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SCIENTIFIC AMERICAN

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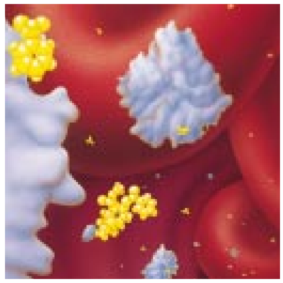
ASTRONOMERS SPOT OVERLOOKED SPIRALS THAT DWARF THE MILKY WAY

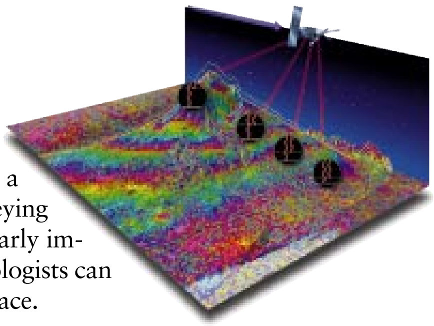
Animal experimentation: the debate continues

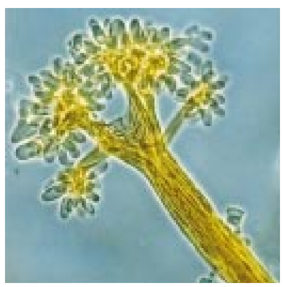
SCIENTIFIC AMERICAN

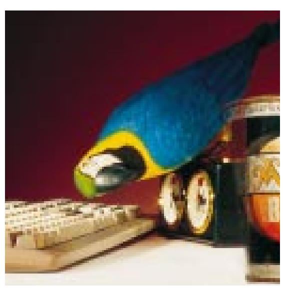
February 1997 Volume 276 Number 2

NEWS AND ANALYSIS









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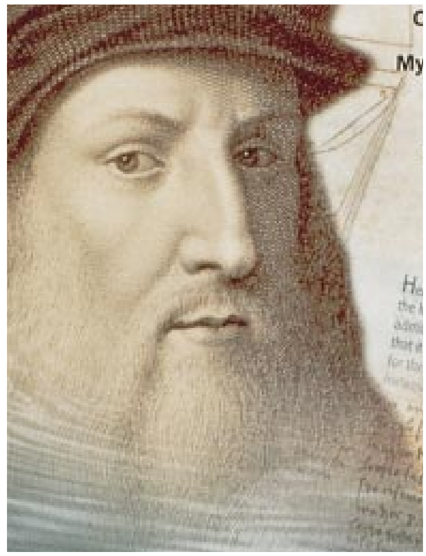
REVIEWS AND COMMENTARIES



About the Cover
Laboratory rats are used by the millions at research centers around the world, along with mice, rabbits, cats, dogs, primates and other species. Are good science and humane practices incompatible? Photograph by Christopher Burke, Quesada/Burke Studios, N.Y.

FROM THE EDITORS

The Animal Question

Some readers, on first seeing our cover story, will think they smell a rat, and not just the one pictured. Researchers may fear that *Scientific American* is giving comfort to the enemy, the animal-rights protesters trying to turn laboratories upside down. Animal welfarists, on the other hand, may assume our coverage will be a biased slam dunk of their arguments. I'm not in the business of disappointing readers, but those are two sets of expectations that won't be met here.

Unfortunately, as our staff writer Madhusree Mukerjee points out in her overview beginning on page 86, it is the polarization of opinions on the experimental use of animals that has often discouraged a reasoned search for a middle ground. We have tried to present some of those divergent views, as well as the efforts at compromise. Some of the ideas expressed here are far from those of the editors, but we are presenting them because one function of this magazine is to be a forum for debate on scientific topics.

JASON GOLTZ

"WHAT HUMANE LIMITS should be on scientific curiosity?"

In my opinion, the arguments for banning experiments on animals—that there are empirically and morally superior alternatives—are unpersuasive. And even some of the moral philosophies favoring reduced use of animals offer little in the way of real guidance. Utilitarians, for instance, ask that the suffering of animals be counterbalanced with good results. But that principle is unmanageably subjective and may even be prejudiced against research realities. The short-term benefits of most experiments are virtually nil, and the long-term benefits are incalculable. How do we enter them in a utilitarian ledger? Does increasing the sum of human knowledge count as a good?

The conflict between animal welfarists and scientists is not just one of differing moral philosophies. Higher animal care costs constrain research budgets and make some investigations unaffordable—and not always the ones that the welfarists would like to see disappear.

The question inevitably revolves back to, What humane limits should we impose on the exercise of our scientific curiosity? Researchers around the world ask and answer that for themselves every day. Their answers may not be perfect, but in general, they are neither ignorant nor willfully bad. Scientists should have the humility to recognize, however, that outsiders have often forced them to reexamine questions of animal welfare they might not otherwise have considered. The debate on animal rights may be frustrating and endless, but it may be constructive after all.

John Rennie

JOHN RENNIE, *Editor in Chief*
editors@sciam.com

WELFARE REFORM

I am always sorry to see SCIENTIFIC AMERICAN stray from science into politics, as you did in October 1996 with the article "Single Mothers and Welfare," by Ellen L. Bassuk, Angela Browne and John C. Buckner. You are not very good at it, which perhaps is not surprising, since scientists are not in general any better at such issues than anyone else. There is no reason, though, why people with credentials in psychiatry and psychology should not say something sensible about welfare economics. But when an article is obviously a tendentious piece of political pleading, you should at least attempt to solicit some contrary remarks from actual economists.

KELLEY L. ROSS
Los Angeles Valley College

I read "Single Mothers and Welfare" with great interest because I spent seven years as a social worker in a public welfare agency in Alabama. I left the field of social work, however, because of a profound sense of disillusionment with the welfare system. One problem I never see addressed is that welfare bureaucracies actually benefit from having unsuccessful clients. If a caseworker gets her clients to find jobs and become self-supporting, she works herself out of a job. The authors of the study—who reveal their own bias against the recent welfare bill, labeling it "draconian"—fail to address the problems with a system that encourages self-destructive behavior and a bureaucracy that requires more clients so it can exist and grow.

KATHERINE OWEN WATSON
Vestavia Hills, Ala.

Bassuk, Browne and Buckner ignore the real inroads states such as Massachusetts, Wisconsin, Indiana and Oklahoma have made in reducing welfare dependency by limiting the time over which they will pay benefits. We have done a terrible disservice to welfare recipients by allowing them to become dependent on a monthly check and expecting nothing in return. I hope those days are over.

WILLIAM D. STEPANEK
Mahopac, N.Y.

Bassuk and Buckner reply:

The economist David Ellwood once observed that "everyone hates welfare." Even so, extremely poor mothers and children cannot be left scrambling to survive without a safety net. We support welfare reform, but sadly, reform has typically been based on stereotypes and myths, rather than rigorously collected information about the realities of life for poor women and children. We have attempted to fill the gap in empirical knowledge with our epidemiological study. Although issues such as welfare cannot be addressed without discussing values, that does not diminish the scientific rigor of our study or the critical need for relevant research about social issues.

We agree that bureaucracies tend to be self-interested and paradoxically at odds with those they serve. Sometimes, as with welfare, the only solution is to overhaul the system. Unfortunately, states have not evaluated the effects of current reforms. Our home state of Massachusetts, for example, has been touted for reducing its welfare rolls by 10,000, but no one knows what has happened to these people; certainly, not all of them are working.


PAUL FUSCO *Magnum*

MOTHERS AND CHILDREN wait in line for lunch vouchers.

ALTERNATIVE VIEWS

Gary Stix's profile of Wayne B. Jonas and the Office of Alternative Medicine ["Probing Medicine's Outer Reaches," News and Analysis, October 1996] was colored by the prejudice often advanced against homeopathy in the U.S., which stands in contrast to more accepting attitudes in Europe. Stix chose to describe the OAM in the peculiar American landscape of personal energy, harmonic resonance, assorted nostrums, potions and electromagnetic-field generators. There is no doubt that the range of therapies within alternative medicine strains credulity, but recognizing those therapies that have been assessed by published clinical trials is a simple way to cut through this complexity.

NORMAN K. GRANT
Michigan Technological University

Congratulations for your objective appraisal of alternative medicine and the director of the OAM. The terms "alternative" and "complementary" themselves are obscurations meant to suggest that unproved treatments are acceptable in place of standard medical care. Those of us on the front lines of medicine have seen the results of uncritical public acceptance of appealing but unproved claims.

EDWARD H. DAVIS
Professor Emeritus,
College of Medicine
State University of New York
at Brooklyn

MINIATURE MICROBES

In the story by Corey S. Powell and W. Wayt Gibbs discussing the possibility that fossilized bacteria may have been found in a meteorite from Mars ["Bugs in the Data?" News and Analysis, October 1996], Carl R. Woese is quoted as saying, "These structures contain one one-thousandth the volume of the smallest terrestrial bacteria." He expresses doubt that anything so small could possibly be alive. But in another article in the same issue, "Microbes Deep inside the Earth," James K. Fredrickson and Tullis C. Onstott explain that when water or other nutrients are in short supply, bacteria stay alive by shrinking to one one-thousandth of their normal volume and lowering their metabolism. Could the shrinkage of such subterranean bacteria provide a model for the very small size of the alleged Martian bacteria?

LES J. LEIBOW
Fair Lawn, N.J.

Letters selected for publication may be edited for length and clarity.

50, 100 AND 150 YEARS AGO

SCIENTIFIC AMERICAN

FEBRUARY 1947

"Uranium metal could be used as an international monetary standard to replace the silver and gold that have traditionally set the world's standards of values. Atomic fission can convert a part at least of any mass of uranium directly into energy, and energy, the ability to do work, is suggested as a far more logical basis of economic value than any possessed by the precious metals. Uranium's hardness and the ease with which it oxidizes preclude its use in actual coins. However, the various proposals for international control of fissionable materials might lend themselves to an international paper currency backed by centrally controlled uranium metal."

"Chemists have finally succeeded in taming fluorine, the most unruly of the elements. The first commercial fluorine plastic is a polymer of tetrafluoroethylene—a translucent, waxy white plastic, stable up to 250 degrees Centigrade. The chemical resistance of Teflon, as the material is called, is outstanding. Because of its cost, however, the field for Teflon is limited. In addition to its use in electrical equipment, it will very likely find applications in the chemical industry as a gasket and as chemically inert tubing."

Snow-melting machine in operation

FEBRUARY 1897

"Miss Lilias Hamilton, who is private physician of the Emir of Afghanistan, has succeeded in convincing her royal patient of the utility of vaccination, says the *Medical Record.* Smallpox ravages Afghanistan every spring, killing about one-fifth of the children. The Emir has decreed obligatory vaccination in all his states. The order has been given to construct stables and to raise vaccine heifers. Miss Hamilton has been deputed to organize a general vaccination service."

"At the bottom of the ocean there is an enormous pressure. At 2,500 fathoms the pressure is thirty times more powerful than the steam pressure of a locomotive when drawing a train. As late as 1880 a leading zoologist explained the existence of deep-sea animals at such depths by assuming that their bodies were composed of solids and liquids of great density, and contained no air. This is not the case with deep-sea fish, which are provided with air-inflated swimming bladders. Members of this unfortunate class are liable to become victims to the unusual accident of falling upward, and no doubt meet with a violent death soon after leaving their accustomed level."

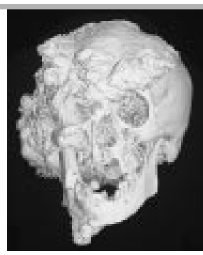
"In New York a heavy snow storm is the signal for the marshaling of all the forces of the Department of Street Cleaning. For days a solid procession of carts, filled with snow, is seen in progress down the side streets toward the river, where it is dumped. There have been many experiments directed toward the elimination of the bulky material by some less clumsy and expensive method. Here we illustrate a naphtha-burning snow melter recently tested in New York. The flame of the naphtha and air comes into direct contact with the snow, melting it instantly. Fourteen men are necessary to feed the insatiable monster."

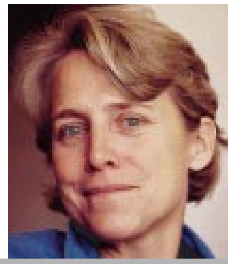
FEBRUARY 1847

"More about the famine—A Liverpool paper states that the arrivals at that port of the starving Irish exceeds 1,000 a day; mostly women and children. In Ireland the guardians of the 'Poor Law' have been compelled to close the doors of the workhouses [poorhouses], and in their own words, to 'adopt the awful alternative of excluding hundreds of diseased and starving creatures who are daily seeking for admission.' Two hundred and sixty have died in three months in one house. It is found impossible to provide coffins for the dead; and the bodies are thrown into the pits without any other covering than the rags they wore when they lived. 400,000 men gladly accepted employment at 10 pence per day, with which many support families, notwithstanding the high price of provisions."

"A Berlin writer states of the Panama project that Prince Louis Napoleon is about to proceed to Central America, for the purpose of putting in progress the work of uniting the two oceans. The celebrated geographer, Professor Charles Ritter, has communicated to the geographical society of Berlin the project of the Prince, which, it appears, he conceived and prepared during his imprisonment at Ham."

NEWS AND ANALYSIS





IN FOCUS

THE NEXT STAR TREK

A budget squeeze and space station woes threaten solar system exploration

With two spacecraft now en route to Mars and another 18 interplanetary probes in various stages of design and construction around the world, solar system science seems poised on the verge of a golden age. Public enthusiasm, fueled by possible evidence of ancient life on Mars as well as startling images from the Galileo probe now orbiting Jupiter, is higher than it has been since the Apollo era. Yet the outlook is not as rosy as it appears at first glance. Russian and European space research will take years to recover from the loss of Mars 96, a seven-ton craft loaded with 22 instruments that crashed into the Pacific last November. And in the U.S., political repercussions from Russia's failure to make progress on its principal contribution to the International Space Station, together with planned budget cuts at the National Aeronautics and Space Administration, threaten missions, including one scheduled for 2005 to return rocks from Mars to Earth. Torrence V. Johnson of the Jet Propulsion Laboratory in Pasadena, Calif., who heads the team of Galileo investigators, says "projections that fit within the push for a balanced budget are very, very bad for space science."

The crisis comes at a time when reasons for exploration of the solar system are stronger than they have ever been. Even before David S. McKay and his colleagues at the NASA Johnson Space Center announced last summer that meteorite ALH84001 had features suggestive of Martian bacteria, NASA

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

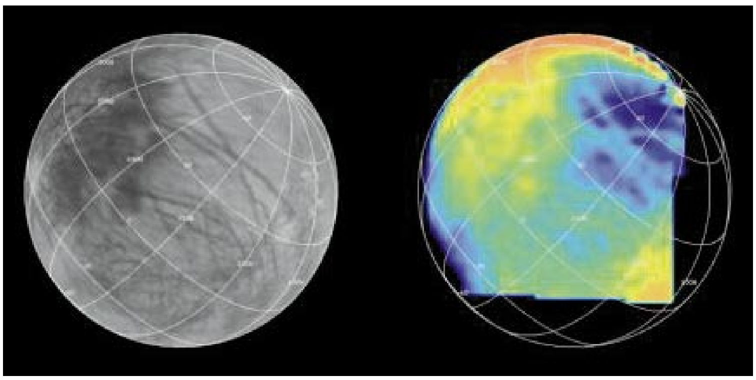
LAUNCH OF MARS PATHFINDER from Cape Canaveral by a Delta 2 rocket took place last December 4. The spacecraft is one of nine slated to visit the planet in the coming decade.

was redefining its objectives to take into account scientific developments. The new focus, which has widespread support among scientists, is the quest to understand the origins of planetary systems and the environments that might support life.

Researchers have collected evidence that life thrives on Earth in almost any place that has usable energy and liquid water, notes Claude R. Canizares, head of the space studies board of the National Research Council. Moreover, it now seems that life appeared on Earth within a geologically brief 100 million years after the planet cooled down enough for organic molecules to evolve, some 3.9 billion years ago. Those insights suggest life might spring up relatively easily and so encourage searches for life elsewhere. Besides Mars, Saturn's moon Titan and Jupiter's moon Europa—which may have water oceans containing organic matter—are considered good prospects.

Some groups of enthusiasts, such as the National Space Society, are riding the wave of excitement to argue for a crash program to send humans to Mars. Fossil hunting cannot be done by a robot, asserts the society's chairman, Robert Zubrin. But Canizares points out that the first mission to Mars to include humans will certainly contaminate the planet enough to cast doubt on the origin of any organic molecules found there later. He therefore urges a vigorous robotic program to explore Mars and other solar system bodies before astronauts arrive.

The White House has apparently accepted that argument. A somewhat ambiguous National Space Policy issued last September endorses both human and robotic exploration but backs away from former president George Bush's earlier announced goal of sending astronauts to Mars. The formula appears to be an attempt to combine support for near-term robotic exploration of the solar system with continued funding for the space station, which the Clinton administration sees as bringing important foreign policy benefits.


NASA/JPL

JOVIAN MOON EUROPA
(left) ***reveals surface ice and mineral mixtures when seen by Galileo in the infrared*** **(right).**

Yet NASA scientists say the budget cuts facing their agency put even relatively inexpensive robotic missions in jeopardy. Budget projections that the administration announced almost a year ago envisage reducing NASA's cash burn rate from $13.8 billion in 1996 to $11.6 billion in 2000, with a gradual increase thereafter. "I don't think they can do a simple sample return within the planned budget," says Louis D. Friedman, executive director of the Planetary Society, an organization that promotes space exploration.

The small robotic planetary missions that NASA has favored since the loss of its Mars Observer probe in 1993 typically cost some $200 million a year to run. The agency spends, in contrast, about $5.5 billion annually on human spaceflight, including $2.1 billion for the space station, a figure capped by agreement with Congress. There is no leeway for diverting funds from human spaceflight to planetary science, because the space station is already falling behind schedule. Indeed, some observers fear that woes besetting the program could add to the pressure on planetary missions. "I am worried that if extra funds have to be provided for the space station, should it come to that, space science is going to be hurt," Friedman says.

Research planned for the space station itself has already suffered from the budget squeeze. In order to release $500 million for station development, NASA last September decided to delay by two years launching eight closet-size racks of the station's scientific equipment. The agency is also trying to gain some financial maneuvering room by negotiating a barter with Japan. That country would supply the station's centrifuge and a life-science research unit in exchange for shuttle launches. The deal could push some of the station's development costs into the future.

Even creative accounting, however, cannot solve the problem of the Russian government's failure to provide funds for the service module, a key early component of the space station now languishing in Moscow. The holdup means that permanent habitation of the station will have to be delayed by up to eight months from the previous target of May 1998. The postponement creates a major political problem, because delays, even more than cost overruns, corrode congressional support. Andrew M. Allen, director for space station services at NASA headquarters, says Russia promised in December 70 percent of the amount needed for work on the module in 1997. But that still leaves a question mark over the other 30 percent, not to mention work in 1998 and follow-on components.

NASA is therefore evaluating contingency plans in case the U.S. decides that the current agreement with Russia has to be recast. A year ago officials indicated that building a substitute service module would cost in the region of $500 million. Allen believes NASA may be able to pare down that figure and stay within its budget limit for the orbiting outpost. But the station would inevitably suffer delays.

The crunch facing NASA has gained high-level recognition. At a meeting billed as a "space summit," to take place this month, congressional leaders will meet with President Bill Clinton to thrash out a long-term space strategy. Scientists are being heard. Canizares and a star-studded team of investigators, including Stephen Jay Gould of Harvard University and Stuart A. Kauffman of the Santa Fe Institute, briefed Vice President Al Gore late last year on the new evidence of life's ubiquity on Earth and its possible existence elsewhere. After the meeting, Gore pledged that NASA "will continue to pursue a robust space science program that will give us greater knowledge about our planet and our neighbors."

Space scientists cannot afford to relax yet. One important player in the debate over NASA will be Representative F. James Sensenbrenner of Wisconsin, a Republican who will chair the House Committee on Science this year. Sensenbrenner is a strong supporter of the space station. He has, moreover, in previous years expressed dismay about the program's dependence on Russian hardware. Unless Russia proves in the next few months that it can be relied on to provide its share of the station near budget and near schedule, Congress may direct NASA to come up with a homemade fix. The resulting budgetary tumult would be unlikely to benefit either human or robotic space exploration.

—Tim Beardsley in Washington, D.C.

PALEONTOLOGY

WHICH CAME FIRST?

Feathered fossils fan debate over the bird-dinosaur link

The descent of birds from dinosaurs has been enshrined in venues as diverse as the American Museum of Natural History and the blockbuster *Jurassic Park*. So readers of the November 15 issue of *Science* may well have been startled to find a challenge to the notion that budgies are the great-great-great- (and so on) grandchildren of *Tyrannosaurus rex*.

The article describes fossils from northern China of birds living as much as 140 million years ago. According to the authors, these birds were too highly developed to have descended from dinosaurs; their ancestors may have been reptilelike creatures that antedated dinosaurs. The mainstream press wasted no time seizing on the heresy. "EARLY BIRD MARS DINOSAUR THEORY," proclaimed a headline in the *New York Times*.

The *Science* report was written by Alan Feduccia of the University of North Carolina and three colleagues. Feduccia is perhaps the most prominent critic of the dinosaur-bird scenario. In *The Origin and Evolution of Birds,* published last fall by Yale University Press, he attempts to refute the theory, which is based primarily on similarities between the bones of birds and dinosaurs.

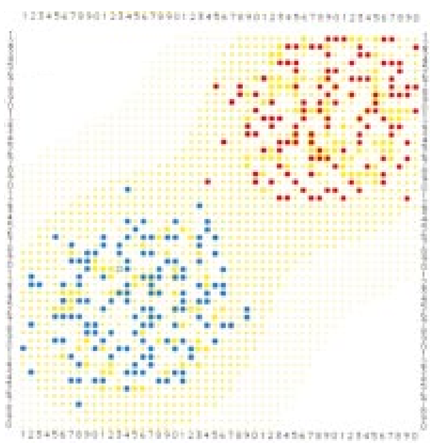
Feduccia argues that many of these shared features stem from convergent evolution—coincidences, really—rather than common ancestry. He points out that most of the fossil evidence for dinosaurs with birdlike features comes from the Upper Cretaceous epoch, less than 100 million years ago. But birds were well established much earlier than that, according to Feduccia.

As evidence, Feduccia points to the fossils described in his recent *Science* paper, which he says demonstrate that surprisingly modern birds were thriving as early as 140 million years ago. The birds include the magpie-size *Confuciusornis* and the sparrow-size *Liaoningor-*

FIELD NOTES

Agent Angst

The audience of academics and journalists gathered at the Brookings Institution had every reason to be excited: the venerable liberal-leaning think tank was announcing the publication of a new book with, in the words of Robert E. Litan, director of economic studies, "revolutionary" implications. It was, Litan declared, the "most innovative, potentially pathbreaking" book ever to bear the Brookings name. The work, *Growing Artificial Societies,* by Joshua M. Epstein and Robert Axtell, describes the two scholars' investigations of their computer-based world called Sugarscape. After the lights went down in the auditorium, Epstein and Axtell provided commentary while a giant display showed how "agents"—simpleminded red and blue blobs representing people—scurry around a grid, competing for yellow resources whimsically named "sugar" and "spice." The agents—more elaborate versions of the dots in John H. Conway's game called Life—eat, mate, trade and fight according to rules set down by their human "gods."



COURTESY OF BROOKINGS INSTITUTION PRESS

The agents' antics invite anthropomorphism. (Epstein referred to one as practicing "subsistence farming" far from the sugar "mountain.") The model's purpose, he explained, is, by employing "radical simplification," to study interacting factors that affect real societies. When agents are let loose in Sugarscape, trends emerge that would be hard to predict. A population may oscillate in size, and often a few individuals garner much of the "wealth," a well-known phenomenon in human societies. The researchers hope to discover which rules, such as inheritance laws, generate which effects. The pair is now using a similar approach to model the population decline of the Anasazi of the American Southwest.

A reporter (this one, truth to tell) asked how the Brookings scholars would know that the critical rules identified in Sugarscape are actually important in the real world. "You don't," Epstein admitted, because many different real-life rules could produce the same outcome. That is a problem with all science, he said, noting that Sugarscape nonetheless provided an improvement on existing economic theory ("mainly just a lot of talk"). But Thomas C. Schelling of the University of Maryland, an early pioneer of agent-based modeling, reinforced SCIENTIFIC AMERICAN's lingering doubt: "You still want to ask, If there are many different ways of producing [a] phenomenon, how do we know we have captured what's really there?" Schelling observed.

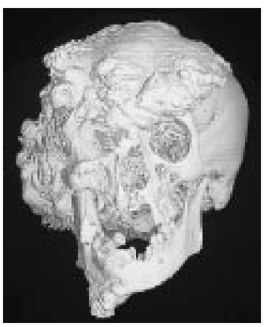
Another reporter rained on Brookings's parade by asking whether Sugarscape has implications for, say, tax policy. That prompted a reminder that the model is still in early development and that Sugarscape would first have to model governments. Epstein earned notoriety in 1991, when he used other computer simulations to calculate that between 600 and 3,750 U.S. soldiers would die in the Gulf War. In fact, only 244 died. But his confidence is apparently undented. On a roll, he started speculating at the Sugarscape book launch that agents could shed light on whether free markets will survive in Russia. John D. Steinbruner, a senior foreign policy fellow at Brookings, interjected that no computer model is ready to answer that question. Soon after, he wound down the discussion, noting that although "well short of a complete account," Sugarscape offers tools "that do appear to be very useful in the process of conceptualization."

—Tim Beardsley in Washington, D.C.

IN BRIEF

Evolutionary Makeovers
Many insects, fish, birds and reptiles adapt their looks to new surroundings and seasons: when the African butterfly *Bicyclus anynana* is born during the rainy season, for example, it sports eye spots to scare off predators, but generations born during drier times do not. How different are these animals? Scientists from the University of Wisconsin at Madison, the University of Leiden and the University of Edinburgh have discovered that it takes the presence of very few genes—half a dozen or so—to vary an animal's appearance radically. The find helps to explain the astounding array of biological diversity.

Elephant Man's Real Disease
Joseph Cary Merrick, the famous Victorian known as the Elephant Man, probably did not have neurofibromatosis, the condition most commonly referred to as Elephant Man's disease. Radiologists at Royal London Hospital, where Merrick lived and his bones remain, have now substantiated the theory that, instead, he suffered from a rarer disorder called proteus syndrome. Recent radiograph and CT scans of Merrick's skull revealed characteristics of the noninherited disease, caused by malfunctions in cell growth.



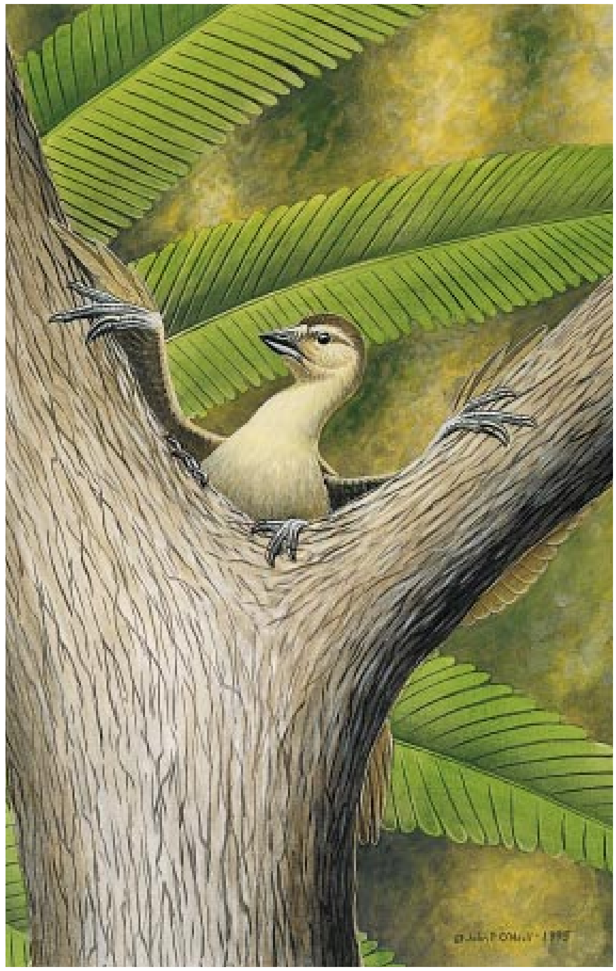
RADIOLOGICAL SOCIETY OF NORTH AMERICA

Holey Microchips
Porous silicon was all the rage when in 1990 it was discovered to emit light. But dreams of incorporating it into microchips were dashed by its fragility, because the material could not withstand the ordinary rigors of chip manufacture. In last November's *Nature,* researchers at the University of Rochester and the Rochester Institute of Technology report that they managed to fortify porous silicon with a double layer of silicon oxide. The team then combined this so-called silicon-rich silicon oxide with a conventional microchip, making for the first time an all-silicon system that in principle can process both light and electricity.

Continued on page 24

nis, both of which had beaks rather than teeth. The latter creature was especially modern-looking, possessing a "keeled" breastbone similar to those found in birds today.

Both birds were more advanced than *Archaeopteryx,* which has generally been recognized as the first feathered bird (although it may have been a glider rather than a true flier) and lived about 145 million years ago. *Archaeopteryx* was not the ancestor of modern birds, as some theorists have suggested, but was an evolutionary dead end, Feduccia asserts. The true ancestors of birds, he speculates, were the archosaurs, lizardlike creatures that predated dinosaurs and gave rise to *Archaeopteryx* as well as *Confuciusornis* and *Liaoningornis*.



JOHN P. O'NEILL; from *The Origin and Evolution of Birds*, Yale University Press, 1996

***MAGPIE-SIZE* CONFUCIUSORNIS**
and other birds are claimed by some to have thrived with dinosaurs 140 million years ago.

Two paleontologists who vehemently reject this scenario are Mark A. Norell and Luis M. Chiappe of the American Museum of Natural History; they wrote a scathing review of Feduccia's new book for the November 21 issue of *Nature*. Feduccia and his colleagues "don't have one shred of evidence," Norell contends. The fossil bed in which Feduccia's team found its specimens, he remarks, has been dated by other researchers at 125 million years, leaving plenty of time for the birds to have evolved from *Archaeopteryx* or some other dinosaur-like ancestor.

Chiappe notes that the anatomical evidence linking birds and dinosaurs is accepted by the vast majority of paleontologists. He does not dispute Feduccia's contention that many of the dinosaurs identified as having birdlike features occurred in the Upper Cretaceous, well after birds were already established. But that fact, Chiappe explains, in no way undermines the notion that birds descended from dinosaurs—any more than the persistence of primates into the present means that they could not have given rise to humans. Moreover, he adds, dinosaur fossils from earlier periods are simply less common.

Ironically, just two weeks before the paper by Feduccia and his co-workers appeared, *Science* published a short news story on a fossil from the same site in northern China—and thus the same epoch—as the birds described by Feduccia's group. But this fossil *bolsters* the bird-dinosaur link—at least according to Philip J. Currie of the Royal Tyrrell Museum in Alberta, Canada, who has analyzed it.

The fossil shows a turkey-size, bipedal dinosaur with what appear to be "downy feathers" running down its back. The finding lends support to the notion that feathers originated as a means of insulation for earthbound dinosaurs and only later were adapted for flight. Currie and several Chinese scientists have written a paper on the fossil that should be published early this year.

"They don't look like feathers to me," declares Larry D. Martin, who has viewed photographs of the dinosaur and was one of Feduccia's co-authors on the *Science* paper. Currie retorts that Martin and Feduccia are so opposed to the standard view of birds' origins that they will reject any evidence. But for most paleontologists, he says, "the evidence is overwhelming that dinosaurs did give rise to birds." *—John Horgan*

MATHEMATICS

PRIZE MISTAKE

The n*-body problem is solved—too late*

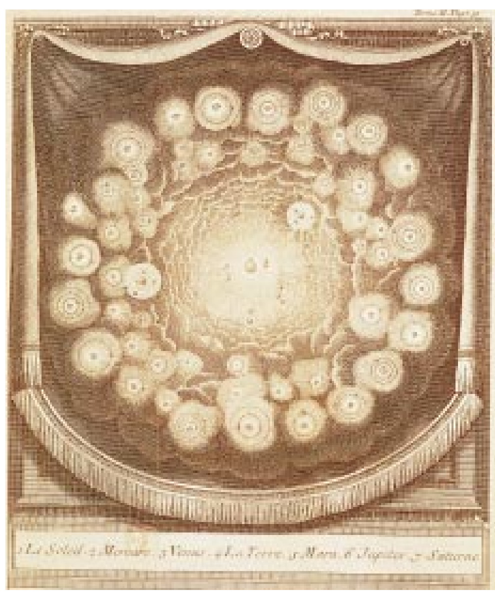
In 1885 three famous mathematicians—Karl Weierstrass, Charles Hermite and Gösta Mittag-Lefler—drew up a list of outstanding problems. Any person who solved one would receive a medal and 2,500 gold crowns on the Swedish king's 60th birthday in 1889. Foremost was the classical *n*-body problem: given the initial positions and velocities of a certain number, *n,* of objects that attract one another by gravity—say, the sun and its planets—one had to predict their configuration at any later time.

More than 100 years later the problem, as stated by Weierstrass, was finally solved in 1991 by Wang Qiu-Dong, a student at the University of Cincinnati. But no one noticed until last year, when Florin N. Diacu of the University of Victoria in British Columbia described it in the *Mathematical Intelligencer.*

Weierstrass had framed the *n*-body problem in a specific way. He was sure that for more than two objects, there is no neat, "closed-form" solution. (An example of a closed-form solution is that of the two-body problem—formed by the sun and one planet—which is an ellipse, with the sun at one of the foci.) For *n* exceeding 2, Weierstrass asked instead for a single series that could yield the answer for all times. So the series had to converge: the successive terms, which serve as refinements to earlier ones, had to get small sufficiently fast. The series $1 - a^2 + a^4 - a^6 + \ldots,$ for example, can be summed only if *a* lies between –1 and 1.

The primary difficulty was collisions. Only a mathematician would worry about point particles—as the bodies are supposed to be approximated—hitting one another. But if they do, their trajectories could cease to exist. Such singular events change the pattern of the series, preventing it from always converging. Wang introduced a measure of time that ran faster as two or more objects approached one another; according to this clock, the collision would occur at infinite time. Having relegated all conflicts to eternity, Wang could then show that there is a converging series.

The solution, unfortunately, is quite useless. As Wang himself states, one has to sum "an incredible number of terms" even for an approximate answer. Nor will he get the prize. It was awarded in 1889 to French mathematician Henri Poincaré, for a paper suggesting that no solution exists. Interestingly, Poincaré's original treatise was so full of mistakes that the publishing journal, *Acta Mathematica,* had to recall and reprint the issue. After correction, however, Poincaré's error-ridden paper laid the foundations of chaos theory. In particular, he elucidated why the motions of the planets are ultimately unpredictable. For this achievement, he surely earned his undeserved prize. *—Christoph Pöppe and Madhusree Mukerjee*



LAUROS-GIRAUDON/ART RESOURCE

***PLANETARY MOTIONS,* depicted here by an 18th-century French artist, are an instance of the n-body problem.**

DEVELOPMENTAL BIOLOGY

LATE BLOOMER

A boy with one hemisphere upsets old ideas on speech acquisition

A keystone in the understanding of how humans acquire language is the critical period theory, which states that the ability to learn to communicate verbally peaks by age six or so and declines as the child gets older. New research, however, may overturn the theory, at least in its simplest form: the ability actually may extend past the age of nine.

Understandably, evidence about the critical period is scarce, because it requires the study of children who have not learned to speak in their early years, either through strange circumstance, accident or disease. One of the first studies took place in 1797, when a "feral child" was discovered wandering in the forests of southern France. The Wild Boy of Aveyron, about age 12 when found, never mastered speech, despite intensive efforts by his mentor, Jean-Marc Itard. This and other cases provided the basis for the critical period theory.

Two centuries later the odyssey of another youngster has provided contrary evidence. January's issue of *Brain* carries a report about "Case Alex," derived from the study of brain-damaged children by Faraneh Vargha-Khadem, Elizabeth Isaacs and their colleagues at the Wolfson Center of the Institute of Child Health in London.

Born brain-damaged, Alex was mute until the age of nine and then rapidly learned to speak over the next two and a half years. He continued to develop increasingly complex language abilities until now, at 15, he produces well-formulated sentences conveying a knowledge of both semantics and syntax that is on a par with that of a normal 10-year-old. As the authors of the *Brain* report put it: "To our knowledge, no previously reported child has acquired a first spoken language that is clearly articulated, well structured and appropriate after the age of about six."

Adding to the surprise is the fact that Alex has acquired speech without a left hemisphere, the region responsible for language in the overwhelming majority of people. That part of the brain had to be surgically removed when Alex was

In Brief, continued from page 18

Scanning for Trouble

Diagnosing appendicitis has always been dicey: one in five patients undergoes costly surgery without cause; another 20 percent go home only to get sicker. But a new CT x-ray technique, unveiled at a December meeting of the Radiological Society of North America, should change that. The focused appendix CT, or FACT scan, capitalizes on dye in the colon to view the appendix—infected or not—more clearly. And because FACT scans home in on the abdomen's lower right quadrant only, they cost half as much as full abdominal scans.

Twirly Birds

This high-speed photograph, taken by biologist Bates Littlehales of the University of California at Los Angeles, reveals why phalaropes spin on the water's surface: when the wading birds chase their tails, they churn up prey. Littlehales and his colleagues caught the kinetic feeding on film by placing the small shorebirds in a tank containing dye-stained brine. When the birds performed their pirouettes, a tornado of fluorescent food funneled up below them.

BATES LITTLEHALES

Protection with Estrogen

Neuroscientists have uncovered sundry ways in which estrogen protects women from brain damage. Patricia Hurn and her colleagues at Johns Hopkins University found that compared with male rats, natural estrogen levels leave females three times less vulnerable to brain damage from stroke. And Sanjay Asthana of the Veterans Medical Center in Tacoma, Wash., has demonstrated the hormone's redemptive potential in Alzheimer's patients: in a small study of elderly women with moderate dementia, estrogen patches temporarily improved both their attention and memory.

Antimatter in the Making

Confirming earlier results from CERN, physicists at Fermilab found seven antihydrogen atoms last November. To make the antiatoms—which contain an antiproton and a positron each—the team sent an antiproton beam through a gas jet, thereby pairing electrons and positrons and, in rarer instances, positrons and antiprotons.

Continued on page 26

eight. Such a hemispherectomy is almost a routine operation for some rare neurological conditions; in Alex's case, it was Sturge-Weber syndrome, which produced a relentless succession of seizures. The epileptic activity interfered so much with the normal operation of his brain that he failed to develop language skills in any form, apart from one or two regularly used words and sounds.

For the first few months after the neurosurgical operation, Alex was kept on anticonvulsive medication. Then, a month after his medication was withdrawn, he suddenly started uttering syllables and single words. His mother recorded in her diary more than 50 words, primarily nouns but also verbs, adjectives and prepositions. Several months later he had progressed to full sentences.

According to the researchers, if there is a critical period, Alex has raised its upper limit to nine, a result consistent with at least one theory that suggests that the hormonal changes of puberty put a stop to the flexibility of the brain's language areas. The next step in studying this remarkable boy is to see if reading and writing can also be learned without a left hemisphere, at least up to a level that will enable him to navigate through the everyday world of signs, forms and cereal boxes. But even before that happens, the *Brain* report is likely to provoke a closer look and possibly a reworking of the critical period hypothesis foreshadowed in a forest in southern France 200 years ago. *—Karl Sabbagh*

MARINE BIOLOGY

SOAKING UP THE RAYS

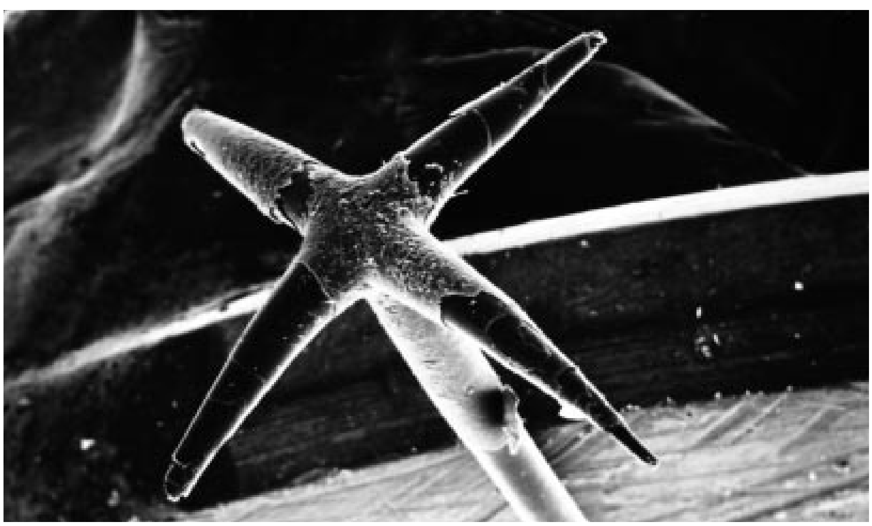
A sponge uses optical fibers to gather sunlight

It is hard to see under the sea—particularly if you are 120 meters down, lying beneath a thick covering of ice during the endless nights of the Antarctic winter. Yet even in this deep night, hoards of tiny algae live inside sponges, soaking up carbon dioxide and, in turn, producing nutrients for their hosts. The mystery has been where these minute green plants get the light they need to drive photosynthesis.

Taking inspiration from the age of telecommunications, Italian scientists recently discovered the secret of the symbionts. It turns out that some sponges have a system of fiber optics that allows them to gather what little light reaches their murky depths and to direct it to the algae. "We don't give sponges much credit. Most people look at them and say 'this is a blobby lump,'" comments Mary K. Harper of the Scripps Institution of Oceanography. "But considering how primitive these animals are, it's amazing how adaptable they are."

Like many sponges, the Antarctic sponge that the team from the universities of Genoa and Perugia examined, *Rossella racovitzae*, has a skeleton composed of little silica spikes called spicules. They support the creature and keep predators away. In the case of *R. racovitzae*, however, each spicule is capped with a cross-shaped antenna of sorts. The flat

***CROSS-SHAPED SPOKES* grab light for an Antarctic sponge known as** Rossella racovitzae.



GIORGIO BAVESTRELLO *University of Genoa*

In Brief, *continued from page 24*

Semiconductors Get Bent
Eager to show that crystal semiconductors could be made flexible, researchers at the State University of New York at Buffalo deposited thin layers of semiconducting materials onto weather-stripping silicone. The resulting semiconductor, when peeled from the silicone, retained most of its properties. According to head researcher Hong Luo, the semiconductor was tougher than those crafted from bendable polymers and possessed better optical properties. They might prove useful in optical circuits and in solar cells.

Rivals of the Fittest
It may not be how far you run but how fast that counts. In a recent study of more than 8,000 athletes, researchers at

BOB THOMAS *Tony Stone Images*

Lawrence Berkeley National Laboratory found that the fleetest of foot had the healthiest of hearts: slower, regular runners had more high-density lipoproteins ("good" cholesterol) than sprinters, but they also had higher blood pressure.

FOLLOW-UP

Prostate Cancer Gene Identified
Collaborators from Johns Hopkins University, the National Center for Human Genome Research and Umeå University in Sweden have found a stretch of chromosome 1 that can predispose men to prostate cancer. Indeed, mutations in a gene in this region, named HPC1 for hereditary prostate cancer 1, probably account for some 30 to 40 percent of all inherited forms of the disease. Some 5 to 10 percent of all prostate cancers are genetic. (See September 1996, page 114.)

Losing on Fusion
A new take on how turbulence affects hot ionized gas in a tokamak may dash all hopes for the first controlled, self-sustaining fusion burn. For a decade, scientists behind the International Thermonuclear Experimental Reactor (ITER)—a $10-billion multinational project—have argued that ITER would demonstrate fusion's practicality by 2010. But two physicists at the University of Texas at Austin suggest technical problems will make the wait much longer. (See April 1992, page 102.) —*Kristin Leutwyler*

SA

spokes of the antenna capture light, which then travels directly down the silica tube of the spicule to the garden of green thriving at the base. (Harper suspects that this mechanism might allow larger numbers of algae to thrive because there is more surface area in the internal folds of the sponge than on its outer surface.)

The researchers discovered *R. racovitzae*'s system after firing red laser light down a straight, 10-centimeter-long spicule and observing its unimpeded travel. They then bent the spicule at various angles to see if it still successfully guided the red light—and it did. Although they have tested just the one sponge—largely because its spicules are long and easy to work with—the scientists think others may use the same device. Group leader Riccardo Cattaneo-Vietti says they will soon begin looking at cave-dwelling sponges for the same adaptation.

Sponges are not the only owners of a natural light-guidance system. According to Jay M. Enoch of the University of California at Berkeley, some copepods—another form of marine organism—have light guides. And certain tropical plants have dome-shaped lenses on their leaves, allowing them to collect and focus any light filtering down through the thick rain-forest canopy. As Thomas Vogelmann of the University of Wyoming described a few years ago, these leaf lenses lead to cells inside the plant, which, in turn, guide light to needy cells at the base. —*Marguerite Holloway*

ASTRONOMY

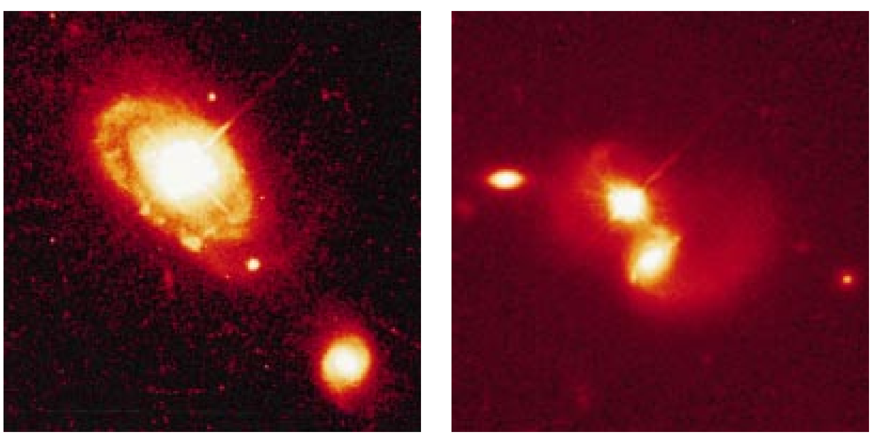
GALACTIC GUSHERS

Evidence mounts that black holes drive all quasars

Shining with the energy of a trillion suns, quasars are the brightest as well as some of the most distant objects in the known universe. Astronomers have devised theories to explain what drives such infernos, but because they are so far away, gathering the evidence has been a challenge. The drought of data is coming to an end, however. Recent surveys conducted with the Hubble Space Telescope have answered some key questions about quasars, although the surveys have also highlighted some gaps in the standard account. Meanwhile a study that combined the observing power of radio telescopes in different countries has found separate evidence that all quasars operate in fundamentally the same way.

