens: the iFeel's twitching becomes an organic part of the computing experience. The mouse's motions provide

gentle reinforcement when one is steering the cursor to a desired point on the screen. In poorly designed Web pages crowded with text, the iFeel can make it easier to find and click on links to other sites. And when a program crashes, the mouse's pal-

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TECHNICALITIES



pable shudder is considerably less annoying than the audible “bonk” with which Windows signals an urgent error message.

Currently most of the creative uses for iFeel are game-related. With the help of Immersion’s special-effects library, the developers of computer games can simulate the jolt of an explosion, the recoil of a gun, the zing of a crossbow and even the hum of a light saber. A handful of Web pages have been modified to take advantage of the iFeel’s abilities, offering exotic effects such as lions roaring and auto engines starting. But these sites scarcely demonstrate the full potential of this technology.

The iFeel mouse can do much more than simply entertain. With touch feedback, for instance, it would be possible for a student to sense the forces at play while folding a molecule in an online biochemistry lesson. The iFeel could also



LOGITECH'S IFEEL MOUSE is only \$10 more expensive than a comparable mouse without touch feedback. An optical device, it detects movement with reflected light rather than with a trackball.

turn Web shopping into a hands-on experience by letting a customer feel, say, the texture of a tweed jacket offered for sale on an e-commerce site. At the moment, however, only one educational site (www.SprocketWorks.com) and one retailing site (www.Blab.com) offer tactile interaction. To convince more people to

buy touch-feedback devices, an enterprising company needs to develop a killer application—a can’t-live-without-it use for computerized touch.

Some people speculate that the first widespread use of tactile feedback might be erotic. A titillating Web site could conceivably attract quite a few customers by offering computer-mediated caresses. The self-appointed forces of decency can save their outrage for now, though; it will probably take a while for software designers to learn how to reproduce the touch of passionate flesh. But regardless of whether its applications are practical or prurient, the iFeel mouse seems to have real appeal for the homunculus in each of us. SA

Steve Ditlea is a freelance journalist who has been writing about personal computers since 1978.

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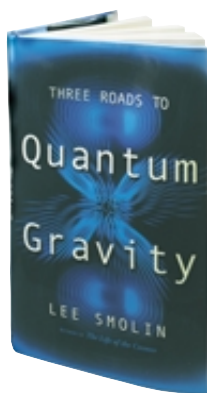
A Spin on Spin Foam

IN WHICH THE AUTHOR TAKES US TO THE CUTTING EDGE OF THE SEARCH FOR AN ULTIMATE THEORY OF REALITY BY CHET RAYMO

THREE ROADS TO QUANTUM GRAVITY

by Lee Smolin

Basic Books, New York, 2001 [\$24]



A colleague of mine, an expert on the foundations of quantum mechanics, recently gave a public lecture at our college called “Quantum Mechanics for Everyone.” Afterward, another colleague, not a scientist, said of the talk: “I understood, but I’m not sure *what* I understood.” Many readers of Lee Smolin’s *Three Roads to Quantum Gravity*

may have the same reaction.

Smolin, professor of physics at Pennsylvania State University, succeeds at giving us what reviews of similar books have called “an illusion of understanding.” We read his description of the cutting-edge search for an ultimate theory of reality, we take aboard his metaphors,

we digest his anecdotes, and we have a feeling that we understand what he is talking about. Even that is a triumph—for us and for Smolin. The subject of this book is so highly abstract, and so far removed from ordinary experience, that an illusion of understanding is perhaps the best we can hope for.

Only a few hundred people in the world may understand the intricacies of loop quantum gravity, Smolin’s particular line of research, and I will confess that I am not one of them. Nevertheless, I am grateful that he has taken the time from his science to write this engaging popularization, for, as he rightly supposes, there are many of us who want to *think* we know what’s going on. It would be hard to imagine a better guide to this difficult subject.