Despite their prodigious luminosity, quasars are not large; they may be even smaller than the solar system. The dominant view is that only a supermassive black hole—a body so dense that not even light escapes it—can generate so much energy in such a small space. Physicists calculate that if something propelled a gas cloud into the vicinity of a black hole, the gas could fuel a quasar. The black hole's gravity would accelerate the gas to near the speed of light, turning it into plasma. Before being consumed, the fuel would be swept into a maelstrom called an accretion disk, where friction would efficiently generate light and other radiation.

The new pictures by Hubble bolster that theory. The telescope has provided the first clear view of the immediate en-



HUBBLE SPACE TELESCOPE

QUASARS IMAGED BY HUBBLE
occur in undisturbed galaxies (left) *and in galaxies in the process of colliding* (right).

vironments of a range of quasars. The images show that most, if not all, lie in the cores of luminous galaxies, including both the common spiral and elliptical types. That suggests the gas cloud theory is on the mark, because galaxies are where gas clouds are found. Moreover, some of the galaxies playing host to a quasar seem to have collided recently with another galaxy. These accident victims display features not found in more quiescent galaxies: parts of some of them seem to have been torn off or distorted. That supports the gas cloud theory, too, because the forces generated in such a collision could easily throw clouds into the feeding zone of a hungry black hole.

Harder to understand is why most of the quasars reside in apparently undisturbed galaxies. "This result is in some ways the most unexpected one that we have obtained," notes John N. Bahcall of the Institute for Advanced Study in Princeton, N.J. Astronomers had tentatively figured that unless a collision delivers large amounts of gas to a black hole, galaxies harboring these cosmic carnivores would supply fuel too slowly to sustain a full-blown quasar. Rather, the theory went, they might sputter just enough to become the lesser lights known as Seyfert galaxies. Michael J. Disney of the University of Wales in Cardiff adds: "We're puzzling over the ones that aren't interacting."

Bahcall suspects that some subtle mechanism that Hubble cannot resolve must be supplying the fuel for these quasars. Planned studies of even more distant quasars might provide a better idea of how they and their host galaxies evolve over time, notes Donald Schneider of Pennsylvania State University.

Despite the diversity of galaxies that harbor quasars, radio-wavelength observations suggest that most quasars share key features in common. "Radio-loud" quasars—the 10 percent of them that emit strongly at radio wavelengths—have previously been observed to have jets of plasma emerging from their "poles" at speeds near that of light. An accretion disk around a black hole is the only imaginable source for plasma jets, but because astronomers have not until now seen such jets emanating from "ra-

ANTI GRAVITY

Dropping One for Science

Okay, let's cut right to the chase. The reason the guy gets into the moose suit is because he couldn't throw the dung far enough.

Well, maybe we should back up. For the past two decades, conservation biologist Joel Berger of the University of Nevada at Reno has studied the behavioral, ecological and reproductive biology of mammals. For the past two years, he has focused on the relationship between predator and prey in the greater Yellowstone National Park area and in south-central Alaska. "Our research is concerned with what happens to prey in systems where large carnivores are absent," he told a group of reporters last November at New York City's Central Park Zoo, part of the Wildlife Conservation Society, which funds his current research. "This is important, because in most of the world, systems are going to be losing large carnivores, rather than gaining them."

Both study sites contain a favorite food of grizzly bears and wolves, namely, moose. (See, we're getting there.) Grizzlies and wolves, however, are much more common in Alaska than around Yellowstone. This discrepancy has some easily quantifiable effects. A century ago moose were rare around Jackson Hole, in the Yellowstone area; they thrive now. More than 90 percent of moose calves survive every year at Jackson Hole, whereas only about 35 percent do in Alaska. From the moose perspective in Yellowstone, times are good.

One thing Berger wants to know, therefore, is how deeply those good times affect behavior: Might prey animals begin to forget sensory cues warning of danger? So he and his colleagues played recordings of predator calls to moose at the different sites. "In Wyoming, moose failed to respond to wolf calls," Berger says. "In Alaska, they are sensitive and reduce the time they spend feeding by about half." Another cue should be odor. To test moose reaction to smell, Berger uses two potent sources of predator scent: urine and dung.

MICHAEL CRAWFORD

Getting the dung is one thing, the basic strategy being to wander around and pick up grizzly and wolf scat. Depositing it close enough to the moose to observe systematically their reactions to the smell is a messier issue. You cannot simply walk up to a moose. They're big, they're dangerous, they're scared—think of the New York Jets. Apparently, Berger did. "I had played some ball in college," the 44-year-old Berger says, "and could still throw reasonably accurately." Those throws weren't far enough, however. "We tried slingshots," he continues, "but they don't work so well. You can only get a small amount through. We tried longer and longer slingshots, but then you get sound effects." And hurling urine remained a problem as well.

Declining the opportunity to experiment with catapults or, for that matter, moosapults or scatapults, Berger was left with an old strategy: if you can't beat 'em, join 'em. A designer from the *Star Wars* movies created the moose suit, which looks like something two people would get into for a Halloween party, but which looks like a moose to other moose, who don't see all that well. The idea is to stroll up to a real moose, drop off some scat, avoid getting mounted and saunter away. Preliminary tests of the suit showed that moose seemed unperturbed. Bison, though, "ran like hell," according to Berger, which may mean that they see better or simply don't like moose.

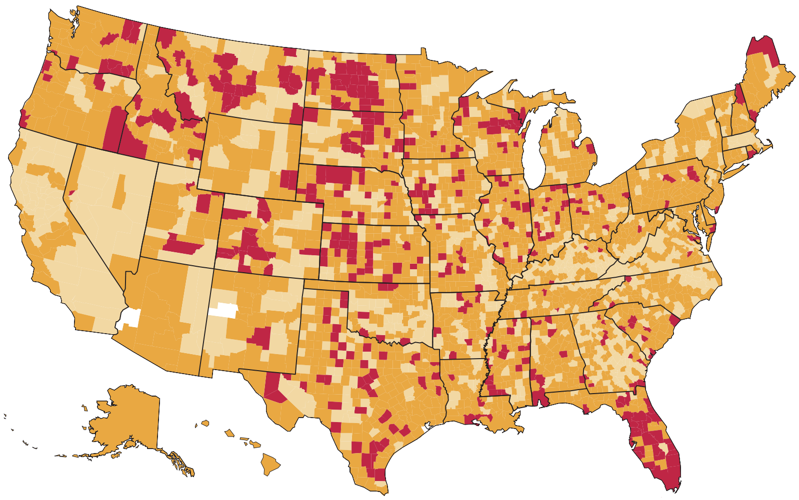
If everything has gone well, Berger and his wife and colleague, Carol Cunningham, will have spent much of this winter in the suit. (At the same time—she's in back.) Before leaving the zoo to return west, Berger was asked if he had any concerns about safety. He answered simply, "Lots." —*Steve Mirsky* dio-weak" quasars, some researchers have suspected that these objects, making up the majority of quasars, work differently. Now radio astronomers at the University of Maryland and the Max Planck Institute for Radio Astronomy in Bonn have found evidence for jets of plasma emerging at almost the speed of light from radio-weak quasars.

The quasars that were studied had previously been classified as members of a small group of "radio-intermediate" quasars, but the new observations indicate that their unusual characteristics arise because their plasma jets happen to point directly toward our galaxy. The new radio-telescope observations, by showing that radio-weak quasars share the key feature of jets with radio-loud quasars, thus indicate that "probably all quasars harbor a very similar engine," according to Heino Falcke of the University of Maryland. The same basic mechanism, he believes, also drives Seyfert galaxies. But many questions remain. If radio-weak and radio-loud quasars indeed share the same mechanism, the explanation for their differences is now "an even deeper mystery," he says.

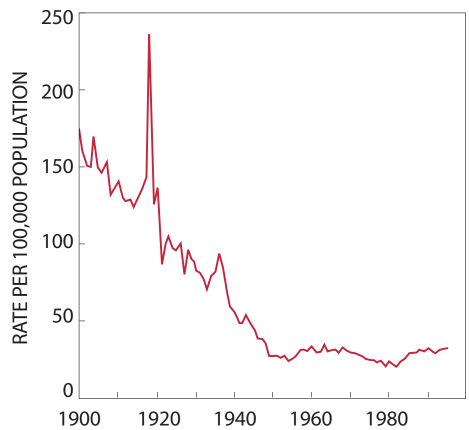
—*Tim Beardsley in Washington, D.C.*

BY THE NUMBERS

U.S. Deaths from Pneumonia



AGE-ADJUSTED RATE PER 100,000 PEOPLE 55 AND OVER, BY COUNTY, 1979–1992
UNDER 50 | 50 TO 79.9 | 80 OR MORE



SOURCE: National Center for Health Statistics. In the graph, rates are for the death registration area, which comprised 12 states in 1900 and 48 states by 1933. Alaska was added in 1959 and Hawaii in 1960. Not adjusted for changing age composition.

Pneumonia, an acute inflammation of the lungs, is not a single disease but more like a family of several dozen diseases, each caused by a different agent. The agents include a variety of bacteria, viruses, fungi, parasites and chemicals and produce different symptoms, but typically patients have fever, difficulty breathing, chest pain and coughing, including the coughing up of blood. The symptoms last a week or more, and in its classic form, lobar pneumonia, 30 percent of patients die if not treated.

Transmission is usually by inhalation but also by hand-to-mouth contact. Patients in hospitals, which abound with pathogens, are vulnerable, especially through invasive devices such as catheters and respirators. The immune system, the mechanical action of coughing and the microscopic motion of cilia normally protect healthy individuals. But old people, who generally have weaker defense mechanisms than the young, are far more likely to die of pneumonia. Those whose defenses are compromised by, say, AIDS or cancer, are also at high risk, as are those given certain medicines such as immunosuppressive drugs. Men are at higher risk than women, partly because they are more prone to alcoholism and nicotine addiction, two of the many risk factors for pneumonia. Blacks are at higher risk than whites, perhaps because they often lack access to good medical care. Air pollution also plays a role.

In recent years, pneumonia was the underlying cause of death for about 80,000 Americans annually, whereas for an additional 100,000 or so, it was a contributing cause of death. The map shows only those deaths for which pneumonia is registered as the underlying cause. There is an ancient theory, suggested by the higher mortality rates documented in winter, that cold temperatures promote pneumonia, but this idea is not consistent with the pattern on the map: Massachusetts has a high rate, but so does Georgia, and North Dakota has the third lowest rate. Florida is lowest, which may reflect the "healthy retiree" effect; that is, the tendency of healthy older people to retire to places like Florida while their less healthy compatriots remain home. California has the highest rate, perhaps in part because of air pollution levels in southern California.

Pneumonia probably affected prehistoric humans and is one of the oldest diagnosed diseases, having been described by the Hippocratic physicians of ancient Greece. In 1900 it was the second deadliest killer in the U.S. after tuberculosis. The extraordinarily high rate in 1918 resulted from the great influenza pandemic that year, which killed more than 540,000 Americans. Since then, pneumonia mortality rates have decreased markedly because of better hygiene and increasingly effective methods of treatment: first, antipneumococcal serum, then sulfa drugs, and finally, in the 1940s, penicillin. The increase in deaths during the past 15 years stems primarily from the growing number of old people.

—*Rodger Doyle*

RODGER DOYLE

PROFILE: Patricia D. Moehlman

Into the Wilds of Africa

Even on the soft, cream-colored carpet of her sparsely decorated house in Connecticut, Patricia D. Moehlman camps out. She takes off her running shoes, sits cross-legged on the floor and hunches over the small, white board on which she is projecting slides in the bright light of a fall afternoon. As she wends her way pictorially through decades of research on the social lives of jackals, work on the plight of wild asses in the war-torn Horn of Africa and her educational projects in Tanzania, Moehlman's joy about being out in the field is palpable. She seems to delight in every face—canine, equid or human—and in every landscape she has photographed.

Although she is showing "very few" slides this particular day, they are still very many. Moehlman has been in Africa for more than 25 years, and she has documented a great deal. Famous for her observations that jackals hardly deserve their ill repute as skulking, slippery scavengers, Moehlman is also renowned for conducting biological surveys in Ngorongoro and the Udzungwa Mountains and for her conservation work in general.

Moehlman is especially outspoken about ensuring that Tanzanian scientists play the major role in studying Tanzanian wildlife and resources—not always a popular position among foreign researchers. But when Moehlman laughs, a very deep, almost gritty, unyielding strength is revealed—the sound suggests the Tanzanians have an unflappable ally.

The daughter of academics, Moehlman grew up first on a farm in Iowa and then in the countryside near Austin, Tex., and was always outdoors. After majoring in biology at Wellesley College, she had just returned to graduate school in Texas—where she studied rodent species on Mustang Island in the Gulf of Mexico—when she heard that Jane Goodall needed assistants. Moehlman, whose father had avidly read Theodore Roosevelt's African adventures, says living in Africa had been a dream since she was young.

So Moehlman abandoned her rodents on their island and, in 1967, moved to East Africa to work with Goodall and her then husband, Hugo van Lawick. During her stay, the couple turned their attention away from chimpanzees for a while to conduct research for a book—*Innocent Killers*—about hyenas, jackals and wild dogs. So, for several months, Moehlman closely watched golden jackals in Ngorongoro Crater.

She returned to the U.S., moved on to the University of Wisconsin to do doctoral work, then settled down in Death Valley National Monument in California to observe feral asses. Moehlman camped alone there for nearly two years, trailing the descendants of the donkeys that the Spanish brought with them in the 1500s—descendants, in turn, of the wild asses found in northeast Africa. (These feral asses continue to be a flash point for controversy because they are considered nonnative and ecologically destructive. Moehlman thinks of them slightly differently: she points out that the mother genus, *Equus,* evolved in North America—so the burros of Death Valley may have simply come home.)

ALEX WEBB *Magnum*

Moehlman ultimately determined that habitat and resource availability dictated the social structure of these wild equids. In arid areas, the stable group would consist of a female and her foal, whereas in regions with lusher vegetation, the stable group was a harem of many females guarded by one or two males. Moehlman argues that large social groups form more easily when one individual's foraging does not adversely affect another's. When food is limited, however, social organization is reduced to a basic unit: mother and offspring.

Moehlman returned to the wild plains of Africa in 1974 and began studying golden and silverbacked jackals on her own—becoming the first woman to get permission to do biological research in the Serengeti. Her years as "jackal woman" had begun. "Out in the field, it was good," she recalls. "It is a great gift to watch animals so intimately."

Jackals are unusual in that they are monogamous—only 3 percent of mammals pair-bond—and the male and female participate equally in raising pups. At the very beginning of her fieldwork, Moehlman noticed something else unusual about jackal families: they use au pairs. These helpers, as Moehlman came to call them, come from the previous year's litter. They stick around for the next season, helping their parents feed and guard the new pups while continuing to act submissively. This arrangement allows helpers to become more experienced, making success more likely once they set out on their own. According to kin selection theory, which tries to explain animal behavior in

PATRICIA D. MOEHLMAN

***RESIDENTS OF THE SERENGETI** migrate near Moehlman's African camp.*

terms of relatedness, the helpers are on average as related to their siblings as they would be to their offspring; therefore, investment in the survival of their younger sisters and brothers makes good genetic sense. Helpers clearly make a choice about whether to stay or go. If they do stay, they must delay their own reproduction—which may not be a bad idea, because it may not be easy to find a mate or a territory in a given year.

Moehlman's jackal discoveries were based on careful identification of individuals: a torn ear, a scar above the muzzle, a dark patch on the tail. She explains that radio-collaring may interfere with survival; further, there is only one spot, about one inch in diameter on the rump, where it is safe to shoot a tranquilizer dart into the small animal. Otherwise, the impact will break bones or damage organs. "I have my gut-level response. I don't want to hurt animals. In addition, it is bad science to intervene with animals in ways that affect their behavior and survival," Moehlman explains. She goes on to say that after years of following research in the Serengeti, she has come to believe that handling animals may interfere in those ways—a belief that is not widely embraced, Moehlman admits: "I am slowly figuring out that if you have opinions you want to express, and they are not part of the general consensus, there is a price to be paid."

Moehlman has particular views about other forms of interference as well, including certain approaches to experimentation. "I would rather take more time and let natural experiments occur and try to understand the components of what is going on," she maintains. She notes that some scientists advised her to remove a helper from a jackal family to determine what its role was. Moehlman counters that if she had removed a helper from, say, a golden jackal family and the pups had died, she might have concluded that helpers consistently ensured pup survival.

Her fieldwork presents a more complex picture. In the first place, some helpers are more peripheral to the family and do not contribute as much. In the second, a parent with a helper may hunt less—and the pups would get the same amount of food as they would have if there were no helper—or the parent may hunt just as much, which means pups would get more food, and so more may survive. Because all individuals in the family are different and change their behavior to reflect varying circumstances, one needs to spend long hours watching the details of behavior to understand the dynamics of cooperative breeding.

After nearly a decade in the Serengeti and Ngorongoro—punctuated by sorties to teach and write at Yale and Cambridge universities and to study feral asses in the Galápagos Islands—Moehlman had fallen in love with Tanzania. And she had become very aware that there were few Tanzanians studying wildlife resources. "Let the Tanzanians be the folks for the long term. They care about Tanzania," she states emphatically. "I care about Tanzania, I care about Tanzanians. But I am not a Tanzanian. I won't stay there forever. And it needs to be in the hands of the nationals."

So Moehlman set about raising funds for students at the University of Dar es Salaam. "Fifteen hundred dollars meant the difference between someone completing a master's and not. Eight hundred dollars meant the difference between a whole class going out and doing a field trip and not. They are not big sums of money." She also established relations with expert biologists around the world, and, so far, about 10 Tanzanians have been able to do graduate work in Tanzania and abroad. Moehlman herself has taught students to conduct biological surveys. "It is the building block for understanding the ecology of the area," Moehlman says. "It also lets the undergraduates know all the possibilities of what you can do out there."

Her most recent scientific efforts also involve working with and training nationals, this time in the Horn of Africa. There, in the harsh deserts of Eritrea, Somalia and Ethiopia, the world's most endangered equid, the African wild ass, is barely surviving. Although her surveys were interrupted by civil war, Moehlman has made several visits since 1989, trying to count animals, to interview local people and to establish protected areas. In the past 20 years, according to Moehlman, the wild ass population fell from between six and 30 per 100 square kilometers to one or two. The accessibility of guns has made it easy to hunt the wild ass—a source of folk medicine for tuberculosis, constipation and backache.

Nevertheless, her forays seem to have had some impact. "I am coming from a long way away, so people are real impressed that I think it is important," she laughs. "They say that if I had not shown up and discussed the wildlife's plight with them, all the asses would be gone now." Many of the Afar and Issa people of the region—often somewhat taken aback by the appearance of a woman—explain that although they recognize its endangered status, the occasional wild ass can mean the difference between someone starving or not.

One Afar elder recounted a tale to illustrate this point, "sort of an interesting story for a desert people," Moehlman notes: A woman is standing in the water with her child on her hip; the water rises, and the woman puts the child on her shoulder; the water rises, and the woman puts the child on her head; the water rises, she stands on the child. True to form, Moehlman responded: "There are many things the woman can do. She can swim to shore. She can build a boat." *Equus africanus* appears to be in good hands. *—Marguerite Holloway*

AVIATION

IT'S A HELICOPTER! IT'S A PLANE!

A nonmilitary tilt-rotor is conceived, but will it fly?

When Bell Helicopter Textron and Boeing Company announced last November that they would build a revolutionary new tilt-rotor aircraft, the superlatives flew, even though no aircraft would for at least five years. Bell chairman Webb Joiner suggested that construction of the tilt-rotor, a hybrid of helicopter and airplane, would be as important as "the very beginning of manned flight itself."

Certainly, the more crowded big-city airports become, the more attractive tilt-rotors seem. In theory, at least, they combine the best features of helicopters and fixed-wing airplanes. They can take off and land vertically, in a compact area the size of a helipad. After taking off, the engine-propeller assembly rotates 90 degrees, turning the craft into something like a conventional turboprop airplane, able to fly with approximately the turboprop's speed and range. Aviation officials say such a craft would not need airports to shuttle people between large cities separated by a few hundred miles; it would take off and land in more convenient locations closer to—or even within—metropolitan areas.

With an advantage like that, why aren't the skies full of tilt-rotors? Because uniting the two great classes of aircraft into a single hybrid has proved to be a major challenge, one that engineers have been working on for more than 40 years. Designed to carry six to nine passengers, the proposed Bell Boeing 609 will actually be an updated version of the experimental, 1970s-era XV-15, which was a test-bed for a military tilt-rotor known as the V-22 Osprey. The V-22's development program, which one secretary of defense struggled to terminate, was marred by two crashes, one of which killed seven people. The Osprey, which holds 24 marines and their gear, is expected to go into service in 1999, after 18 years of design and development.

Tilt-rotors are a study in trade-offs. They must have rotors large enough to lift the craft vertically but small enough for reasonably efficient cruising in airplane mode. "It's intuitively obvious that you have to give away something," notes David S. Jenney, editor of the *Journal of the American Helicopter Society* and a retired helicopter engineer. According to Bell, the V-22 has a lift-to-drag ratio of eight, meaning that eight times as much thrust is required to lift the vehicle vertically as to move it forward. This ratio is important because it determines the extremes of thrust for which the tilting rotors must be efficient. When it is cruising, the aircraft is essentially overcoming drag—which is, according to the ratio, eight times less than the weight.

Another requirement is an airframe that can withstand the distinct vibrations and stresses of both vertical and horizontal flight. This hurdle was for the most part insurmountable until the development in the 1970s of advanced carbon-fiber composite materials.

With a projected maximum cruising speed of 509 kilometers per hour and a maximum range of 1,400 kilometers, the 609 will go "twice as fast and twice as far" as a helicopter, Bell officials claim. Not all experts share that view, however. "The tilt-rotor should be more efficient and burn less fuel per mile than a helicopter," Jenney says. "But the two-to-one claim is probably exaggerated."

The greatest difficulties for the 609 will not be technical, though. "I don't doubt they can make it work," Jenney adds. "The challenge will be financial viability." A 1987 study estimated that maintenance of a civilian V-22 would cost about $835 for each hour spent in flight; for a comparable turboprop the cost was $180 an hour. Nevertheless, Bell spokesman Terry Arnold asserts that "we think [maintenance costs] will be comparable to turboprops and small jets, and much lower than for helicopters." The 609 is expected to cost about $10 million when it is delivered, probably around 2002. A helicopter with similar lift capability would cost in the neighborhood of $7 million.

With its limited cargo capacity, the 609 will be targeted to several niche markets now served mainly by helicopters. The uses include shuttling executives among scattered corporate sites, transporting crews and equipment to offshore oil rigs, search and rescue, disaster relief and medical evacuation, and various border-patrol activities.

Commercial shuttle service between cities would await larger tilt-rotors (preliminary designs have already been sketched for 19-, 31-, 39- and 75-passenger craft) and new federal regulations governing the certification and operation of tilt-rotors in heavily populated areas. Such regulations, now being formulated by the Federal Aviation Administration, may determine as much as anything else whether the tilt-rotor concept finally flies or becomes yet another intriguing idea that never quite got off the ground. —*Glenn Zorpette*

BELL BOEING

***V-22 MILITARY TILT-ROTOR** will have a diminutive civilian counterpart.*

MATERIALS SCIENCE

NATURAL SYNTHETICS

Genetically engineered plants produce cotton/polyester blends and nonallergenic rubber

Farmers have long bred crop strains to resist cold, pests and disease. More recently, biotechnologists have tinkered with plants' genes as a more efficient means to the same ends. Now two experiments have demonstrated that breeders and genetic engineers can do more with plants than just boost their yield: they can actually grow entirely new materials—including some, like plastics, heretofore considered synthetic. If the techniques prove commercially viable, they could produce warmer clothing and safer medical supplies from all-natural sources.

In November, scientists at Agracetus in Middleton, Wis., reported creating transgenic cotton plants that fill the hollow middle of their fibers with a small amount of the plastic polyester, polyhydroxybutyrate (PHB). The team built on earlier work first published in 1992 by Chris Somerville of the Carnegie Institution, who hoped to engineer plants that produced so much PHB that farmers could harvest plastics as cheaply as refineries manufacture them. Although Somerville's plants never grew enough PHB to be commercially viable, the research grabbed the attention of Agracetus.

There Maliyakal E. John and Greg Keller used a gene gun to shoot gold beads coated with genes for PHB production into a cotton seedling. As the plant grew, they pruned any leaves and buds that did not express the genes until at last they had a mature plant whose entire length held at least one layer of genetically transformed tissue. Although the process is hardly efficient—John and Keller had to shoot 14,000 seedlings to obtain 30 mutant plants—it has two advantages over test-tube techniques. The gene gun works with whole plants (commercial cotton does not grow well from tissue culture), and it can insert several genes at once.

Don't expect wrinkle-free, 50/50-blend shirts coming out of cotton fields just yet. So far even the best bolls are still mostly cellulose and less than 1 percent PHB by weight. Not much, but enough to make

RALF-FINN HESTOFT *SABA*

POLYESTER-LACED COTTON was grown by Maliyakal E. John.

a difference: Agracetus claims that cotton fabric woven from these polyester hybrids retains 8.6 percent more heat than unaltered fabric. John concedes that commercial applications will probably require boosting PHB levels by three times or more, which may take years.

In the meantime, the company plans to stick other useful polymers inside cotton fibers. More complex forms of PHB, polymers from other plants, and even keratin (the protein that makes up hair), Keller says, could help mutant cotton hold heat, retain colors and wick away moisture better than the wild type.

Genetic engineering may not be necessary to grow improved materials, however. Consider the case of an unassuming Chihuahuan desert shrub called guayule (pronounced gwah-YOO-lee). The plant naturally produces latex—although not nearly as profusely as the tropical trees from which all rubber products currently flow. But 15 years of classical breeding has tripled its rubber output to about 900 pounds per acre—comparable to tropical trees, says breeder Dennis Ray of the University of Arizona.

Guayule rubber is as durable and strong as tropical rubber, and it has two advantages. It grows in such arid regions as Arizona, where tropical trees cannot. More important, guayule rubber is nonallergenic. This property, says Katrina Cornish of the U.S. Department of Agriculture, is what gives guayule its niche. There are 57 allergenic proteins in tropical rubber. As a result, latex allergy, with symptoms ranging from simple skin irritation to anaphylactic shock, is common among health care workers and others who frequently come in contact with rubber. Unfortunately, synthetic alternatives such as nylon tend to allow fluids and viruses to leak through.

Guayule rubber should perform better. In a 1994 study of 21 latex-sensitive patients, none responded to guayule proteins. Even so, Cornish is modifying the guayule latex extraction process to keep protein concentrations low. Meanwhile Ulex Corporation in Philadelphia is negotiating with the USDA to license Cornish's process. If all goes well, the next few years should see the blooming of fields full of manufacturing plants.

—Samuel K. Moore in San Francisco

COMPUTING

MAKING SENSE

Microsoft uses a dictionary to teach computers English

In a lab at Microsoft Research in Redmond, Wash., Xuedong Huang sits me down at his computer to show off the company's new speech-recognition software. "It is just a matter of time," he asserts, until people operate computers using their mouths more than their hands.

Time, Huang's demonstration reveals, is precisely the issue. To his attentive dictation program, I enunciate: "Microsoft Corporation is working on advanced speech-recognition systems." The program obediently spells out my sentence but substitutes "Petras" for "advanced." I highlight the mistake and say "advanced" again; the computer writes "bitterness." Another try, and the program suggests "pariahs." Finally, Huang types the correct word. The entire exercise takes about 30 seconds—twice the time required to simply type the sentence.

Such frustrating behavior is hardly peculiar to Microsoft's software. Oblivious to grammar and context, even the best speech-recognition systems stumble over homonyms ("write their weight" or "right there, wait?"). To do more than just dictation—to actually follow spoken orders—such systems still make users memorize long lists of permissible commands. "Send message" may work, but "e-mail this letter" may not.

They do this to avoid dealing with ambiguity. Told to "scan this text for typos," should the machine search for the word "typo"? Common sense says of course not. But how, short of typing in millions of facts can one endow computers with a modicum of common sense?

Down the hall from Huang, a team of computational linguists led by Karen Jensen believes it is onto an answer. "Our system pulls itself up by its bootstraps, using natural language to understand natural language," Jensen says.

The process works in four stages. Starting with a database of all English root words labeled with their simplest attributes—singular or plural, noun or verb, and so on—the researchers first coded the rules for adding prefixes and suffixes. Next they wrote a parser that can diagram the words in a sentence according to function. In the third stage, a program used the words, rules and parser to page through an unabridged dictionary, creating a new database entry for each meaning of each word. "A," for example, has three senses: as a noun, a preposition and an indefinite article. The system links each sense with the entries for all the significant words that appear in its definition. So entry one for "a" is connected to "first," "letter," "English" and "alphabet." After 24 hours or so, the program at last reaches "zymurgy," having woven an enormous web of words.

The database is still riddled with ambiguity, however; "a" is linked to "letter," but "letter" has several meanings. Should "a" be linked to "a symbol or character" or to "a written message?" The fourth stage resolves many such questions using a second program guided by a copy of the web itself. Scanning the several senses of "letter," the program finds that the first definition (a symbol or character) contains the words "English" and "alphabet," which match the first definition of "a," so it refines its link between the two words.

The technique, says Martin S. Chodorow of the City University of New York Graduate Center, can extract many semantic relationships from almost any text—including those in other languages. (Microsoft is building similar systems for French, German, Spanish, Chinese, Japanese and Korean.) Theoretically, Jensen says, the system could use a bilingual dictionary to generate a web linking English words with their semantic counterparts in another language—a big step toward automatic translation.

Microsoft is focusing, predictably, on more immediate applications. Its new word processor uses simplified versions of the team's early work as a grammar checker. The next step, Chodorow speculates, might be an intelligent thesaurus that spots misused words and recommends alternatives. Jensen responds that the entire information base still is too big and slow to go into a commercial product. But history suggests that day may come sooner than expected.

—W. Wayt Gibbs in San Francisco

PATHOLOGY

BEATING BACTERIA

New ways to fend off antibiotic-resistant pathogens

Exotic diseases such as Ebola and hantavirus capture headlines, but the real hot zone encompasses familiar infectious diseases such as tuberculosis, malaria, cholera, diarrhea and pneumonia: more than 10 million people died from these conditions in 1995. More disturbingly, the bacteria responsible for these ailments are becoming ever more resistant to today's drugs. In response, researchers have come up with novel ways to find antibiotics and are exploring several possible treatments—even some that derive from the days before antibiotics—that could defeat the resistant pathogens.

Although physicians have known for some time that bacteria can develop resistance to a particular antibiotic, until recently they were confident that another drug in stock would work. The antibiotics arsenal is now close to empty. For example, certain strains of enterococci bacteria no longer respond to vancomycin—the drug of last resort that doctors thought could beat any bacterial infection. In its *World Health Report 1996,* the World Health Organization stated that "too few new drugs are being developed to replace those that have lost their effectiveness. In the race for supremacy, microbes are sprinting ahead."

Researchers are only beginning to catch up. Drug companies scaled back their antibiotic development efforts after the 1950s, but a recent survey showed that the number of medicines and vaccines in development for infectious disease is up 33 percent since 1994. Most of these drugs remain in preclinical development or early clinical trials, however, and are not expected to reach the market for several years.

Many of the potential drugs have emerged from novel search methods. Vincent Ahonkhai, vice president for anti-infective agents at SmithKline Beecham, notes that because of the lack of rapid progress, "companies are loathe to continue in the same old ways" to discover antibiotics, such as altering the chemical structure of current drugs or screening microorganisms for potent antibiotics. "There's a rush to explore other methods," he says. One such approach is genomics, which involves sequencing the genetic code of disease-

ALLAN TANNENBAUM *Sygma*

MEDICATION AT HOME FOR A TUBERCULOSIS PATIENT
ensures proper use of antibiotics and helps to prevent the rise of resistant strains.

causing microbes to determine new targets for drugs to attack (this technique has also been instrumental in producing antiviral agents against HIV infection). Antibiotics developed using a genomics approach are still in the early stages of research.

Scientists are also turning to new natural sources. Daniel Bonner, executive director of anti-infective microbiology at Bristol-Myers Squibb, suggests that "there has been a change of thinking" in the search for naturally occurring antibiotics. Historically, people relied on antibiotic compounds produced by microorganisms (penicillin and erythromycin, for instance, are both produced by bacteria). But now Bonner says companies are considering a panoply of living creatures—plants, bees, grasshoppers and algae, to name a few. For example, researchers discovered that shark stomachs contain a compound called squalamine, which has antibiotic properties.

Investigators occasionally find an entirely new class of antibiotics serendipitously, usually by routine testing of thousands of synthetic chemicals. Last November Merck Research Laboratories announced the discovery of a class of novel antibiotics that in initial tests killed several strains of drug-resistant bacteria.

Still, it is not clear that an antibiotic can ever be immune to the problem of evolving resistance. W. Michael Scheld of the University of Virginia School of Medicine notes that previous generations of antibiotics at first appeared invincible: "History tells us to be cautious," he advises. At best, new drugs might remain potent for longer.

In the face of this quandary, some scientists are turning to drugs other than antibiotics. Jan van de Winkel of Utrecht University has been working with Medarex on what he calls "bispecific antibodies": chimeric molecules with one region that recognizes the microbial target and a second region that recognizes phagocytic cells of the immune system—in effect, these molecules escort the harmful pathogens to their enemies. According to van de Winkel, this approach "is a more natural way to combat infectious disease" because it employs the body's immune system. As a result, he believes, "the chances are probably much smaller that resistance will develop."

Even more unusual suggestions, harkening back to the days before antibiotics, have been proposed. One such approach relies on bacteria-attacking viruses, called bacteriophages. Another proposes irradiating a patient's blood with ultraviolet radiation to kill microorganisms. Neither, however, has garnered significant support among the medical community as a whole, which doubts the efficacy of such procedures.

While patients wait for new infection-fighting treatments, physicians emphasize the proper administration of antibiotics. The Centers for Disease Control and Prevention is currently putting together a campaign to warn about the risks of improper or unnecessary use of antibiotics. The series of videos, pamphlets and other educational material should come out within the next few months, just in time for the spring cold season. —*Sasha Nemecek*

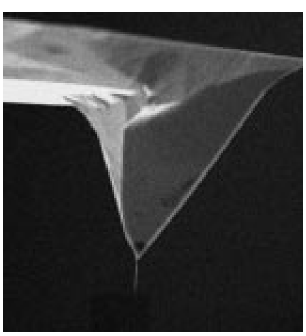
NANOTECHNOLOGY

Scoring with Buckyballs

All the hauling, lugging and lifting to construct the ancient pyramids one block at a time was, no doubt, tedious work. But forming an object one molecule at a time can be even more intricate. Now two groups exploring nanotechnology have recently incorporated buckminsterfullerene and related structures into their repertoire, thereby bringing buckyballs—those spherical molecules made of carbon—a step closer to genuine applications.

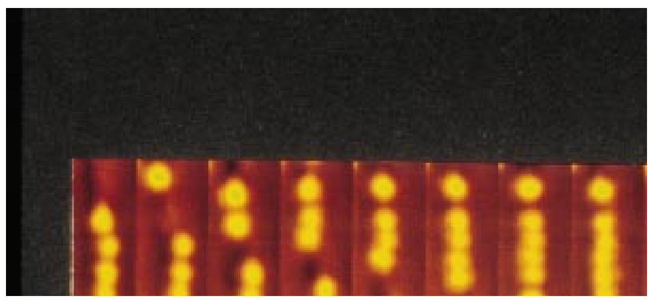
One group's work may improve an existing specialized tool of nanoengineering—the scanning-force microscope (SFM), which relies on fine tips to detect and nudge molecules. Until now, tips were rather large, up to 2,000 nanometers thick. Hongjie Dai of Rice University, working with buckyball co-discoverer and Nobelist Richard E. Smalley, fashioned some fullerenes into a pipe, or "nanotube," to replace some SFM tips. The photograph below shows the new tip dangling from the old.

Shaped like concentric cylinders of chicken wire, these multiwall tubes can range between five and 20 nanometers thick, thus facilitating more accurate atomic manipulation. When capped at one end with a hemispheric fullerene, the tip can serve as a chemical probe. What makes them even more appealing is their durability. Fellow researcher Daniel Colbert explains that although they tried to "crash," or damage, the tubes, the inherent flexibility allows them to return to their original shape.



HONGJIE DAI

To make nanotubes, the team vaporized carbon with an electric current. The vapor condenses to form a sooty gob, rich in nanotubes. The workers mine the clump with cellophane tape, and then, holding a glue-dipped conventional tip, they lightly touch it to the wad of nanotube bundles and gingerly pull one out.



IBM RESEARCH DIVISION

A continent away, scientists at the IBM Zurich Research Laboratory incorporated buckyballs for a less practical purpose: a smaller-than-Lilliputian-size abacus (*above*). Researcher James Gimzewski and his colleagues lined up buckyballs on a multigrooved copper plate, mimicking beads on a string, and proceeded to manipulate the beads with a scanning tunneling microscope (STM), using them to calculate. The authors write in *Applied Physics Letters* that because hundreds of buckyballs can fit in the width of a processor chip, they could be exploited in building a better computer chip. That vision, though, may be a while in coming, considering how slow the computation is. Gimzewski notes that moving the buckyballs with an STM probe is the equivalent of operating a standard abacus with the Eiffel Tower. But by showing what is possible, buckyballs are starting to score big in the small field of nanotechnology. —*Erica Garcia*

Universal Disservice

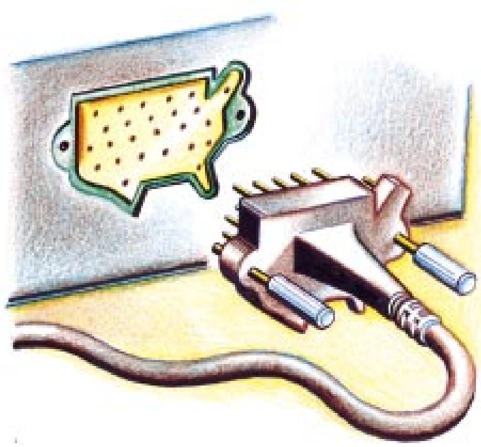
Universal service is one of the most noble legacies of the days when telephones were made of black Bakelite and came only from AT&T. The policies evolved to make sure that everybody, no matter how remote or how poor they might be, could get access to basic telephone services, and they mostly worked. Now politicians are trying to adapt universal service to the Internet and today's new communications technologies. Noble instinct; bad idea. The more politicians try to update universal service, the more they demonstrate why such policies should be scrapped.

At the heart of efforts to modernize universal service is a review board composed of both federal and state regulators. Created in March by the Telecommunications Act of 1996, the board last November reported its recommendations, which the Federal Communications Commission (FCC) plans to rule on early this year. Problem is, though, that for all its work the board still hasn't come up with consistent answers to the two most basic questions facing universal-service policies. Who is universal service trying to help, and what is universal service trying to help them do?

Traditionally, universal service tries to provide basic telephone services to the poor and those in rural areas. The board wants to keep up those traditions, but it also wants to wire schools, libraries and hospitals to the Internet. To do all these things at once requires massive and complicated regulations and cross-subsidies that will leave just about everyone worse off—except big, entrenched telephone companies. To see the problems, look at some of the board's recommendations in detail.

Today the "universal-service fund"—which amounts to about $750 million—gives money to any telephone company that can show that costs to consumers are higher than 115 percent of the national average. The point is to ensure that even people with inefficient telephone companies pay average prices, although it also has the unfortunate side effect of removing any incentive inefficient companies might have to improve themselves.

For the future, the joint board still wants to continue the subsidies, but instead of awarding them to companies with high costs, it plans to create an econometric "proxy model" that can distinguish between those companies that are inefficient and those serving areas that have unavoidably high costs. Sounds great but for one snag: the board doesn't say how this model might actually work. This is no trivial omission. Effectively, the creators of the model will have to decide which technologies will reduce costs and which won't—before anybody has tried them. Rather than encouraging innovation among the telephone companies, the proxy model threatens to force them all into lockstep with bureaucratic preconceptions.



DAVID SUTER

Similar hubris plagues the board's plans to help schools and libraries connect to the Internet. The board wants to offer discounts of 20 to 90 percent on the cost of giving every classroom and library a basic connection. In theory, just giving the schools money would provide them both with freedom to buy the services and clout to negotiate the best prices. But the FCC has no powers of taxation, and presumably grants are not as legally practical as discounts. (Nevertheless, some telecommunications lawyers reckon that the whole scheme to put schools on the Net would lie well beyond the FCC's powers.) Given that the total cost of wiring classrooms could be $5 billion to $8 billion, the discounts therefore shift a lot of clout to Washington—particularly when nobody has yet defined what the "adequate" connection called for by the board might be.

Where the problems of universal service become even more vexing is in determining who should foot the bill. Presumably to avoid levying charges with one hand on the same services it would subsidize with the other, the joint board proposes to exempt providers of the Internet and other on-line services from the obligation of contributing to the funds that will constitute universal-service subsidies. (Here, too, the board glosses over the fuzzy distinction between Internet service and traditional voice telephony.)

But the local telephone companies are already lobbying hard to get Internet service providers to contribute more to the cost of subsidizing residential telephone service. With pricing policies being proposed by the joint board, the result is a growing threat of much higher prices for the Internet.

Specifically, the board recommends that line-rental charges not be raised—and in some cases be lowered. But because the income from local calls is negligible, and monthly line-rental charges do not cover the (mostly fixed) costs of providing residential service, the board decision would leave local telephone companies dependent on "access charges." Such charges are levied on each minute that long-distance telephone service providers connect to the local network. Not surprisingly, local telephone companies are lobbying the FCC to require Internet service providers to pay similar access charges, which would both force prices up for Internet service and push Internet providers to bill on usage. (No prize for guessing who has the best systems to handle the complicated task of billing by the minute.)

Of course, such price-raising regulations are absurd and counterproductive. But they are also the inevitable consequence of systems that, like universal service, try to set prices where politicians think they should be rather than where consumers in the marketplace decide. Should Americans determine that the poor do need help in getting wired, it would be far cheaper and more efficient to relieve their poverty the old-fashioned way—by giving them money. Tellingly, this argument does not go down well with universal-service advocates, who argue that Americans would never authorize taxes on the scale of existing universal-service subsidies. But perhaps, for all the noble rhetoric, that is exactly the point. *—John Browning*

Immunotherapy for Cocaine Addiction

Newly developed compounds derived from the immune system may help combat cocaine abuse by destroying the drug soon after it enters the bloodstream

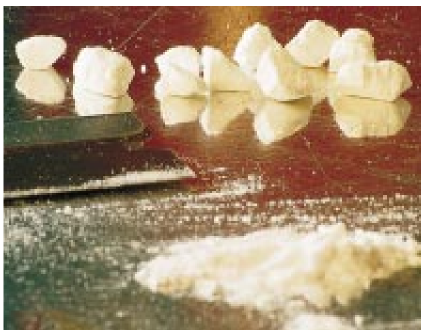
by Donald W. Landry

The epidemic of cocaine abuse that has raged through the U.S. for more than a decade has left no part of the nation untouched. Millions take the drug, with medical consequences that include severe psychological disturbance and sudden heart attack. The social effects of illegal cocaine distribution have contributed to the devastation of many cities, draining both human and financial capital that might otherwise be put to productive use.

Many factors have contributed to the present crisis, including the social acceptance of drug taking, the ineffective antismuggling policies that have led to increased availability of inexpensive cocaine, and the development of a higher-potency, smokable form of the drug, "crack." Unfortunately, as a society we have not been able to reverse the tide, and biomedical science has thus far failed to offer a pharmacological solution.

In fact, despite decades of effort, medical research has not yet produced any agent able to treat effectively either cocaine addiction or cocaine overdose. This protracted failure has prompted my colleagues and me at Columbia University to embark on a radically new approach. Traditional therapeutic research has attempted to interfere with cocaine in the brain; our strategy aims to destroy the drug before it has any chance of reaching the brain at all.

The appeal of this new approach is based on the peculiarities of cocaine's effects on the brain. Essentially all addictive drugs stimulate a neural "reward pathway" that evolved in the ancestors of mammals more than 100 million years ago. This pathway activates the so-called limbocortical region of the brain, which controls the most basic emotions and behaviors. In preconscious creatures, activation of reward pathways during behaviors as diverse as feeding and copulation aided learning and undoubtedly conferred a survival advantage. The same structures persist today and provide a physiological basis for our subjective perception of pleasure. When natural brain chemicals known as neurotransmitters stimulate these circuits, a person feels "good."


JASON GOLTZ

CRACK and powdered cocaine are the two forms of the drug.

Substance abuse is rooted in the normal neurobiology of reinforcement. Every substance that people commonly self-administer to the point of abuse—alcohol, nicotine, barbiturates, amphetamines, heroin, cannabis or cocaine—stimulates some part of the reward pathway, thereby "teaching" the user to take it again. Furthermore, these substances alter the normal production of neurotransmitters so that abandoning the drugs once the addiction has taken root can trigger withdrawal: physical or psychological upsets whose effects vary from deeply unpleasant to dangerous. Humans and other animals will perform work, sacrifice other pleasures or endure pain to ensure a continuing supply of a drug they have come to depend on.

The magnitude of reinforcement differs intrinsically among the addictive drugs. It also rises with the amount of drug that reaches the brain and the speed with which the drug's concentration mounts. Intravenous injection typically provides the most efficient delivery. For substances that can be vaporized, however, such as cocaine in its crack form, smoking is equally effective in producing the experience that addicts want. Cocaine, particularly when injected or smoked as crack, is the most potent of the common reinforcers. Its peculiar mechanism of action makes it unusually difficult to combat.

The Cocaine Challenge

Cocaine works by locking neural switches in the reward pathway into the "on" position. Reward pathways, like all neural circuits, contain synapses—points of near contact between two neurons—that are bridged by neurotransmitters. When a neuron on one side of the synapse fires, it releases a transmitter, such as dopamine, into the narrow gap between cells, and the neuron on the other side of the synapse responds by changing its own rate of firing. To prevent excessive signaling, the first neuron actively takes up the neurotransmitter from the synaptic space.

Cocaine interferes with this system. Removal of dopamine from a synapse relies on transport proteins that carry the neurotransmitter from the outside of the cell to the inside. Cocaine prevents the transport proteins from working, and so, when the drug is present, too much dopamine remains in the synapse. The dopamine overstimulates the reward pathway and reinforces cocaine use.

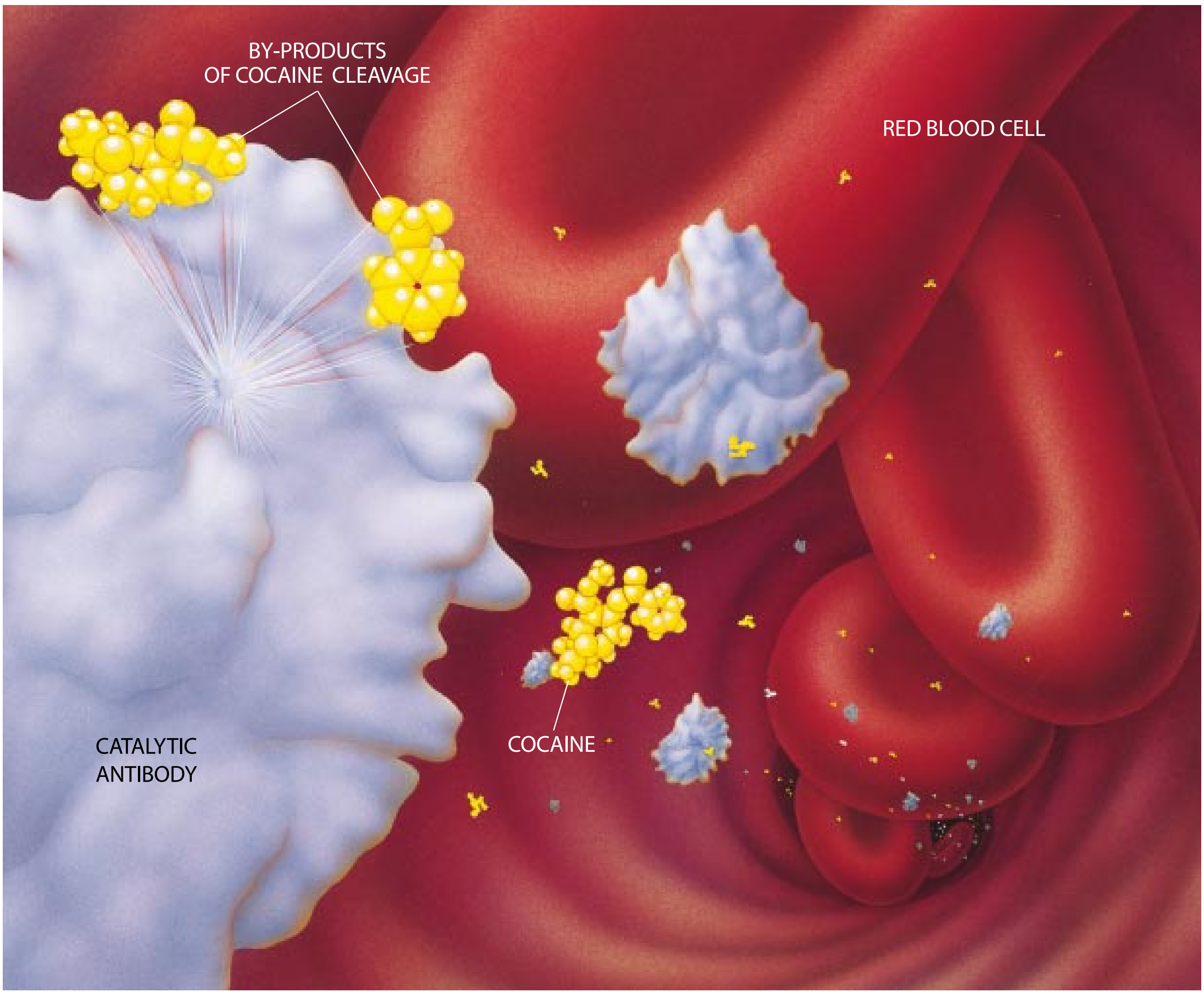
Contrast the way cocaine works with the way heroin works: heroin binds to a neurotransmitter receptor and stimulates reward pathways directly. Cocaine stimulates the same circuits indirectly, by prolonging the action of neurotransmitters that are already present. This difference is what makes interfering with cocaine such a challenge. Heroin can be stopped by inactive, dummy compounds (such as naltrexone) that bind to the same receptors and thereby block heroin's access to them. But any agent that impedes cocaine's access to its target—the dopamine transporter—will also most likely disrupt the transporter's ability to remove dopamine from the synaptic space. It will thus have virtually the same effect as cocaine. Newly discovered subtleties in the ways dopamine and cocaine interact with the transporter suggest that a usable cocaine blocker may eventually be found, but so far intensive efforts have not borne mature fruit.

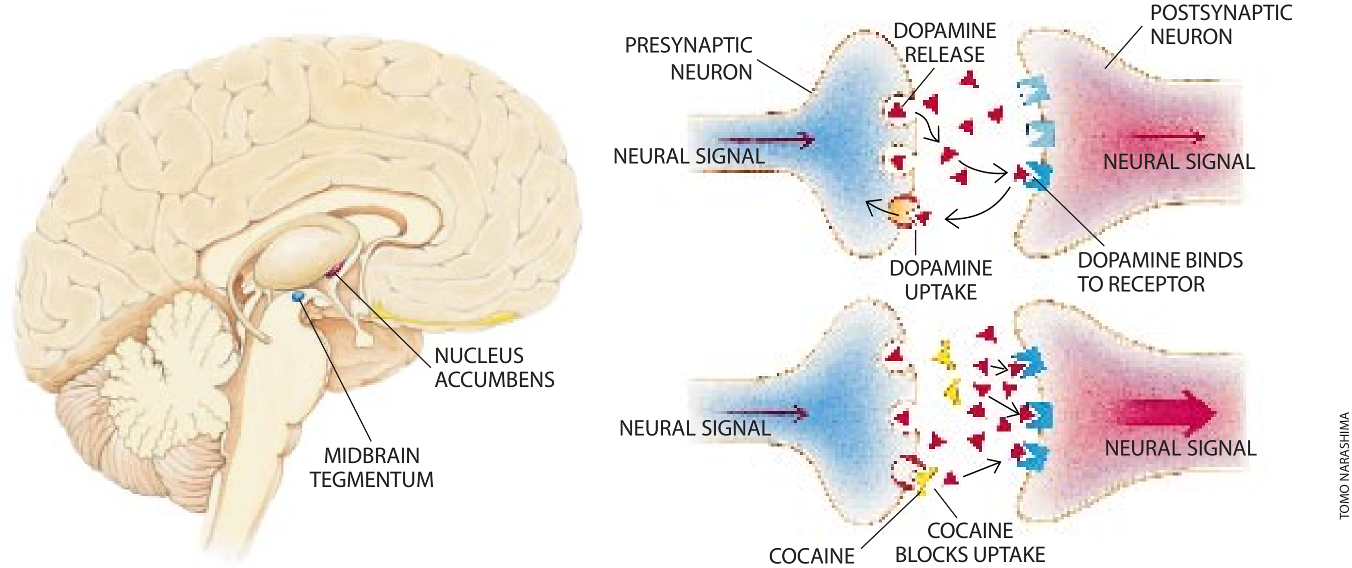
As an alternative approach, my colleagues and I began several years ago to consider whether it might be possible to interrupt the delivery of cocaine to the brain. Regardless of how cocaine enters the body, it must be carried to the brain by circulating blood. The natural choices for blood-borne interceptors are antibodies—molecules of the immune system designed by nature to bind to a variety of target molecules. We found an exciting, almost forgotten report published in 1974, in which Charles R. Schuster, now at Wayne State University in Detroit, discovered in monkeys that immunization with a heroin analogue (which induced the immune system to make antibodies against the analogue) blocked some of the drug's effects.

Unfortunately, the circulating antibodies quickly vanished from the bloodstream as they formed complexes with their target. Because cocaine addiction involves taking repeated doses, it was clear to us that an anti–cocaine antibody would need to eliminate the drug without itself being inactivated or eliminated. Furthermore, cocaine can bind 250 times its weight in antibody—even a single dose of 100 milligrams or so would overwhelm any reasonable amount of a typical circulating antibody.

Luckily, advances in organic chemistry since 1974 had provided just the practical solution we needed: catalytic antibodies. In the late 1980s Richard A. Lerner of the Scripps Research Institute and Stephen J. Benkovic of Pennsylvania

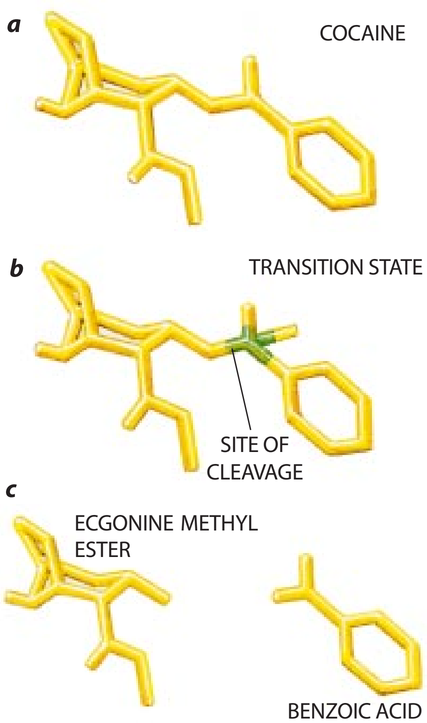
APPROACH UNDER STUDY for combating cocaine addiction would deliver antibody molecules to the bloodstream, where they would trap cocaine and break it apart. The antibodies would thus inactivate the drug before it had a chance to work in the brain.





COCAINE FOSTERS ADDICTION by overexciting a brain circuit that gives rise to exhilaration. This circuit includes (*diagram at left*) neurons that extend from the midbrain tegmentum and form contacts, or synapses, with neurons of the nucleus accumbens. Stimulation occurs (*top diagram at right*) when the neurotransmitter dopamine binds to receptors on postsynaptic cells. In the nondrugged brain, the signaling is dampened because the dopamine is cleared from the synapse by the neurons that release it. Cocaine blocks this clearance (*bottom diagram*), causing dopamine to accumulate in the synapse and to activate the circuit intensely.

State University and, independently, Peter G. Schultz of the University of California at Berkeley discovered that they could make antibodies that would both bind to selected molecules and facilitate chemical reactions leading to their breakup. Once the chemical change has taken place, the catalytic antibodies release the products and emerge unchanged, ready to bind again. Some antibodies with particularly potent catalytic activity can drive scores of reactions a second. Such high turnover rates, we realized, would allow a small amount of antibody to inactivate a large quantity of drug.



BREAKUP OF COCAINE involves altering its structure. The native form (*a*) is converted to a less stable, transition state (*b*). Then it is cleaved to yield two inactive substances (*c*).

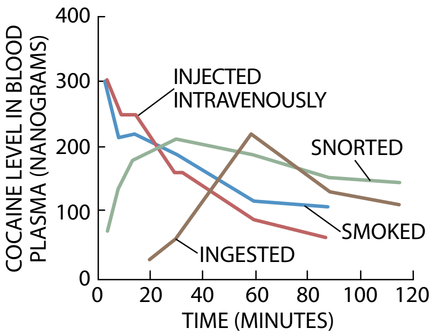
Easy to Break Up

Cocaine seemed a great candidate for the catalytic antibody approach in part because it can be deactivated by a simple cleavage reaction that yields two inactive products. An enzyme in human blood promotes precisely this reaction, but too slowly to blunt the addicting high. In contrast, cleaving heroin produces morphine and so merely exchanges one addictive drug for another.

We also knew that some of the catalytic antibodies able to degrade esters—a class of chemical structures that includes cocaine—acted quite efficiently. Antibodies can catalyze more than 40 distinct chemical transformations, but the reaction rates vary widely and are frequently low. Yet certain antibodies that cleave esters (otherwise known as esterases) are nearly as efficient as natural enzymes, and so we had reason to think that antibodies to cocaine could work fast enough to deprive an abuser of most of the drug's effect. They would thereby break the cycle of reinforcement that maintains addiction.

As a proof of this concept, we could also look to a fascinating experiment involving natural cocaine and its biologically inactive mirror image, known as (+)-cocaine. (The two compounds have the same constituents, but their structures differ as do our left and right hands.) When both compounds were injected into a monkey, only natural cocaine reached the brain. It turns out that the biological enzyme that degrades cocaine also degrades the mirror-image compound, but 2,000 times faster. The half-life of (+)-cocaine in the bloodstream is only five seconds. An enzyme that had the same kind of effect on natural cocaine would make snorting or smoking the drug essentially innocuous.

My colleagues and I therefore set out to develop catalytic antibodies able to degrade cocaine. Our plan was to create a cocaine analogue that would spur the immune systems of laboratory animals to produce antibodies to cocaine; these antibodies could then be purified and manufactured in quantity. More specifically, we wanted to create a molecule whose structure resembled that of cocaine in what is called its transition state. The folds, pockets and active sites of a catalytic antibody are not shaped for the normal configuration of the target compound but rather for its transition state—the shape the molecule takes in the midst of a chemical reaction. As a result, the antibody encourages the target to take on this configuration, there-



SOURCE: Marian Fischman, Columbia University

JOHNNY JOHNSON

SMOKING OR INJECTING cocaine raises blood (and brain) levels of the drug more quickly than snorting or ingesting it does and so produces a stronger effect. Antibody therapy may not eliminate the drug completely. But it should reduce cocaine's appeal by decreasing its potency.

by making the reaction more likely. The state of the art for designing transition-state analogues is a combination of theory and empiricism. Despite researchers' best efforts, some analogues idiosyncratically fail to elicit catalytically active antibodies.

We made our transition-state mimic by replacing one atomic grouping in the transition state with another that would stabilize the structure yet maintain the normal transition architecture. We had to devise a new method for synthesizing this particular compound because all known methods failed to produce the desired structure. Once our cocaine mimic had been made, we had to attach a carrier protein to it to ensure that it would engender an immune response. Small molecules such as cocaine do not generally elicit antibodies by themselves—which is why, for example, people do not make antibodies to aspirin.

We immunized mice with our compound and isolated cells that produced antibodies to it. Among those cells, we found two strains making antibodies that bound cocaine, degraded the drug, released inactive products and repeated the cycle—the first artificial enzymes to degrade cocaine. Since then, we have synthesized two additional transition-state analogues and now have nine different catalytic antibodies. Each molecule of our most potent agent to date can degrade more than two cocaine molecules per minute. Such activity is sufficient for initial animal studies.

We will very likely want a more active antibody for human use. An addict's bloodstream would need to contain 10 grams or more of our current best performer to neutralize a 100-milligram snort of cocaine. If we can achieve a turnover rate of two reactions per second, 500 milligrams of antibody—which could easily be injected by syringe—would be sufficient to exclude a large dose of cocaine from the brain. Because catalytic antibodies with activities greater than 40 turnovers per second have been reported, this goal seems realistic.

To improve the chemical activity, we are pursuing a three-pronged approach. First, we have developed a strategy for designing additional transition-state analogues that should elicit highly active catalytic antibodies—any antibodies that bind our new analogues will warp cocaine into a particularly fragile configuration that cleaves almost spontaneously. We are also developing screening methods that will allow us to select antibodies directly for catalytic activity rather than first selecting for tight binding to a transition-state analogue. Finally, we have cloned our catalytic antibodies, creating pure populations of each type, so that we can alter their structures selectively.

Putting Antibodies to Work

Even after we have developed a catalytic antibody that can degrade cocaine efficiently, we will have to face other hurdles to devising an effective drug treatment. Physicians cannot immunize addicts with a transition-state analogue directly, because only a small fraction of the various antibodies a patient produced against it would likely be catalytic. To ensure high levels of a catalytic antibody in the blood, doctors would have to infuse it directly—a process known as passive immunization. That being the case, manufacturers would have to develop cell lines able to make large amounts of these antibodies. Monoclonal antibodies have become established pharmaceutical agents, however, so this task seems manageable.

A catalytic antibody could be designed to remain in the body for several weeks or more, roughly as long as natural human antibodies. Such a long duration would be essential to simplify treatment programs, as a single injection could block cocaine for a month. That would be long enough for the most intense psychological pangs to subside and for conventional treatment of addiction to be established. The majority of those participating in current treatments continue to take cocaine even as they undergo counseling and other therapy designed to wean them from the drug. If the cocaine could be blocked, other treatments might be more effective; heroin treatment programs that employ both counseling and methadone to block that drug's effects report abstinence rates between 60 and 80 percent, in contrast with 10 to 30 percent for treatment regimens that rely on behavioral changes alone.

Even if a cocaine blocker does not prevent every bit of the drug from reaching a user's brain, it may still act against addiction by blunting the intensity of the drug's high. The rush of smoking a large dose of crack might be reduced to the less overwhelming level of snorting a few milligrams of powdered cocaine. And that difference could be enough to start addicts on the road to recovery. SA

The Author

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Further Reading

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Satellite Radar Interferometry

From hundreds of kilometers away in space, orbiting instruments can detect subtle buckling of the earth's crust

by Didier Massonnet

Tectonic plates creep silently past one another; glaciers flow sluggishly down mountains; ground level slowly rises and falls. The geologic forces that shape the surface of the earth usually act with such stealth that most people remain entirely unaware of them. But then the sudden break of a geologic fault or the explosive eruption of a volcano occurs in a populated area, and the devastation instantly makes thousands frighteningly aware that the solid earth is indeed prone to motion.

To better understand and, perhaps, forecast such catastrophic events, scientists have labored to measure the ongoing bending and stretching of the earth's crust. For this task, they have employed instruments of many types, from simple surveyor levels to sophisticated electronic positioning equipment. With all such methods, a person must travel to the site that is to be evaluated to set up some sort of apparatus and make observations. Yet this commonsensical requirement, as it turns out, is not an absolute prerequisite.

In 1985 I carried out a study—then an entirely theoretical exercise—that showed a way, without putting any equipment at all on the ground, to monitor the deformation caused by tectonic forces. At that time scientists had used satellites and aircraft for many years to construct radar images of the land below, and I envisioned that, with some additional tricks, these same devices could detect the subtle shifts that the surface of the earth undergoes. I immediately tried to convince geologists of the value of this endeavor, but most of the people I approached remained dubious. Measuring ground motion of only a few millimeters from hundreds of kilometers away in space seemed too miraculous to be feasible. Fortunately, I was able to persuade my employer, the French Space Agency, to allow me to pursue this exciting prospect.

It would take years of diligent work, but my research group, along with other investigators around the world, has succeeded in carrying out what seemed quite fantastic to most scientists just a dozen years ago. My colleagues and I have used a new technique, called satellite radar interferometry, to map geologic faults that have ruptured in earthquakes and to follow the heaving of volcanic mountains as molten rock accumulates and ebbs away beneath them. Other researchers have harnessed radar interferometry to survey remote landslides and the slow-motion progress of glacial ice. Former skeptics must now concede that, miraculous or not, radar satellites can indeed sense barely perceptible movements of the earth's surface from far away in space.

Helpful Interference

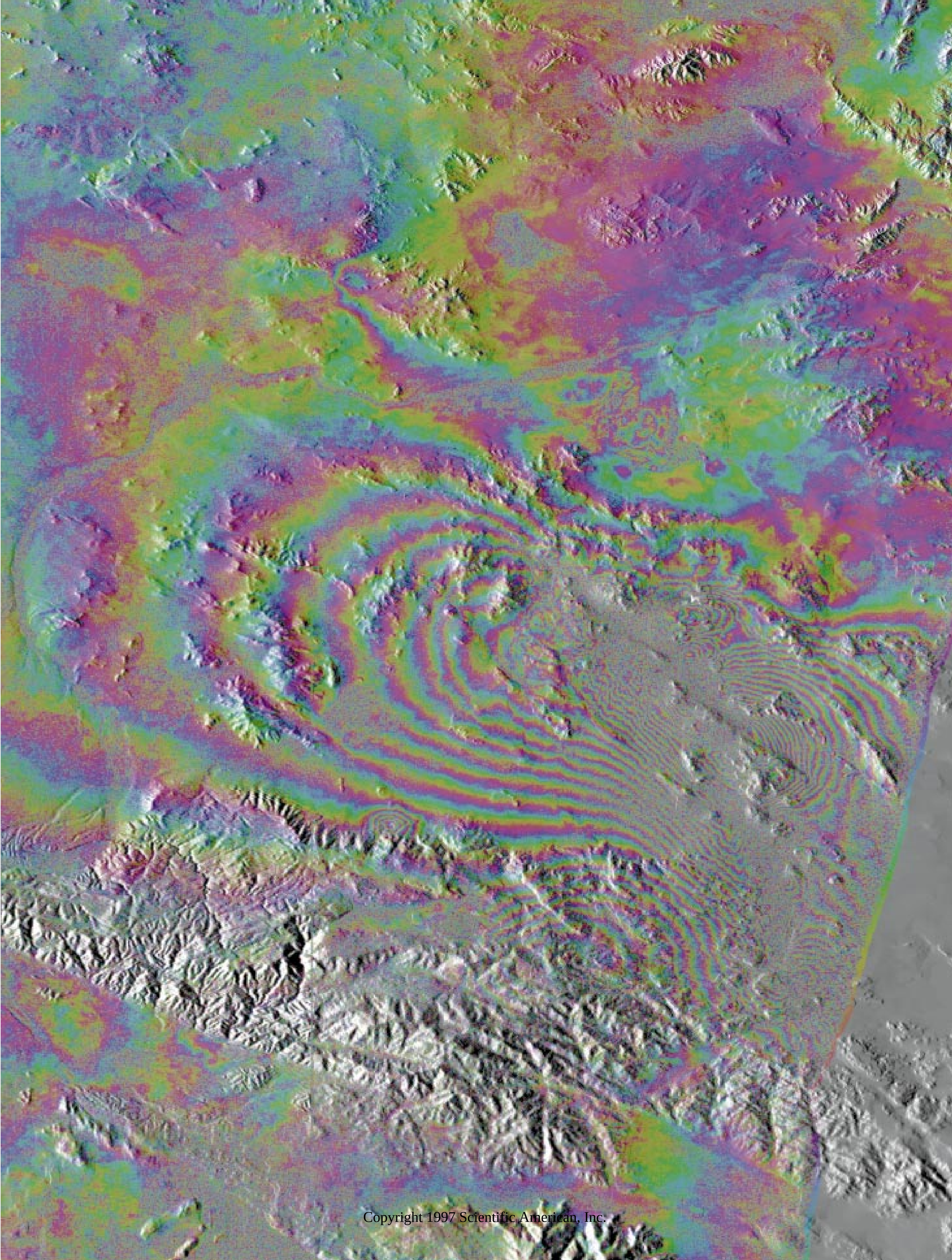
Although the dramatic successes of satellite radar interferometry are quite recent, the first steps toward accomplishing such feats took place decades ago. Soon after radar (shorthand for *ra*dio *d*etecting *a*nd *r*anging) became widely used to track airplanes using large rotating dish antennas, scientists devised ways to form radar images of the land surface with small, fixed antennas carried aloft by aircraft [see "Side-Looking Airborne Radar," by Homer Jensen, L. C. Graham, Leonard J. Porcello and Emmett N. Leith; Scientific American, October 1977]. Even thick cloud cover does not obscure such images, because water droplets and ice crystals do not impede the radio signals. What is more, aircraft and orbiting satellites fitted with radar antennas can take these pictures equally well during the day or night, because the radar provides, in a sense, its own light source.

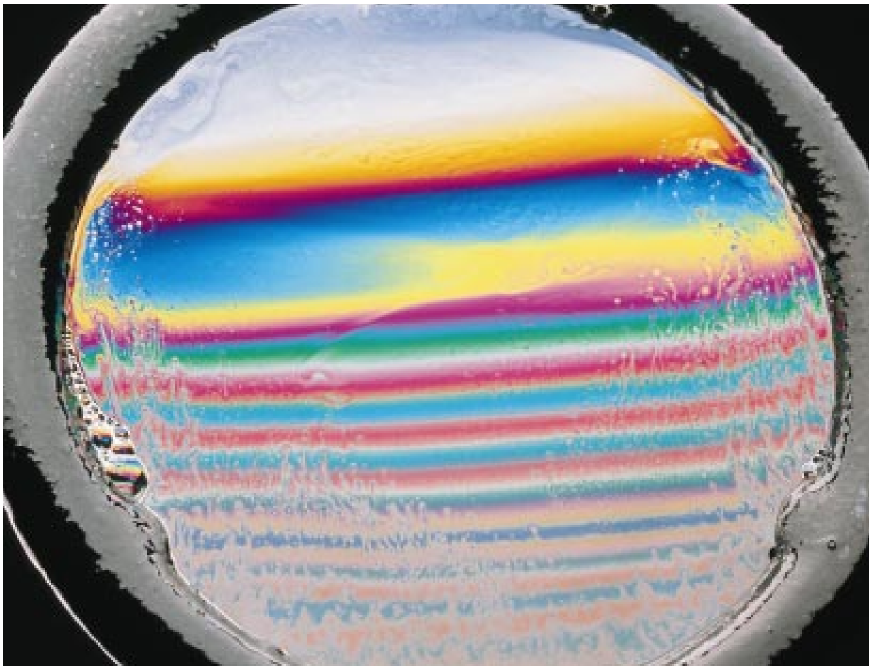
But the distinction between radar imaging and conventional aerial photography is more profound than the ability of radar to operate in conditions that would cause optical instruments to falter. There are fundamental differences in the physical principles underlying the two approaches. Optical sensors record the amount of electromagnetic radiation beamed from the sun (as countless independent light waves, or photons) and reflected from the ground. Thus, each element of the resulting image—called a pixel—is characterized by the brightness, or amplitude, of the light detected. In contrast, a radar antenna illuminates its subject with "coherent" radiation: the crests and troughs of the electromagnetic wave emitted follow a regular sinusoidal pattern. Hence, radar instruments can measure both the amplitude and the exact point in the oscillation—called the phase—of the returned waves, whereas optical sensors merely record the quantity of reflected photons.

A great benefit arises from measuring phase, because radar equipment operates at extremely high frequencies, which correspond to short radio wavelengths. If a satellite radar functions, for

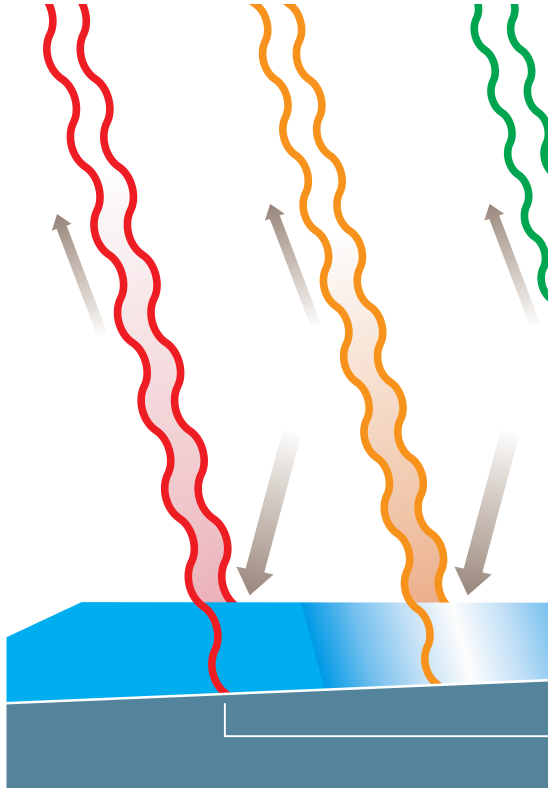
INTERFERENCE FRINGES (*colored bands at right*) obtained from a sequence of radar scans by the ERS-1 satellite (*above, left*) show the deformation of the ground caused by an earthquake near Landers, Calif., in 1992. Each cycle of interference colors (*red through blue*) represents an additional 28 millimeters of ground motion in the direction of the satellite. The radar interference caused by the mountainous relief of the area (*black-and-white background*) was removed to reveal this pattern of ground deformation.

DIDIER MASSONNET





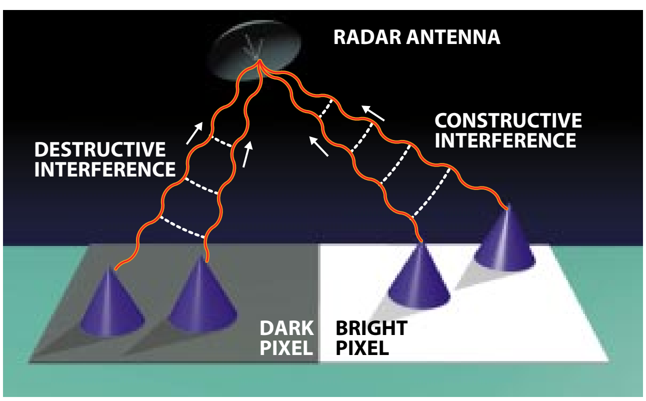
RICHARD MEGNA *Fundamental Photographs*



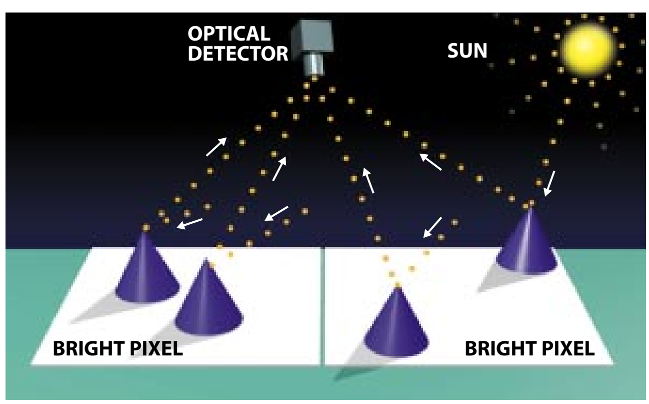
SOAP FILM of tapering thickness can separate light into its component colors (*above*), each of which corresponds to a particular wavelength of electromagnetic radiation. A fringe of one color shows where the light rays of that wavelength reflect from the top and bottom surfaces of the thin film and combine constructively (*right*).

instance, at a frequency of six gigahertz (six billion cycles per second), the radio signal will travel earthward at the speed of light for only five centimeters during the tiny amount of time the wave takes to complete one oscillation. If the distance from the radar antenna to a target on the ground is, for example, exactly 800 kilometers, the 1,600-kilometer round-trip (for the radar signal to reach the earth and bounce back up) will correspond to a very large—but whole—number of wavelengths. So when the wave returns to the satellite, it will have just completed its final cycle, and its phase will be unchanged from its original condition at the time it left. If, however, the distance to the ground exceeds 800 kilometers by only one centimeter, the wave will have to cover an additional two centimeters in round-trip distance, which constitutes 40 percent of a wavelength. As a result, the phase of the reflected wave will be off by 40 percent of a cycle when it reaches the satellite, an amount the receiving equipment can readily register. Thus, the measurement of phase provides a way to gauge the distance to a target with centimeter, or even millimeter, precision.

Yet for decades, most practitioners of radar imaging completely overlooked the value of phase measurements. That oversight is easy to understand. A single pixel in a radar image represents an appreciable area on the ground, perhaps 100 square meters. Such a patch will generate multiple radar reflections from the countless small targets contained within it—scattered pebbles, rocks, leaves, branches and other objects—or from rough spots on the surface. Because these many radar reflections will combine in unpredictable ways when they reach the antenna, the phase mea-

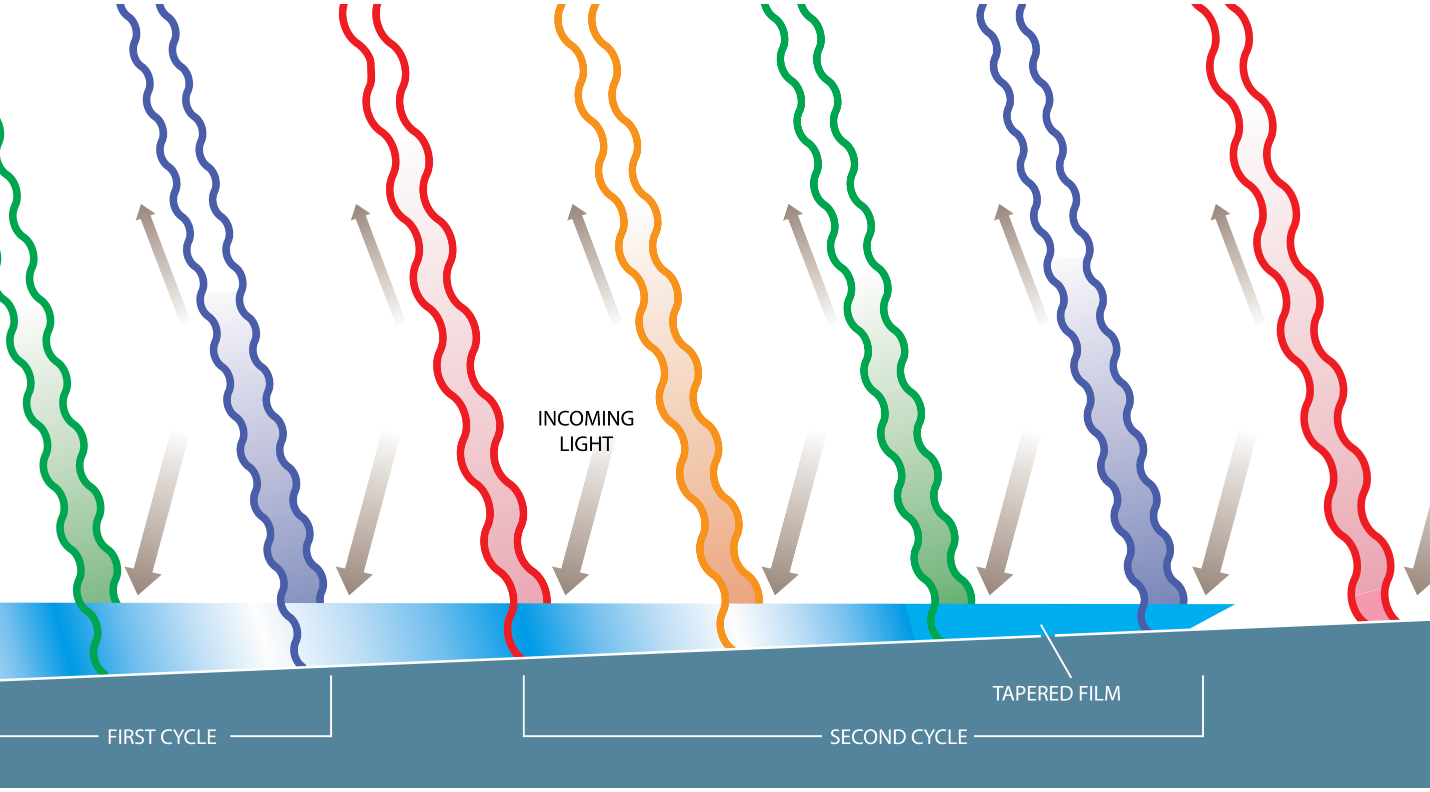


RADAR REFLECTIONS (*red lines*) from a pair of nearby objects can interfere constructively (*right*) or destructively (*left*). Minor differences in geometry can therefore give rise to large changes in the amplitude of the pixels in a radar image.



SLIM FILMS

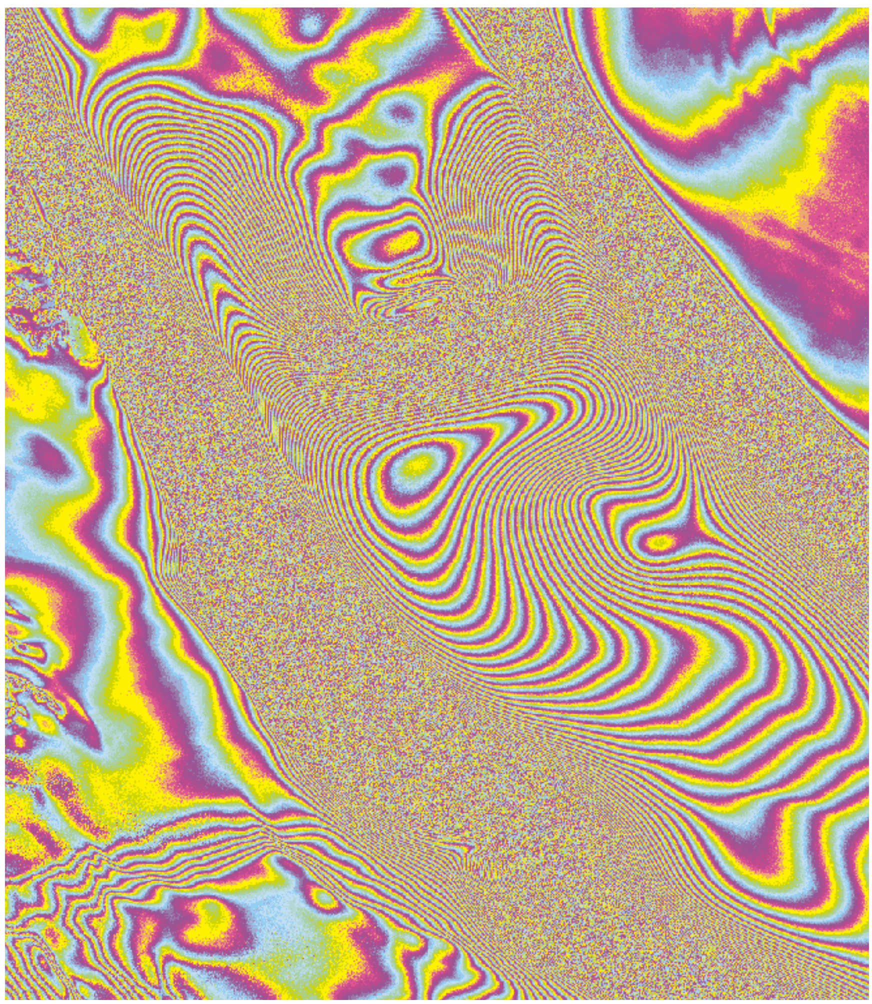
OPTICAL REFLECTIONS from a pair of objects always produce a similar number of reflected photons (*orange*), regardless of the exact position of the objects. Thus, the brightness of a pixel does not vary with slight shifts in the configuration of reflectors.



sured for a given pixel seems random. That is, it appears to have no relation to the phase measured for adjacent pixels in the radar image.

The amplitude associated with a given pixel in such an image will, however, generally indicate whether many or few elementary reflectors were present at the corresponding place on the ground. But the amplitude measurements will also have a "noisy" aspect, because the individual reflections contributing to one pixel can add together and make the overall reflection stronger (constructive interference), or they can cancel one another out (destructive interference). This phenomenon in the reflection of coherent radiation—called speckle—also accounts for the strange, grainy appearance of a spot of laser light.

For many years, scientists routinely overcame the troubling effects of speckle by averaging the amplitudes of neighboring pixels in their radar images. They followed this strategy in an attempt to



RICHARD M. GOLDSTEIN *Jet Propulsion Laboratory*; BARCLAY KAMB AND HERMANN ENGELHARDT *California Institute of Technology*

GLACIAL ICE at the margins of Antarctica flows toward the sea relatively rapidly along confined channels, or "ice streams," such as the one mapped here using a pair of satellite radar images. Two parallel bands of highly sheared ice (*speckled areas*) mark the borders of the ice stream.

mimic the results of conventional black-and-white aerial photography, and to that end they were quite successful. Yet by averaging amplitudes, they lost all knowledge of the phase of the radar reflections, which unbeknownst to them contained much hidden information.

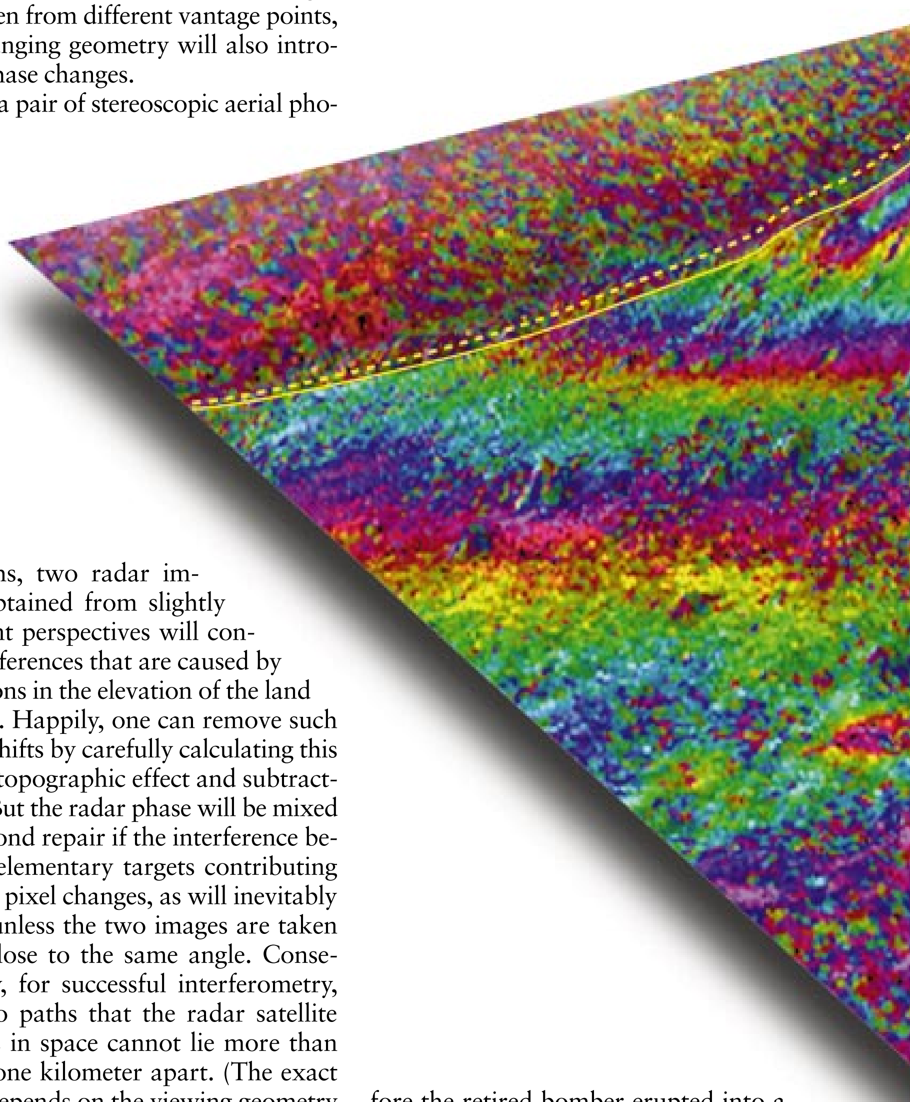
But that state of affairs did not continue indefinitely. In 1974 L. C. Graham, working at Goodyear Aerospace, first demonstrated that it was possible to take advantage of the phase measured by an airborne radar. Then, in the early 1980s, scientists at the Jet Propulsion Laboratory in Pasadena, Calif., showed that they could extract similar results from the phase measured by SEASAT, the first civilian radar satellite, which was launched in 1978 (but worked for only three months). They did so by comparing two radar images taken from roughly the same position but at different times. In a sense, that exercise was akin to taking two widely separated frames of time-lapse photography. Although the phase itself appeared random every time, the phase differences between corresponding pixels in the two radar images produced a relatively straightforward interference pattern.

In principle, if two sequential satellite images are taken from exactly the same position, there should be no phase difference for any pair of corresponding pixels. But if the scene on the ground changes ever so slightly in the interim between the two radar scans, the phases of some pixels in the second image will shift. Radar satellites can thus track minute movements of the earth's surface.

In the usual presentation, radar "interferograms" produced in this way show ground motion using a series of colored bands, which are meant to resemble the interference fringes produced from a thin film of soap or oil. One complete set of colored bands represents a shift of half a wavelength, because the radar wave must cover the round-trip distance back and forth. For the European satellite ERS-1, a set of fringes marks a change of just three centimeters in the amount of ground motion. Although these fringes record only the component of ground movement that is in the direction of the satellite (or directly away from it), they nonetheless prove extraordinarily useful, because a single radar view can span vast stretches of land that would take years for geologists and surveyors to map in similar detail.