The first half of the 20th century saw the invention of two highly successful theories

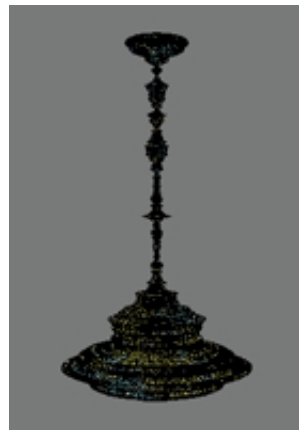
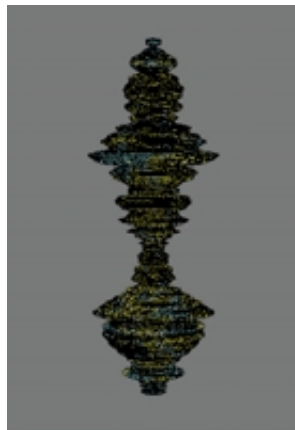
for describing the world: quantum mechanics and general relativity (gravity). Each theory reigns supreme in its domain of application: quantum theory on the scale of elementary particles, relativity on the cosmic scale. Only occasionally, as in discussions of black holes, do the two theories rub against each other.

The rubbing can be abrasive. Quantum theory radicalizes our assumptions about the relationship between observer and observed but pretty much buys into Newton’s ideas of space and time. General relativity changes our notions of space and time but accepts Newton’s view of observer and observed. This situation is deemed unacceptable by most physicists, and the race is on to find a unifying theory of quantum gravity, sometimes called a Theory of Everything.

Smolin describes the three most promising approaches to such a theory, all of

QUANTUM UNIVERSE doing its foamy thing. (From “Simulation of Lorentzian 2d Quantum Gravity,” by J. Ambjorn, K. N. Anagnostopoulos and R. Loll; www.nbi.dk/~ambjorn/lqg2/)

BETH PHILLIPS (above)



REVIEWS

which operate on the so-called Planck scale of reality, 20 orders of magnitude smaller than the atomic nucleus.

One approach applies thermodynamics and information theory to black holes. Another is string theory, which proposes that the ultimate elements of reality are vibrating linear mathematical entities existing (in one version of the theory) in nine spatial dimensions that give rise in their various states of excitation to the elementary particles. Smolin pushes hard for a third approach, which involves something called quantum loops—quantized elements of spacetime that in their shimmerings evoke everything else, perhaps even strings.

Quantum loop theory proposes that spacetime is a kind of “spin foam,” a pure geometry of Planck-scale loops and nodes, that in its “knots, links and kinks” spins

out a universe. A note in the book led me to a Web site [see illustration on preceding page] where one can view a quantum universe of one space and one time dimension doing its foamy thing. The prospect is exhilarating that behind the world of our senses this ceaseless Planck-scale fandango is going on.

All roads to quantum gravity, when they have battered their way to a common vision, will probably suggest that space and time, like matter and energy, come in quantized, indivisible units and that relationships, rather than things, are the fundamental elements of reality. Alas, it is difficult to conceive how any such theory of quantum gravity can be tested with present technology, although Smolin is confident it will happen.

Readers will perhaps best enjoy the first chapters of the book, where the au-

thor neatly lays out the philosophical principles that guide the search, and the penultimate chapter, where he explores how quantum gravity relates to our understanding of ourselves and God.

Are books like this one, which the typical reader will only partly understand, useful? Absolutely. Quantum gravity theorists may be engaged in the modern equivalent of calculating how many angels can dance on the head of a pin, but we shouldn't forget that some of the best minds of our species once pondered the properties of celestial spirits. It may be that practicing with angels helped to prepare our collective imaginations for quantum loops. SA

Chet Raymo teaches at Stonehill College in Massachusetts and writes a science column for the Boston Globe.