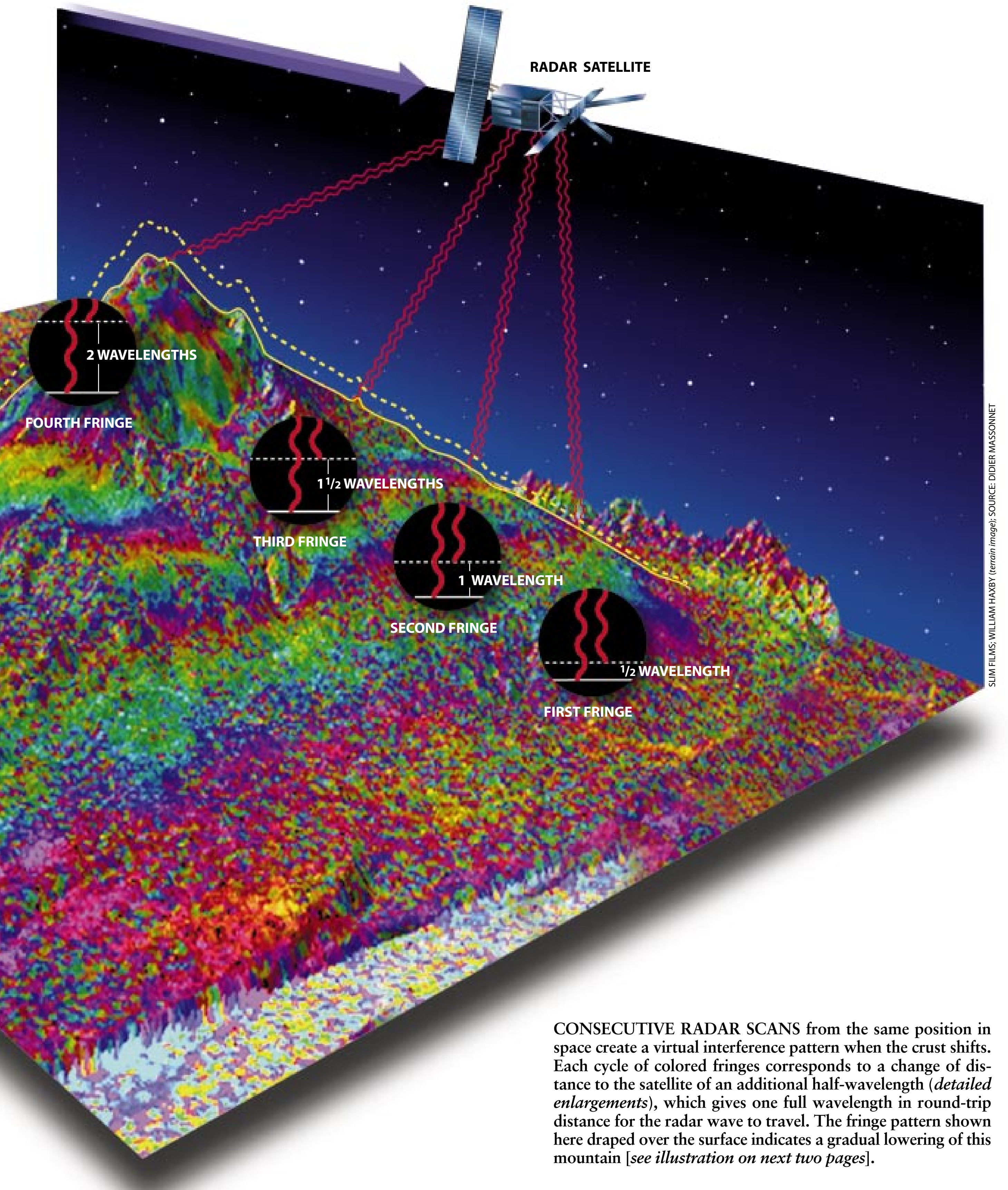
Radar interferometry does, however, require that the many small reflective objects contributing to each pixel—be they rocks or pockets of vegetation—remain unchanged (so that the random component of the phase is exactly the same for both images). This rather stringent condition creates some bothersome limitations. If the time elapsed between the acquisition of the two images is excessive, the small targets encompassed by each pixel will shift erratically. Leaves can fall off trees; clumps of grass might grow where there were none before; rainstorms may wash out ruts in the ground. Another, even more subtle, problem arises: if the two radar images are taken from different vantage points, the changing geometry will also introduce phase changes.

Like a pair of stereoscopic aerial photographs, two radar images obtained from slightly different perspectives will contain differences that are caused by variations in the elevation of the land surface. Happily, one can remove such phase shifts by carefully calculating this purely topographic effect and subtracting it. But the radar phase will be mixed up beyond repair if the interference between elementary targets contributing to each pixel changes, as will inevitably occur unless the two images are taken from close to the same angle. Consequently, for successful interferometry, the two paths that the radar satellite follows in space cannot lie more than about one kilometer apart. (The exact value depends on the viewing geometry and the particulars of the radar satellite used.) The four radar satellites now in operation—the Canadian Radarsat, the European ERS-1 and ERS-2, as well as the Japanese JERS-1—usually comply with this requirement, although none was designed with interferometry in mind. Aircraft have a much more difficult time flying along the same path twice, a difficulty I did not fully appreciate when I first began working to prove the concept.



Watching the Earth Move

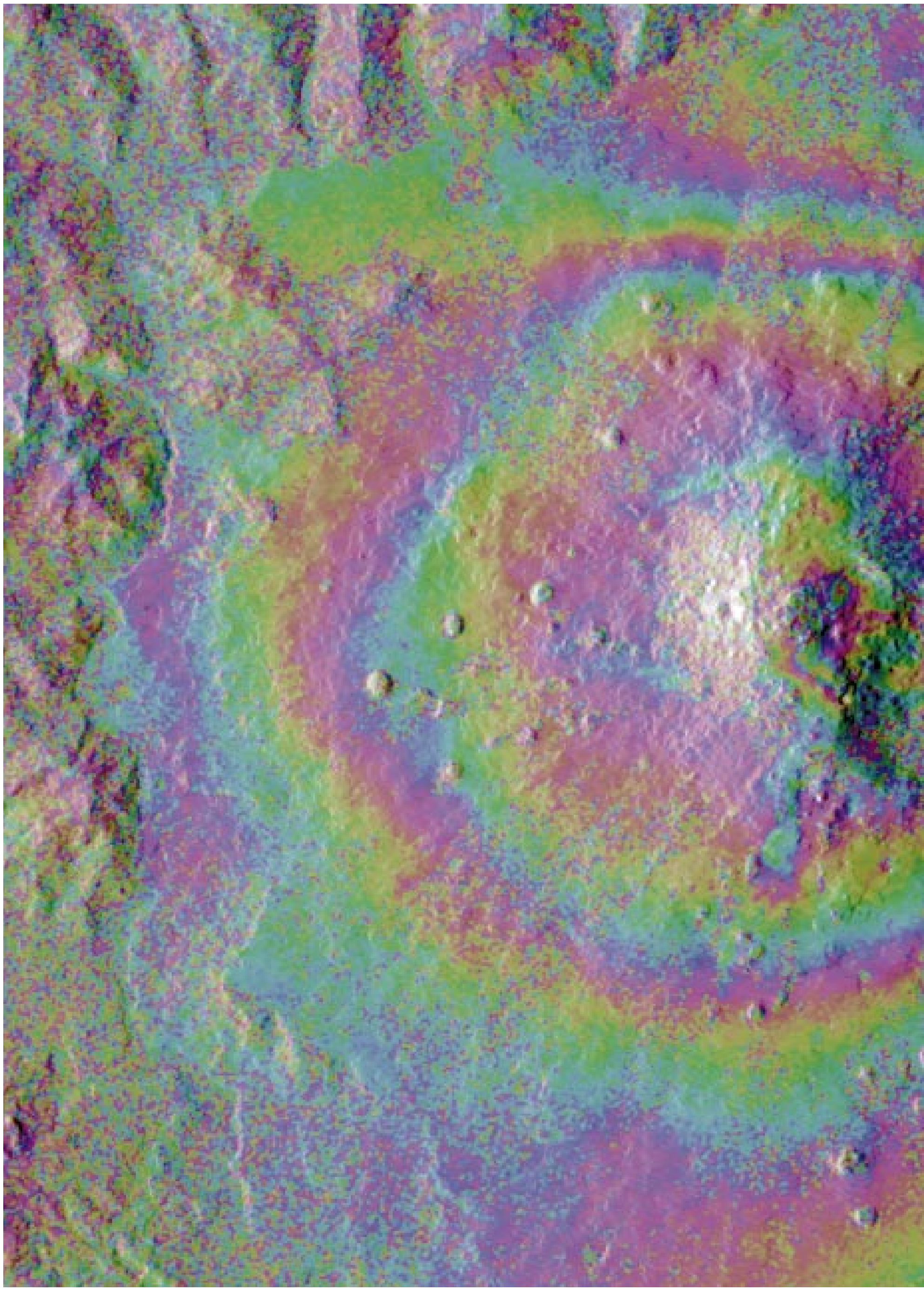
Shortly after I proposed that radar interferometry could detect tectonic motion, my colleagues and I began experiments to demonstrate the idea using an airborne radar. Our progress was set back severely when the vintage B-17 flying fortress that usually carried our radar crashed on takeoff in 1989. Fortunately, the crew managed to escape before the retired bomber erupted into a fireball. But we had to start afresh. Rather than adapting our equipment to another aircraft, we attempted to demonstrate our scheme with an airborne radar provided by some German colleagues. Yet we missed our goal, because the aircraft was not able to fly sufficiently close to its previous path. A. Laurence Gray and his colleagues at the Canadian



SLIM FILMS; WILLIAM HAXBY (*terrain image*); SOURCE: DIDIER MASSONNET

CONSECUTIVE RADAR SCANS from the same position in space create a virtual interference pattern when the crust shifts. Each cycle of colored fringes corresponds to a change of distance to the satellite of an additional half-wavelength (*detailed enlargements*), which gives one full wavelength in round-trip distance for the radar wave to travel. The fringe pattern shown here draped over the surface indicates a gradual lowering of this mountain [*see illustration on next two pages*].

MOUNT ETNA, a volcanic peak in Sicily, subsided as magma drained away below it. An interferogram produced by two radar scans made 13 months apart by the ERS-1 satellite displays four cycles of interference fringes, indicating that the top of the mountain settled by about 11 centimeters during this interval.



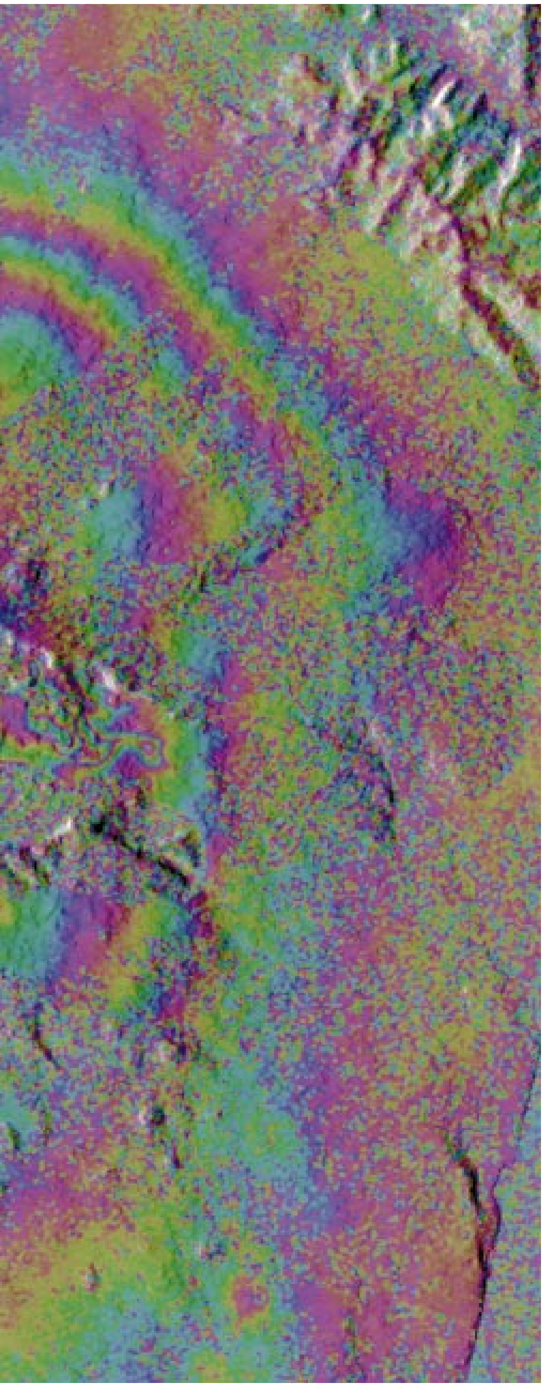
Center for Remote Sensing accomplished this tour de force in 1991.

The next year a major earthquake struck near the town of Landers in southern California, and my colleagues and I realized that this desert locale might be an ideal place to test whether a satellite radar could measure the associated deformation of the earth's crust. So we assembled all the radar images of the area available from the ERS-1 satellite and formed several interferograms by combining one image taken before the earthquake with another one taken afterward from approximately the same position. Because the satellite tracks were never identical, the rugged relief in the region affected these interferograms markedly. Yet with the help of a digitized map of elevations, we were able to calculate the topographic contribution and remove it. Doing so unveiled a tantalizingly rich picture of interference fringes. But were these colored bands truly showing what the earthquake had done to the surface of California's Mojave Desert?

To test whether our representation of ground movement was indeed valid, we calculated an idealized interferogram based on measurements that geologists had made for the motion along the main fault. The model interferogram showed a striking resemblance to the radar pattern we found, and that match bolstered our confidence enormously. We were also pleased to see that in some places the fringe pattern revealed tiny offsets on other geologic faults known to be crisscrossing the area. In one case, we detected a mere seven millimeters of motion on a fault located 100 kilometers away from where the quake had struck.

Soon after our study of the Landers earthquake, Richard M. Goldstein of the JPL and his co-workers used radar interferometry to track the movement of glacial ice in Antarctica. They took advantage of an exceptional opportunity presented by the ERS-1 satellite when it passed within a few meters of the path it had followed six days previously. Because the satellite had taken "before" and "after" radar images from virtually the same position, the topography of the glacier did not influence the pattern of fringes, and the resulting picture directly indicated the motion of the ice. That image displayed movement of an ice stream (where flow is relatively rapid) in superb detail.

Having shown its ability to track slipping faults and surging glaciers, radar interferometry had displayed great promise by 1993, and we wondered whether the technique could detect deformation that was even more subtle. So we next experimented with a set of radar images of the Mount Etna volcano in Sicily. That volcano had been nearing the end of an eruptive cycle during an 18-month period in 1992 and 1993 when the ERS-1 satellite passed over it 30 times. With those many radar images and an elevation map of the area, my colleagues and I were able to produce dozens of interferograms that were free from topographic effects. Some of our results were clearly degraded by changes in vegetation on the flanks of the volcano. (Certain pairs of images used in construct-



DIDIER MASSONNET

ing these interferograms spanned many months; others encompassed more than a year.) Nevertheless, with the help of researchers at the Institute for the Physics of the Earth in Paris, we were able to follow the deflation of Mount Etna, as the last of the magma erupted and the pressure within the mountain declined. Our radar images showed that Mount Etna subsided by two centimeters each month during the final seven months of eruption. This deformation extended for a large distance around the volcano, suggesting that the subterranean magma chamber was much deeper than geologists had previously thought.

Although Mount Etna is located in one of the best surveyed parts of the world, radar interferometry uncovered surprising revelations (just as it had done by locating minute cracks in the Mojave Desert). The technique should prove even more valuable for studying the hundreds of other active volcanoes on earth that can be viewed using the existing radar satellites. Radar interferometry cannot replace conventional ground surveys, but at the very least it should serve to focus the attention of geologists toward slowly awakening volcanoes as they begin to inflate and become dangerous. This new form of remote sensing also offers a way to monitor volcanic peaks in otherwise inaccessible locales.

As we probe more places, we have come to realize that short-lived variations in the atmosphere and ionosphere can sometimes alter the fringe pattern. Changes in soil properties, too, can induce the interference fringes to shift, even though the ground does not actually move. Such effects can complicate the interpretation of radar interferograms, and we have had to design some clever procedures to discriminate between them and true ground motion. But looked at more positively, these secondary influences represent features of the earth that are also of inherent interest—and it may prove a boon to some scientists that a radar satellite can map these features in great detail.

More Surprises to Come

What else is in store for radar interferometry? Forecasting specific advances is difficult, but one can safely predict that scientists will find plenty of opportunity to apply this technique all over the world. The four radar satellites currently in operation can scan most of the earth's surface, and Europe, Japan and Canada will soon launch others to add to the fleet of orbiting sensors. My colleagues and I have investigated possible future missions by studying the accuracy that a specially designed satellite could achieve in repeating its trajectory. Such an exact-repetition satellite would be the ideal platform for radar interferometry. The same satellite could also serve to measure surface elevation if its trajectory were purposely shifted in order to create the proper stereoscopic effect. (The National Aeronautics and Space Administration is, in fact, planning a space shuttle mission for the year 2000 to exploit this use of radar interferometry.) In this way, the overall topography of the entire planet could finally be obtained.

Will radar interferometry be able to detect the precursory motions needed for scientists to predict earthquakes and volcanic eruptions? As of yet, no one can say for sure. But in scientific research every new tool brought to bear invariably uncovers crucial facts and deepens the understanding of fundamental principles. Radar interferometry will undoubtedly do the same for the study of the solid but ever restless earth. SA

The Author

DIDIER MASSONNET entered the Ecole Polytechnique in 1979, where he began his scientific training. He later specialized in signal processing and ultimately completed a doctoral thesis on radar imaging at the University of Toulouse. In 1984 he joined the French Space Agency (CNES) but spent his first year at the Jet Propulsion Laboratory in Pasadena, Calif., working with American scientists on data obtained from a shuttle imaging radar mission. He then developed radar processing at CNES. Since 1996, he has been deputy manager of CNES's image-processing division in Toulouse.

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The Ghostliest Galaxies

Astronomers have found more than 1,000 "low-surface-brightness" galaxies over the past decade, significantly altering our views of how galaxies evolve and how mass is distributed in the universe

by Gregory D. Bothun

Throughout human history, people have peered into the night sky in search of clues that might help them understand the universe—its size, structure and evolution. As observational tools became more sophisticated, so, too, did our conception of the universe. At the end of World War I, for example, the construction of a giant telescope at California's Mount Wilson Observatory allowed the astronomer Edwin Hubble to confirm that the universe extended far beyond our own galaxy. Hubble found that the universe contained innumerable galaxies much like our own, each with tens of billions or hundreds of billions of stars.

In time, astronomers were able to estimate that there are hundreds of millions, if not a billion or more, observable galaxies. They also found that galaxies generally exist in groups, or clusters, with up to hundreds of members. Clusters, too, may aggregate into so-called superclusters. Filamentary in shape, some superclusters extend hundreds of millions of light-years across space, making them the largest structures known.

Astronomers have known for decades that galaxies exist in three basic types: elliptical, spiral and irregular. The ellipticals are spheroidal, with highest light intensity at their centers. Spirals, which include our own Milky Way, have a pronounced bulge at their center, which is much like a mini-elliptical galaxy. Surrounding this bulge is a spiral-patterned disk populated with younger, bluish stars. And irregular galaxies have relatively low mass and, as their name implies, fit none of the other categories.

With only minor refinements, this system of galactic classification has changed little since Hubble originated it some 70 years ago. Technological advances, however, have significantly improved astronomers' ability to find objects outside our own Milky Way that are extraordinarily hard to detect. Over the past decade my colleagues and I have used an ingenious method of photographic contrast enhancement invented by the astronomer David J. Malin of the Anglo-Australian Observatory as well as electronic imaging systems based on improved charge-coupled devices (CCDs).

Using these techniques, we have discovered that the universe contains, in addition to the other types, galaxies that, because of their extreme diffuseness, went essentially unnoticed until the mid- to late 1980s. These galaxies have the same general shape and even the same approximate number of stars as a conventional spiral galaxy. In comparison, though, the diffuse galaxies tend to be much larger, with far fewer stars per unit volume. In a conventional spiral galaxy, for example, the arms are hotbeds of stellar formation and are ordinarily populated with young stars emitting more bluish light. In the diffuse galaxies, the arms have much more gas and much less of a spiral structure. Apparently these low-surface-brightness galaxies, as they are known, take much longer to convert gas to stars. The result is galaxies that evolve four or five times more slowly; the universe literally is not old enough for these galaxies to have evolved fully.

Our work over the past decade demonstrates that, remarkably, these galaxies may be as numerous as all other galaxies combined. In other words, up to 50 percent of the general galaxy population of the universe has been missed.

The prevalence of these galaxies may be extraordinary, but it is still not nearly enough to clear up one of the central mysteries in cosmology today: that of the universe's "missing mass." For decades, astronomers have been aware that the known matter in the universe cannot

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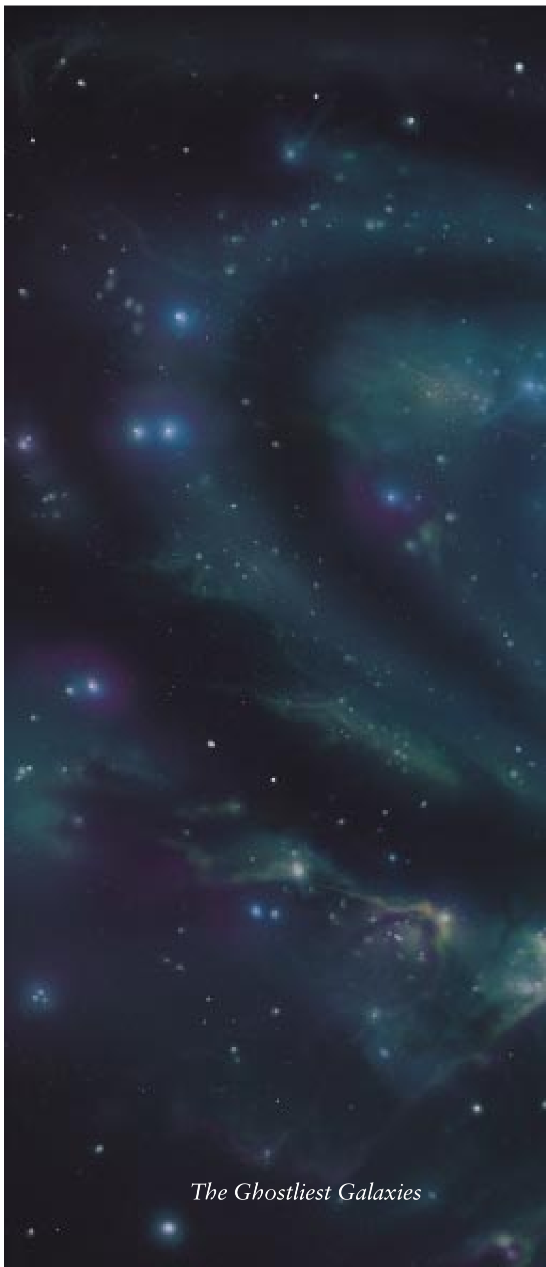


LOW-SURFACE-BRIGHTNESS galaxy Malin 1 dwarfs a conventional spiral galaxy about the size of the Milky Way, shown for scale at the upper right in this artist's conception.

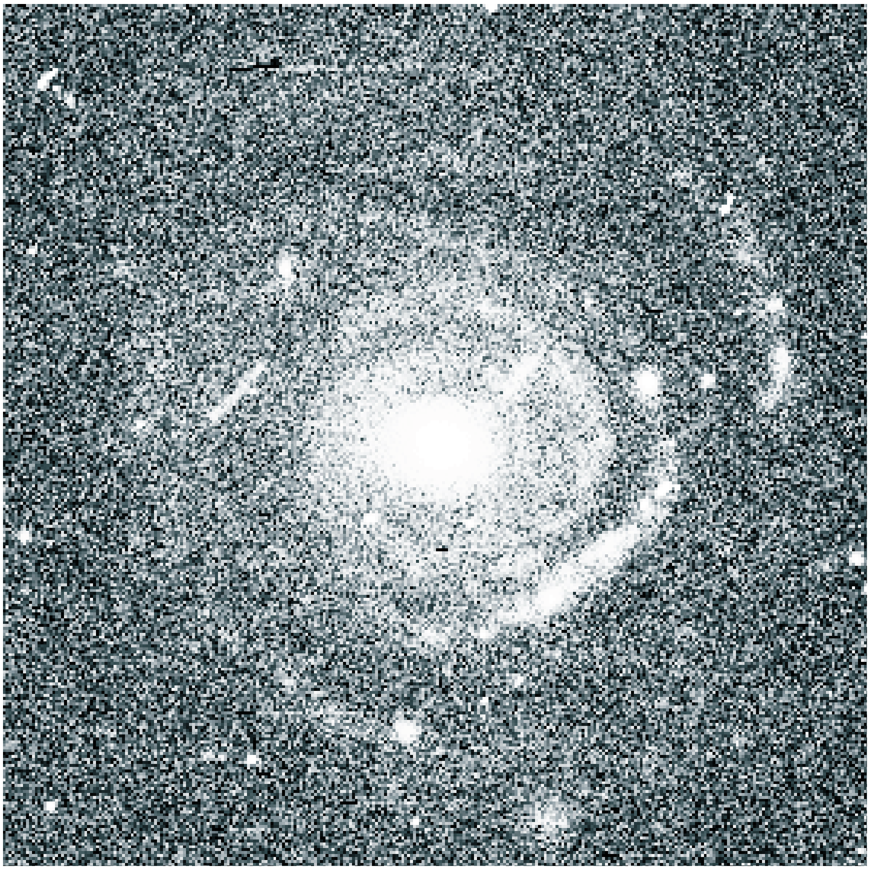
account for its large-scale physical behavior. Eventually they concluded that at least 90 percent of the mass in the universe must be so-called dark matter, nonluminous and therefore not observable.

Although low-surface-brightness galaxies are not numerous and massive enough to be cosmologists' long-sought dark matter, they may solve a different long-standing cosmological puzzle, concerning the baryonic mass in galaxies. Baryons are subatomic particles that are generally either protons or neutrons. They are the source of stellar—and therefore galactic—luminosity. But the amount of helium in the universe, as measured by spectroscopy, indicates that there should be far more baryons than exist in the known population of galaxies. The missing baryons may be in intergalactic space, or they may be in an unknown or difficult-to-detect population of galaxies—such as low-surface-brightness galaxies. More knowledge about these galaxies may not only settle this issue but may also force us to revise drastically our current conception of how galaxies form and evolve.

An Astronomer Vindicated

Low-surface-brightness galaxies have only recently begun shaking up the world of extragalactic astronomy, although the first temblors were felt 20 years ago. In 1976 the astronomer Michael J. Disney, now at the University of Wales in Cardiff, realized that the catalogues of galaxies discovered by optical telescopes were potentially seriously biased. Disney noted that astronomers had catalogued only the most conspicuous galaxies—those relatively detectable because they exhibited high contrast with respect to the background of the night sky. There was no reason to believe these galaxies were representative of the general population, Disney maintained. At that time, however, astronomers had not yet detected any very diffuse galaxies to substantiate Disney's suspicions. Thus, for a decade or so, the astronomical community dismissed his theory as applicable to, at most, an inconsequential population of extragalactic objects.

Ultimately, Disney was vindicated. In 1986 my colleagues and I serendipitously discovered an extremely large, low-surface-brightness disk galaxy that is the most massive (and luminous) disk galaxy yet observed. In extragalactic terms, it is fairly close—a mere 800 million light-years away. If this galaxy were as close as the spiral Andromeda galaxy (2.3 million light-years away), it would subtend an arc of fully 20 degrees



MALINIZATION TECHNIQUE enables the imaging of low-surface-brightness galaxies. This one is known, appropriately enough, as Malin 2; it was discovered in 1990 and was the second such galaxy to be found. It is about 450 million light-years away and, with a scale length of 15 kiloparsecs, is about five times the size of the Milky Way.

in the earth's sky—40 times the apparent width of a full moon.

Why did an object this massive and nearby elude us for so many years? The answers require some background on galactic characteristics and the way astronomers measure them. As mentioned earlier, spiral galaxies have two main components: a central bulge and a surrounding disk with spiral arms. The disks usually emit light in a specific pattern, in which the intensity falls off exponentially with radial distance away from the galaxy's center.

This characteristic provides astronomers with a convenient means of measuring the size of a galaxy. The scale length of a spiral galaxy (the size indicator preferred by astronomers) is a measure of the distance from the center of the galaxy to the point in the disk where the surface brightness falls to the reciprocal of *e*, the base of natural logarithms. (This number is commonly used in characterizations of natural systems that display such an exponential falloff.) The scale length is typically given in thousands of parsecs, or kiloparsecs; a parsec is a unit of astronomical distance equal to about 3.26 light-years, or 3.0857×10^{16} meters. Our own Milky Way, which is of fairly modest size, has a scale length of about three kiloparsecs.

The other key parameter astronomers use to characterize galaxies is the central surface light intensity, which is a measure of bluish light in the center of the galaxy, an indicator of stellar density [*see illustration on opposite page*]. The word "surface" in this expression refers to the fact that galaxies, which are three-dimensional, are viewed on the two-dimensional plane of the sky; thus, their brightness is projected onto this two-dimensional "surface."

Central surface light intensity is expressed in apparent magnitudes per square arc second. The magnitude scale ranks the brightness of an astronomical body on a numerical scale. On this scale, the less luminous an object is, the *higher* its numerical magnitude value.

The scale is also logarithmic; a difference of five magnitudes corresponds to a 100-fold difference in brightness. A typical spiral galaxy might have a central surface light intensity (in the blue part of the spectrum) of about 21.5 magnitudes per square arc second. For the purposes of this article, we might define a low-surface-brightness galaxy as one whose central surface light intensity has a value of at least 23 magnitudes per square arc second. (Remember, the higher the magnitude value, the *less* luminous the object.) To put this value of 23 magnitudes per square arc second into perspective, it is about equal to the brightness of the background night sky, as measured in the bluish spectrum between 4,000 and 5,000 angstroms, on a dark, moonless night at a good astronomical observing site.

Together, by simple integration, the scale length and the central surface light intensity can give us a galaxy's total mass and luminosity. Astronomers' standard catalogues of galaxies generally list them according to diameter or luminosity, as derived from scale length and central surface light intensity. As the discovery of low-surface-brightness galaxies attests, however, the complete range of galactic types is still being determined. Thus, the full range of scale lengths and central surface light intensities is not yet known. The range of these parameters is controlled by the process of galaxy formation, which remains a mystery. This fact underscores the importance of the discovery of these galaxies—they have significantly extended the known range of these parameters. When it is finally ascertained, the total range will meaningfully constrain physical theories of galaxy formation, because these theories will have to be compatible with the observed range of scale lengths and surface light intensities.

First Glimpses

It was in 1983 that astronomers assembled the first noteworthy evidence that there were galaxies with central surface light intensities significantly fainter than those generally accepted as the dimmest. William J. Romanishin, now at the University of Oklahoma, and his collaborators Stephen E. Strom and Karen M. Strom, now at the University of Massachusetts at Amherst, uncovered the evidence while combing through the *Uppsala General Catalogue of Galaxies.*

Few of the galaxies in the sample compiled by Romanishin and the Stroms actually met the aforementioned criterion for a low-surface-brightness galaxy—a central surface light intensity fainter than 23. But their survey did identify a class of galaxies that had large amounts of gas and other unusual properties.

Reading their results, I began to suspect that the prevailing view of the way in which galaxies are distributed in the universe was biased. This distribution can be thought of as a kind of three-dimensional map of the known universe, showing all the galaxies that have been detected by various means, their types and their locations with respect to one another. The locations were obtained by measuring the galaxies' optical redshift—the Doppler reduction in the frequency of light or radio emissions—from rapidly receding bodies. Low-surface-brightness galaxies, though, would be too diffuse to have a redshift measurable by optical spectroscopy.

Then, early in 1984, the astronomer Allan R. Sandage of the Carnegie Institution of Washington published some of the first results from his photographic survey of the galaxies in the Virgo cluster, done at Las Campanas in Chile. Sandage had found some vivid examples of dwarf galaxies that were quite diffuse.

Both I and my postdoctoral colleague at the California Institute of Technology, Chris D. Impey, began to suspect that the Sandage survey had missed galaxies of even lower surface brightness, and we decided to undertake a search for them. The galaxies we sought would be so diffuse as to have escaped the notice of countless other astronomers. This meant we would need patience and, most of all, exceptional technology. From journal articles, we were aware that Malin, the Australian astronomer, had developed a method of enhancing the contrast in photographs that had enabled him to find low-surface-brightness shells and other tidal debris around normal galaxies. There was no reason why the technique could not be used to find entire galaxies of very low surface brightness. Indeed, Malin piqued our curiosity by declaring that whenever he applied his technique to a plate, he would find these "faint little buggers" everywhere.

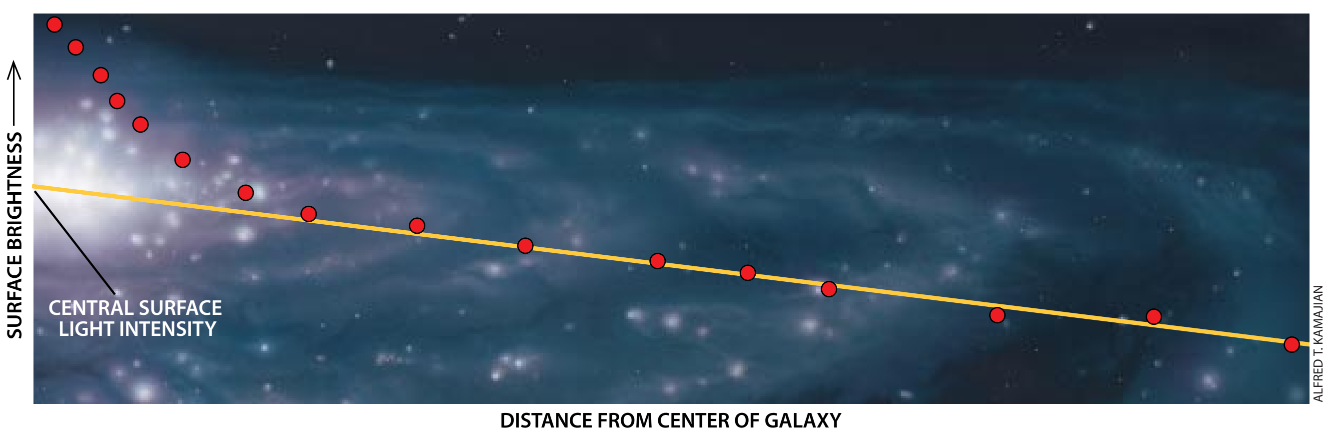
Malin's technique ("malinization") increases the contrast of a photographic image by stacking together multiple glass plates of the same image and illuminating them through the stack. The image that appears on the far side of the stack from the light source is of greater contrast. The more images in the stack, the higher the resulting contrast. The system works only when the images are aligned with extreme precision; Malin's breakthrough was in finding a way to achieve this precision.

Malin agreed to apply his technique to images of some selected one-square-degree areas of the Virgo cluster. Using the *Uppsala General Catalogue,* Sandage's survey and Malin's processing, we compiled a list of low-surface-brightness objects for follow-up imaging through the use of CCDs and for distance measurements through redshift analysis. Our endeavor was going along according to plan when we had the kind of rare discovery that suddenly turns a routine science project into something much more significant and compelling.

By February 1986 we were into the second phase of the plan, which entailed using the Las Campanas 254-centimeter (100-inch) telescope to make digital images of Malin's Virgo fields, particularly of those objects we had identified in the first phase as being worth another look. Most of these galaxies turned out to be diffuse blobs, with little apparent structure. But one of these objects had what looked to be a very faint spiral structure that was connected to a pointlike central region. In one photographic sky survey, this center was visible as a faint star, without any associated nebula, as one would expect of a galaxy.

Although rather dim, the center of this unusual object was bright enough, if barely, for optical spectroscopy. In May 1986 Jeremy Mould and I measured the object's spectrum using the 508-centimeter (200-inch) telescope at California's Palomar Mountain Observatory. We were astonished to find that the object's spectrum exhibited emission lines, the sharp "peaks" of luminous energy at specific wavelengths. Only certain well-known physical processes in galaxies, such as star formation and other processes in which gases are ionized, are known to give rise to emission lines, and we had never seen any of those processes in the galaxies we were observing at Palomar.

Some quick calculations at the telescope, based on redshift analysis of these emission lines, indicated that this object was 25 times farther away than Virgo. Incredibly, its angular size on our CCD frame was about 2.5 arc minutes. A quick scaling indicated that if this object were a galaxy, and if it were indeed 25 times more distant than Virgo, it would be roughly 20 times the size of the Milky Way (as measured by scale lengths)—by far the largest galaxy ever discovered.



SURFACE BRIGHTNESS of a spiral galaxy declines more or less exponentially with radial distance away from the galaxy's center. Past the central bulge, however, the decline in brightness is almost linear. If this linear region is extended leftward to the vertical axis, it intersects the axis at a value known as the central surface light intensity, an indicator of stellar density.

This possibility seemed so far-fetched that I offered to bet Mould a six-pack of Foster's beer that we were detecting the spectrum from a galaxy far behind the Virgo cluster shining through a much closer dwarf galaxy within the cluster. Mould, now at the Australian National University, took the bet.

In October 1986 I traveled to Arecibo, a radio-astronomical observatory in Puerto Rico, determined to win the beer. My plan was to tune the observatory's central observing frequency to the mean redshift of the Virgo cluster. Galaxies have rather large amounts of certain gases, such as hydrogen, which emit radio-frequency waves that are redshifted in the same way as light. If my hypothesis about the foreground dwarf galaxy in Virgo was correct, then by tuning to the frequency of redshifted, gaseous emissions from Virgo, I should have been able to detect signals emanating from the gas of my hypothesized foreground dwarf. But I found no such signals.

I was briefly stymied before coming up with the best idea of my entire career. At Palomar the signals we had received from Virgo were redshifted by 8.3 percent. Although Arecibo is a radio telescope rather than an optical telescope, this redshift would still apply to any radio-frequency radiation from the object. So two days before my allotted time was up on the Arecibo dish, I tuned the observing frequency to 21.1 centimeters—the radio-frequency wavelength of emissions from atomic hydrogen—redshifted by 8.3 percent. Ten minutes later I was rewarded with a huge signal.

Found: Largest Known Galaxy

Atomic hydrogen makes up roughly 10 percent of the mass of many galaxies and concentrates in the arms of spiral galaxies. So its emissions can often be analyzed to determine whether a very far-off object is a galaxy. The signature of the 21.1-centimeter signal I received at Arecibo was exactly that of a rotating disk galaxy. I lost my bet but discovered Malin 1, an absolutely immense and extraordinarily diffuse disk galaxy. Malin 1 has a central surface light intensity of 26.5 magnitudes per square arc second—only 1 percent as bright as a typical, conventional spiral. This was the first direct verification of the existence of low-surface-brightness galaxies.

Based on these results, Impey and I initiated three new surveys, hoping to characterize the extent and nature of this apparent population of previously undetected galaxies. The first survey relied heavily on the goodwill of James M. Schombert, at that time a postdoctoral researcher at Caltech. Schombert was associated with the new Palomar Sky Survey and had access to the survey's plates, which he let us inspect for diffuse galaxies with sizes larger than one arc minute.

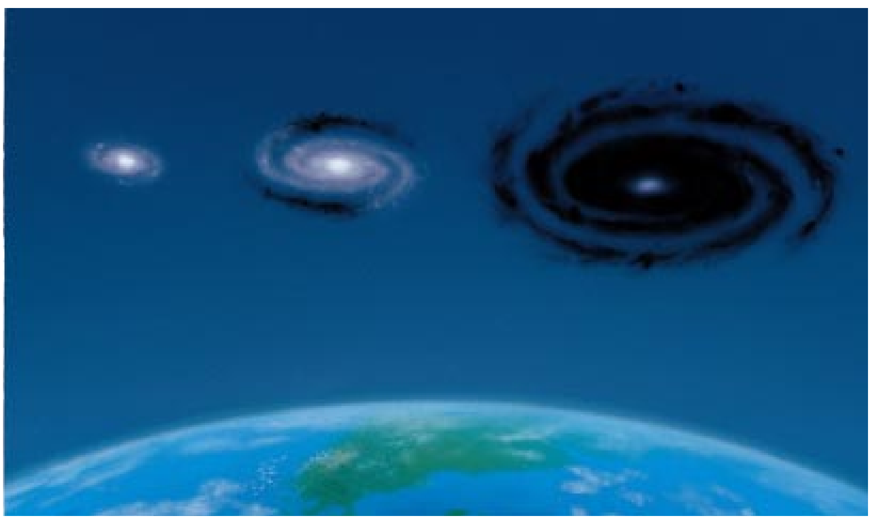
A second survey using the malinization technique was initiated in the Fornax cluster. In this survey, we could detect galaxies with central surface light intensities as low as 27 magnitudes per square arc second—a mere 2 percent brighter than the background night sky. The final survey was initiated with Michael J. Irwin of the Royal Greenwich Observatory in Cambridge, England; it made use of automatic techniques to scan photographic plates.

As a result of these surveys, we detected a total of approximately 1,000 objects that we believe to be low-surface-brightness galaxies. The group is quite varied and includes both very small, gas-poor dwarfs and about a dozen extremely large, gas-rich objects like Malin 1. (A decade after its discovery, though, Malin 1 remains the largest known galaxy.) In general, these galaxies span the same range of physical size, rotation velocity and mass as conventional spiral galaxies. But a small percentage of the low-surface-brightness population is relatively gigantic, with scale lengths that exceed 15 kiloparsecs.

We found that in clusters of galaxies—and perhaps in the universe at large—low-surface-brightness galaxies seem to be much more numerous than conventional ones. Furthermore, if the ratio of mass to luminosity increases with decreasing surface brightness (that is, if there is more mass in less visible galaxies), then these diffuse galaxies harbor a great deal—perhaps most—of the baryonic mass in the universe.

The most startling result of these surveys has come from a recent analysis by Stacy S. McGaugh, now at the Carnegie Institution of Washington. McGaugh found that if the space density of galaxies is plotted as a function of their central surface brightness intensity, the plot is flat out to the limits of the data [*see illustration on opposite page*]. In other words, there seem to be just as many very diffuse galaxies with a central surface light intensity of 27 magnitudes per square arc second as there are conventional galaxies for which this value is 21—or 23.5 or 22 or 20, and so on. This fact means that up to 50 percent of all galaxies are spirals with a central surface light intensity fainter than 22 magnitudes per square arc second.

Interestingly, low-surface-brightness galaxies are similar in several ways to the enormous number of faint, blue gal-



ALFRED T. KAMAJIAN

THREE SPIRAL GALAXIES show why low-surface-brightness galaxies escaped detection for so long. All of the conventional galaxy (*left*) is brighter than the background of the night sky. In the middle galaxy the central bulge and some of its surrounding spiral exceed the night sky's brightness; it might be detected as a galaxy. But almost all of the low-surface-brightness galaxy (*right*) has a surface brightness almost the same as that of the night sky. Against a night sky full of innumerable luminous objects, astronomers relying solely on optical techniques would probably miss this galaxy completely or perhaps mistake its barely visible central bulge for a faint star.

axies detected in CCD surveys of very, very distant galaxies. The two galactic types share such attributes as color, luminosity, mean surface brightness and extent of clustering. It may well be that these faint, blue galaxies are low-surface-brightness galaxies in their initial phase of star formation. At closer distances, where the objects are seen as they were in the less distant past, these objects have faded to surface brightness levels that are not intense enough for us to detect. If these faint, blue galaxies are indeed young low-surface-brightness galaxies, then there must be a still larger space density of these low-surface-brightness galaxies than is accepted at present.

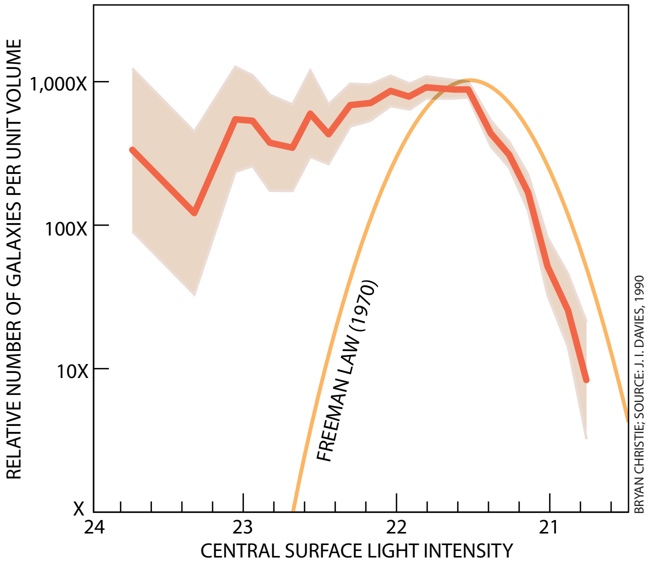


CHART OF RELATIVE SPACE DENSITY of galaxies shows that there are probably as many very diffuse galaxies, with central surface light intensities of 23 or 24 apparent magnitudes per square arc second, as there are conventional galaxies for which this value is about 21.5 or 22. (The shading indicates the range of uncertainty in the values.) The orange arc indicates how galaxies were thought to be distributed before the discovery of low-surface-brightness galaxies in the mid-1980s.

This view is supported by studies of the color of low-surface-brightness galaxies, which are generally quite blue. This bluishness, typically a sign of star formation, is difficult to understand. It generally indicates a galaxy that has not progressed past an early formative stage, a fact consistent with the low densities of these structures. Thus, it appears that most low-surface-brightness galaxies collapsed quite late and that their first stars formed rather late as well.

Several other findings had intriguing implications for our views about how galaxies evolve. For example, the amounts of neutral hydrogen in low-surface-brightness and conventional galaxies tend to be similar, except that the low-surface-brightness galaxies have much lower densities of the gas. This and other data support the idea that a rotating gas disk must reach a minimum, or threshold, surface gas density before widespread star formation can occur. Furthermore, low-surface-brightness spirals are comparatively deficient in molecular gas.

Taken together, these observations suggest that the density of neutral hydrogen gas on the surface of the diffuse galaxies is insufficient to transform the gas into the giant molecular clouds that, in conventional galaxies, subsequently fragment to form massive stars. It seems that low-surface-brightness spiral galaxies are on a parallel evolutionary track, one in which only small stars form within lower-density clouds of neutral hydrogen gas. Because they lack massive stars, low-surface-brightness galaxies produce the heavier elements (those with atomic numbers greater than 12) at quite low rates. Ordinarily, the more massive a galaxy is, the more heavy elements it tends to contain. That low-surface-brightness galaxies, regardless of their mass, are so deficient in heavy elements suggests that these diffuse galaxies are among the most unevolved objects in the universe and have changed little over the course of billions of years.

In just over a decade, a whole new population of galaxies has presented us with a unique window onto the evolution of galaxies and the distribution of matter in the universe. Over the next few years we will search for these galaxies more rigorously, with CCD surveys of wide fields of the sky at the darkest sites. In these new surveys, we should be able to find galaxies with central surface light intensities of 27 magnitudes per square arc second. As the data accumulate, we may be able to determine whether the density of galaxies throughout space, as a function of their central surface light intensity, continues to remain flat even as the central surface light intensity varies by a factor of 100.

Of course, the full range of possible findings and their implications for our understanding of galactic evolution and the structure of the universe can scarcely be imagined. But for now, it is gratifying simply to be reminded that discovery in astronomy remains possible and that the universe still has not revealed all. SA

The Author

GREGORY D. BOTHUN is professor of physics at the University of Oregon. After receiving a Ph.D. in astronomy in 1981 from the University of Washington, he held positions at Harvard University, the California Institute of Technology and the University of Michigan. His research interests center on observational cosmology, especially involving large-scale structure in the universe and the formation and evolution of galaxies. He currently serves as director of Pine Mountain Observatory at the University of Oregon, which is now being transformed into a "digital observatory" accessible to the public over the Internet.

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More information and images related to the author's work can be found at his World Wide Web site: http://zebu.uoregon.edu

The Lesser Known Edison

In addition to his famous inventions, Thomas Edison's fertile imagination gave the world a host of little known technologies, from talking dolls to poured-concrete houses

by Neil Baldwin

As we celebrate the sesquicentennial this month of the birth of America's most renowned inventor, Thomas Alva Edison (1847–1931), our thoughts turn naturally to his "big three"—the electric lightbulb, the phonograph and the motion-picture camera. In fact, his creative energies were much more prolific: Edison obtained some 1,000 patents over six decades.

An essentially uneducated man, a dropout from the first grade, Edison's genius lay in hiring the best scientists and engineers to help fill the lacunae in his knowledge. His compulsive mind filled hundreds of laboratory notebooks with ideas to be enacted by this cadre of experienced co-workers.

Through Edison's lesser known endeavors, a selection enumerated in these pages, runs a strong, common thread—a pluralistic, Whitmanesque desire to do good things for the greatest number of Americans, to harness the technology of a nation emerging out of the industrial revolution into the modern era.

On the one hand, the electric pen, direct precursor of the mimeograph, was a successful step in communications; on the other, the Talking Doll, one of Edison's few genuine toys, something he sincerely wanted to produce for the delight of children, failed to catch hold because its delicate internal mechanism fell apart in shipping. During the 1890s, Edison invested at most $40,000 in glamorous research and development for the motion pictures, at the same time sinking uncounted millions into the iron-mining business.

Thomas Edison should be remembered for his incessant commitment to the underlying *process* of invention—he called it an art, never labor. He refused to recognize failure; he lived by the necessity to forge ahead, regardless of the ultimate practicality of any enterprise.

Thomas Edison was born 150 years ago—on February 11, 1847, in this little room overlooking the new, much heralded interstate canal at Milan, Ohio. By age 15, intrepid "Little Al" Edison, a gleam already in his eye, was at work as a news butch, selling dime novels, newspapers, candy and sundries on the three-hour railroad commute between Port Huron, Mich., and Detroit.

1847 1862

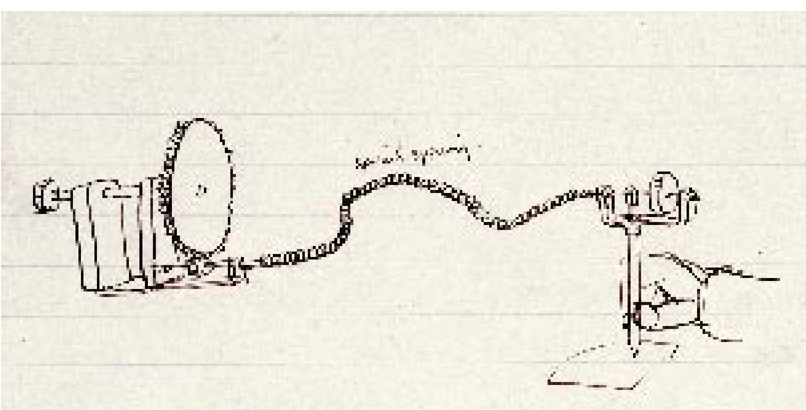
The Chicago, Detroit and Canada Grand Trunk Junction Railway (seen here under construction in 1859), the first major north-south line in the Midwest, was Edison's first employer. When the three-year-old son of the stationmaster at Mount Clemens, Mich., wandered blithely out onto the tracks, Tom, without a moment's thought, darted into the path of an oncoming freight car and shoved Jimmie to safety. The child's grateful father offered to teach young Tom the intricate skills of telegraphy.

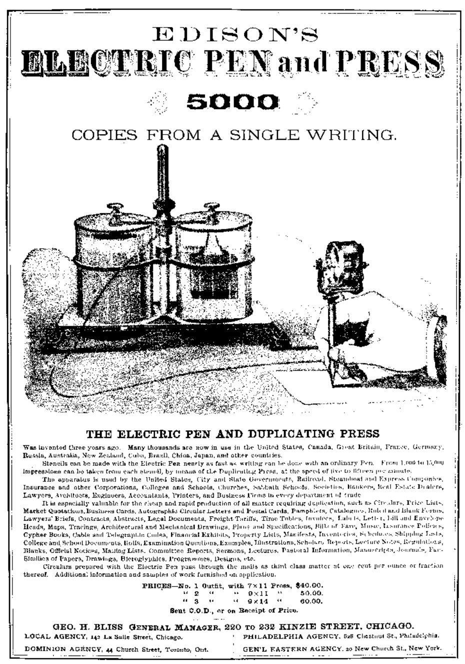
By early 1876, Edison (*seated, wearing cap, sixth from left*) had established the first R&D facility in America at Menlo Park, in rural New Jersey. He would be ensconced here for the long haul, living and working with a handpicked team of "scientific men." The second floor of the main laboratory building was equipped with 2,500 bottles of chemicals lining the walls, as well as a massive pipe organ, the focal point for after-hours singing and beer drinking.

PHOTOGRAPH OF THOMAS EDISON'S ROOM AT THE EDISON BIRTHPLACE MUSEUM, MILAN, OHIO, COURTESY OF TOM KOBA; ALL OTHER PHOTOGRAPHS AND DOCUMENTARY MATERIAL COURTESY OF THE COLLECTIONS OF THE EDISON NATIONAL HISTORIC SITE, NATIONAL PARK SERVICE; BETH PHILLIPS (*photographs of notebooks*)

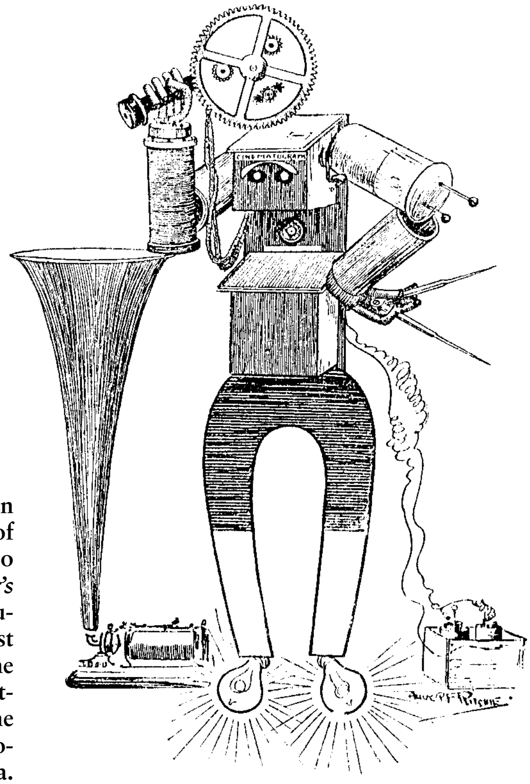
1876

One of Edison's first creations to come out of Menlo Park was "An Improvement in Autographic Printing," or Electric Pen, a prototype for document reproduction. An early mechanical version (*notebook drawing below*) cut stencils by hand, powering the incising needle with a spring. In the final invention, a portable galvanic battery drove an electromagnetic motor. Ink was then applied by roller over the punctured sheet, to create multiple impressions. Edison eventually sold the patent to A. B. Dick, pioneer of the mimeograph.



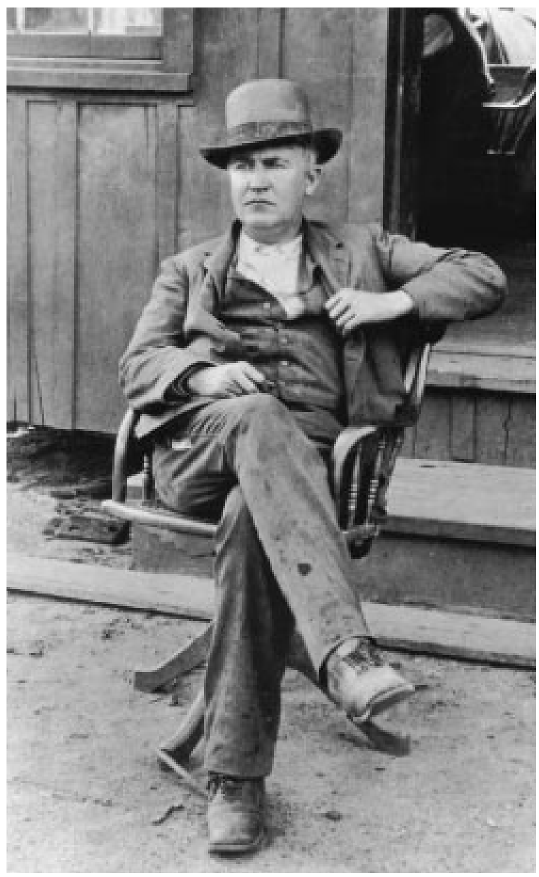


In the hollow innards of the sadly short-lived Talking Doll, a miniature phonograph cylinder on a screw-threaded shaft connected to a crank protruding from the doll's back. There was just enough space on each cylinder for the first verse of "Mary Had a Little Lamb," "Jack and Jill" or "Little Bo Peep."

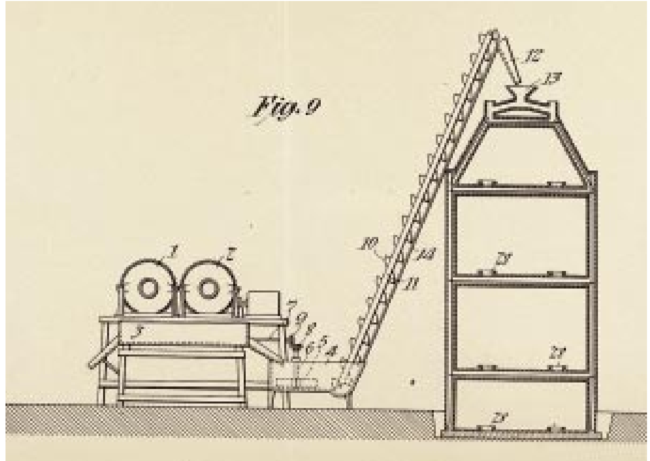


By the early 1890s, when this satirical caricature of "The Wizard of Menlo Park" appeared in *Harper's Weekly,* Edison was popularly defined by his most renowned inventions—the phonograph, electric lightbulb, improved telephone receiver and cinematographic camera.

1890 — **1895**



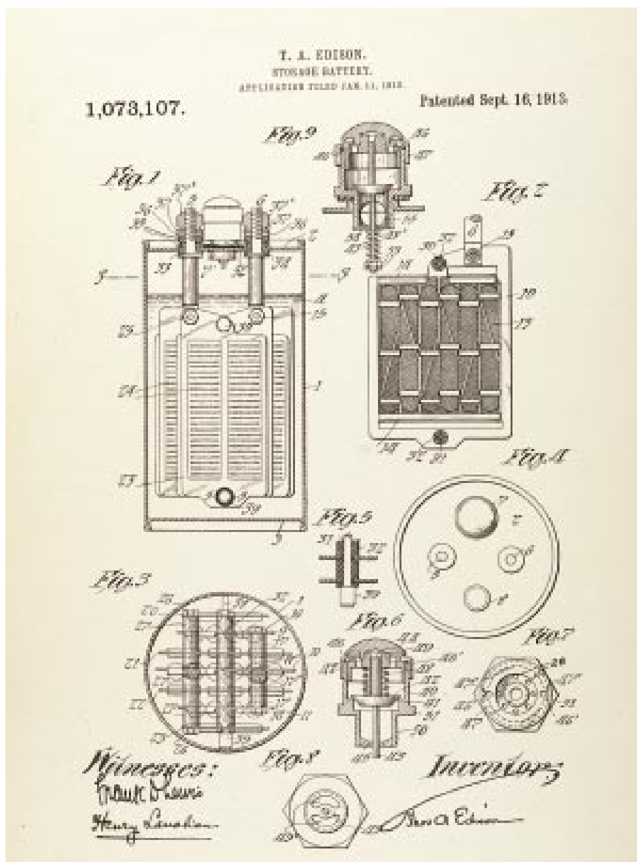
But meanwhile Edison had embarked on the most consuming obsession of his career, a far cry from the safe confines of the laboratory. He purchased a 2,500-acre site in Sparta, in northwestern New Jersey, and set up a mining camp, where he would live in dust and grime for most of the next decade, determined to extract and refine magnetic iron from the Musconetcong Mountains. The Morgan Electric Overhead Traveling Crane (*above*) picked up 10-ton-capacity railroad cars and tipped the raw ore onto giant crushing rolls. Edison's notebook plan illustrates how dried ore fragments less than 1/16 of an inch in diameter were dropped in a thin stream through a tower, past banks of electromagnetic sorters that pulled out the concentrated product.



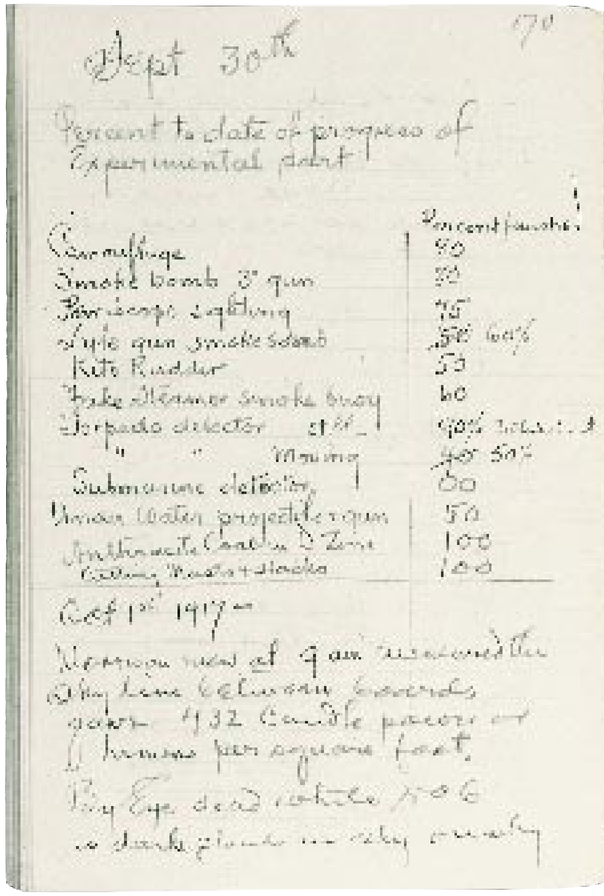
In 1901 Edison vowed to create mass housing that would be within reach of every hardworking American family: the poured-concrete house. Designed to be produced in planned communities, it cost less than $1,200. The patent drawing illustrates that all the parts—including sides, roof, partitions, stairs, floors, dormers, even cupboards and ornamental ceilings—were formed from quartz-strengthened and clay-tempered cement poured into a cast-iron mold from the top downward, over a six-hour period. Ten days after the molds were removed and the cement fully hardened, only doors and windows remained to be added.

1901 **1910**

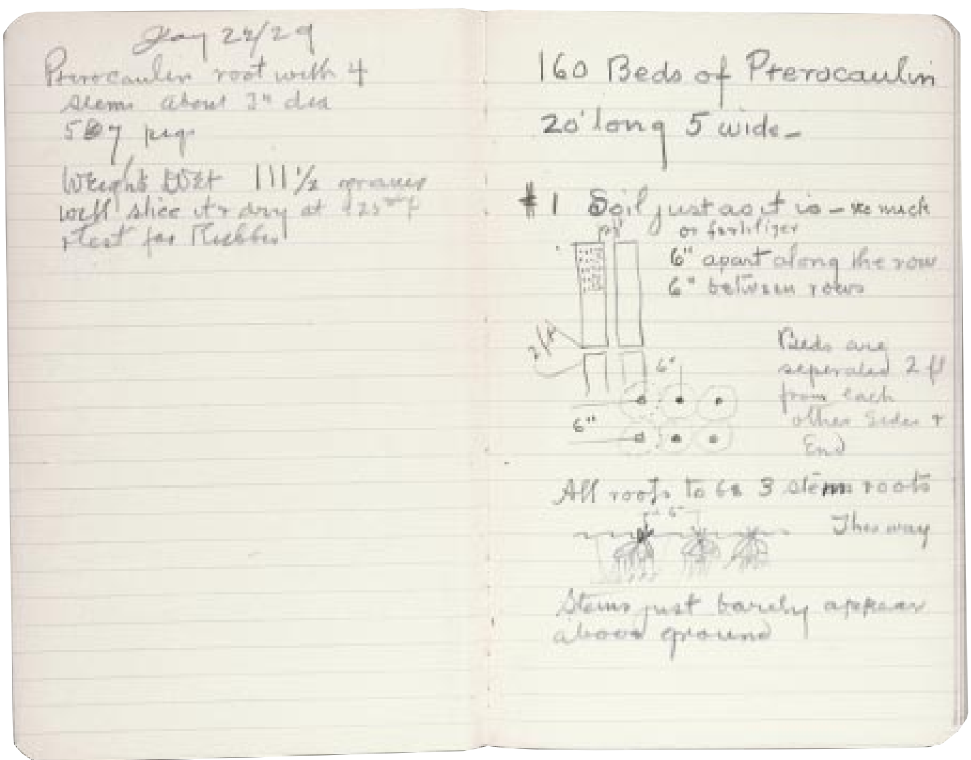
Edison was prescient in his fear that "the seething mass" of machine-made industrial progress would generate ever greater environmental pollution. Despite the advances in internal combustion made by his old friend Henry Ford, Edison declared that "the future belong[ed] to the electric car." This 1910 S. R. Bailey Company model was powered by Edison's revamped storage battery: noncorroding plates of steel immersed in an aqueous electrolyte solution (rather than lead immersed in sulfuric acid), which could be charged quickly and cleanly.



During World War I, Edison the patriot spent little time with his family, shown here at their Llewellyn Park estate near West Orange, N.J. (*left to right:* daughter Madeleine, wife Mina and sons Theodore and Charles). As chairman of the Naval Consulting Board, an inventors' think tank, Edison was most often to be found on board ships off the coasts of Annapolis, Long Island, and Key West, developing defensive "peace insurance" ideas, as he called them, "to protect our boys at sea" against dreaded submarines.

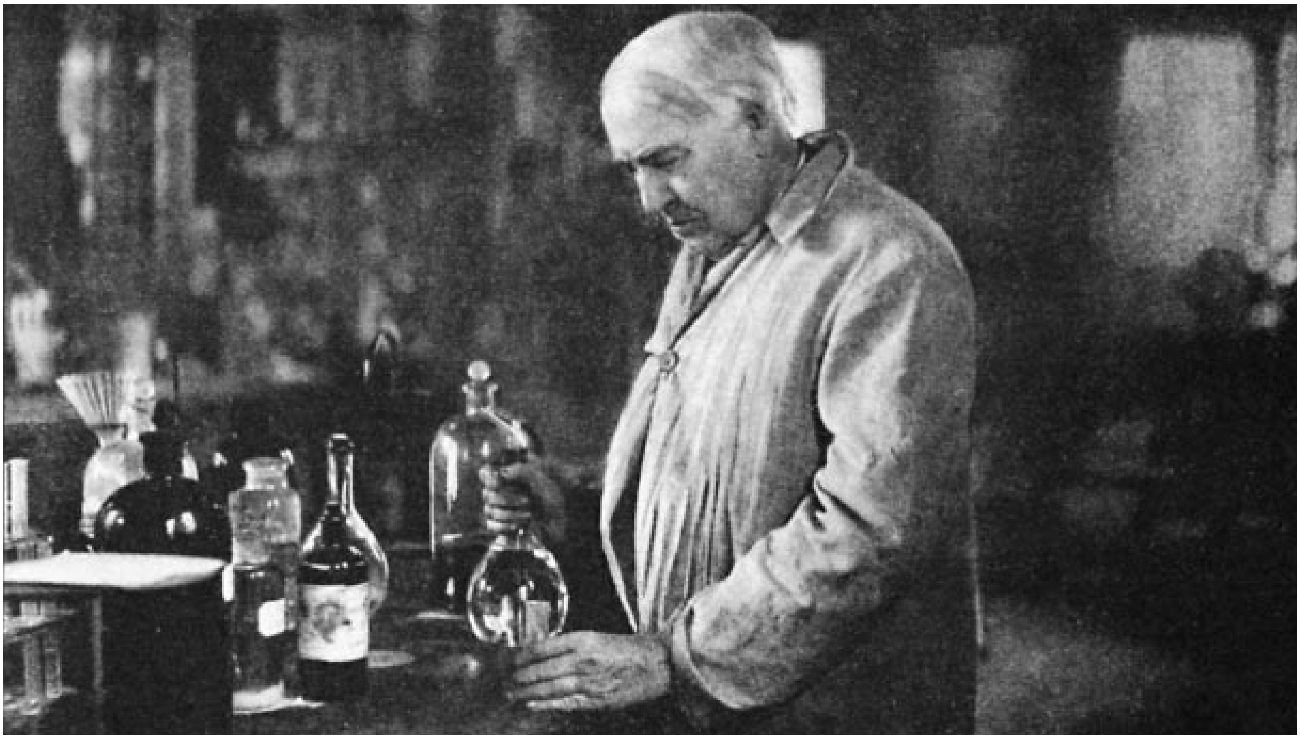


1915 1929

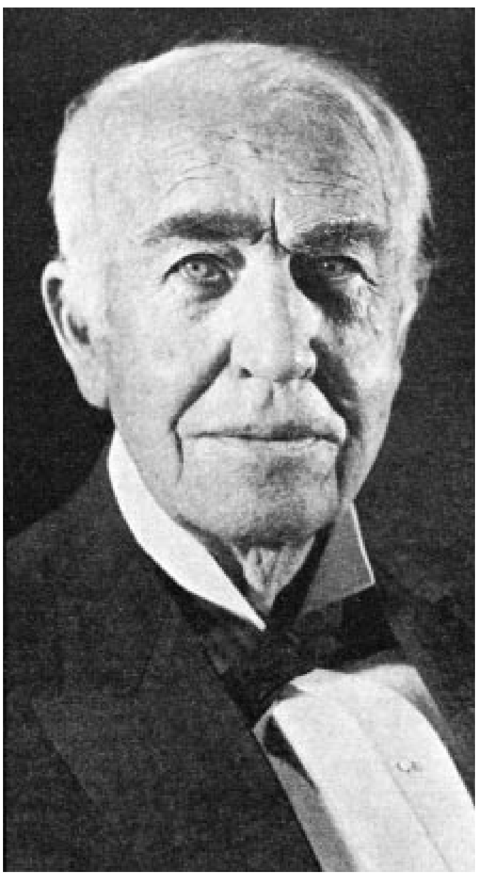


Shocked to learn from the American horticulturist Luther Burbank that the U.S. depended on foreign markets for more than 75 percent of its domestic rubber consumption, Edison embarked over the final two decades of his life on a crusade to cultivate "milky sap"–bearing plants on native ground, converting his winter estate in Fort Myers, Fla., into a vast plantation. The sturdy *Pterocaulon* (misspelled by the inventor), a popular herb in the southeastern U.S., is a member of the Carduaceae (thistle) family. Edison found that its characteristic winged leaves contained slightly more than 2 percent natural rubber.

“I have not yet gone far enough to find out if my schemes [for producing rubber] are practicable,” a 1929 journal entry reads in Edison’s shaky hand. Past the time of the “Golden Jubilee” celebration of the first incandescent light, the octogenarian inventor still visited the West Orange laboratory every day, defiantly punching in and out on his very own time card.



1931



Edison did not believe in exercise, chewed tobacco continuously and smoked several cigars a day. For many years, his only foods were milk and the occasional glass of orange juice. And yet ulcers, diabetes and Bright’s disease could not dim the persistent luster in Edison’s gaze, as this picture testifies, taken six months before his death on October 18, 1931. Toward the end, he emerged from a coma, looked upward at his wife, Mina, and said, “It is very beautiful over there.”

The Author

NEIL BALDWIN received his Ph.D. in modern American poetry in 1973 from the State University of New York at Buffalo. He is executive director of the National Book Foundation in New York City, sponsor of the National Book Awards. His article on “The Laboratory Notebooks of Thomas Edison” appeared in the October 1995 issue of *Scientific American*. Baldwin is the author of the biography *Edison: Inventing the Century* (Hyperion, 1995; paperbound, 1996) and writer/associate producer for the documentary based on his biography of artist Man Ray, to appear this spring on the PBS©WNET series *American Masters*. He acknowledges the kind assistance of Douglas Tarr and George Tselos of the Edison National Historic Site in West Orange, N.J., and Susan Fraser of the New York Botanical Garden.

To obtain high-quality reprints of this article, please see page 36.

Why and How Bacteria Communicate

Bacteria converse with one another and with plants and animals by emitting and reacting to chemical signals. The need to "talk" may help explain why the microbes synthesize a vast array of compounds

by Richard Losick and Dale Kaiser

The 4th of June in the morning I saw great abundance of living creatures; and looking again in the afternoon of the same day, I found great plenty of them in one drop of water.... They looked to my eye, through the Microscope, as common sand doth to the naked eye.

So wrote the great microscopist Anton van Leeuwenhoek in 1676, when he described what probably was one of the earliest observations of bacteria. Leeuwenhoek's rudimentary, single-lens equipment could barely discern the microbes. Today scientists know that bacteria, which are among the oldest and most abundant organisms on the earth, are structurally simple creatures. Viewed under the electron microscope, they seem to be little more than rigid vessels filled with DNA and an amorphous cytoplasm. In contrast, the cells of most other organisms contain elaborate architectural features, including a nucleus, internal scaffolding and energy-producing organelles called mitochondria.

The structural simplicity of bacteria belies their extraordinary sophistication in manipulating their environment. Nowhere is their versatility more apparent than in their ability to communicate with one another and with higher organisms. Sometimes the interactions, which are effected through the exchange of chemical signals, result in only modest changes in the behavior of the "discussants," but at other times the alterations are nothing short of remarkable.

Biologists have long understood that bacteria live in colonies. But until recently, most thought the colony members were essentially rugged individual-

ists, looking out solely for themselves and having little to say to their kin. Now it seems that most, if not all, bacteria communicate with their neighbors. Here we will touch on some of the best-studied and most intriguing examples uncovered so far.

Let There Be Light

That bacteria are capable of chemical communication first emerged from investigations into marine bacteria able to glow in the dark. In 1970 Kenneth H. Nealson and John Woodland Hastings of Harvard University observed that luminous bacteria in culture do not glow at a constant intensity. In fact, they emit no light until the population reaches a high density.

Nealson and Hastings knew the light resulted from chemical reactions catalyzed by the enzyme luciferase. They postulated that this enzyme was ultimately controlled not by some mechanism inside each bacterial cell but by a molecular messenger that traveled between cells. Once inside target cells, the messenger, which the researchers called autoinducer, could induce expression of the genes coding for luciferase and for the other proteins involved in light production; that is, autoinducer could stimulate synthesis of the encoded proteins and, thus, of light. Their theory met with skepticism at first but has since been confirmed and expanded.

Investigators have learned that autoinducer does exist. And it does indeed pass freely from one bacterial cell, through the surrounding medium and into other cells, where it activates a protein known as LuxR that can stimulate the expression of genes involved in luminescence. But low levels of autoinducer cannot yield a glow. Light erupts when the concentration of cells is high enough to push autoinducer levels in the medium past a threshold value. At that point, autoinducer causes LuxR to stimulate expression of the genes for luciferase and for its light-producing collaborators, as well as for autoinducer itself. This first round of protein synthesis creates a positive feedback loop that results in more autoinducer production, more gene activity and, finally, a burst of light.

How do luminescent bacteria benefit from having an intercellular messenger in control of light production? One answer is suggested by the fact that these creatures provide the gleam emitted by the light organs of certain marine fish and squid.

Consider the case of the squid *Euprymna scolopes,* which selects the bacterium *Vibrio fischeri* to grow in its light organ, choosing that species over all others in the sea. When the bacterial cells live freely in the ocean, their concentration, and that of autoinducer, is extremely dilute; hence, the microbes give off no light. But if the squid cultivates a large population of the cells in its light organ, where the bacteria become packed like sardines, autoinducer accumulates to high concentrations and triggers maximal light production.

The squid, a nocturnal forager, benefits because the luminescing bacteria camouflage it from predators below; the glow, resembling moonlight, erases the shadow that would normally be cast when the moon's rays struck the squid from above. And the bacterium benefits because the squid provides a nourishing, sheltering haven. The autoinducer system ensures that the bacteria waste little energy on light production until they have reached a high density; at that point, the resulting large concentration of autoinducer essentially "tells" the cells that they are clustered together in an enclosed space. If they now begin to radiate light, the energy they expend on providing illumination for the squid is likely to be repaid richly in food and protection.

Autoinducer belongs to a family of small molecules termed homoserine lactones, which are derived from an amino acid. A wide variety of bacteria have been found to employ these and structurally related molecules as devices for measuring cell density. Exactly why the cells assess this property of the colony is not always obvious. But, as is true of *V. fischeri,* the measurements often determine the behavior of the community as a whole, pushing it down one developmental pathway instead of another.

Signals Spur Spore Formation

In *V. fischeri* the intercellular chatter does not lead to a radical alteration in the shape or behavior of the cells. Chemical signaling in myxobacteria, though, causes those microbes to undergo astonishing changes in structure and activity. Myxobacteria are motile, rod-shaped bacteria that inhabit cultivated soils the world over.

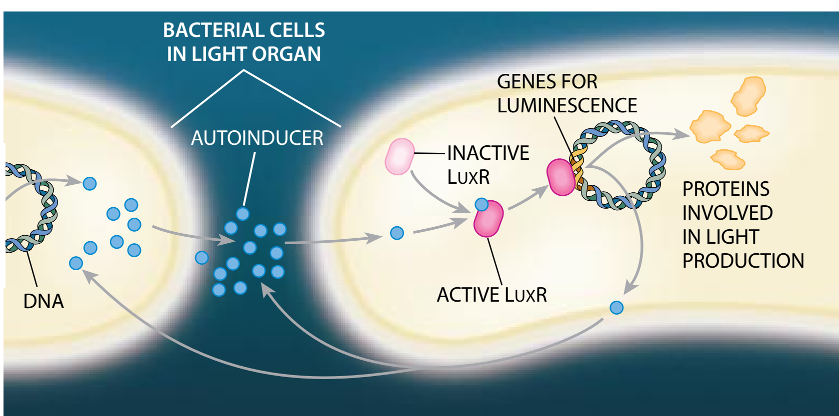
These bacteria typically grow as individual cells. But when water or nutrients are in short supply, thousands of cells of one species assemble into multicellular structures called fruiting bodies. Some of these structures are so complex that myxobacteria were once classified as fungi, which are higher than bacteria on the evolutionary tree. Fruiting bodies make it possible for thousands of spores—thick-coated cells that are resistant to heat, desiccation and long-term starvation—to be picked up as a package by wind, water or a passing animal and carried to destinations more suitable for establishing a new colony.

Incredibly, most of the cells that participate in forming myxobacterial fruiting bodies seem to sacrifice themselves to ensure that others will form spores and survive to reproduce. (The individual cells and spores are microscopic, but the fruiting bodies are large enough to be seen by the unaided eye; they are visible as brightly colored yellow, red or green specks in decaying vegetation or on the bark of trees.)

During the past 10 years, researchers have uncovered some of the intricate

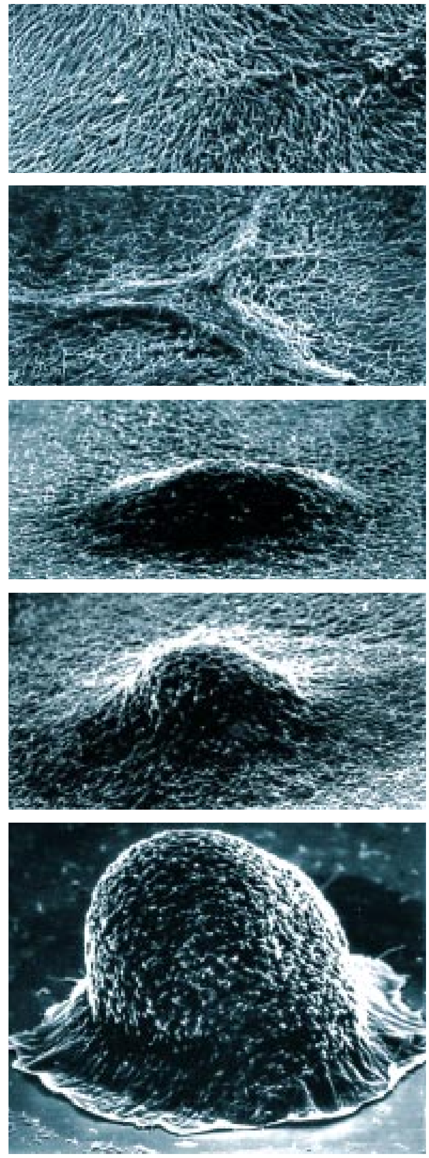
MARGARET McFALL-NGAI AND EDWARD G. RUBY *University of Hawaii*

LAURIE GRACE



SQUID *Euprymna scolopes* (*opposite page*) has been opened from underneath to show its light organ (*butterfly shape near center*). The organ glows because it is densely colonized by the luminescent bacterium *Vibrio fischeri*. The microbes light up after being instructed to do so by autoinducer (*blue in diagram*), a messenger that travels between the bacterial cells. A high level of autoinducer leads to activation of the protein LuxR. LuxR stimulates genes to give rise to the proteins directly responsible for light production and to more autoinducer, which stimulates both the cell that produces it and neighboring cells.

SOIL-DWELLING BACTERIA of the species *Myxococcus xanthus* live in small groups of cells unless resources dwindle. When cells begin to starve, they signal their plight by secreting a chemical called factor A. A low density of factor A (*panel* a *in diagram*) has little effect on a colony, but when the density exceeds a threshold (*b*), the rise signifies widespread trouble and spurs the cells to band together (*c*) to begin forming a fruiting body (*micrograph sequence*). Such bodies can contain 100,000 spores, cells able to withstand a lack of food. Wind or an animal then transports the entire package to more fertile territory, where the spores can germinate and establish a new colony.



signaling that controls fruiting-body formation in a fascinating species: *Myxococcus xanthus*. Approximately four hours after starvation sets in, the rod-shaped *M. xanthus* cells start to travel from various parts of the community and congregate at focal points. Eventually about 100,000 cells accumulate at each focus and form a golden mound (*xanthus* means "golden") that can reach a tenth of a millimeter in height (the width of a hair) and is visible without magnification. By 20 hours after starvation ensues, some cells in the mound have begun to differentiate into spores. By about 24 hours, assembly of the basic structure is complete.

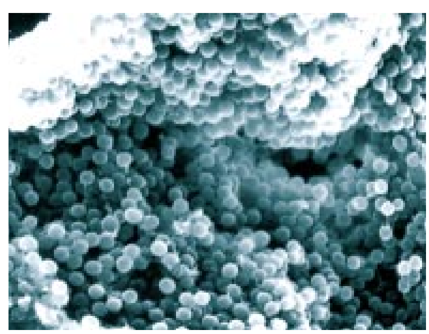
Two of the best-studied chemical messengers controlling fruiting-body formation in *M. xanthus* go by the names factor A and factor C. Factor A is needed for cells to aggregate at a focus, and factor C helps cells to complete aggregation and initiate spore production.

As is true of autoinducer and the other homoserine lactones, factor A is a cell-density signal. It is released into the surrounding area and triggers aggregation only if a threshold concentration is achieved. We can think of factor A as a kind of SOS signal indicating that a cell is in danger of starving. If only a few cells in a community are releasing it, the overall ("summarizing") concentration in the region will be low, and the community will deduce that the environment contains adequate resources for growth as individual cells. If, on the other hand, enough cells emit SOS signals, the high regional concentration will act as a warning that the entire community is imperiled. Then the cells will begin to assemble the fruiting body. Supporting this idea, the number of cells that must secrete factor A to trigger fruiting-body synthesis is the minimum needed to compose a full spore-forming organ.

Factor C, which is a small protein, comes into play after starvation has been evaluated and clustering at a focus has commenced. Unlike factor A, it stays attached to the cell that makes it and projects from the surface. Interestingly, cells must move about in order for factor C's spore-forming message to be transmitted between cells in a nascent aggregate. Researchers have long puzzled over why extensive movement is required, but experiments by one of us (Kaiser), Seung K. Kim, Brian M. Sager, Frank J. Slack and Lotte Søgaard-Andersen of Stanford University have helped solve the mystery.

The answer lies with the organism's need to be transported to a location where food will once again be available. The likelihood that a fruiting body will be carried away and establish a thriving new colony rises as the number of spores and the density of packing within a fruiting body increase. For the rod-shaped cells to pack themselves most closely, they must touch at their sides and their tips, and for such contacts to be made, the cells must move.

When proper alignment is somehow achieved, the factor C that protrudes from the touching cells informs others of the success. A high degree of C signaling tells the community that optimal (close) packing has been accomplished. So assured, the cells stop moving and



OPENED FRUITING BODY of *M. xanthus*, shown at high magnification, reveals the spores inside. Spore formation is triggered by a chemical known as factor C.

activate the genes needed for spore formation. In other words, C signaling is a sign of high cell density and of proper completion of the early steps of fruiting-body development.

Intensive signaling has also been detected in another family of soil-dwelling bacteria, streptomycetes. Pharmacologists cherish streptomycetes as sources of many antibiotics and other compounds valuable in medicine, such as avermectin (which kills parasites) and FK506 (administered to prevent immune rejection of organ transplants). Nature lovers also have these organisms to thank for the earthy odor of forests.

Streptomycete colonies grow as a branching network of long, fiberlike cells, or hyphae, and resemble certain filamentous fungi. The hyphae penetrate and degrade vegetation, feeding on the decaying matter. When food supplies dwindle, the community, like that of *M. xanthus,* cooperates to produce spores—in this case, in a specialized structure known as an aerial mycelium.

An observer watching the construction of the aerial mycelium would first see many hyphae rise up from the colony and point into the air. These hyphae give the colony a white, fuzzy appearance. Then, over several days, each of the aerial hyphae, which initially consisted of a single long cell, would become partitioned and would differentiate into a long chain of thick-coated spores (resembling a string of pearls). Often spores become pigmented as they mature, eventually imparting a hue to the fuzzy surface of a colony.

Much evidence indicates that an active exchange of chemical signals within the community governs the lifting of the aerial hyphae. One of the best studied of these chemicals is similar to molecules of the homoserine lactone family (the one that includes the density-detecting autoinducer manufactured by luminescent bacteria). Presumably this signal promotes formation of aerial hyphae when enough of the soil dwellers detect a drop in food supplies.

Cells of the hyphal community also cooperate by secreting SapB, a small protein that accumulates in copious quantities outside the cells. SapB seems to participate directly in constructing aerial hyphae, a discovery made by Joanne Willey of Harvard in 1990. It coats the surface of the colony, perhaps helping the uppermost filaments to break surface tension and rise up from the ground. Thus, somewhat akin to a Quaker barn raising, erecting aerial hyphae is a kind of community enterprise in which cells coordinate their activities through the exchange and accumulation of various chemicals.

Talking with Higher-ups

Beyond conversing with their own kind, bacterial cells sometimes conduct elaborate chemical conversations with higher organisms. The luminescent bacterium *V. fischeri* offers a case in point. We have already described how the cells, once ensconced in the light organ of the squid, direct one another to switch on their light-producing machinery. But the microbes do more than that; they also spur maturation of the light organ. When hatchling squid are raised in sterile seawater, they fail to enlarge the pouches that become the fully developed organ. Presumably a chemical signal from the bacterium induces that development, although the specific substance involved has yet to be isolated.

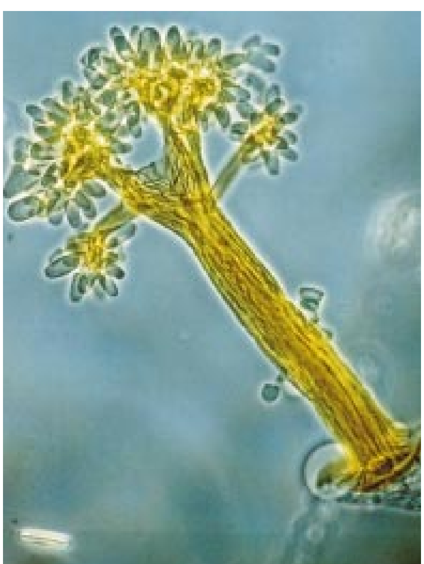
Investigators have, however, learned a great deal about the bacterial signaling that promotes the development of some plants. Certain soil bacteria engage in a mutually beneficial, or symbiotic, relationship with the leguminous plants that produce peas, soybeans and the like. Those bacteria are members of the genus *Rhizobium,* and their association with legumes is part of a much larger biogeochemical story: the cycling of the element nitrogen between the atmosphere and terrestrial life.

All life-forms depend on nitrogen. Although the earth is bathed in an atmosphere rich in nitrogen gas, few organisms can assimilate that form into their tissues. For atmospheric nitrogen to be incorporated into cellular material, the strong chemical bonds that hold the atoms of the gas together in pairs must be broken by an energy-intensive process known as nitrogen fixing. In nature, fixing is carried out by only a few specialized kinds of bacteria. Without nitrogen-fixing bacteria, life would surely have perished long ago, because these organisms make it possible for nitrogen to remain in use. Fixed nitrogen is ultimately returned to the atmosphere through other microorganisms that release nitrogen gas as they degrade dead plant and animal matter. Today we still obtain usable nitrogen from the natural fixing process, although man-made chemical factories that incorporate nitrogen into fertilizers augment the work of the bacteria.

Free-living *Rhizobium* is incapable of carrying out nitrogen fixing. It does this essential job only when it colonizes a legume. Bacteria in the soil invade tiny hairs on the roots of the legume. Then they migrate deep into the root tissues, settling in specialized nodules built for them by the plant. There the bacteria undergo dramatic changes in shape and size, becoming rounder and bigger as they differentiate into nitrogen-fixing factories known as bacteroids. In this mutually beneficial association, bacteroids supply their host with a readily assimilated form of nitrogen (ammonia), and the plant supplies the bacteria with food (carbohydrates).

The profound changes that occur in both microbe and host stem from a reciprocal molecular conversation that commences even before the bacterium and plant come into contact. The plant issues a chemical signal, known as a flavonoid, discovered in the 1980s by Sharon R. Long and her colleagues at Stanford. This flavonoid apparently penetrates into the bacterial cells and stimulates a gene-activating protein. The protein then switches on several "nodulation" genes involved in inducing the plant to proceed with forming nodules.

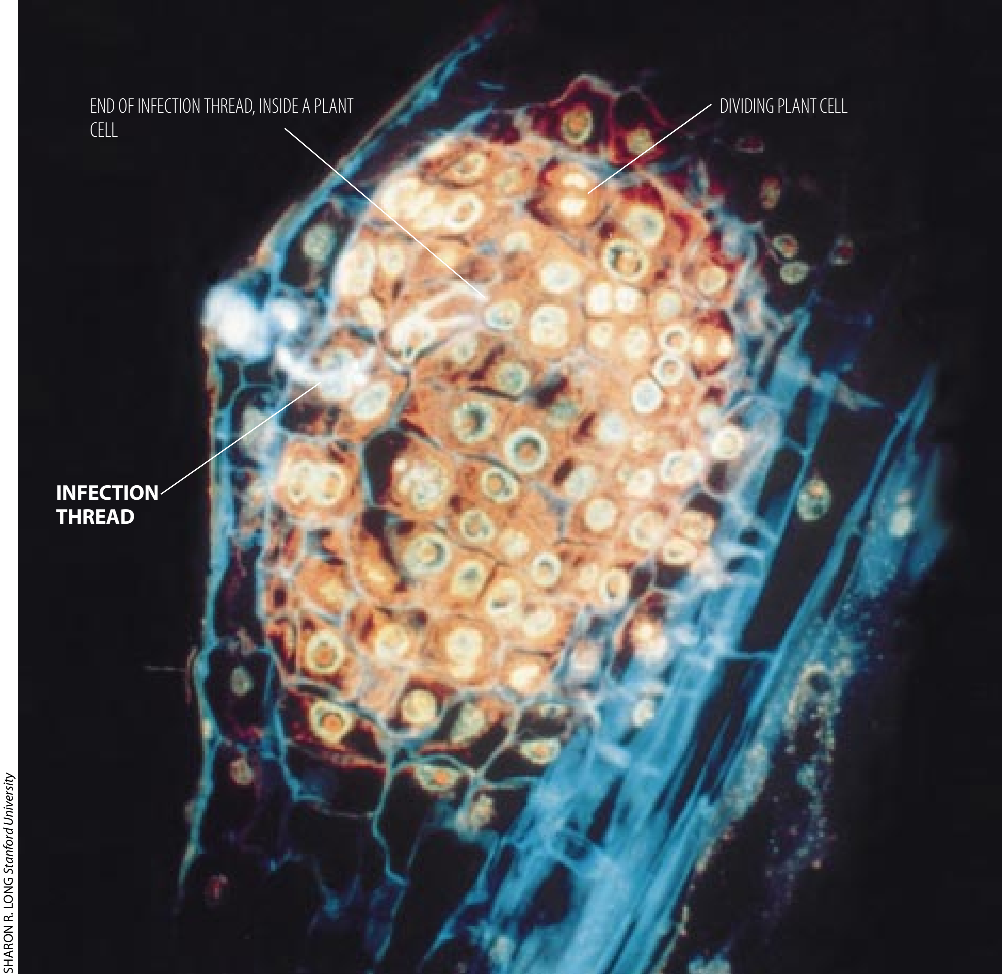
Others have provided a closer look at how the nodulation genes in the *Rhizobium* cells produce a reaction in the



HANS REICHENBACH *Institute for Biotechnical Research, Braunschweig, Germany*

FRUITING BODY of the myxobacterium *Chondromyces crocatus* is more intricate than that of *M. xanthus. C. crocatus* starts down the same road as *M. xanthus,* but instead of forming spores at the mound stage, it produces a stalk. Then it forms branches that finally support about 20 spore-filled packages at the tips. This complexity highlights the organizing power of signaling among bacterial cells.