THE EDITORS RECOMMEND

THE SEVEN SINS OF MEMORY: HOW THE MIND FORGETS AND REMEMBERS

by Daniel L. Schacter. Houghton Mifflin Company, Boston, 2001 (\$25)

You've put your glasses down somewhere, and now you can't find them. That is the memory's sin of absent-mindedness. Schacter, chairman of the psychology department at Harvard University, cites that and six other sins of memory: transience, the weakening of memory over time; blocking, the inability to recall a familiar name or fact; misattribution, in which one assigns an item of memory to the wrong source; suggestibility, the implanting of memories through leading questions; bias, the unconscious reshaping of a memory under the influence of later events or opinions; and persistence, the repeated recall of disturbing information or events that one would prefer to forget. Do these aberrations serve a useful function? Yes, Schacter says, they protect against overload, helping the memory "to retain information that is most likely to be needed in the environment in which it operates."



FLATTERLAND: LIKE FLATLAND ONLY MORE SO

by Ian Stewart. Perseus Publishing, Cambridge, Mass., 2001 (\$25)

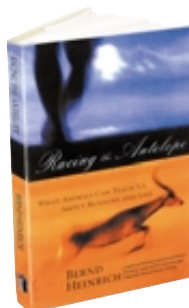
Flatland, published in 1884, portrayed a two-dimensional world in which women were lines and men were polygons. The author was A. Square, a pseudonym of British headmaster and Shakespearean scholar Edwin Abbott Abbott. His aim was to show the inhabitants of our three-dimensional world that there could be a fourth dimension—time—as strange to them as three dimensions were to the inhabitants of Flatland. Stewart, professor of mathematics at the University of Warwick in England and conductor until this year of the Mathematical Recreations department in these pages, wants to show the inhabitants of Planiturth—the three-dimensional world—that there is a Mathiverse with all conceivable "Spaces and Times." And so one reads of wormholes, cosmic strings, multiple universes and branes, among other wonders, in a presentation that is as entertaining as it is enlightening.



RACING THE ANTELOPE: WHAT ANIMALS CAN TEACH US ABOUT RUNNING AND LIFE

by Bernd Heinrich. Cliff Street Books (HarperCollins Publishers), New York, 2001 (\$23)

Zoologist Heinrich is also what many people would regard as a superhuman runner. In 1981, at the age of 41, he set a record of 6:38:21 for the North American 100-kilometer race. Here, among other things, he tells the story of that grueling race and his preparations for it. The other things include the physiology of running and analyses of what makes certain animals noteworthy for speed or endurance—among them pronghorn antelopes, migrating birds and camels, "which show us how to handle an oversupply of heat with an undersupply of water." Now, along with his work as professor of zoology at the University of Vermont, he has begun "a new training regimen, to try for some age-group (over sixty) records."



All the books reviewed are available for purchase through www.sciam.com

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The Delphi Flip BY DENNIS E. SHASHA

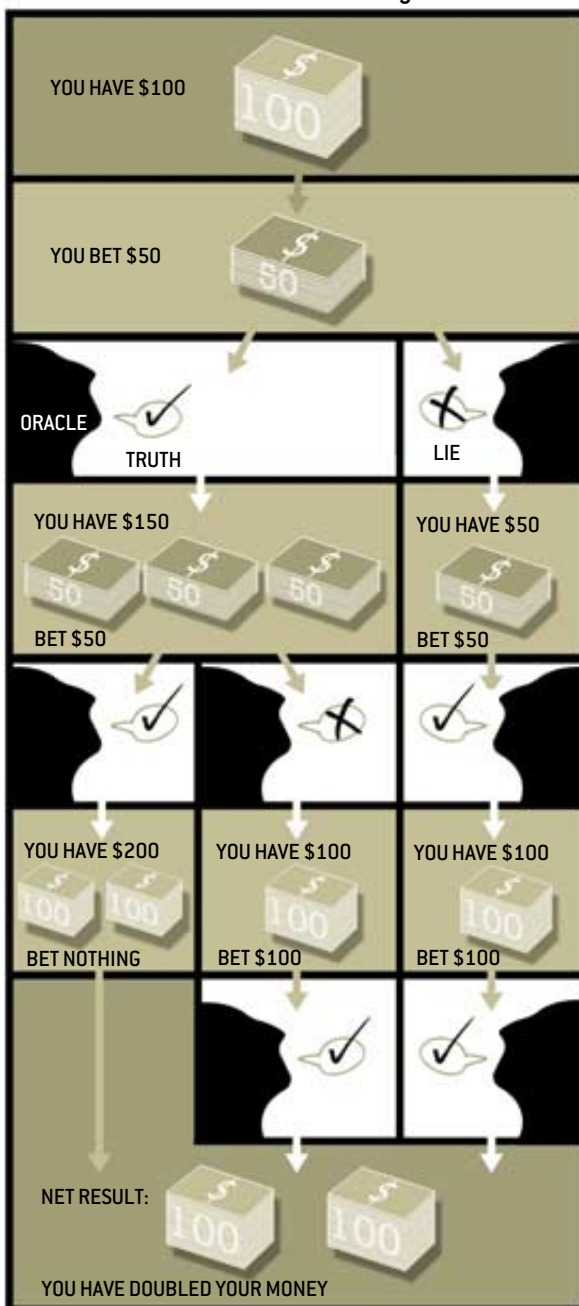
Predicting the future accurately is most useful in betting games—the stock market comes to mind. Unfortunately, perfect oracles are hard to come by (the stock market comes to mind, again). This puzzle considers how to take advantage of the flaky oracles one is likely to find.