HUGH SPENCER *Photo Researchers, Inc.*



SHARON R. LONG *Stanford University*

NODULES on the roots of a pea plant (*above*) contain *Rhizobium* bacteria, which fix nitrogen, converting the gas into a form plants can use. In exchange, the bacteria gain a safe, nourishing place to live. Such nodules form and become colonized by bacteria as a result of chemical conversations between the roots and the microbes (*diagram*). The young nodule in the micrograph (*right*), from alfalfa, displays dividing cells and an infection thread through which bacteria will enter the root.

plant. The protein products of some nodulation genes are enzymes that manufacture a sugar-rich molecule called Nod factor; this molecule then talks back to the plant, triggering the cell division needed to form the nodules that ultimately house the bacteroids.

Later, when *Rhizobium* cells come into contact with root hairs, the bacteria stimulate the hairs to produce tunnel-like passages called infection threads. Carbohydrates on *Rhizobium* then enable the bacteria to enter the threads and burrow into the root. It would not be surprising to discover that the nodules reply by producing yet to be identified signals able to induce the transformation of the invading bacteria into nitrogen-fixing bacteroids. In any case, it is clear that signaling here goes two ways; the bacterium and its host prod each other to carry out successive steps in a pathway that regulates the development of both organisms.

Pathogenic Patter

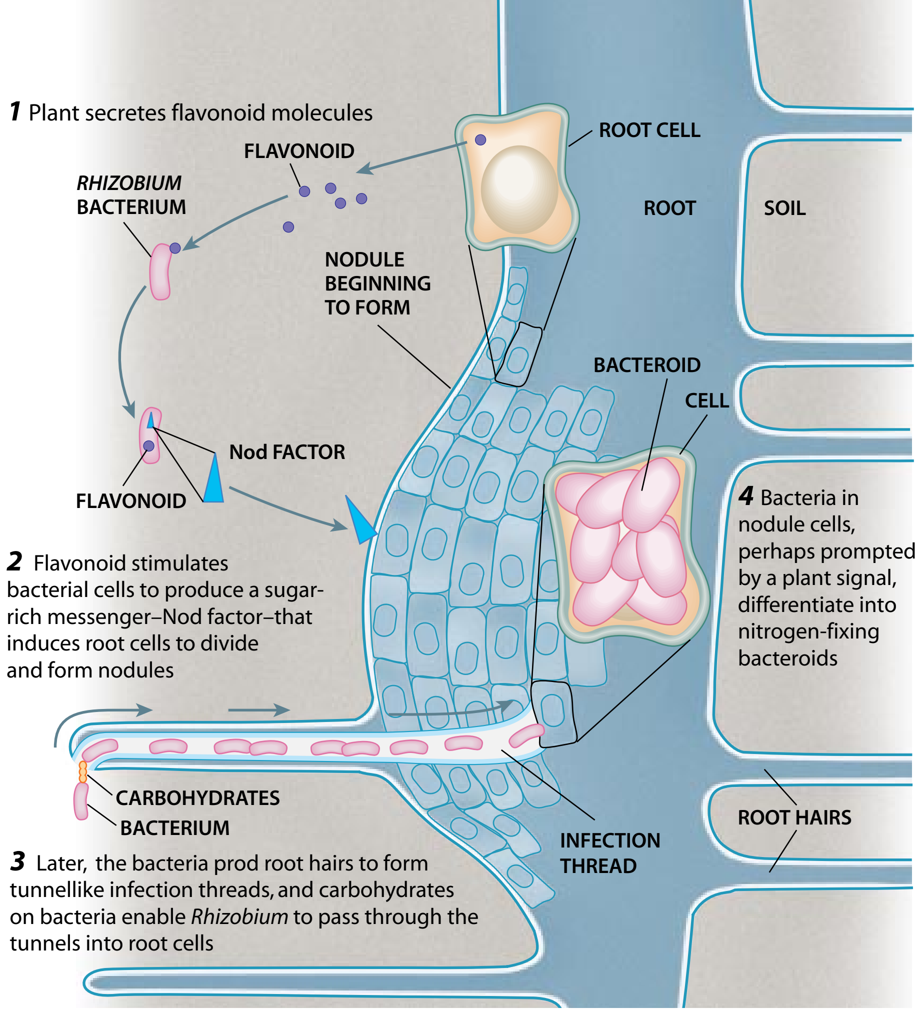
Not all signaling between bacteria and higher organisms works to the benefit of both. Like symbiotic bacteria, disease-causing species transmit chemical signals that instruct the cells of a host to alter their behavior. But in the case of pathogens, the signals elicit responses that are detrimental to the host, disabling its defenses and enabling the pathogens to gain a foothold. Of these dangerous bacteria, one that applies particularly clever tactics is *Yersinia pestis,* the pathogen responsible for the bubonic plague that decimated much of the population in 14th- and 15-century Europe.

Y. pestis, which still causes isolated outbreaks of disease, infects lymphoid tissues in humans and undermines the activity of defensive cells known as lymphocytes. To carry out this mission, it must first escape ingestion by macrophages—scavenger cells of the immune system. Macrophages swallow and destroy pathogenic bacteria and also help to activate other components of the immune system. *Y. pestis* evades assault by producing proteins that enter macrophages and disarm them. Some of those proteins directly injure macrophages, but others, such as one called YopH, forestall attack by interfering with the macrophage's internal communications network.

Like the bacterial colonies we have been discussing, higher multicellular organisms have intricate signaling systems that enable cells to communicate with one another. Signaling molecules of various kinds, such as hormones, bind to receptors on the surface of some target cell. These receptors convey the external message to molecules inside the cell, which relay them to the cell nucleus, where the genes are housed. The signal then alters the pattern of gene expression, thereby altering the activities of the cell. Investigators refer to the chain of events from the cell surface to the nucleus as a signal transduction pathway.

A key component of many transduction pathways, including those in macrophages, is the enzymatic addition of phosphate molecules to selected proteins in the signaling chain—a change that typically activates quiescent proteins and enables them to keep the chain alive. Jack E. Dixon, when he was at Purdue University, discovered that YopH belongs to a class of enzymes that detaches the added phosphates. It is easy to imagine that phosphate removal by YopH would disrupt the transduction pathways in macrophages and stop the cells from responding to *Y. pestis.*

Certain species of *Yersinia* also com-



LAURIE GRACE

mandeer the signal transduction systems of other kinds of cells and use the systems to their own ends. For example, some *Yersinia* bacteria must travel through intestinal cells to colonize lymph nodes in the gut of their host. These bacteria often switch on signal transduction pathways that cause the intestinal cells to take up the bacteria.

The bacteria set the pathways in motion by displaying the protein invasin, which binds to a receptor on the host cells. Invasin may thus be part of the mechanism by which these *Yersinia* species are able to pass through layers of cells in their host to reach deeper tissues. That invasin could be responsible for triggering engulfment was demonstrated in an elegant experiment by Ralph Isberg of the Tufts University School of Medicine. In the laboratory, cells of the bacterium *Escherichia coli* are noninvasive. But when they are endowed with the ability to produce the *Yersinia* invasin protein, they become able to penetrate mammalian cells.

The signaling molecules made by bacteria belong to a larger group of chemicals called secondary metabolites. In contrast to such primary metabolites as amino acids and vitamins, the secondary types are inessential to cell maintenance and growth. For years, scientists have wondered why bacteria make an extensive array of these compounds.

Signals Worth Listening to

Clearly, many of the secondary metabolites are agents of the wars bacteria wage against competing microorganisms; these are the chemicals that have provided human society with many antibiotic drugs. But some of the secondary metabolites are ordinarily synthesized at levels too low to afford the microbes much protection. We suspect many of these other compounds are used for communication. Moreover, the need for varied communiqués may well help explain why, over the aeons, bacteria have continued to make a vast array of seemingly expendable chemicals.

Interestingly, some work hints that a subset of secondary metabolites can play a dual role, acting defensively at high levels and serving as messengers at lower ones. For instance, Julian Davies and Charles J. Thompson, both then at the Pasteur Institute in Paris, discovered that at doses too low to inhibit the growth of target microbes, certain antibiotics released by bacterial cells can stimulate the expression of genes in other cells of the same type. Perhaps other secondary metabolites with no known antibiotic effects are signaling molecules rather than agents of biochemical warfare.

Listening in on the conversations bacteria hold with their neighbors should provide new insights into the survival tactics of the earth's simplest creatures. If we pay close attention, our eavesdropping may also uncover novel substances of value to humankind. SA

The Authors

RICHARD LOSICK and DALE KAISER are both fascinated by the unexpected communicative prowess of bacteria. Losick is Maria Moors Cabot Professor and chairman of the department of molecular and cellular biology at Harvard University. Kaiser is Wilson Professor of Biochemistry and professor of developmental biology at the Stanford University School of Medicine. He is also the 1997 recipient of the Abbott–American Society for Microbiology Lifetime Achievement Award.

Further Reading

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The Challenge of Large Numbers

As computer capabilities increase, mathematicians can better characterize and manipulate gargantuan figures. Even so, some numbers can only be imagined

by Richard E. Crandall

Large numbers have a distinct appeal, a majesty if you will. In a sense, they lie at the limits of the human imagination, which is why they have long proved elusive, difficult to define and harder still to manipulate. In recent decades, though, computer capabilities have dramatically improved. Modern machines now possess enough memory and speed to handle quite impressive figures. For instance, it is possible to multiply together million-digit numbers in a mere fraction of a second. As a result, we can now characterize numbers about which earlier mathematicians could only dream.

Interest in large numbers dates back to ancient times. We know, for example, that the early Hindus, who developed the decimal system, contemplated them. In the now commonplace decimal system the position of a digit (1s, 10s, 100s and so on) denotes its scale. Using this shorthand, the Hindus named many large numbers; one having 153 digits—or as we might say today, a number of order 10^{153}—is mentioned in a myth about Buddha.

The ancient Egyptians, Romans and Greeks pondered large values as well. But historically, a large number was whatever the prevailing culture deemed it to be—an intrinsically circular definition. The Romans initially had no terms or symbols for figures above 100,000. And the Greeks usually stopped counting at a *myriad,* a word meaning "10,000." Indeed, a popular idea in ancient Greece was that no number was greater than the total count of sand grains needed to fill the universe.

In the third century B.C., Greek mathematician Archimedes sought to correct this belief. In a letter to King Gelon of Syracuse, he set out to calculate the actual number of sand grains in the universe. To do so, Archimedes devised a clever scheme involving successive ratios that would effectively extend the prevailing Greek number system, which had no exponential scaling. His results, which in current terms placed the number somewhere between 10^{51} to 10^{63}, were visionary; in fact, a sphere having the radius of Pluto's orbit would contain on the order of 10^{51} grains.

Scholars in the 18th and 19th centuries contemplated large numbers that still

29384732625364758192049586738271635241827364655948372645362718205678893543627190983452167894320984563

have practical scientific relevance. Consider Avogadro's number, named after the 19th-century Italian chemist Amedeo Avogadro. It is roughly 6.02×10^{23} and represents the number of atoms in 12 grams of pure carbon. One way to think about Avogadro's number, also called a mole, is as follows: if just one gram of carbon were expanded to the size of planet Earth, a single carbon atom would loom something like a bowling ball.

Another interesting way to imagine a mole is to consider the total number of computer operations—that is, the arithmetic operations occurring within a computer's circuits—ever performed by all computers in history. Even a small machine can execute millions of operations per second; mainframes can do many more. Thus, the total operation count to date, though impossible to estimate precisely, must be close to a mole. It will undoubtedly have exceeded that by the year 2000.

Today scientists deal with numbers much larger than the mole. The number of protons in the known universe, for example, is thought to be about 10^{80}. But the human imagination can press further. It is legendary that the nine-year-old nephew of mathematician Edward Kasner did coin, in 1938, the googol, as 1 followed by 100 zeroes, or 10^{100}. With respect to some classes of computational problems, the googol roughly demarcates the number magnitudes that begin seriously to challenge modern machinery. Even so, machines can even answer some questions about gargantua as large as the mighty googolplex, which is 1 followed by a googol of zeroes, or $10^{10^{100}}$. Even if you used a proton for every zero, you could not scribe the googolplex onto the known universe.

LARGE NUMBERS—such as the 100-digit, or googol-size, ones running across the tops of these pages—have become more accessible over time thanks to advances in computing. Archimedes, whose bust appears at the left, had to invent new mathematics to estimate the number of sand grains required to fill the universe. His astonishingly accurate result, 10^{51}, was by ancient standards truly immense. Modern machines, however, routinely handle vastly greater values. Indeed, any personal computer with the right software can completely factor a number of order 10^{51}.

Manipulating the Merely Large

Somewhat above the googol lie numbers that present a sharp challenge to practitioners of the art of factoring: the art of breaking numbers into their prime factors, where primes are themselves divisible only by 1 and themselves. For example, 1,799,257 factors into $7{,}001 \times 257$, but to decompose a sufficiently large number into its prime factors can be so problematic that computer scientists have harnessed this difficulty to encrypt data. Indeed, one prevailing encryption algorithm, called RSA, transforms the problem of cracking encrypted messages into that of factoring certain large numbers, called public keys. (RSA is named after its inventors, Ronald L. Rivest of the Massachusetts Institute of Technology, Adi Shamir of the Weizmann Institute of Science in Israel and Leonard M. Adleman of the University of Southern California.)

To demonstrate the strength of RSA, Rivest, Shamir and Adleman challenged readers of Martin Gardner's column in the August 1977 issue of *Scientific American* to factor a 129-digit number, dubbed RSA-129, and find a hidden message. It was not until 1994 that Arjen K. Lenstra of Bellcore, Paul Leyland of the University of Oxford and then graduate student Derek Atkins of M.I.T. and undergraduate student Michael Graff of Iowa State University, working with hundreds of colleagues on the Internet, succeeded. (The secret encrypted message was "THE MAGIC WORDS ARE SQUEAMISH OSSIFRAGE.") Current recommendations suggest that RSA encryption keys have at least 230 digits to be secure.

Network collaborations are now commonplace, and a solid factoring culture has sprung up. Samuel S. Wagstaff, Jr., of Purdue University maintains a factoring newsletter listing recent factorizations. And along similar lines, Chris K. Caldwell of the University of Tennessee at Martin maintains a World Wide Web site (http://www.utm.edu/research/primes/largest.html) for prime number records. Those who practice factoring typically turn to three powerful algorithms. The Quadratic Sieve (QS) method, pioneered by Carl Pomerance of the University of Georgia in the 1980s, remains a strong, general-purpose attack for factoring numbers somewhat larger than a googol. (The QS, in fact, conquered RSA-129.) To factor a mystery number, the QS attempts to factor many smaller, related numbers generated via a clever sieving process. These smaller factorizations are combined to yield a factor of the mystery number.

A newer strategy, the Number Field Sieve (NFS), toppled a 155-digit number, the ninth Fermat number, F_9. (Named

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for the great French theorist Pierre de Fermat, the nth Fermat number is $F_n = 2^{2^n} + 1$.) In 1990 F_9 fell to Arjen Lenstra, Hendrik W. Lenstra, Jr., of the University of California at Berkeley, Mark Manasse of Digital Equipment Corporation and British mathematician John Pollard, again aided by a substantial machine network. This spectacular factorization depended on F_9's special form. But Joseph Buhler of Reed College, Hendrik Lenstra and Pomerance have since developed a variation of the NFS for factoring arbitrary numbers. This general NFS can, today, comfortably factor numbers of 130 digits. In retrospect, RSA-129 could have been factored in less time this way.

The third common factoring tactic, the Elliptic Curve Method (ECM), developed by Hendrik Lenstra, can take apart much larger numbers, provided that at least one of the number's prime factors is sufficiently small. For example, Richard P. Brent of the Australian National University recently factored F_{10} using ECM, after first finding a single prime factor "only" 40 digits long. It is difficult to find factors having more than 40 digits using ECM. For arbitrary numbers between, say, 10^{150} and $10^{1,000,000}$, ECM stands as the method of choice, although ECM cannot be expected to find *all* factors of such gargantuan numbers.

Even for numbers that truly dwarf the googol, isolated factors can sometimes be found using a centuries-old sieving method. The idea is to use what is called modular arithmetic, which keeps the sizes of numbers under control so that machine memory is not exceeded, and adroitly scan ("sieve") over trial factors. A decade ago Wilfrid Keller of the University of Hamburg used a sieving technique to find a factor for the awesome F_{23471}, which has roughly $10^{7,000}$ decimal digits. Keller's factor itself has "only" about 7,000 digits. And Robert J. Harley, then at the California Institute of Technology, turned to sieving to find a 36-digit factor for the stultifying (googolplex + 1); the factor is 316,912,650, 057,057,350,374,175,801,344,000,001.

Algorithmic Advancements

Many modern results on large numbers have depended on algorithms from seemingly unrelated fields. One example that could fairly be called the workhorse of all engineering algorithms is the Fast Fourier Transform (FFT). The FFT is most often thought of as a means for ascertaining some spectrum, as is done in analyzing birdsongs or human voices or in properly tuning an acoustic auditorium. It turns out that ordinary multiplication—a fundamental operation between numbers—can be dramatically enhanced via FFT [*see box below*]. Arnold Schönage of the University of Bonn and others refined this astute observation into a rigorous theory during the 1970s.

FFT multiplication has been used in celebrated calculations of π to a great many digits. Granted π is not a bona fide large number, but to compute π to millions of digits involves the same kind of arithmetic used in large-number studies. In 1985 R. William Gosper, Jr., of Symbolics, Inc., in Palo Alto, Calif., computed 17 million digits of π. A year later David Bailey of the National Aeronautics and Space Administration Ames Research Center computed π to more than 29 million digits. More recently, Bailey and Gregory Chudnovsky of Columbia University reached one billion digits. And Yasumasa Kanada of the University of Tokyo has reported five billion digits. In case anyone wants to

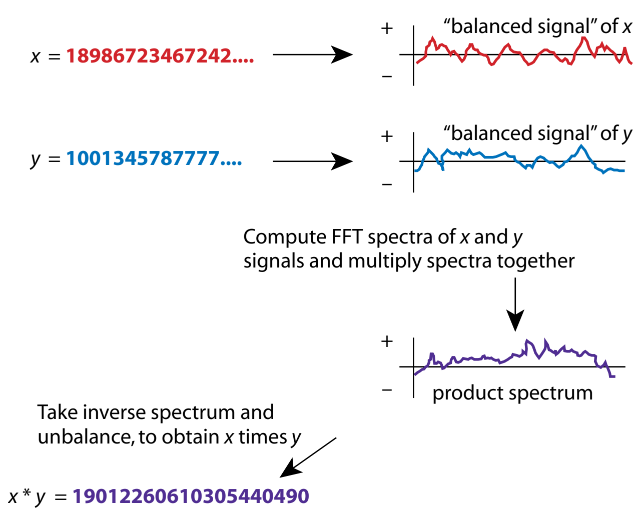
Using Fast Fourier Transforms for Speedy Multiplication

Ordinary multiplication is a long-winded process by any account, even for relatively small numbers: To multiply two numbers, *x* and *y*, each having *D* digits, the usual, "grammar school" method involves multiplying each successive digit of *x* by every digit of *y* and then adding columnwise, for a total of roughly D^2 operations. During the 1970s, mathematicians developed means for hastening multiplication of two *D*-digit numbers by way of the Fast Fourier Transform (FFT). The FFT reduces the number of operations down to the order of *D* log *D*. (For example, for two 1,000-digit numbers, the grammar school method may take more than 1,000,000 operations, whereas an FFT might take only 50,000 operations.)

A full discussion of the FFT algorithm for multiplication is beyond the scope of this article. In brief, the digits of two numbers, *x* and *y* (actually, the digits in some number base most convenient for the computing machinery) are thought of as signals. The FFT is applied to each signal in order to decompose the signal into its spectral components. This is done in the same way that a biologist might decompose a whale song or some other meaningful signal into frequency bands. These spectra are quickly multiplied together, frequency by frequency. Then an inverse FFT and some final manipulations are performed to yield the digits of the product of *x* and *y*.

There are various, powerful modern enhancements to this basic FFT multiplication. One such enhancement is to treat the digit signals as bipolar, meaning both positive and negative digits are allowed. Another is to "weight" the signals by first multiplying each one by some other special signal. These enhancements have enabled mathematicians to discover new prime numbers and prove that certain numbers are prime or composite (not prime).

—*R.E.C.*



check this at home, the one-billionth decimal place of π, Kanada says, is nine.

FFT has also been used to find large prime numbers. Over the past decade or so, David Slowinski of Cray Research has made a veritable art of discovering record primes. Slowinski and his coworker Paul Gage uncovered the prime $2^{1,257,787}-1$ in mid-1996. A few months later, in November, programmers Joel Armengaud of Paris and George F. Woltman of Orlando, Fla., working as part of a network project run by Woltman, found an even larger prime: $2^{1,398,269}-1$. This number, which has over 400,000 decimal digits, is the largest known prime number as of this writing. It is, like most other record holders, a so-called Mersenne prime. These numbers take the form 2^q-1, where q is an integer, and are named after the 17th-century French mathematician Marin Mersenne.

For this latest discovery, Woltman optimized an algorithm called an irrational-base discrete weighted transform, the theory of which I developed in 1991 with Barry Fagin of Dartmouth College and Joshua Doenias of NeXT Software in Redwood City, Calif. This method was actually a by-product of cryptography research at NeXT.

Blaine Garst, Doug Mitchell, Avadis Tevanian, Jr., and I implemented at NeXT what is one of the strongest—if not the strongest—encryption schemes available today, based on Mersenne primes. This patented scheme, termed Fast Elliptic Encryption (FEE), uses the algebra of elliptic curves, and it is very fast. Using, for example, the newfound Armengaud-Woltman prime $2^{1,398,269}-1$ as a basis, the FEE system could readily encrypt this issue of *Scientific American* into seeming gibberish. Under current number-theoretical beliefs about the difficulty of cracking FEE codes, it would require, without knowing the secret key, all the computing power on earth more than $10^{10,000}$ years to decrypt the gibberish back into a meaningful magazine.

Just as with factoring problems, proving that a large number is prime is much more complicated if the number is arbitrary—that is, if it is not of some special form, as are the Mersenne primes. For primes of certain special forms, "large" falls somewhere in the range of $2^{1,000,000}$. But currently it takes considerable computational effort to prove that a "random" prime having only a few thousand digits is indeed prime. For example, in 1992 it took several weeks for François Morian of the University of Claude Bernard, using techniques developed jointly with A.O.L. Atkin of the University of Illinois, and others, to prove by computer that a particular 1,505-digit number, termed a partition number, is prime.

Colossal Composites

It is quite a bit easier to prove that some number is not prime (that it is composite, that is, made up of more than one prime factor). In 1992 Doenias, Christopher Norrie of Amdahl Corporation and I succeeded in proving by machine that the 22nd Fermat number, $2^{2^{22}}+1$, is composite. This number has more than one million decimal digits. Almost all the work to resolve the character of F_{22} depended on yet another modification of FFT multiplication. This proof has been called the longest calculation ever performed for a "one-bit," or yes-no, answer, and it took about 10^{16} computer operations. That is roughly the same amount that went into generating the revolutionary Pixar-Disney movie *Toy Story,* with its gloriously rendered surfaces and animations.

Although it is natural to suspect the validity of any machine proof, there is a happy circumstance connected with this one. An independent team of Vilmar Trevisan and João B. Carvalho, working at the Brazilian Supercomputer Center with different machinery and software (they used, in fact, Bailey's FFT software) and unaware of our completed proof, also concluded that F_{22} is composite. Thus, it seems fair to say, without doubt, that F_{22} is composite. Moreover, F_{22} is also now the largest "genuine" composite known—which means that even though we do not know a single explicit factor for F_{22} other than itself and 1, we do know that it is not prime.

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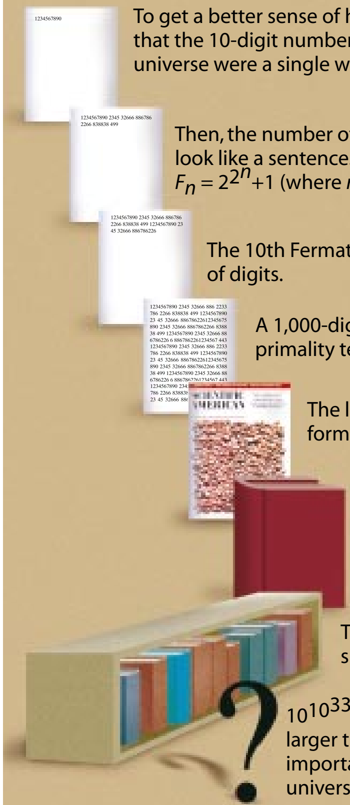
COLOSSI become somewhat easier to contemplate—and compare—if one adopts a statistical view. For instance, it would take approximately $10^{3,000,000}$ years before a parrot, pecking randomly at a keyboard, could reproduce by chance *The Hound of the Baskervilles*. This time span, though enormous, pales in comparison to the $10^{10^{33}}$ years that would elapse before fundamental quantum fluctuations might topple a beer can on a level surface.

How Large Is Large?



To get a better sense of how enormous some numbers truly are, imagine that the 10-digit number representing the age in years of the visible universe were a single word on a page.

Then, the number of protons in the visible universe, about 10^{80}, would look like a sentence. The ninth Fermat number—which has the value $F_n = 2^{2^n}+1$ (where n is nine)—would take up several lines.

The 10th Fermat number would look something like a paragraph of digits.

A 1,000-digit number, pressing the upper limit for random primality testing, would look like a page of digits.

The largest known prime number, $2^{1,398,269} - 1$, in decimal form, would essentially fill an issue of *Scientific American*.

A book could hold all the digits of the 22nd Fermat number, which possesses more than one million digits and is now known to be composite.

To multiply together two "bookshelves," even on a scalar supercomputer, takes about one minute.

$10^{10^{33}}$, written in decimal form, would fill a library much larger than the earth's volume. In fact, there are theoretically important numbers that cannot be written down in this universe, even using exponential notation.

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Just as with Archimedes' sand grains in his time, there will always be colossal numbers that transcend the prevailing tools. Nevertheless, these numbers can still be imagined and studied. In particular, it is often helpful to envision statistical or biological scenarios. For instance, the number 10 to the three-millionth power begins to make some intuitive sense if we ask how long it would take a laboratory parrot, pecking randomly and tirelessly at a keyboard, with a talon occasionally pumping the shift key, say, to render by accident that great detective epic, by Sir Arthur Conan Doyle, *The Hound of the Baskervilles*. To witness a perfectly spelled manuscript, one would expect to watch the bird work for approximately $10^{3,000,000}$ years. The probable age of the universe is more like a paltry 10^{10} years.

But $10^{3,000,000}$ is as nothing compared with the time needed in other scenarios. Imagine a full beer can, sitting on a level, steady, rough-surfaced table, suddenly toppling over on its side, an event made possible by fundamental quantum fluctuations. Indeed, a physicist might grant that the quantum wave function of the can does extend, ever so slightly, away from the can so that toppling is not impossible. Calculations show that one would expect to wait about $10^{10^{33}}$ years for the surprise event. Unlikely as the can toppling might be, one can imagine more staggering odds. What is the probability, for example, that sometime in your life you will suddenly find yourself standing on planet Mars, reassembled and at least momentarily alive? Making sweeping assumptions about the reassembly of living matter, I estimate the odds against this bizarre event to be $10^{10^{51}}$ to 1. To write these odds in decimal form, you would need a 1 followed by a zero for every one of Archimedes' sand grains. To illustrate how unlikely Mars teleportation is, consider that the great University of Cambridge mathematician John Littlewood once estimated the odds against a mouse living on the surface of the sun for a week to be $10^{10^{42}}$ to 1.

These doubly exponentiated numbers pale in comparison to, say, Skewes's number, $10^{10^{10^{34}}}$, which has actually been used in developing a theory about the distribution of prime numbers. To show the existence of certain difficult-to-compute functions, mathematicians have invoked the Ackermann numbers (named after Wilhelm Ackermann of the Gymnasien in Luedenscheid, Germany), which compose a rapidly growing sequence that runs: 0, 1, 2^2, $3^{3^{3^3}}$.... The fourth Ackermann number, involving exponentiated 3's, is approximately $10^{3,638,334,640,024}$. The fifth one is so large that it could not be written on a universe-size sheet of paper, even using exponential notation! Compared with the fifth Ackermann number, the mighty googolplex is but a spit in the proverbial bucket. SA

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The Benefits and Ethics of Animal Research

Experiments on animals are a mainstay of modern medical and scientific research. But what are the costs and what are the returns?

by Andrew N. Rowan

For the past 20 years, we have witnessed an intense but largely unproductive debate over the propriety and value of using animals in medical and scientific research, testing and education. Emotionally evocative images and simple assertions of opinion and fact are the usual fare. But we do not have to accept such low standards of exchange. Sound bites and pithy rhetoric may have their place in the fight for the public's ear, but there is always room for dispassionate analysis and solid scholarship.

When it comes to animal research, there is plenty of reason for legitimate dispute. First, one has to determine what values are being brought to the table. If one believes animals should not be used simply as means to ends, that assumption greatly restricts what animal research one is willing to accept. Most people, though, believe some form of cost-benefit analysis should be performed to determine whether the use of animals is acceptable. The costs consist mainly of animal pain, distress and death, whereas the benefits include the acquisition of new knowledge and the development of new medical therapies for humans.

There is considerable disagreement among scientists in judging how much pain and suffering occur in the housing and use of research animals. More attention is at last being given to assessing these questions and to finding ways of minimizing such discomfort. Developing techniques that explicitly address and eliminate animal suffering in laboratories will reduce both public and scientific uneasiness about the ways animals are used in science. At present, indications are that public attention to the animal research issue has declined somewhat; however, the level of concern among scientists, research institutions, animal-rights groups and those who regulate animal use remains high.

There is also much room to challenge the benefits of animal research and much room to defend such research. In the next few pages, you will find a debate between opponents and supporters of animal research. It is followed by an article that sets out the historical, philosophical and social context of the animal-research controversy. We leave it to you to judge the case.

ANDREW N. ROWAN is director of the Tufts University Center for Animals and Public Policy.

CHRISTOPHER BURKE/QB

Animal Research Is Wasteful and Misleading

by Neal D. Barnard and Stephen R. Kaufman

The use of animals for research and testing is only one of many investigative techniques available. We believe that although animal experiments are sometimes intellectually seductive, they are poorly suited to addressing the urgent health problems of our era, such as heart disease, cancer, stroke, AIDS and birth defects. Even worse, animal experiments can mislead researchers or even contribute to illnesses or deaths by failing to predict the toxic effects of drugs. Fortunately, other, more reliable methods that represent a far better investment of research funds can be employed.

The process of scientific discovery often begins with unexpected observations that force researchers to reconsider existing theories and to conceive hypotheses that better explain their findings. Many of the apparent anomalies seen in animal experiments, however, merely reflect the unique biology of the species being studied, the unnatural means by which the disease was induced or the stressful environment of the laboratory. Such irregularities are irrelevant to human pathology, and testing hypotheses derived from these observations wastes considerable time and money.

The majority of animals in laboratories are used as so-called animal models: through genetic manipulation, surgical intervention or injection of foreign substances, researchers produce ailments in these animals that "model" human conditions. This research paradigm is fraught with difficulties, however. Evolutionary pressures have resulted in innumerable subtle, but significant, differences between species. Each species has multiple systems of organs—the cardiovascular and nervous systems, for example—that have complex interactions with one another. A stimulus applied to one particular organ system perturbs the animal's overall physiological functioning in myriad ways that often cannot be predicted or fully understood. Such uncertainty severely undermines the extrapolation of animal data to other species, including humans.

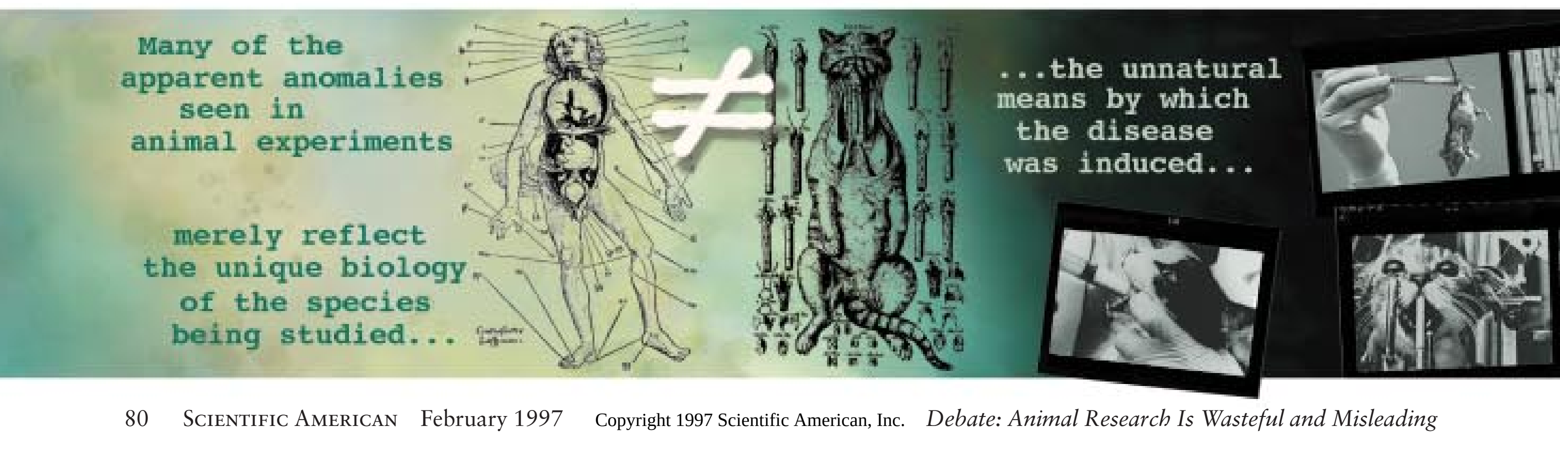
Animal Tests Are Inapplicable

Important medical advances have been delayed because of misleading results derived from animal experiments. David Wiebers and his colleagues at the Mayo Clinic, writing in the journal *Stroke* in 1990, described a study showing that of the 25 compounds that reduced damage from ischemic stroke (caused by lack of blood flow to the brain) in rodents, cats and other animals, none proved efficacious in human trials. The researchers attributed the disappointing results to disparities between how strokes naturally occur in humans and how they were experimentally triggered in the animals. For instance, a healthy animal that experiences a sudden stroke does not undergo the slowly progressive arterial damage that usually plays a crucial role in human strokes.

During the 1920s and 1930s, studies on monkeys led to gross misconceptions that delayed the fight against poliomyelitis. These experiments indicated that the poliovirus infects mainly the nervous system; scientists later learned this was because the viral strains they had administered through the nose had artificially developed an affinity for brain tissue. The erroneous conclusion, which contradicted previous human studies demonstrating that the gastrointestinal system was the primary route of infection, resulted in misdirected preventive measures and delayed the development of a vaccine. Research with human cell cultures in 1949 first showed that the virus could be cultivated on nonneural tissues taken from the intestine and limbs. Yet in the early 1950s, cell cultures from monkeys rather than humans were used for vaccine production; as a result, millions of people were exposed to potentially harmful monkey viruses.

In a striking illustration of the inadequacy of animal research, scientists in the 1960s deduced from numerous animal experiments that inhaled tobacco smoke did not cause lung cancer (tar from the smoke painted on the skin of rodents did cause tumors to develop, but these results were deemed less relevant than the inhalation studies). For many years afterward, the tobacco lobby was able to use these studies to delay government warnings and to discourage physicians from intervening in their patients' smoking habits.

Of course, human population studies provided inescapable evidence of the tobacco-cancer connection, and recent human DNA studies have identified tobacco's "smoking gun," showing how a derivative of the carcinogen benzo(a)-pyrene targets human genes, causing cancer. (It turns out that cancer research is especially sensitive to differences in physiology between humans and other animals. Many animals, particularly rats



DIGITAL COLLAGE BY JENNIFER C. CHRISTIANSEN; NEW YORK ACADEMY OF MEDICINE (*left*); NATIONAL LIBRARY OF MEDICINE (*center*); PETA (*right*) and mice, synthesize within their bodies approximately 100 times the recommended daily allowance for humans of vitamin C, which is believed to help the body ward off cancer.)

The stress of handling, confinement and isolation alters an animal's physiology and introduces yet another experimental variable that makes extrapolating results to humans even more difficult. Stress on animals in laboratories can increase susceptibility to infectious disease and certain tumors as well as influence levels of hormones and antibodies, which in turn can alter the functioning of various organs.

In addition to medical research, animals are also used in the laboratory to test the safety of drugs and other chemicals; again, these studies are confounded by the fact that tests on different species often provide conflicting results. For instance, in 1988 Lester Lave of Carnegie Mellon University reported in the journal *Nature* that dual experiments to test the carcinogenicity of 214 compounds on both rats and mice agreed with each other only 70 percent of the time. The correlation between rodents and humans could only be lower. David Salsburg of Pfizer Central Research has noted that of 19 chemicals known to cause cancer in humans when ingested, only seven caused cancer in mice and rats using the standards set by the National Cancer Institute.

Indeed, many substances that appeared safe in animal studies and received approval from the U.S. Food and Drug Administration for use in humans later proved dangerous to people. The drug milrinone, which raises cardiac output, increased survival of rats with artificially induced heart failure; humans with severe chronic heart failure taking this drug had a 30 percent increase in mortality. The antiviral drug fialuridine seemed safe in animal trials yet caused liver failure in seven of 15 humans taking the drug (five of these patients died as a result of the medication, and the other two received liver transplants). The commonly used painkiller zomepirac sodium was popular in the early 1980s, but after it was implicated in 14 deaths and hundreds of life-threatening allergic reactions, it was withdrawn from the market. The antidepressant nomifensine, which had minimal toxicity in rats, rabbits, dogs and monkeys, caused liver toxicity and anemia in humans—rare yet severe, and sometimes fatal, effects that forced the manufacturer to withdraw the product a few months after its introduction in 1985.

These frightening mistakes are not mere anecdotes. The U.S. General Accounting Office reviewed 198 of the 209 new drugs marketed between 1976 and 1985 and found that 52 percent had "serious postapproval risks" not predicted by animal tests or limited human trials. These risks were defined as adverse reactions that could lead to hospitalization, disability or death. As a result, these drugs had to be relabeled with new warnings or withdrawn from the market. And of course, it is impossible to estimate how many potentially useful drugs may have been needlessly abandoned because animal tests falsely suggested inefficacy or toxicity.

Better Methods

Researchers have better methods at their disposal. These techniques include epidemiological studies, clinical intervention trials, astute clinical observation aided by laboratory testing, human tissue and cell cultures, autopsy studies, endoscopic examination and biopsy, as well as new imaging methods. And the emerging science of molecular epidemiology, which relates genetic, metabolic and biochemical factors with epidemiological data on disease incidence, offers significant promise for identifying the causes of human disease.

Consider the success of research on atherosclerotic heart disease. Initial epidemiological investigations in humans—notably the Framingham Heart Study, started in 1948—revealed the risk factors for heart disease, including high cholesterol levels, smoking and high blood pressure. Researchers then altered these factors in controlled human trials, such as the multicenter Lipid Research Clinics Trial, carried out in the 1970s and 1980s. These studies illustrated, among many other things, that every 1 percent drop in serum cholesterol levels led to at least a 2 percent drop in risk for heart disease. Autopsy results and chemical studies added further links between risk factors and disease, indicating that people consuming high-fat diets acquire arterial changes early in life. And studies of heart disease patients indicated that eating a low-fat vegetarian diet, getting regular mild exercise, quitting smoking and managing stress can reverse atherosclerotic blockages.

Similarly, human population studies of HIV infection elucidated how the virus was transmitted and guided intervention programs. In vitro studies using human cells and serum allowed researchers to identify the AIDS virus and determine how it causes disease. Investigators also used in vitro studies to assess the efficacy and safety of important new AIDS drugs such as AZT, 3TC and protease inhibitors. New leads, such as possible genetic and environmental factors that contribute to the disease or provide resistance to it, are also emerging from human studies.

Many animals have certainly been used in AIDS research, but without much in the way of tangible results. For instance, the widely reported monkey studies using the simian immunodeficiency virus (SIV) under unnatural conditions suggested that oral sex presented a transmission risk. Yet this study

PETA (*left*); BRIAN GUNN IAAPEA (*center*); CHRISTOPHER BURKE/QB (*right*)

did not help elucidate whether oral sex transmitted HIV in humans or not. In other cases, data from animal studies have merely repeated information already established by other experiments. In 1993 and 1994 Gerard J. Nuovo and his colleagues at the State University of New York at Stony Brook determined the route of HIV into the female body (the virus passes through cells in the cervix and then to nearby lymph nodes) using studies of human cervical and lymph node samples. Later, experimenters at New York University placed SIV into the vaginas of rhesus monkeys, then killed the animals and dissected the organs; their paper, published in 1996, arrived at essentially the same conclusion about the virus's path as did the previous human studies.

Research into the causes of birth defects has relied heavily on animal experiments, but these have typically proved to be embarrassingly poor predictors of what can happen in humans. The rates for most birth defects are rising steadily. Epidemiological studies are needed to trace possible genetic and environmental factors associated with birth defects, just as population studies linked lung cancer to smoking and heart disease to cholesterol. Such surveys have already provided some vital information—the connection between neural tube defects and folate deficiency and the identification of fetal alcohol syndrome are notable findings—but much more human population research is needed.

Observations of humans have proved to be invaluable in cancer research as well. Several studies have shown that cancer patients who follow diets low in fat and rich in vegetables and fruit live longer and have a lower risk of recurrence. We now need intervention trials to test which specific diets help with various types of cancers.

The issue of what role, if any, animal experimentation played in past discoveries is not relevant to what is necessary now for research and safety testing. Before scientists developed the cell and tissue cultures common today, animals were routinely used to harbor infectious organisms. But there are few diseases for which this is still the case—modern methods for vaccine production are safer and more efficient. Animal toxicity tests to determine the potency of drugs such as digitalis and insulin have largely been replaced with sophisticated laboratory tests that do not involve animals.

A Rhetorical Device

Animal "models" are, at best, analogous to human conditions, but no theory can be proved or refuted by analogy. Thus, it makes no logical sense to test a theory about humans using animals. Nevertheless, when scientists debate the validity of competing theories in medicine and biology, they often cite animal studies as evidence. In this context, animal experiments serve primarily as rhetorical devices. And by using different kinds of animals in different protocols, experimenters can find evidence in support of virtually any theory. For instance, researchers have used animal experiments to show that cigarettes both do and do not cause cancer.

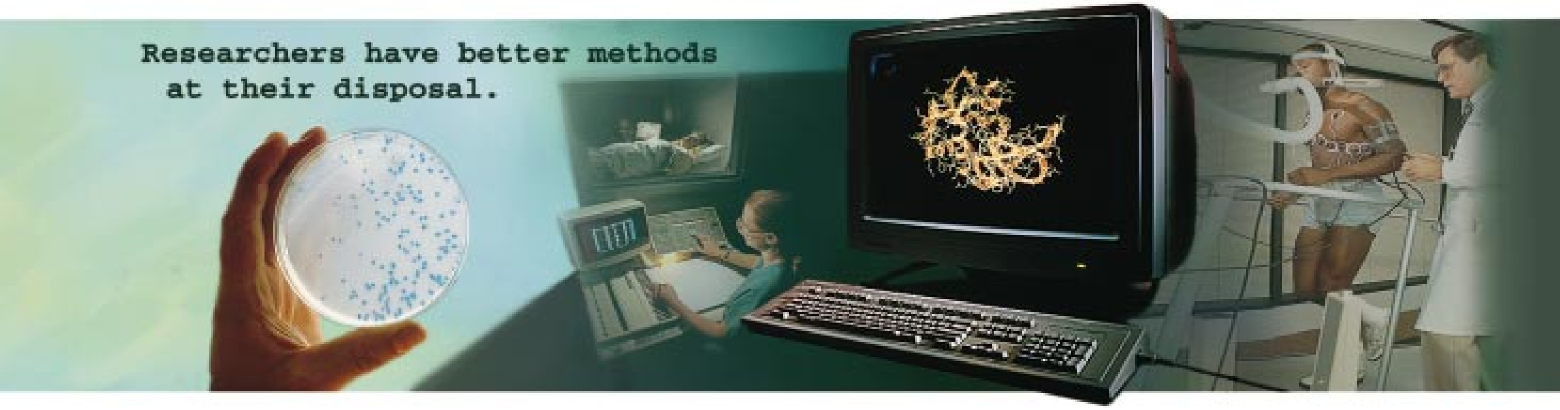
Harry Harlow's famous monkey experiments, conducted in the 1960s at the University of Wisconsin, involved separating infant monkeys from their mothers and keeping some of them in total isolation for a year. The experiments, which left the animals severely damaged emotionally, served primarily as graphic illustrations of the need for maternal contact—a fact already well established from observations of human infants.

Animal experimenters often defend their work with brief historical accounts of the supposedly pivotal role of animal data in past advances. Such interpretations are easily skewed. For example, proponents of animal use often point to the significance of animals to diabetes research. But human studies by Thomas Cawley, Richard Bright and Appollinaire Bouchardat in the 18th and 19th centuries first revealed the importance of pancreatic damage in diabetes. In addition, human studies by Paul Langerhans in 1869 led to the discovery of insulin-producing islet cells. And although cows and pigs were once the primary sources for insulin to treat diabetes, human insulin is now the standard therapy, revolutionizing how patients manage the disease.

Animal experimenters have also asserted that animal tests could have predicted the birth defects caused by the drug thalidomide. Yet most animal species used in laboratories do not develop the kind of limb defects seen in humans after thalidomide exposure; only rabbits and some primates do. In nearly all animal birth-defect tests, scientists are left scratching their heads as to whether humans are more like the animals who develop birth defects or like those who do not.

In this discussion, we have not broached the ethical objections to animal experimentation. These are critically important issues. In the past few decades, scientists have come to a new appreciation of the tremendous complexity of animals' lives, including their ability to communicate, their social structures and emotional repertoires. But pragmatic issues alone should encourage scientists and governments to put research money elsewhere. SA

NEAL D. BARNARD and STEPHEN R. KAUFMAN are both practicing physicians. Barnard conducts nutrition research and is president of the Physicians Committee for Responsible Medicine. Kaufman is co-chair of the Medical Research Modernization Committee.



left to right: SPL/PHOTO RESEARCHERS, INC.; CHARLES GUPTON *UNIPHOTO*; DOE/SPL/PHOTO RESEARCHERS, INC.; JIM OLIVE *UNIPHOTO*

Animal Research Is Vital to Medicine

by Jack H. Botting and Adrian R. Morrison

Experiments using animals have played a crucial role in the development of modern medical treatments, and they will continue to be necessary as researchers seek to alleviate existing ailments and respond to the emergence of new disease. As any medical scientist will readily state, research with animals is but one of several complementary approaches. Some questions, however, can be answered only by animal research. We intend to show exactly where we regard animal research to have been essential in the past and to point to where we think it will be vital in the future. To detail all the progress that relied on animal experimentation would require many times the amount of space allotted to us. Indeed, we cannot think of an area of medical research that does not owe many of its most important advances to animal experiments.