You have \$100 to start with and 10 bets to make. Each bet turns on the result of a coin flip. The oracle will tell you which way the coin will fall but may lie on just one occasion and may do so after seeing your bet for that flip. You can find a counterparty who will give you even odds on any bet you make, so placing an x -dollar bet means he will return $2x$ dollars to you if the oracle tells the truth and will pocket your bet if the oracle lies. How do you end up with the greatest possible final amount, no matter when the oracle chooses to lie?

Here is a second problem: suppose you have to decide the amount of all your bets in advance without knowing when the oracle will lie. What should your bets be in that case, and what final amount can you be sure to get no matter when (and if) the oracle chooses to lie? Just one more thing: you lose everything if you plan to make a bet on a particular move but end up having too little money at that time.

Warm-up for the first problem: Suppose there are three flips and at most one lie. You have \$100. How much should you bet the first time? Given the outcome, how much should you bet the second and third times? The figure shows some good alternatives.

WARM-UP PUZZLE: How much should you bet?



Answer to Last Month's Puzzle

For a circle with a radius of 10 centimeters or more, any pattern of red and blue must satisfy the 10-centimeter bicolouration condition. Here's the proof: Consider two points in the circle— R (which is red) and B (which is blue)—that are between 10 and 20 centimeters apart (for the proof that two such points must exist, see the Puzzling Adventures page at www.sciam.com). Draw circles with a radius of 10 centimeters around each point. These circles must intersect at one or two points, and at least one of these points must lie within the original circle. Label this point Q .

If Q is red, then the line segment $B-Q$ is 10 centimeters long and bicolored. If Q is blue, then the segment $R-Q$ is 10 centimeters long and bicolored. Either way the pattern satisfies the 10-centimeter rule.

Web Solution

For a peek at the answer to this month's problem, visit www.sciam.com



And the Winner Really Is . . .

THE BEST YEARS OF THEIR LIVES MAY BE OSCAR WINNERS' EXTRA ONES, AS THEY SLOW DOWN THE JOURNEY FROM HERE TO ETERNITY BY STEVE MIRSKY

At the annual Oscars ceremony, the presenters in recent years have avoided saying, "And the winner is" in favor of "And the Oscar goes to." This way the other four poor nominees allegedly aren't losers. Except that everyone knows that the *Gladiator* guy, Russell Crowe, won for best actor this year and the other four guys lost, and if you need proof that what they did was lose, try to name them. (If you guessed Tom Hanks, well, yes, but that's pretty much a given.) Anyway, if the competition for an Oscar has been cutthroat up until now, wait until next year: according to new research, winning an Academy Award for acting gets you a little statue for your mantel plus about four extra years of life in which to savor the victory.