In the mid-19th century, most debilitating diseases resulted from bacterial or viral infections, but at the time, most physicians considered these ailments to be caused by internal derangements of the body. The proof that such diseases did in fact derive from external microorganisms originated with work done by the French chemist Louis Pasteur and his contemporaries, who studied infectious diseases in domestic animals. Because of his knowledge of how contaminants caused wine and beer to spoil, Pasteur became convinced that microorganisms were also responsible for diseases such as chicken cholera and anthrax.

To test his hypothesis, Pasteur examined the contents of the guts of chickens suffering from cholera; he isolated a possible causative microbe and then grew the organism in culture. Samples of the culture given to healthy chickens and rabbits produced cholera, thus proving that Pasteur had correctly identified the offending organism. By chance, he noticed that after a time, cultures of the microorganisms lost their ability to infect. But birds given the ineffective cultures became resistant to fresh batches that were otherwise lethal to untreated birds. Physicians had previously observed that among people who survived a severe attack of certain diseases, recurrence of the disease was rare; Pasteur had found a means of producing this resistance without risk of disease. This experience suggested to him that with the administration of a weakened culture of the disease-causing bacteria, doctors might be able to induce in their patients immunity to infectious diseases.

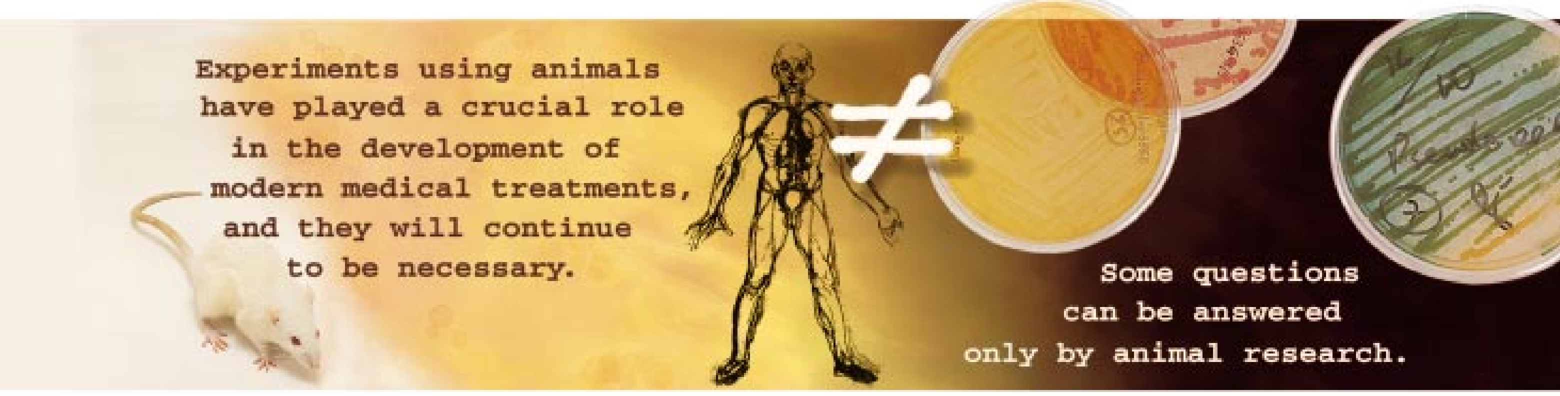
In similar studies on rabbits and guinea pigs, Pasteur isolated the microbe that causes anthrax and then developed a vaccine against the deadly disease. With the information from animal experiments—obviously of an extent that could never have been carried out on humans—he proved not only that infectious diseases could be produced by microorganisms but also that immunization could protect against these diseases.

Pasteur's findings had a widespread effect. For example, they influenced the views of the prominent British surgeon Joseph Lister, who pioneered the use of carbolic acid to sterilize surgical instruments, sutures and wound dressings, thereby preventing infection of wounds. In 1875 Queen Victoria asked Lister to address the Royal Commission inquiry into vivisection—as the queen put it, "to make some statement in condemnation of these horrible practices." As a Quaker, Lister had spoken publicly against many cruelties of Victorian society, but despite the request of his sovereign, he was unable to condemn vivisection. His testimony to the Royal Commission stated that animal experiments had been essential to his own work on asepsis and that to restrict research with animals would prevent discoveries that would benefit humankind.

Dozens of Vaccines and Antibiotics

Following the work of Pasteur and others, scientists have established causes of and vaccines for dozens of infectious diseases, including diphtheria, tetanus, rabies, whooping cough, tuberculosis, poliomyelitis, measles, mumps and rubella. The investigation of these ailments indisputably relied heavily on animal experimentation: in most cases, researchers identified candidate microorganisms and then administered the microbes to animals to see if they contracted the illness in question.

Similar work continues to this day. Just recently, scientists developed a vaccine against *Hemophilus influenzae* type B (Hib), a major cause of meningitis, which before 1993 resulted in death or severe brain damage in more than 800 children each year in the U.S. Early versions of a vaccine produced only poor, short-lived immunity. But a new vaccine, prepared and tested in rabbits and mice, proved to be powerfully immunogenic and is now in routine use. Within two months of the vaccine's in-



CHRISTOPHER BURKE/QB (left); CORBIS-BETTMANN (center); GEOFF TOMPKINSON SPL/Photo Researchers, Inc. (right) troduction in the U.S. and the U.K., Hib infections fell by 70 percent.

Animal research not only produced new vaccines for the treatment of infectious disease, it also led to the development of antibacterial and antibiotic drugs. In 1935, despite aseptic precautions, trivial wounds could lead to serious infections that resulted in amputation or death. At the same time, in both Europe and the U.S., death from puerperal sepsis (a disease that mothers can contract after childbirth, usually as a result of infection by hemolytic streptococci) occurred in 200 of every 100,000 births. In addition, 60 of every 100,000 men aged 45 to 64 died from lobar pneumonia. When sulfonamide drugs became available, these figures fell dramatically: by 1960 only five out of every 100,000 mothers contracted puerperal sepsis, and only six of every 100,000 middle-aged men succumbed to lobar pneumonia. A range of other infections could also be treated with these drugs.

The story behind the introduction of sulfonamide drugs is instructive. The team investigating these compounds—Gerhard Domagk's group at Bayer Laboratories in Wuppertal-Elberfeld, Germany—insisted that all candidate compounds be screened in infected mice (using the so-called mouse protection test) rather than against bacteria grown on agar plates. Domagk's perspicacity was fortunate: the compound prontosil, for instance, proved to be extremely potent in mice, but it had no effect on bacteria in vitro—the active antibacterial substance, sulfanilamide, was formed from prontosil within the body. Scientists synthesized other, even more powerful sulfonamide drugs and used them successfully against many infections. For his work on antibacterial drugs, Domagk won the Nobel Prize in 1939.

A lack of proper animal experimentation unfortunately delayed for a decade the use of the remarkable antibiotic penicillin: Alexander Fleming, working in 1929, did not use mice to examine the efficacy of his cultures containing crude penicillin (although he did show the cultures had no toxic effects on mice and rabbits). In 1940, however, Howard W. Florey, Ernst B. Chain and others at the University of Oxford finally showed penicillin to be dramatically effective as an antibiotic via the mouse protection test.

Despite the success of vaccines and antibacterial therapy, infectious disease remains the greatest threat to human life worldwide. There is no effective vaccine against malaria or AIDS; physicians increasingly face strains of bacteria resistant to current antibacterial drugs; new infectious diseases continue to emerge. It is hard to envisage how new and better vaccines and medicines against infectious disease can be developed without experiments involving animals.

Research on animals has been vital to numerous other areas in medicine. Open-heart surgery—which saves the lives of an estimated 440,000 people every year in the U.S. alone—is now routine, thanks to 20 years of animal research by scientists such as John Gibbon of Jefferson Medical College in Philadelphia. Replacement heart valves also emerged from years of animal experimentation.

The development of treatments for kidney failure has relied on step-by-step improvement of techniques through animal experiments. Today kidney dialysis and even kidney transplants can save the lives of patients suffering from renal failure as a result of a variety of ailments, including poisoning, severe hemorrhage, hypertension or diabetes. Roughly 200,000 people require dialysis every year in the U.S.; some 11,000 receive a new kidney. Notably, a drug essential for dialysis—heparin—must be extracted from animal tissues and tested for safety on anesthetized animals.

Transplantation of a kidney or any major organ presents a host of complications; animal research has been instrumental in generating solutions to these problems. Experiments on cats helped develop techniques for suturing blood vessels from the host to the donor organ so that the vessels would be strong enough to withstand arterial pressure. Investigators working with rabbits, rodents, dogs and monkeys have also determined ways to suppress the immune system to avoid rejection of the donor organ.

The list continues. Before the introduction of insulin, patients with diabetes typically died from the disease. For more than 50 years, the lifesaving hormone had to be extracted from the pancreas of cattle or pigs; these batches of insulin also had to be tested for safety and efficacy on rabbits or mice.

When we started our scientific careers, the diagnosis of malignant hypertension carried with it a prognosis of death within a year, often preceded by devastating headaches and blindness. Research on anesthetized cats in the 1950s heralded an array of progressively improved antihypertensive medicines, so that today treatment of hypertension is effective and relatively benign. Similarly, gastric ulcers often necessitated surgery with a marked risk of morbidity afterward. Now antiulcer drugs, developed from tests in rats and dogs, can control the condition and may effect a cure if administered with antibiotics to eliminate *Helicobacter pylori* infection.

Common Misconceptions

Much is made in animal-rights propaganda of alleged differences between species in their physiology or responses to drugs that supposedly render animal experiments redundant or misleading. These claims can usually be refuted by proper examination of the literature. For instance, opponents of animal research frequently cite the drug

LONNY SHAVELSON *Impact Visuals* (*left*); UNIPHOTO (*right*) thalidomide as an example of a medicine that was thoroughly tested on animals and showed its teratogenic effect only in humans. But this is not so. Scientists never tested thalidomide in pregnant animals until after fetal deformities were observed in humans. Once they ran these tests, researchers recognized that the drug did in fact cause fetal abnormalities in rabbits, mice, rats, hamsters and several species of monkey. Similarly, some people have claimed that penicillin would not have been used in patients had it first been administered to guinea pigs, because it is inordinately toxic to this species. Guinea pigs, however, respond to penicillin in exactly the same way as do the many patients who contract antibiotic-induced colitis when placed on long-term penicillin therapy. In both guinea pigs and humans, the cause of the colitis is infection with the bacterium *Clostridium difficile*.

In truth, there are no basic differences between the physiology of laboratory animals and humans. Both control their internal biochemistry by releasing endocrine hormones that are all essentially the same; both humans and laboratory animals send out similar chemical transmitters from nerve cells in the central and peripheral nervous systems, and both react in the same way to infection or tissue injury.

Animal models of disease are unjustly criticized by assertions that they are not identical to the conditions studied in humans. But they are not designed to be so; instead such models provide a means to study a particular procedure. Thus, cystic fibrosis in mice may not exactly mimic the human condition (which varies considerably among patients anyway), but it does provide a way to establish the optimal method of administering gene therapy to cure the disease. Opponents of animal experiments also allege that most illness can be avoided by a change of lifestyle; for example, adoption of a vegan diet that avoids all animal products. Whereas we support the promulgation of healthy practices, we do not consider that our examples could be prevented by such measures.

A Black Hole

Our opponents in this debate claim that even if animal experiments have played a part in the development of medical advances, this does not mean that they were essential. Had such techniques been outlawed, the argument goes, researchers would have been forced to be more creative and thus would have invented superior technologies. Others have suggested that there would not be a gaping black hole in place of animal research but instead more careful and respected clinical and cellular research.

In fact, there was a gaping black hole. No outstanding progress in the treatment of disease occurred until biomedical science was placed on a sound, empirical basis through experiments on animals. Early researchers, such as Pasteur and the 17th-century scientist William Harvey, who studied blood circulation in animals, were not drawn to animal experiments as an easy option. Indeed, they drew on all the techniques available at the time to answer their questions: sometimes dissection of a cadaver, sometimes observations of a patient, sometimes examination of bacteria in culture. At other times, though, they considered experimentation on animals to be necessary.

We would like to suggest an interesting exercise for those who hold the view that animal experiments, because of their irrelevance, have retarded progress: take an example of an advance dependent on animal experiments and detail how an alternative procedure could have provided the same material benefit. A suitable example would be treatment of the cardiac condition known as mitral valve insufficiency, caused by a defect in the heart's mitral valve. The production of prosthetic heart valves stemmed from years of development and testing for efficacy in dogs and calves. The artificial valve can be inserted only into a quiescent heart that has been bypassed by a heart-lung machine—an instrument that itself has been perfected after 20 years' experimentation in dogs. If, despite the benefit of 35 years of hindsight, critics of animal research cannot present a convincing scenario to show how effective treatment of mitral valve insufficiency could have developed any other way, their credibility is suspect.

Will animal experiments continue to be necessary to resolve extant medical problems? Transgenic animals with a single mutant gene have already provided a wealth of new information on the functions of proteins and their roles in disease; no doubt they will continue to do so. We also anticipate major progress in the treatment of traumatic injury to the central nervous system. The dogma that it is impossible to restore function to damaged nerve cells in the mammalian spinal cord has to be reassessed in the light of recent animal research indicating that nerve regeneration is indeed possible. It is only a matter of time before treatments begin to work. We find it difficult to envision how progress in this field—and so many others in biological and medical science—can be achieved in the future without animal experiments. SA

JACK H. BOTTING and ADRIAN R. MORRISON have been active in the defense of animal research since the 1980s. Botting, a retired university lecturer, is the former scientific adviser to the Research Defense Society in London. Morrison is director of the Laboratory for Study of the Brain in Sleep at the University of Pennsylvania School of Veterinary Medicine.

LLEWELLYN *UNIPHOTO*

Trends in Animal Research

Increased concern for animals, among scientists as well as the public, is changing the ways in which animals are used for research and safety testing

by Madhusree Mukerjee, *staff writer*

There is no question about it: the number of animals used in laboratory experiments is going down. In the U.K., the Netherlands, Germany and several other European countries, the total has fallen by half since the 1970s. In Canada, mammals have largely been replaced by fish. The figures for the U.S. are unclear. The U.S. uses between 18 and 22 million animals a year, but exact numbers are unknown for roughly 85 percent of these—rats, mice and birds. Primate use has stayed constant, whereas the use of dogs and cats is down by half since the 1970s.

No one reason accounts for the decline, but several factors are obvious. In 1975 the animal-rights movement exploded onto the scene with the publication of *Animal Liberation* by the Australian philosopher Peter Singer. The book's depiction of research, and a series of exposés by suddenly vigilant activists, threw a harsh spotlight on scientists. In the following years, public perceptions of animals became increasingly sympathetic. Dian Fossey, Jane Goodall and other ethologists related to an enthralled audience tales of love, sorrow, jealousy and deceit among primates. Although not so popular with scientists, such anthropomorphic views of animals fueled the passage of laws regulating experimentation.

And the scientists have changed. Those entering the biomedical profession in recent decades have imbibed at least some of the concerns of the movement, if not its ideals; many are willing to acknowledge the moral dilemmas of their craft. Some experiments that were applauded in the 1950s would not be done today, because they would be deemed to cause too much suffering. Oftentimes biotechnology is allowing test tubes to be substituted for animals. And a few researchers, cognizant that only their expertise can help reduce the need for animals, are avidly seeking alternatives. All these efforts are bearing fruit.

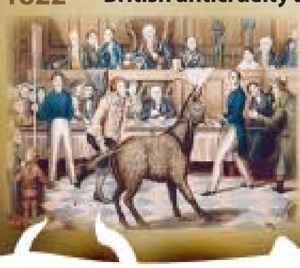
The Philosophers

The underlying force behind these changes appears to be society's evolving views of animals. These perceptions owe a great deal to philosophy and to science—and very little to religion. The Bible is unequivocal about the position of animals in the natural order: God made man in his image and gave him dominion over all other creatures. And although Hinduism and Buddhism envisage a hierarchy of organisms rather than a sharp division, their influence on the animal-rights movement is limited to vague inspiration and vegetarian recipes. The real roots lie in secular philosophy. In 1780 the English barrister Jeremy Bentham asked what "insuperable line" prevented humans from extending moral regard to animals: "The question is not, Can they reason? nor, Can they talk? but, Can they suffer?"

The question became more poignant in 1859 with the advent of Charles Darwin's theory of evolution. The theory provided a scientific rationale for using animals to learn about humans, and Darwin endorsed such use. But he also believed in an emotional continuum between humans and animals and was troubled by the suffering that experimentation could cause. This dichotomy inspired clashes between animal lovers and experimenters in 19th-century England, culminating in the 1876 British

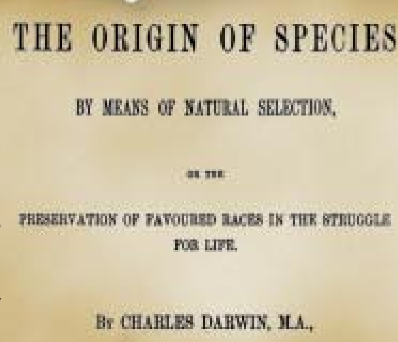
The Evolution of Animal Use in Research

1822 **British anticruelty act** introduced by Richard Martin (holding donkey). He later founded the RSPCA



ROYAL SOCIETY FOR THE PREVENTION OF CRUELTY TO ANIMALS

1859 **Charles Darwin** publishes the theory of evolution



THE ORIGIN OF SPECIES

BY MEANS OF NATURAL SELECTION,

OR THE

PRESERVATION OF FAVOURED RACES IN THE STRUGGLE FOR LIFE.

BY CHARLES DARWIN, M.A.,

CORBIS–BETTMANN

1866 **Henry Bergh** founds ASPCA in U.S.

CORBIS–BETTMANN

Cruelty to Animals Act regulating animal experimentation. But the phenomenal success of medicine in the next century made the animal-protection movement recede into the background.

It rebounded in the 1970s, with Singer's attack. A philosopher in the utilitarian tradition of Bentham, Singer holds that in all decisions the total amount of good that results—human and animal—should be weighed against the suffering—human and animal—caused in the process. Not that to him the interests of humans and animals have equal weight: life is of far greater value to a human than, for example, to a creature with no self-awareness. But if there is something one would not do to, say, a severely incapacitated child, then neither should one do it to an animal that would suffer as much. Ignoring the interests of an animal just because it is not human is, to Singer, "speciesism," a sin akin to racism. Invoking the connections between humans and the great apes, Singer, Goodall and others have issued a call for these creatures, at least, to be freed from experimentation.

Although Singer started the modern animal-rights movement, it takes its name and its most uncompromising ideas from Tom Regan's *The Case for Animal Rights* (University of California Press, 1983). Regan believes that all humans and most animals have inherent rights, which he describes as invisible "no trespassing" signs hung around their necks. They state that our bodies may not be transgressed, no matter how much good might thereby result. Regan does not equate humans with animals—to save survivors in a lifeboat, a dog could be thrown overboard before a human would—yet he states that animals cannot be experimented on, because they are not merely means to an end.

Many other philosophers have lent their voices to the animals, but few have come to the aid of researchers. One who did so, Michael A. Fox, author of *The Case for Animal Experimentation* (University of California Press, 1986), later declared himself convinced by his critics and became an advocate for animals. Attempts to refute Singer and Regan usually involve pointing to morally relevant criteria that separate humans from animals. Raymond G. Frey of Bowling Green State University has written that animals cannot have interests, because they cannot have desires, because they cannot have beliefs, because they do not have language. Regan counters that a dog may well believe "that bone is tasty" without being able to formulate the phrase and that a human infant would never learn to speak unless it could acquire preverbal concepts to which it could later assign words, such as "ball."

Another supporter of research, Carl Cohen of the University of Michigan, has argued that rights are not inherent: they arise from implicit contracts among members of society, and they imply duties. Because animals cannot reciprocate such duties, they cannot have rights. This argument meets with the retort that infants and the mentally ill cannot fulfill such obligations either but are not left out of the realm of rights: Why omit animals? (One response is that human rights are based on characteristics of "typical" humans, not on borderline cases, prompting animal advocates to ask what these special qualities are—and so on and on.)

Some research proponents also note that nature is cruel: lions kill zebras, cats play with mice. Evolution has placed humans on top, so it is only natural for us to use other creatures. This argument, which some say elevates "survival of the fittest" to a moral philosophy, falls prey to a proposition called the naturalistic fallacy. To paraphrase the 18th-century philosopher David Hume, what "is" cannot dictate what "ought to be." So natural history may well illuminate why human morals evolved into their present form, but humans can transcend their nature. One animal advocate declares: "Killing and eating [meat] is an integral part of the evolution of human beings. Not killing and not eating [meat] is the next step in our evolution."

Many philosophers fall into the troubled middle, arguing for interests or rights to be ordered in a hierarchy that allows some uses of animals but bars others. Such distillations of animal-liberation ideas have been finding their way into legislation. The U.K., Australia, Germany and several other nations require a utilitarian cost-benefit analysis to be performed before an animal experiment can proceed. And in November 1996 the Netherlands passed into law the statement that animals have "intrinsic value": they are sentient beings, entitled to the moral concern of humans.

The Public

Not that, of course, all the Dutch are vegetarians. Rational argumentation may have influenced public opinion, but as Harold A. Herzog, Jr., a psychologist at Western Carolina University, remarks, the average person's stance on animal issues remains wildly inconsistent. In one survey, questions phrased in terms of rats yielded a far more provivisection outcome than those mentioning dogs. Jesse L. Owens, a neuroscientist at the University of Alaska, protests

ILLUSTRATION OF SCROLL BY LAURIE GRACE

SCIENTIFIC AMERICAN SCIENTIFIC AMERICAN OLIVER MECKES *Photo Researchers, Inc.*

that medical research is "the only use of animals that is essential" and like other researchers is bewildered by people who eat meat and in the same gulp condemn experimentation.

Not surprisingly, the animal-liberation movement has coincided with society's becoming increasingly distant from farms—and shielded from the reality behind dinner. Those who grew up on farms often see animals as objects to be used, whereas those who had pets tend to express more sympathy. One line along which attitudes divide is gender. In all countries surveyed, women are more pro-animal and antivivisectionist than men, and three quarters of American animal-rights activists are women. Also noticeable is a generation gap. Surveys by Stephen R. Kellert of Yale University find that those who are older or less educated are more likely to see animals as resources, whereas those who are younger or more educated tend to view animals with compassion.

Public support of animal experimentation, though higher in the U.S. than in Europe, has been slowly declining. In 1985, 63 percent of American respondents agreed that "scientists should be allowed to do research that causes pain and injury to animals like dogs and chimpanzees *if* it produces new information about human health problems"; in 1995, 53 percent agreed. Even in disciplines that have traditionally used animals, the trend is unmistakable. A survey by Scott Plous of Wesleyan University finds that psychologists with Ph.D.'s earned in the 1990s are half as likely to express strong support for animal research as those with Ph.D.'s from before 1970. (Part of this result comes from the increased presence of women, but there is a significant drop among men as well.)

Opposition to animal experimentation is often said to derive from antiscience sentiments, aggravated by poor public knowledge of science. But according to a 1994 survey led by Linda Pifer of the Chicago Academy of Sciences, negative attitudes toward animal experimentation in the U.S. correlate only weakly with lack of knowledge about science. And in Belgium, France and Italy, for instance, greater scientific literacy is connected with an increased rejection of animal experimentation.

Sociologists agree that opposition to vivisection derives primarily from sympathy for animals. Almost all animal rightists are vegetarians; many are "vegans," eschewing milk, eggs, leather and other animal products. "My philosophy of living as softly on the earth as I can is my life," one activist told Herzog. In striving to cause the least suffering possible, these individuals labor under a heavy moral burden that sits lightly on the rest of us. Some activists have indulged in threatening researchers, breaking into laboratories or even arson. But the number of such illegal acts, listed by the U.S. Department of Justice, dropped from about 50 a year in 1987 to 11 in 1992. (More recent figures are unavailable but are believed to be small.)

Many animal experimenters are also animal lovers. Surveys by Harold Takooshian, a sociologist at Fordham University, reveal that biomedical researchers have the same mixed feelings about animals and animal research as does the general public. (The groups that gave animals the lowest rating and vivisection the highest were farmers, hunters and the clergy.) Thomas M. Donnelly, a veterinarian at the Rockefeller University's animal center, also runs a shelter to which he takes cats that are no longer needed for research. Almost all the toxicologists and pharmacologists at a 1996 meeting on alternatives to animal experimentation had experience with using animals and were moved enough by it to seek substitutes. Scientists choose to use animals because they feel it is the only way to help humans. Donald Silver, who did cancer studies on mice at Sloan-Kettering Hospital in the 1970s, recounts that whenever he had doubts about his work, he had only to think about the terminally ill patients in the children's ward.

The Scientists

Of course, scientists' perceptions of animals have evolved as well. In the early 20th century Darwinian worries about emotions were dispelled by the rise of behaviorism. Because thoughts cannot be measured, but behavior can, practitioners such as C. Lloyd Morgan and, later, B. F. Skinner sought to describe animals purely in terms of their responses to stimuli. Bernard Rollin, author of *The Unheeded Cry* (Oxford University Press, 1989), argues that at some point, the animal psyche went from being impossible to measure to being nonexistent. The test of a good theory, "Morgan's canon," required all actions to be interpreted in terms of the lowest psychological faculties possible. In practice, this meant that a rat would not be feeling pain even if its "writhes per minute" were being used to test the efficacy of an analgesic. Its neurochemistry was merely inducing a physiological reflex.

"We were taught as undergraduates not to think of animals as other than stimulus-response bundles," asserts Melanie Stiassney, an ichthyologist at the American Museum of Natural History. "The dogma is you can't credit them with feelings." In turn, it is often thought undesirable for a researcher to have feelings about the animal under study: emotions can impair professional judgment and also make it hard to perform cer-

UPI/CORBIS-BETTMANN

1951

Christine Stevens founds Animal Welfare Institute in U.S.

UPI/CORBIS-BETTMANN

1952

Jonas Salk develops killed-virus polio vaccine

1954

Humane Society of the U.S. founded

1953

Albert Sabin develops live, attenuated polio vaccine tain procedures. Arnold Arluke, a sociologist at Northeastern University who studied animal laboratories from 1985 to 1993, reports that some technicians were deeply disturbed when a playful dog or a roomful of mice had to be put down. Such distress was officially discouraged and therefore kept secret. But after being "burned" by the death of a favorite animal, laboratory workers learned to avoid emotional connections with the creatures.

The resulting dissociation, which is often likened to that of a surgeon from a patient, allows a researcher to function with a minimum of stress. But given the emotional separation, a scientist may not realize when an animal is in pain—especially if the very existence of pain is in doubt. Nowadays, many researchers are aware of dissociation and seek objective ways to detect distress. And animal pain has come into its own. At a 1996 meeting on the *Guide to the Care and Use of Laboratory Animals*—a collection of guidelines that all researchers funded by the National Institutes of Health have to follow—veterinarian Gerald F. Gebhart of the University of Iowa stated that the pain-sensing apparatus is the same throughout the vertebrate kingdom and offered this rule of thumb: "If it hurts you, it probably hurts the animal."

Increasingly, animal experimenters try to balance scientific imperatives with humaneness. Keith A. Reimann, a veterinarian at Harvard University's animal facility, does AIDS-related research in monkeys. He insists that a macaque be euthanized as soon as it becomes sick, even if additional information might be gained by following the course of the illness. Franz P. Gruber of the University of Konstanz in Germany, who serves on a board overseeing animal experimentation, says his committee does not allow "death as an end point"—studies in which the animal dies of the disease or procedure being studied. Instead the committee works with the researcher to define a stage at which the creature can be put out of its misery.

One area of concern to American veterinarians involves paralytic drugs. These agents immobilize an animal for surgery, for six or more hours at a time; anesthesia, however, may wear off in an hour or two. A few researchers are reportedly reluctant to administer additional anesthetics for fear that an overdose could kill the animal before the experiment is over, leading to a loss of data. But without such "topping up," the animal may become conscious during the operation and not be able to convey, by twitch or cry, that it is in agony. And some scientists object to using painkillers because they do not want to introduce a new variable into the experiment.

Compassionate feelings for animals also influence studies, although researchers rarely admit to such unscientific, if creditable, motivations. When asked about their choice of species subjects, for example, three neuroscientists—working on monkeys, rats and frogs, respectively—replied unhesitatingly that it was determined by the scientific question at hand. But later in the conversation, the frog experimenter confided that he, personally, could not work on "a furry animal," and the rat experimenter said he would not work with a cat or even with a rat in a more painful protocol.

The Three Rs

Scientists' concern for animals first became visible professionally in the 1950s, when the behavioristic paradigm came under attack. British zoologist William M. S. Russell and microbiologist Rex L. Burch published *The Principles of Humane Experimental Technique* (Methuen, London, 1959), in which they put forth the "three Rs." This principle sets out three goals for the conscientious researcher: replacement of animals by in vitro, or test-tube, methods; reduction of their numbers by means of statistical techniques; and refinement of the experiment so as to cause less suffering. Although they took some decades to catch on, the three Rs define the modern search for alternatives.

Starting in the 1960s, humane organizations and governments began to fund studies in alternative methods. European governments, especially, have invested considerable resources. For the past 15 years, Germany has been giving out about $6 million a year in research grants alone; the Netherlands spends $2 million a year (including overheads for its alternatives center). The European Center for the Validation of Alternative Methods, a body set up in 1992 by the European Commission, requires another $9 million annually. In the U.S., governmental interest has been comparatively low; the National Institute of Environmental Health Sciences (NIEHS) is now offering $1.5 million worth of grants a year, for three years. And industry provides the $1 million a year that the Center for Alternatives to Animal Testing (CAAT) at Johns Hopkins University disburses in grants. (Although 15 federal agencies have recently formed the Interagency Coordinating Committee for Validation of Alternative Methods, this venture is as yet unfunded.)

All this effort has yielded a variety of means for reducing animal use. Statistical sophistry, for example, is allowing the classical LD50 (or lethal dose 50 percent) test for acute toxicity to be eliminated. This test requires up to 200 rats, dogs or other animals to be force-fed different amounts of a substance, to determine the dose that will kill half a

1959
William M. S. Russell and Rex L. Burch state **three Rs** of animal experimentation

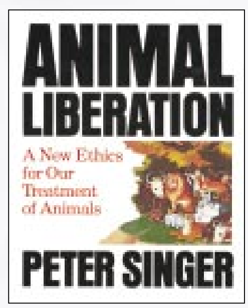
REPLACE
REDUCE
REFINE

1966
Animal Welfare Act (AWA) passed in the U.S.

1969
Dorothy Hegarty founds Fund for the Replacement of Animals in Medical Experiments in U.K.

1970
Amendments to AWA cover warm-blooded animals and require pain relief

1975



Peter Singer publishes animal-liberation philosophy

COURTESY OF *NEW YORK REVIEW OF BOOKS*

group. Although in vitro alternatives are still far away—because the mechanisms underlying toxicity are poorly understood—protocols currently accepted worldwide call for a tenth the number of animals. The Organization for Economic Cooperation and Development, for example, asks for between three and 18 animals to be used: if the substance kills the first three, it need be tested no further.

Another unpleasant procedure is the LD80 test for vaccines. Experimental animals are vaccinated against a disease; they and a control group are then exposed to it. The vaccine passes only if at least 80 percent of the experimental group remains healthy and if 80 percent of the control group dies. Again using statistics, Coenraad Hendriksen of the National Institute of Public Health and the Environment in the Netherlands found a way of testing diphtheria and tetanus vaccines that requires simply checking the level of antibodies. Apart from greatly reducing the suffering, it uses half the number of animals.

"Data mining"—the sifting of mountains of information for relevant new findings—has also proved astonishingly helpful. Horst Spielmann of ZEBET, the German center for alternatives to animal testing, surveyed decades of industry data on pesticides and concluded that if mice and rats prove sensitive to a chemical, it does not have to be tested on dogs. Spielmann anticipates that 70 percent of the dog tests can be dispensed with. Klaus Cussler of the Paul Ehrlich Institute in Langen, Germany, reviewed data on the "abnormal safety test" for vaccines (called the "mouse and guinea pig safety test" in the U.S.), which involves vaccinating mice and guinea pigs and watching for untoward reactions. Their findings led to the test being dropped for vaccines checked in other standard ways. "It was so senseless," Cussler shakes his head.

In 1989, after observing that production of monoclonal antibodies in mice with tumors causes much suffering, ZEBET funded industry research into test-tube alternatives. Consequently, the antibodies, used in cancer therapy, are now rarely manufactured in mice in Europe (although mice remain the norm in the U.S.). Production of polio vaccines is another success story. In the 1970s the Netherlands used 5,000 monkeys a year; now kidney cell cultures from just 10 monkeys provide enough vaccine for everyone. Hormones or vaccines manufactured in cell cultures are also purer than those made in vivo (that is, in the animals themselves), so each batch need not be tested as before for safety and efficacy.

In 1993 the Department of Transportation became the first U.S. agency to accept in vitro tests, for skin corrosivity. The traditional test requires placing a substance on a rabbit's shaved back to see how far it eats in. The test's replacement uses reconstructed human skin or a biomembrane such as Corrositex—testimony to the role played by venture capital in finding alternatives. Several cosmetics manufacturers have entirely eliminated animal testing: they rely on in-house substitutes or use ingredients that have been tested in the past.

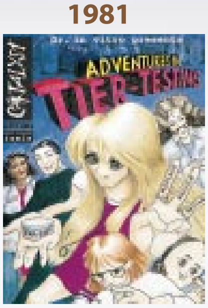
As yet, most researchers in the basic sciences see little hope of replacing animals. They stick to reduction or refinement, such as using an animal lower on the phylogenetic tree. The next spate of cuts in animal use, Spielmann predicts, will come in the field of medical education, for which alternative teaching tools have been devised. British surgeons, in fact, have not trained on animals since the 1876 act banned such use; instead they practice on human cadavers and later assist experienced surgeons in actual operations. In the U.S., more than 40 of the 126 medical schools do not use animals in their regular curricula.

The most significant change has been in mind-set. Since 1985 in the Netherlands, every scientist starting research on animals has been required to take a three-week course. They learn hands-on procedures, proper anesthesia, specifications of inbred strains and so on—as well as the three Rs. First the students design an animal experiment; then they are asked to find ways of answering the same question without animals. The resulting discussion and hunt for information induces a new way of thinking. "It gives them time for reflection," says Bert F. M. van Zutphen of Utrecht University, who pioneered the course. "It's of utmost importance. To know how far I can go for my own conscience."

The Laws

Another source of change in scientists' attitudes has been legislation. In the U.S., laws tend to derive from isolated incidents. The Animal Welfare Act of 1966—the federal law regulating animal use—came into being because of Pepper, a Dalmatian believed by its owners to have been stolen and sold to a lab, and a *Life* magazine article depicting starving dogs in dealers' pens. Perhaps the most significant change came in 1985, in the wake of two exposés involving primates. In Silver Spring, Md., macaques belonging to Edward Taub of the Institute for Behavioral Research were found to be chewing on their limbs, to which the nerves had been cut. And in 1984 videotapes from the University of Pennsylvania Medical Center displayed laboratory personnel mocking baboons whose heads had been smashed in dur-

1981



Center for Alternatives to Animal Testing founded in U.S.

JOHNS HOPKINS SCHOOL OF PUBLIC HEALTH

1985

Amendments to AWA result from Silver Spring, Md., and Pennsylvania primate exposés

COURTESY OF NATIONAL PRESS BOOKS

1992

European Center for the Validation of Alternative Methods founded

1993

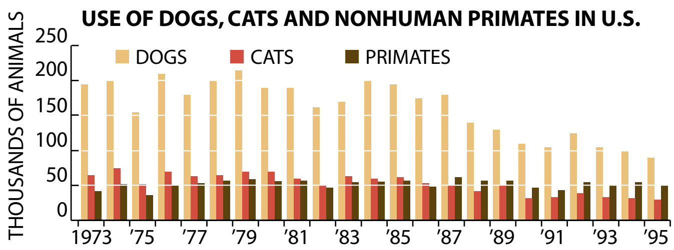
First World Congress on Alternatives held in the U.S.

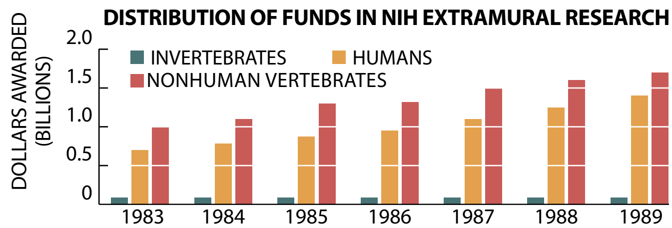
1996

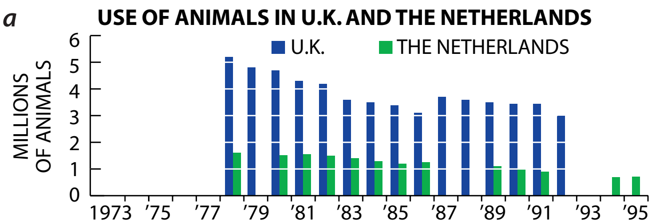
Second World Congress on Alternatives held in the Netherlands

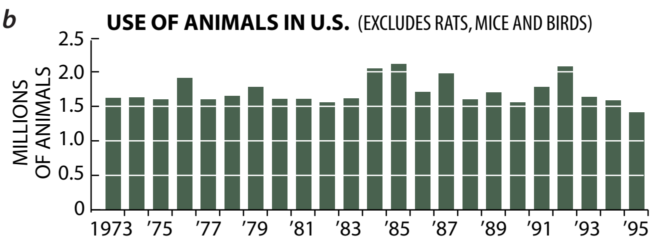
The Numbers of Research Animals

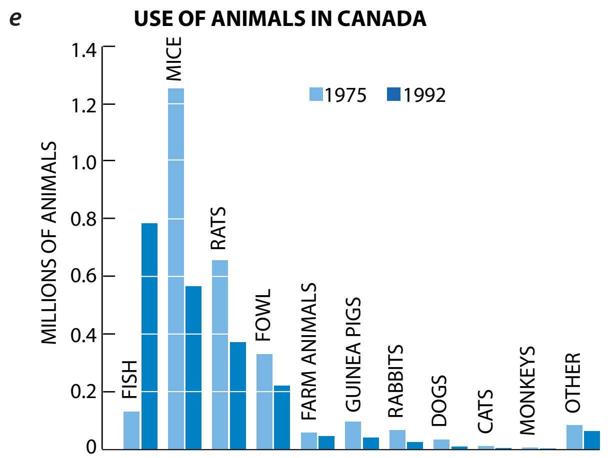
Use of animals in European laboratories has been slowly declining (*a*). In the U.S., the available statistics (*b*) include primates, dogs, cats, guinea pigs, rabbits, hamsters and others but exclude rats, mice and birds—an estimated 17 million additional animals per year. Primate use is roughly constant, although the numbers of cats and dogs (*c*) is declining. (In many instances, dogs are being replaced by pigs, calves and other farm animals. These have been counted since 1990 but are not included in the chart.) The National Institutes of Health supports research into invertebrate models (*d*); however, funding has been increasing more steeply for vertebrate (and human) studies. In Canada, animal numbers (*e*) have hovered at around two million a year, but fish have replaced mammals in many areas, especially toxicology.











BRYAN CHRISTIE; SOURCES: USDA (*a–c*); NATIONAL CENTER FOR RESEARCH RESOURCES, NIH (*d*); CANADIAN COUNCIL ON ANIMAL CARE (*e*)

ing experiments on head trauma. The outcry following these revelations allowed Senator Robert Dole of Kansas to bring an amendment to the act. It established institutional animal care and use committees (IACUCs) at each facility using regulated animals and required laboratories to exercise dogs and to ensure the psychological well-being of primates.

The "well-being" clause can be considered an instance of the public's imposing a scientific paradigm on scientists. An inspector from the U.S. Department of Agriculture, which administers the Animal Welfare Act, sought expert advice at that time on primate psychology. There was no such thing, he was told. Now, just 10 years later, primates have emotions. At the 1996 NIH meeting, Gebhart listed fear, anxiety, boredom, separation and isolation as conditions to which experimenters should attend in their subjects. And a few labs are even trying to enrich the lives of their rabbits.

The laws have generally had the effect of driving up the costs of animal research. Animal protectionists complain, however, that the Animal Welfare Act and its amendments invariably get diluted at the implementation stage. The act, for instance, refers to warm-blooded animals, but the regulations written by the USDA exclude rats, mice and birds. The agency says it does not have funds for inspecting the laboratories that use these creatures, which is true; animal welfarists, however, say the omission originally came from lobbying by the biomedical community. In 1990 humane organizations sued to have these animals included. Although they initially won, the suit was thrown out on appeal, on the grounds that animal protectionists have no legal standing: only those who are injured—that is, the rats, mice and birds—can bring a civil suit. Dale Schwindaman of the USDA has promised, however, to include these animals within the next five years.

Another controversy has to do with so-called performance standards. When writing regulations for the 1985 amendments, the USDA refrained, for example, from stating how many times a week the dogs had to be walked. Such specifics are referred to as engineering standards. Instead the agency allowed each facility to come up with its own plans for dog and primate well-being, the "performance" of which was to be evaluated. (Because these plans are kept in-house, and not with the USDA, the public cannot obtain them through the Freedom of Information Act.)

Researchers are enthusiastic about the flexibility of performance standards, whereas Martin L. Stephens of the Humane Society of the U.S. calls them "euphemisms for no standards." USDA inspectors are divided. Some argue that the standards are vague and unenforceable. Among others, Harvey McKelvey of the USDA's northwestern region says they let him use his judgment: "If I see

PETA

ANTIVIVISECTION POSTER attacks the rationales behind animal research.

an animal is bored with its toy, I can write that it needs a new one. I couldn't do that with engineering standards." The new NIH guide also embraces performance standards.

The animal care committees have empowered those scientists who wish to cut down on wastage and improve conditions for animals. "If you have an institution with conscientious people, the IACUC system works fairly well," says Ralph A. Meyer of Carolinas Medical Center. Cathy Liss of the Animal Welfare Institute in Washington, D.C., agrees that some committees do far better than the law. But there is concern about the remainder. In 1992 an audit of the USDA's enforcement activities by the Office of the Inspector General revealed that out of 26 institutions selected at random, 12 "were not adequately fulfilling their responsibilities under the act." Everyone agrees that enforcement is inadequate: at present, there are only 69 inspectors, who may not be able to visit each of the 1,300 regulated laboratories (and also animal dealers, transporters and exhibitors) every year.

As a result, the inspectors rely on whistle-blowers. "We need eyes out there," McKelvey explains. It might be an animal-rights activist who has infiltrated a laboratory: groups such as People for the Ethical Treatment of Animals (PETA) prepare detailed case histories that they present to the USDA or the NIH. Or it might be a researcher or technician.

Still, the USDA can offer few reassurances to informants. A former member of the animal care committee at New York University Medical Center claims to have been fired in August 1995 for protesting irregularities in N.Y.U.'s labs and cooperating with the USDA's investigations. The university states that his position became redundant. But the scientist, along with an administrator who was also dismissed, is suing N.Y.U., as well as the USDA—which, he says, failed to provide whistle-blower protection. (The agency did fine N.Y.U. $450,000 for assorted violations of the Animal Welfare Act.) Several USDA inspectors express frustration with their agency's provisions on informants. "We can't protect a whistle-blower," McKelvey says. "The regulation is weak." Unlike civil-discrimination suits, which require only a concatenation of circumstances, the USDA needs to prove that the person was fired because of having blown the whistle.

Also controversial are the statistics on pain and distress provided by the IACUCs to the USDA. They indicate that in 1995, 54 percent of the regulated animals had no pain or distress, 37 percent had distress alleviated by painkillers, and only 8.8 percent suffered unalleviated pain or distress. The data have been widely criticized for being unreliable, because the USDA does not specify how to classify pain. Andrew N. Rowan of the Tufts University Center for Animals and Public Policy has noted that some rather painful procedures, such as toxicity testing or antibody production, are commonly placed in the nonpainful category. Although the USDA proposed a pain scale in 1987, it was withdrawn after objections by researchers.

There are difficulties with assessing animal distress. Nevertheless, many European nations, as well as Canada, Australia and New Zealand, have developed pain scales in which each procedure is assigned a grade. As a result, their reports are more informative. The Netherlands listed in 1995 that 54 percent of animals had minor discomfort, 26 percent had moderate discomfort, and 20 percent suffered severe discomfort.

A pain scale would make it easier for IACUCs to rate the suffering involved in different schemes for doing an experiment. At present, the committees are required to certify that the animal researcher has looked for alternatives and that the number of animals used is reasonable. Alan M. Goldberg of CAAT wishes that they would also evaluate the experimental design. "Right now, using method A, they check: Is it the right number of animals? They don't look at method B or C"—which could involve in vitro techniques. Nor—unlike committees in Germany, Australia and elsewhere—are they required to weigh the benefits of research against the suffering or to include representatives of animal-welfare organizations in the review process. (The IACUCs do have to include someone unaffiliated with the institution, but who fills that position is again a source of controversy.)

The Propaganda

Change in the U.S. has been slow and painful. Notwithstanding some evolution of practices, the ferocity of the attacks by the most fervent animal rightists has led to a sense of moral outrage and an unwillingness to compromise—on both sides. Almost all activists insist that animal research is unnecessary; to them, investigators using animals are cruel and corrupt, consumed by a desire for ever more papers and grants. One antivivisection tract is entitled *Slaughter of the Innocent,* and the cover of another features splashes of blood. To animal liberators, the killing of more than six billion animals a year, mostly for food, represents a holocaust, and Adolf Hitler's doctors are proof that experimenters can be inhumane.