Donald A. Redelmeier and Sheldon M. Singh, whose report "Survival in Academy Award-Winning Actors and Actresses" appeared in the May 15 issue of *Annals of Internal Medicine*, thought that examining the Oscars would be an innovative way to see how social status and health are intertwined. "We are trying to take advantage of these high-profile performers," Redelmeier says, "to make a much more serious point that is relevant to every person in society—namely, that social factors have a major influence on a person's health."

(Redelmeier, an epidemiologist whose affiliations include a professorship in medicine at the University of Toronto, was probably best known before this star turn as the man who took the cell phone

out of your hand in the car. His 1997 *New England Journal of Medicine* investigation found that yapping while driving makes for about a fourfold increase in the risk of crashing.)

The Academy Award study subjects included all 762 actors and actresses ever nominated for a leading or supporting

category catches Lorne Greene, who was a chemical engineering student before coming to his senses.

The researchers analyzed the data in multiple ways to make sure that winning an Oscar led to increased longevity and not the other way around. Satisfied that they were looking in the right direction, they determined that Oscar winners live 3.9 years longer than members of the other two groups. (Shirley MacLaine can presumably divvy up the time over her next few lives.) Nominees who don't win live no longer than those never nominated. Apparently, it is "an honor just to be nominated," and it is *just* an honor to be nominated.

The 3.9 years to the victors is an even more astounding statistic than it may at first seem. "For perspective," Redelmeier says, "if you were to cure all cancers in all people for all time for all of North America, you add only about 3.5 years to life expectancy." And if you win additional Oscars, you get another two years.

Perhaps the Oscar winner has more help keeping healthy, in the form of personal trainers, chefs, nannies and managers. Whatever the underlying factors, winning an Oscar today is a bigger deal than ever. The first awards ceremony, in 1929, took place in a hotel banquet room; the latest one was watched by perhaps a billion television viewers, who saw Julia Roberts cop the prize for best actress. Dentures may eventually stand in for her teeth, but that smile looks like it's going to get flashed across movie screens for a long, long time.



Oscar. Another 887 non-nominees who appeared in the same films and were about the same age acted, in some of their best work, as controls. Redelmeier divided the entire cohort into three groups. "Winners" include 94-year-old Katharine Hepburn (a record four Oscars), who we sincerely hope is still alive when this issue hits the stands. Among the "nominees" is Robert Downey, Jr., about whom we can say the same thing. The "controls" cate-

Why doesn't stainless steel rust?


—NANCY AVERY, NEW LONDON, CONN.

Metallurgical engineer Michael L. Free of the University of Utah offers this explanation:

Because of its durability and aesthetic appeal, stainless steel is used in a wide variety of products, ranging from eating utensils to bank vaults to kitchen sinks. This form of steel remains stainless, or does not rust, because of the interaction between its alloying elements and the environment. Stainless steel contains iron, chromium, manganese, silicon, carbon and, in many cases, significant amounts of nickel and molybdenum. These elements react with oxygen from water and air to produce a very thin, stable film that consists of such corrosion products as metal oxides and hydroxides. Chromium plays a dominant role in reacting with oxygen to form this film. In fact, all stainless steels by definition contain at least 10 percent chromium.

This stable film prevents additional corrosion by acting as a barrier that limits the access of oxygen and water to the underlying metal surface. Because the film forms so readily and tightly, even just a few atomic layers of the material reduce the rate of corrosion to very low levels. The film is much thinner than the wavelength of visible light, and so it is difficult to see without the aid of modern instruments. Thus, although the steel is in fact corroded at the atomic level, it appears stainless to the unaided eye. Common inexpensive steel, in contrast, reacts with oxygen from water to form a relatively unstable iron oxide/hydroxide film that continues to grow with time and exposure to water and air. As such, this film, otherwise known as rust, achieves sufficient thickness to be easily observable soon after exposure to water and air.



In summary, because it is sufficiently reactive to protect itself from further attack by forming a passive corrosion product layer, stainless steel does not rust. Important met-

als such as titanium and aluminum also rely on passive film formation for their corrosion resistance. 

For the complete text of this answer and many others, visit Ask the Experts (www.sciam.com/askexpert).



WHY NEWTON GOT THE CREDIT.

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