Many animal researchers, in turn, think of animal rightists as being brainless "bunny huggers" at best and dangerous fanatics at worst. Leaflets published by the American Medical Association represent the animal-rights position as equating humans with animals; a quote from Ingrid Newkirk of PETA, "A rat is a pig is a dog is a boy," is offered as evidence. (Newkirk claims her statement was "When it comes to feeling pain, a rat is a pig is a dog is a boy.")

In an essay entitled "We Can't Sacrifice People for the Sake of Animal Life," Frederick K. Goodwin, former head of the National Institute of Mental Health, has argued that the issue of animal rights threatens public health. In this vein, research advocates sometimes portray proposals to control animal research as being attacks on human life. For instance, one organization advises this response to a query about experimentation on pound animals: "How would you feel if the one research project that may save your child's life was priced out of existence because pound animals were banned?" Some writers invoke Hitler as proof that animal advocates are antihuman: he was an animal lover who passed anticruelty laws in 1930s Germany.

Finding itself under moral—and sometimes physical—siege, the research community has often retreated behind electronic surveillance systems—and an ethical code that frequently denounces internal dissent as treason, "giving ammunition to the enemy." One scientist interviewed for this article said that if his criticisms became known, he would be fired. In 1991 two animal researchers, John P. Gluck and Steven R. Kubacki of the University of New Mexico, wrote a treatise deploring the lack of ethical introspection in their field. Gluck testifies that the article quickly changed his status from an insider to a distrusted outsider. Arluke's studies revealed an absence of discussion about ethics: in 33 of 35 laboratories, moral positions were defined institutionally. Newcomers were given to understand that senior scientists had answered all the difficult questions, leaving them little to worry about.

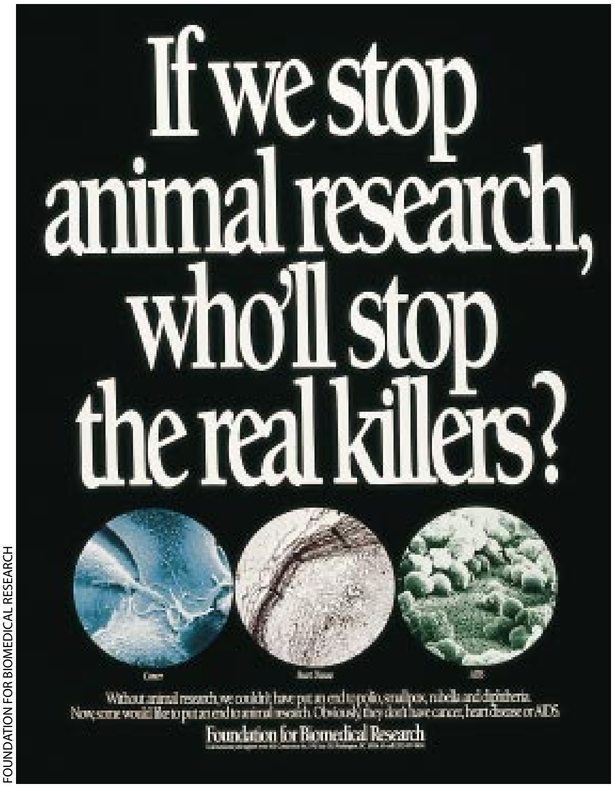
The insulation has made it difficult for changes in other branches of the life sciences—or from across the Atlantic—to filter in. Primatologists, for instance, have been discussing complex emotions in their subjects for decades. But many American experimenters still refuse to use the word "suffering," because it suggests an animal has awareness. Even the word "alternatives" is suspect; instead the NIH describes these as "adjuncts" or "complements" to animal research. Some researchers seem to regard the three Rs as an animal-rights conspiracy. Robert Burke of the NIH has stated: "To argue that we must refine our methods suggests that they are currently inadequate or unethical.... In my view, it is intellectually dishonest and hypocritical to continue to advocate the original three Rs as a goal for science policy. It is also, without question, dangerous to give our enemies such useful tools with which to pervert the scientific enterprise."

Of the 17 institutes included in the NIH, only the NIEHS has been active in researching alternatives. Following a directive by Congress, the NIH awarded about $2.5 million in earmarked grants between 1987 and 1989. But F. Barbara Orlans of the Kennedy Institute of Ethics at Georgetown University charges that the money did not constitute a special allocation for alternatives: 16 of the 17 grants went to studies that had traditionally been funded. (Like other public health agencies worldwide the NIH supports research into invertebrate, in vitro and computer models that are not billed as alternatives.)

In 1993 Congress directed the NIH to come up with a plan for implementing the three Rs. The resulting document, entitled "Plan for the Use of Animals in Research," is an overview of biomedical models, with some emphasis on nonmammalian systems. "The central message of the plan," explains Louis Sibal of the NIH, "is that scientists have to decide for themselves what the best method of solving their problem is." Whereas the European Union plans to cut animal use in half by the year 2000, a 1989 NIH report stated that animal use is not likely to decrease.

One arena in which the propaganda battles have been especially fierce is the classroom: both sides see dissection as the key to the next generation's sympathies. Animal advocates say dissection in schools is unnecessary and brutalizing and that the 5.7 million vertebrates (mostly wild frogs, but also cats, fetal pigs, pigeons and perch) used every year are procured in inhumane ways. Research advocates fear that without dissection, instruction will be inadequate, and fewer students will be attracted to or equipped for the life sciences.

In 1989, when the National Association of Biology Teachers (NABT) announced a new policy encouraging alternatives, it provoked a violent reaction. Barbara Bentley of the State University of New York at Stony Brook, for instance, denounced the monograph on implementing the policy as "an insidiously evil publication—evil because it is a barely disguised tract produced by animal rightists." An intense campaign followed, and in 1993 the NABT issued a new policy statement, warning teachers to "be aware of the limitations of alternatives." There is no high school dissection in most European countries.



FOUNDATION FOR BIOMEDICAL RESEARCH

MEDICAL NECESSITY of animal experiments is emphasized in a pro-research poster.

"It is possible to be both pro research and pro reform," Orlans says. She and others in the troubled middle have a simple message: the impasse must end. Animal liberators need to accept that animal research is beneficial to humans. And animal researchers need to admit that if animals are close enough to humans that their bodies, brains and even psyches are good models for the human condition, then ethical dilemmas surely arise in using them. But the moral burden is not for scientists alone to bear. All of us who use modern medicine and modern consumer products need to acknowledge the debt we owe to our fellow creatures and support science in its quest to do better by the animals. SA

Further Reading

IN THE NAME OF SCIENCE: ISSUES IN RESPONSIBLE ANIMAL EXPERIMENTATION. F. Barbara Orlans. Oxford University Press, 1993.

THE MONKEY WARS. Deborah Blum. Oxford University Press, 1994.

THE ANIMAL RESEARCH CONTROVERSY: PROTEST, PROCESS AND PUBLIC POLICY. Andrew N. Rowan and Franklin M. Loew, with Joan C. Weer. Center for Animals and Public Policy, Tufts University School of Veterinary Medicine, 1995.

More coverage of the animal-rights debate is available on-line at http://www.sciam.com by Shawn Carlson

COMET HALE-BOPP captured on film

HERMAN MIKUZ *Crni Vrh Observatory (left);*
TIM PUCKETT *Puckett Observatory (center and right)*

A Picture-Perfect Comet

I spent my formative years in what was then rural San Diego County. Our front porch opened onto an expanse of foothills so wild that we often startled coyotes away from our front yard when we retrieved the morning paper. The night sky was absolutely dazzling, and the millions of stars overhead enticed me out to enjoy them in secret.

Throughout the summer that separated second from third grade, my head never hit the pillow before I was scheming that night's escape. I had recently heard about Halley's comet—of its famous appearance of 1910 and of its imminent return. So, armed with a noisy party favor to scare off the coyotes, I posted scores of predawn hours atop a nearby hill, fully expecting to be the first person to see the comet on its return journey. By the time autumn's chill finally drove me off my hill, I felt utterly defeated. Only years later did I discover that I had misheard the year of Halley's return as 1968 instead of 1986.

In the decades since that disappointment, I've continued my love affair with the night sky, but I've never seen a cometary display to match the description of Halley's 1910 appearance. Halley's pathetic showing in 1986 left that stiff-lipped little boy within me still waiting for the heavens to redeem themselves.

Well, it looks like they finally might. Comet Hale-Bopp (C/1995 O1) looks even more impressive than it did just a month ago. The comet's nucleus is at least three times larger than Comet Halley's, and it has been ejecting bright jets of dust for many months, as seen in the photographs above. Some astronomers now believe Hale-Bopp may be the brightest comet this century. Here's how to make a detailed photographic record of the comet's passage.

If you think that so many pictures are going to be taken of this comet that yours can't be scientifically useful, think again. Professional astronomers want your help. A comet's tail changes rapidly, and the professionals need an army of observers to track these changes. For example, every few days, when the magnetic field created by the solar wind changes direction, the gas tail can separate from the comet's head. The comet can repair these "disconnection events" in just 30 minutes; you could be the only person who records it.

With a good 35-millimeter camera (single-lens reflex), a few lens attachments and a little practice, you can take vivid portraits of Hale-Bopp. Manual cameras are better for this work than the newer electronic automatic models. They perform better in cold weather, and you never risk a power failure during a long exposure. Try to find one that will let you lock up the internal mirror so that it won't jar the camera when you trip the shutter. If, while prowling around a used camera shop, you find a much coveted Olympus OM-1, Nikon F series or Pentax LX, buy it! Finally, because any vibration can spoil your image, you'll also need a cable release (available through camera supply companies for about $20) to activate the shutter without touching the camera.

When it comes to film, there is a trade-off between speed and grain size. Faster films require shorter exposures to catch the same detail, but they have a larger grain size and so give poorer resolution. As a general rule, you should use the slowest film your subject will allow, but nothing slower than ISO 400. Many astronomers prefer black-and-white film for its superior resolution. Kodak's T-Max 400 gives excellent results. If you decide to take color pictures, Fuji's Super G 800 and Kodak's Royal Gold 1000 get high marks for prints, and for slides Kodak's Ektachrome P1600 nudges out Fuji's Provia 1600 in side-by-side comparisons.

The correct exposure time depends on too many factors to guess accurately. The best advice is to shoot the comet at several exposures ranging from 10 seconds to 10 minutes. In general, a wide-angle lens requires shorter exposures than a telephoto lens of the same aperture, and the larger the aperture of the lens, the shorter the required exposure time. After reviewing the results of a roll or two, you should be able to narrow the range of exposure times.

The earth's rotation steadily shifts the sky, causing stars (and comets) to create curved streaks on any extended-exposure picture taken by a stationary camera. To compensate, you'll need to shift the camera with the sky throughout the exposure for any exposure longer than one minute. If you have a telescope with a sidereal drive, you can buy a piggyback mount to attach your camera to the telescope. (Lumicon in Livermore, Calif., sells one for $60; telephone: 510-

447-9570.) Battery-operated drives for cameras are also available but very expensive. (Pocono Mountain Optics in Daleville, Pa., sells one for $295; telephone: 800-569-4323 or 717-842-1500.) Or you can build a hand guider for less than $20 [*see box below*]. This design comes compliments of Dennis Mammana, resident astronomer of the Fleet Space Theater and Science Center in San Diego, and is the product of the collective cleverness of Dennis and other gifted astrophotographers. By manually twisting the adjusting screw one quarter turn every 15 seconds, you can eliminate star trails for up to 10 minutes on wide-field shots. Or use a high-torque DC motor powered by a car battery to turn the screw, then sit back and enjoy the comet.

Many astrophotographers take beautiful wide-angle portraits of comets that contrast the feathery tails against a stark landscape. Though often stunning, these images fail to capture many of the tail's most interesting features. Better science requires a closer view. The ideal field of view for recording tail features is about five degrees, which requires a lens with a 400-millimeter focal length. Because the tail may extend 20 degrees or more, you'll need to make a mosaic of images to catch the whole comet.

Remember, the longer the shutter is open, the more bad things can happen to your picture, so keep exposures as short as possible. This means you want a "fast"—that is, wide aperture—lens. The highest-quality 400-millimeter lenses can cost up to $6,000. Don't fret if you have to go to a shorter lens and a wider angle. A standard 135-millimeter telephoto is still scientifically useful. You will have to do some market research and balance your budget against the science you wish to accomplish. If possible, avoid mirror telephoto lenses and zoom lenses, whose optics are generally unsuitable for the sharp contrasts of astrophotography.

A few things to keep in mind: To help avoid darkroom catastrophes, begin each roll of film with a well-lit picture of something—anything. Without a reference image, darkroom technicians often can't identify the edges of a starry frame and sometimes miscut the film (to eliminate the risk entirely, many astrophotographers have their slides or negatives returned uncut). Also, carefully log the date, time and sky conditions for every observation you make. Most important, you must commit yourself to a regular observing schedule. A series of consistent observations made from the same site over many nights is much more valuable than a scattering of disjointed observations taken around the world. To do the job right, you've got to be out there on every clear night possible.

To find out more about observing comets or to learn how to contribute your observations, contact the Harvard-Smithsonian Center for Astrophysics via e-mail at icq@cfp.harvard.edu or visit their World Wide Web site at http://cfa-www.harvard.edu/cfa/ps/icq.html (Also see the January column for details about comets' tails.) I gratefully acknowledge informative conversations with Daniel W. E. Green of the Smithsonian Astrophysical Observatory and Dennis Mammana. SA

Check out the Society for Amateur Scientists's Web page at http://www.thesphere.com/SAS/ or call (800) 873-8767 or (619) 239-8807.

Further Reading

ASTROPHOTOGRAPHY II. Patrick Martinez. Willmann-Bell Publishers, 1987.

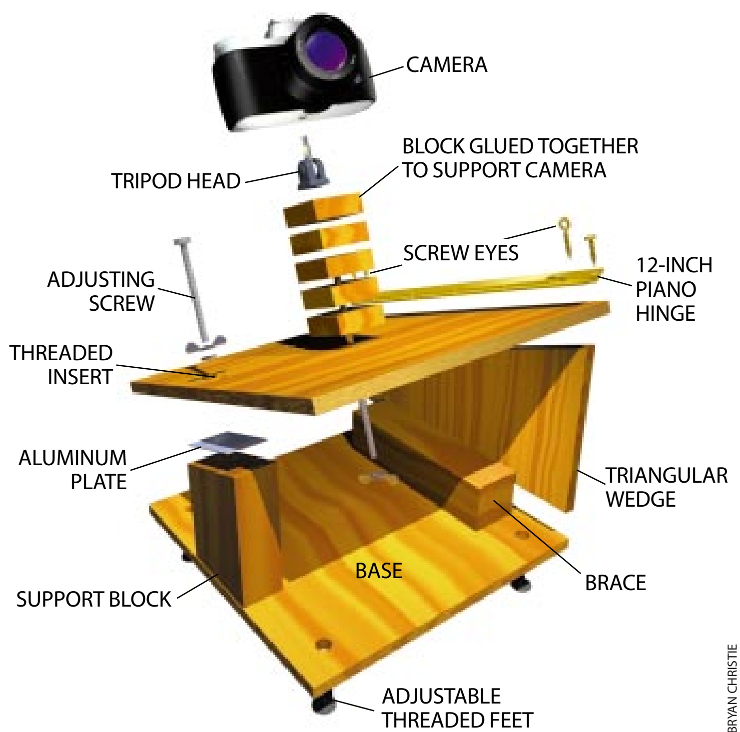
GUIDE TO OBSERVING COMETS. Smithsonian Astrophysical Observatory. Available for $15 from *International Comet Quarterly*, 60 Garden St., Cambridge, MA 02138.

ASTROPHOTOGRAPHY: AN INTRODUCTION. H.J.P. Arnold. Sky Publishing, 1995.

Hand Guider for Sky Photography

The guider is essentially a hinged wedge that can hold a camera steady while rotating its field of view to keep up with the movement of the stars through the night sky. Its crucial components are a wooden wedge, cut so that its angle matches the latitude of your observing site; a piano hinge to align the camera platform with the wedge; and an adjusting screw that turns inside a threaded insert to move the platform. For the one-turn-per-minute rate given in the text, the adjusting screw must be one quarter inch in diameter, with a pitch of 20 threads per inch; its centerline must be located precisely 11 $^{3}/_{8}$ inches from the hinge line. The top of the block on which it bears should be cut to the same angle as the wedge and protected by a small aluminum plate so that the screw does not cut into the wood.

To use the guider, set it up on a smooth, level surface and turn it so that the line of the piano hinge points directly at the North Star. Without moving the platform, turn the camera so that its viewfinder captures your item of interest. Lock up the shutter and begin your exposure, turning the adjusting screw gently one quarter turn every 15 seconds.



BRYAN CHRISTIE

MATHEMATICAL RECREATIONS

by Ian Stewart

Crystallography of a Golf Ball

Who would imagine that there is significant mathematics in the humble golf ball? Not me, certainly, until my attention was drawn to the fact by Tibor Tarnai, an engineer at the Technical University of Budapest. Golf balls have an interesting structure because they are not perfect spheres. They are made with dimples, which improve their aerodynamic performance by reducing drag [see "Tackling Turbulence with Supercomputers," by Parviz Moin and John Kim; SCIENTIFIC AMERICAN, January]. Manufacturers employ an amazing variety of dimple patterns, and nearly all of them are highly symmetric—which is where the mathematics comes in. It is the same kind of mathematics that crystallographers use to analyze the symmetries of crystal lattices.

The symmetries and the number of dimples are connected, leading to "magic" numbers of dimples that occur more often than others, such as 252, 286, 332, 336, 360, 384, 392, 410, 416, 420, 422, 432, 440, 480, 492 and 500. All of these are found in commercial balls. One manufacturer made a ball with 1,212 dimples, but not for actual play, just to show how clever it was at making golf balls.

The dimples must cover the surface of the ball in a fairly even manner. Otherwise the ball will tend to swerve, because the air resistance depends on the density of dimples. So the problem of designing golf balls is closely related to that of distributing tiny, circular disks uniformly over the surface of a sphere. There are practical considerations, however. In particular, the ball is molded from two hemispheres, so there must always be at least one parting line: a great circle on the surface that does not meet any of the dimples. To ensure aerodynamic balance, most designs have many pseudo–parting lines arranged symmetrically. These lines provide excellent clues to the symmetry of the ball.

In ordinary language, "symmetry" is used in a rather vague way, to indicate something well proportioned or elegant—such as William Blake's "Tyger" with its "fearful symmetry." In mathematics, symmetry is much more rigidly defined. It refers not to a shape but to a transformation—a mathematical rule for moving a shape around. If the object fits into exactly the same space after the transformation as it did before, then that transformation is a symmetry of the object. For example, a square has exactly eight symmetries (leaving out deformations such as bending or stretching). These are (counterclockwise) rotations through 90, 180 or 270 degrees, together with reflections about either of the axes or diagonals. The eighth symmetry is the "trivial" transformation in which the square is left exactly as it is.

The symmetries of an object form a "group": if two symmetry transformations are performed one after another, the result—known as their composite or product—is also a symmetry transformation. For example, if a square is rotated through 90 degrees and then through 180 degrees, the result is a rotation through 270 degrees—a member of the group. This "group property" is one reason why we include the trivial symmetry: if this were omitted, the product of two symmetries might not count as a symmetry. For example, the product of a 90-degree rotation with a 270-degree rotation is a 360-degree rotation. Because the latter leaves every point of the square in the original place, it is just another name for the trivial symmetry.

The group structure lets us classify symmetric objects into various types. Two objects have the same symmetry type if their group of symmetry transformations has the same abstract structure. So, for example, a square has the same symmetry type as a square with its corners rounded off.

In two- and three-dimensional geometry, the most important types of symmetry are rotations and reflections. A rotation in two dimensions "spins" the object through some angle about a fixed point; in three dimensions, it spins

TIBOR TARNAI *Technical University of Budapest*

GOLF BALLS illustrate the subtleties of finite symmetry groups.

the object through some angle about a fixed axis. A reflection in two dimensions exchanges points that are similarly situated on either side of a fixed "mirror line"; in three dimensions, it does the same, but now there is a fixed mirror plane.

An important feature of the symmetry group is its order—the number of distinct symmetry transformations it contains. So the order of the symmetry group of the square is eight. Some of the most symmetric objects in three dimensions are the famous regular solids—the tetrahedron, cube, octahedron, dodecahedron and icosahedron. The orders of their symmetry groups are:

- tetrahedron (four triangular faces) 24
- cube (six square faces) 48
- octahedron (eight triangular faces) 48
- dodecahedron (12 pentagonal faces) 120
- icosahedron (20 triangular faces) 120

In every case, the order of the symmetry group is equal to twice the number of faces, multiplied by the number of sides on a face. For example, for the dodecahedron, we have $2 \times 12 \times 5 = 120$. This relation is a consequence of the regular geometry of these solids. To see why it holds, choose a particular face: the dodecahedron can be rotated so that any of the 12 faces is chosen. While preserving that face, it can then be rotated to any one of five positions. That gives $12 \times 5 = 60$ rotational symmetries. But the chosen face can also be reflected before performing these rotations, and that doubles the final number of possibilities.

Note that the cube and octahedron have the same order of symmetry, as do the dodecahedron and the icosahedron. This is a consequence of duality. The midpoints of the faces of an octahedron form the vertices of a cube, and conversely; this implies that the octahedron and the cube have the same symmetry group. Ditto for the dodecahedron and the icosahedron.

The maximum order of symmetry groups in three dimensions is not 120. But the only way to exceed this order is to possess infinitely many symmetries. A dimpled golf ball, however, must have a symmetry group of finite order, because there are only a finite number of dimples, so its maximum order of symmetry is 120.

The number of dimples, of course, may be larger than this. Early golf balls used two distinct patterns. In the first, the dimples were arranged along lines of latitude, which were situated relative to an equatorial parting line. Usually there were 392 dimples, and the golf ball had fivefold rotational symmetry about an axis running from its north to its south pole [*see* a *in illustration on page 96*], but often eight dimples were omitted for obscure reasons (*b*). The second pattern had the same symmetry type as the regular octahedron, a shape formed from eight equilateral triangles (such as two square-based pyramids joined base to base). The classic octahedral golf ball (*c*) has 336 dimples; it has three parting lines that meet one another at right angles, just like the earth's equator and the meridians at zero and 90 degrees.

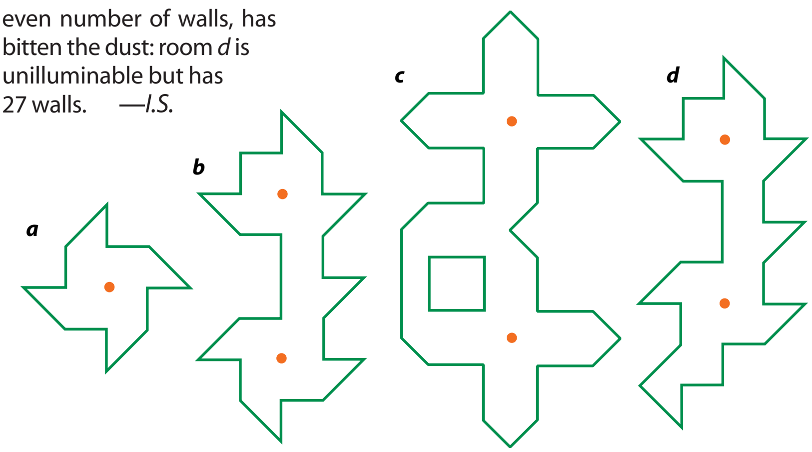
A more esoteric design possesses icosahedral symmetry (*d*) with six parting lines. An icosahedron is formed from 20 equilateral triangles, arranged in fives around each vertex. The same arrangement is found in geodesic domes such as those used to house radar equipment and in the protein units of many viruses. The adenovirus, for instance, has 252 protein units configured as an "icosadodecahedron," whose faces are either regular hexagons or equilateral triangles arranged five around a vertex. Uniroyal makes a golf ball (*e*) with exactly this structure: oddly, its 252 dimples are five-sided pyramids.

In 1973 Titleist introduced a ball (*f*) that at first sight looks icosahedral in form. But its symmetry is imperfect. The construction begins with an icosahedron, packing each triangular face with dimples; this particular arrangement, however, does not possess a parting line, so a row of dimples along the equator was doubled up to leave a clear gap in between. This pattern breaks the icosahedral symmetry but produces an entirely practical golf ball.

There is far more to the symmetries of golf balls. Specifically, I have ignored some important but esoteric distinctions between subtly different symmetry groups. You can find the details in Tarnai's article in *Katachi U Symmetry*, edited by T. Ogawa, K. Miura, T. Masunari and D. Nagy (Springer-Verlag, Tokyo, 1996). Or buy some golf balls and investigate for yourself. SA

FEEDBACK

In the August 1996 column I described the work of George W. Tokarsky of the University of Alberta on the existence of unilluminable rooms. These are rooms with mirrored walls such that a point source of light, when placed in a suitable position, does not illuminate the entire room. Tokarsky sent me some of his latest results, which are equally remarkable: it is possible to have a self-unilluminable room, one in which no reflection of the point source is visible from the source itself. Room *a* is conjectured to be minimal—no room with fewer walls is self-unilluminable; however, no proof of minimality is known. Room *b* is conjectured to be the minimal unilluminable room, whereas room *c* shows an unilluminable room with a hole. And one conjecture, that an unilluminable room must have an even number of walls, has bitten the dust: room *d* is unilluminable but has 27 walls. —*I.S.*



JENNIFER C. CHRISTIANSEN

PALOMAR OBSERVATORY/CALIFORNIA INSTITUTE OF TECHNOLOGY

SCHMIDT TELESCOPE on Palomar Mountain in California compiled the canonical map of the heavens—now available on CD-ROM.

HEAVEN ON EARTH

Review by Timothy Ferris

RealSky CD: The Palomar Observatory Sky Survey
Astronomical Society of the Pacific, 1996
(Nine compact discs; PC or Macintosh format, $250)

The release of the *RealSky* CD-ROM collection provides a dramatic example of the growing egalitarian power of the personal computer. Rarely has so powerful a research tool been placed within the grasp of amateur scientists. These discs bring to the general public a digital edition of what has long been an icon of astronomical exclusivity: the coveted photographic plates of the National Geographic Society–Palomar Observatory Sky Survey.

The POSS plates, as they are known, constitute the world's most comprehensive atlas of the northern skies. Accumulated over nine years of photography using the 48-inch Oschin Schmidt telescope atop Palomar Mountain in southern California, they cover nearly the entire sky visible from that latitude, imaged in both red- and blue-sensitive emulsions, down to the 20th magnitude in red light (roughly 500,000 times fainter than can be seen with the naked eye).

Since their publication in 1958, the POSS plates have been indispensable to professional astronomers. It was by poring over them that Bart Bok identified the "Bok globules" wherein new stars form and that George Abell discovered the many galaxy clusters that still bear his name. Hundreds of observers have used them to distinguish supernovae and uncharted asteroids from ordinary stars, and many thousands more undoubtedly have wished they could do so. But a full set of the 1,870 POSS plates cost $15,000, enough to limit their possession to professional observatories and a few exceedingly well heeled amateurs.

The revolution began when a team at the Space Telescope Science Institute in Baltimore scanned into a computer the images on the 14-inch-square glass POSS plates. This initial effort yielded a third of a terabyte of raw data, stored on 55 gleaming silver laser discs—an imposing collection, but one so unwieldy that the workers developed a compression algorithm to boil down the data by a factor of 10.

The compressed version, commonly known as the 10X POSS, was released in 1994 on 102 compact discs, at a price of $3,500 per set. It is now available on the World Wide Web from the Hubble Space Telescope Data Archive (http://stdatu.stsci.edu/dss/dss_form.html).The 10X POSS is useful for those who want to scrutinize a particular patch of sky, but it is too massive to appeal to browsers. With a 28.8-baud modem, it can take more than three hours to download a field one degree on a side—about the area visible at low power through a typical amateur telescope. To accomplish at home the kind of serendipitous sky browsing that benefited Bok and Abell, one needs ready access to a complete digital POSS, at a manageable price.

Now we have it. *RealSky* consists of the red-light POSS plates (the ones most observers favor, because they bring out the ruddy glow of interstellar nebulae), compressed to 1 percent of their original volume and squeezed into nine CDs for $250. Elegantly housed in a star-studded case no larger than a boxed set of the complete Mahler symphonies, *RealSky* is intelligently designed and delightfully easy to use. Boot up any disc, click on the "target list," and you are presented with a catalogue of bright, deep-sky objects that includes many of the galaxies and nebulae observers know best. Hit "view," and you have on your computer screen a sharp POSS plate segment showing the selected object at its center.

The image can be manipulated in several useful ways. It can be rendered as positive or negative (white sky background), superimposed with an east-north orientation mark, modified in brightness and contrast, sharpened or smoothed, and so forth; the image can also be exported to other graphics programs for further enhancement. Handy buttons on the screen make it easy to zoom in and out, to shrink or enlarge the field of view, and to pan across the sky. Moving the mouse pointer around on the plate instantly displays its location on the sky, accurate to better than one second of arc. Alternatively, one can select a site by coordinates alone. This exceptionally powerful and felicitous program is like a musical instrument, limited less by its own structure than by the proficiency and expertise of the user.

But how much has been lost in reducing the POSS data by a factor of 100? To find out, I downloaded an image of the distorted spiral galaxy NGC 3027 from the Hubble Space Telescope Web site (where the plates are compressed only by a factor of 10) and compared it with a *RealSky* depiction of the same galaxy. At first glance the two photographs looked remarkably similar. But when I viewed them through a digital blink comparitor—a system that flashes back and forth between the two, so that differences leap out to the eye—it was evident that a number of dim stars visible in the 10X POSS plate had vanished in the *RealSky* version, as had much of the galaxy's outer envelope.

The results were happier when I tested *RealSky* against the real sky. I printed out a dozen galaxy fields on a laser printer in preparation for undertaking a visual search for supernovae through the 0.46-meter reflecting telescope at Rocky Hill Observatory, located 100 kilometers north of San Francisco. The brightness of the sky at that location limits the telescope's grasp for such work to about magnitude 14.5, fairly typical of the conditions encountered by amateur astronomers in today's light-polluted world.

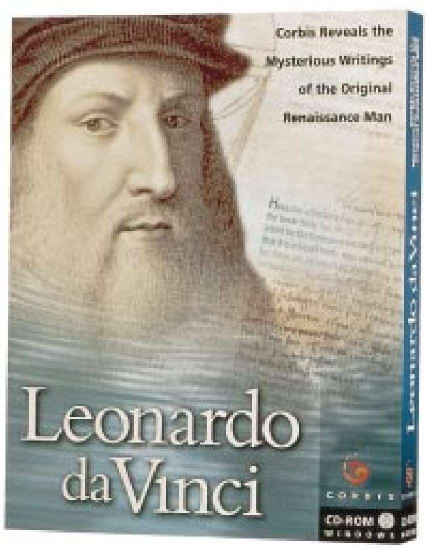
To find a supernova, one must notice a star that was not evident before. The

THE CD EXAMINED

Leonardo da Vinci
Corbis, 1996
(CD-ROM for Windows or Macintosh, $35)

Although it does contain broad overviews of Leonardo's life and work, the real focus of this disc is the Codex Leicester, a collection of 36 folios penned by Leonardo around 1508 that contain his insights into a variety of natural phenomena. (The Codex Leicester was acquired in 1994 by Bill Gates, who, not coincidentally, owns Corbis.) *Leonardo da Vinci*'s primary innovation is a set of clever viewing tools that let the user examine English translations of the Codex superimposed onto lavish facsimiles of its pages. Leonardo's studies still make fascinating reading; he deduced, quite accurately, that reflected light from the earth illuminates the whole of the crescent moon and clearly explained why the distribution of fossils could not be explained by the Biblical flood. The rest of the disc is beautifully designed but oddly sparse. Instructional "guided tours" (slide shows, really) fail to provide a depth of analysis to match Leonardo's brilliant scientific gropings.

—Corey S. Powell



CORBIS

BRIEFLY NOTED

SPINELESS WONDERS: STRANGE TALES FROM THE INVERTEBRATE WORLD, *by Richard Conniff. Henry Holt, 1996 ($25).*
Ants, worms, slime eels: the invertebrate world holds a repugnant fascination. Close up, many of these creatures are not only intriguing but beautiful and—in the case of tarantulas—even a bit cuddly. How many people know that eelskin wallets are a product of the hagfish, a boneless genus more than 200 million years old? Before the exotic-leather boom, the hagfish was best known for its ability to tie itself in a knot and to suffocate would-be predators by exuding masses of slime.

SALLY BENSUSEN

THE BIOLOGICAL UNIVERSE: THE TWENTIETH-CENTURY EXTRATERRESTRIAL LIFE DEBATE AND THE LIMITS OF SCIENCE, *by Steven J. Dick. Cambridge University Press, 1996 ($54.95).*
Steven J. Dick, a historian at the U.S. Naval Observatory, has written a sober, exhaustively researched analysis of popular and scientific attitudes toward alien life. He picks apart topics ranging from UFOs to the Search for Extraterrestrial Intelligence (SETI) to the ever shifting ideas on the origin of life. The book's measured tone sometimes verges on the comically deadpan, but its wealth of detail offers a welcome perspective above the current media din about life on Mars.

THOUGHT CONTAGION: HOW BELIEF SPREADS THROUGH SOCIETY, *by Aaron Lynch. BasicBooks, 1996 ($24).*
Can epidemiology be a valid tool for understanding the spread of ideas? Some scientists argue that memes, or individual units of belief, spread like diseases and compete with one another much as genes compete in biological evolution. Aaron Lynch's account of the "science of memes" is fun but ultimately facile—memes appear simply to stand in for older, less trendy concepts about social evolution and sociobiology. And the specter of infinite regression (the concept of memes is a meme, as is the concept of the concept of memes, and so on) is enough to make a postmodernist's head spin.

Continued on page 103

finder chart should, therefore, show all the stars in the sky, down to the observer's limiting magnitude. *RealSky* passed this test effortlessly. In every case, it represented galaxies in a way that was passably close to their visual appearance, and it covered all the stars I could see. Observers using charge-coupled devices, or CCDs (electronic light detectors), and big telescopes under truly dark skies will see more than *RealSky* records, but in many cases, the same would be true even if they were using the original, uncompressed POSS.

Further improving its utility, *RealSky* can interface with *TheSky,* a popular commercial planetarium program [see "Hands-on Astronomy," by Timothy Ferris; Reviews and Commentaries, Scientific American, February 1996]. An appropriately updated version of *TheSky* can superimpose POSS images onto its digital sky charts at the correct scale and orientation. The results look crude and may involve a bit of disc swapping, but they vastly enhance the reach of *TheSky* and point the way toward better things to come.

Digital egalitarianism is taking place in many fields of science, but its consequences are particularly stunning in astronomy. POSS-II, a new Palomar survey now being completed in three bands (blue, red and far-red) is being digitized, and many compressed POSS-II plates are already available on the Space Telescope Science Institute Web site. These images make it possible for students or dedicated dabblers to make genuine discoveries—for instance, identifying transient phenomena by blink-comparing the same piece of sky as photographed at dates decades apart. POSS-II will also probably make the transition to home use, probably on digital videodiscs (DVDs) the size of CDs but having 10 times the data capacity and read speed.

Anyone who fears that digital technology threatens to turn humans into a race of navel-gazing couch potatoes need look no further than these ongoing sky surveys, which invite us to gaze not at the pointing finger but at the stars.

TIMOTHY FERRIS is emeritus professor of journalism at the University of California, Berkeley. His latest book, The Whole Shebang, *will be published by Simon & Schuster in May.*

CHEAP MATERIAL

Review by Jeffrey L. Meikle

Plastic: The Making of a Synthetic Century
BY STEPHEN FENICHELL
HarperBusiness, 1996 ($25)

First impressions of *Plastic* are encouraging. The dust jacket of Stephen Fenichell's historical survey of plastic in American life displays a life-size jumble of brightly colored plastic knives, forks and spoons. The inside flap promises a "fresh, irreverent look at the substance we all love to hate." A blurb by Douglas Coupland, the chronicler of Generation X, declares the book to be "oddly funny, grippingly readable, and crammed with wads of cool facts that make you see the twentieth century in a whole new light." More than a generation older and possessed of a darker vision, Norman Mailer rejoices that here at last, "for anyone who hates plastic and likes good writing," is a book "to satisfy your anger, your pleasure, and your instinctive judgment."

Having recently published a scholarly history of plastic, I picked up Fenichell's attractively packaged survey with keen anticipation; I was curious to see how a freelance journalist would interpret synthetic materials in a book for a popular audience. Fenichell advances a clear notion of the significance of plastic: it "combines the ultimate twentieth-century characteristics—artificiality, disposability, and synthesis—all rolled into one." The proliferation of plastic in everyday life indicates "the victory of pack-

THE ILLUSTRATED PAGE

Ships and Shipwrecks of the Americas: A History Based on Underwater Archaeology
EDITED BY GEORGE F. BASS
Thames and Hudson, 1996
(paperbound, $24.95)

On Christmas Eve of 1492, the *Santa María*—the flagship of Christopher Columbus's mission of discovery—became the first European ship wrecked in American waters. Many others followed; between 1492 and 1520 alone, at least 50 sailing vessels sank in and around the Caribbean. Since the proliferation of scuba diving in the 1950s, many of these wrecks have been discovered, excavated or even salvaged. This book describes in splendid detail some of the most spectacular or unusual finds, including four ships bound for Spain from Veracruz that wrecked off Padre Island in 1554. A large galleon, the Conde de Tolosa, was on its way to Mexico with mercury for silver production when it sank off Hispaniola in 1724 (*right*).

George F. Bass has skillfully edited essays by 12 contributors into a seamless, readable whole; the illustrations, too, are numerous and of good quality. The main drawback to this affordable paperback reissue is that it seems not to have been revised since its original release in 1988, so it lacks a discussion of how remotely operated vehicles and technical diving are transforming marine archaeology. For the average reader, however, this book serves as a fascinating lesson that there is a lot more to the Caribbean than piña coladas and Club Med. —*Glenn Zorpette*

age over product, of style over substance, of surface over essence."

Unfortunately, the book displays similar qualities. Despite its outward promise, it is riddled with errors of fact and of interpretation. All that *Plastic* has going for it is a genuine enthusiasm for the protean manifestations of synthetic materials.

Fenichell's narrative proceeds chronologically, driven by anecdotal tales of eccentric entrepreneurs and serendipitous inventions. It starts with "protoplastics" such as vulcanized rubber in the mid-19th century and winds up among the engineered polymers of the 1980s. Along the way the author traces the progress of celluloid from billiard balls to motion-picture film, surveys the development of cellophane, rayon and nylon, and details the 1950s explosion of plastic consumer goods, from Tupperware to hula hoops.

COURTESY OF PEDRO J. BORRELL

The chapters are uneven in quality, varying with the types of sources Fenichell apparently relied on ("apparently" because the book contains neither references nor bibliography—not even the suggested readings essential to any popularization of science or technology). When Fenichell clearly follows a major source—as he does when discussing nylon—the narrative line is relatively strong. But when no such source was available, as in the chapters on the 1950s and 1960s, the text becomes a disorganized mosaic of catchily titled subsections each defined, or perhaps generated, by whatever newspaper or magazine articles happened to be at hand.

Even so, *Plastic* is sometimes entertaining, offering historical glosses on such fascinating topics as the Crystal Palace exhibition of 1851, for which Charles Goodyear commissioned a "Vulcanite Court" whose walls, vaulted roof and contents were all fabricated from hard rubber. In the midst of tracing the development of celluloid movie film, Fenichell pauses to tell the story of the Lumière brothers of France, whose projection system delivered moving images to a large audience, a major improvement over Thomas Edison's kinetoscope with its peepshow audience of one.

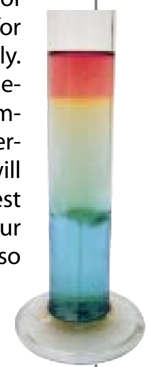
We also learn about the development of a plastic bugle, intended to conserve precious copper during World War II. Although familiar with the bugle itself, I was unaware of the intriguing story behind it (which makes the absence of solid documentation all the more frustrating). Reluctantly procured by a U.S. Army quartermaster officer who preferred brass, the prototype was hurled against a brick wall before being tested by the military's top bugler as scientific instruments measured the accuracy of its tone. An order for 200,000 followed.

At first glance the information set out in *Plastic* all seems plausible, and unsuspecting readers might naturally assume that Fenichell knows what he is talking about. But *Plastic* contains so many inaccuracies that it simply cannot be trusted. When Fenichell tells the story of Formica, for instance, he garbles the first name of one of its inventors and the last name of the other; he goes on to weave a tale of their entrepreneurial success that is distinctly at odds with the facts.

BRIEFLY NOTED

Continued from page 101

CHEMICAL CURIOSITIES, *by Herbert W. Roesky and Klaus Möckel. Translated by T. N. Mitchell and W. E. Russey. VCH Verlagsgesellschaft, 1996 ($39.95).*
For most people—those who do not have access to fume hoods and acid-resistant gloves—this book of chemical recipes should be for reading and daydreaming only. But the photographs and descriptions of spectacular demonstrations, ranging from underwater fire to invisible inks, will delight anyone with an interest in the materials from which our world is made. The authors also include a remarkable array of passages from the history of chemistry.



BETRAYAL OF SCIENCE AND REASON, *by Paul R. Ehrlich and Anne H. Ehrlich. Island Press, 1996 ($24.95).*
THE ULTIMATE RESOURCE 2, *by Julian L. Simon. Princeton University Press, 1996 ($35).*
The near-simultaneous release of these two books is the environmentalist equivalent of the "Rumble in the Jungle." Paul and Anne Ehrlich deliver a stinging rebuttal of the antienvironmental "brownlash," whereas Julian Simon equally vehemently attacks green notions of resource scarcity. There are revealing excesses on both sides—Simon proclaims that resources are effectively infinite. After the dust settles, these books make a persuasive case for a middle ground between capitalist innovation and preservationist caretaking.

HOW NATURE WORKS: THE SCIENCE OF SELF-ORGANIZED CRITICALITY, *by Per Bak. Copernicus, 1996 ($27).*
As the title hints, Per Bak is not shy about the claims he makes for his research on self-organized criticality, the tendency of systems to experience periods of stasis followed by sharp transitions to a new state of equilibrium. Sometimes he overreaches, as when trying to explain the workings of the brain. On the whole, however, Bak has concocted a profoundly fresh way of viewing the world—one in which earthquakes, mass extinctions and collapsing piles of sand all express the same, episodic rules written into the laws of nature.

MARTIN BARRAUD *Tony Stone Images*

***PLASTIC PRODUCTS** are a ubiquitous and complex presence in the modern world—even on the beach.*

Also, Daniel O'Conor and Herbert Faber did not leave Westinghouse—where they developed the product first sold about 1910 as "Micarta"—because the company would not manufacture their invention. Instead they went into business for themselves (infringing Westinghouse patents to produce the first Formica in 1913) so that they could cut into Westinghouse's near monopoly of an expanding market.

Errors in dating, both explicit and implicit, are even more prevalent throughout the book. J. B. Dunlop commercialized the pneumatic tire in 1888, not during the 1910s (when it would have come far too late to play its essential role in the cycling craze of the 1890s). And Bobby Darin landed his first recording contract in 1957; he was not, as Fenichell implies, a hit singer in 1948. Such compressions of time are common in the book, collapsing events separated by years into an undifferentiated historical present. Fenichell merges the Art Deco style of the late 1920s with the distinctive streamlining of the mid-1930s, then goes on to conflate two years of changes in Du Pont's nylon exhibit at the 1939–1940 New York World's Fair into a single event.

In fact, the company put its new synthetic fiber through a series of successively more dramatic displays at the World's Fair in response to the incessant clamor of visitors intent on seeing nylon stockings. The exhibit started as a dull scientific display, progressed to an impromptu fashion show and culminated in an extravaganza in which a mysterious "Miss Chemistry" emerged from a test tube to display her nylon-clad legs. Fenichell ignores these telling changes and tosses in a description of mechanical hands endlessly stretching a nylon stocking—a demonstration that New York visitors never saw, because it appeared only at San Francisco's Golden Gate Exposition of 1939.

Plastic abounds with such errors. Although Fenichell tells us that British scientists discovered polyethylene during World War II, he later correctly traces its discovery to 1933. Twice he states that Nazi Germany did not manufacture polyethylene; in reality, the U.S. Army captured an intact polyethylene plant at the end of the war. Norman Mailer is misquoted, with one of his sinuous riffs chopped into three short sentences for easy reading.

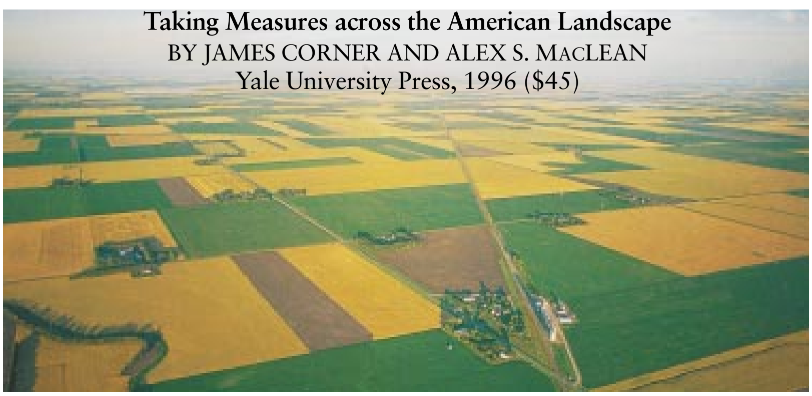
It appears that Fenichell was ill served by his editors at HarperBusiness, who also let numerous stylistic oddities pass and even missed a glaring typo in the book's opening sentence. But no amount of editing could repair a book whose research is so casually flawed. The author seems to consider facts to be as malleable as plastic. As long as the surface is seamless, artificially smooth and styled for entertainment, why should anyone question the book's deeper substance? *Plastic* is a simulacrum corresponding only approximately to reality.

At one time, I might have referred to this sort of publishing as just another example of "plastic." But my own research has made me aware that such a dismissal trivializes synthetic materials' complex, ambiguous contributions to the 20th century. In choosing surface over substance, Fenichell merely glides over the rich details.

JEFFREY L. MEIKLE, a professor of American studies and art history, is the director of the American studies program at the University of Texas at Austin. His book American Plastic: A Cultural History *(Rutgers University Press) won the 1996 Dexter Prize of the Society for the History of Technology.*

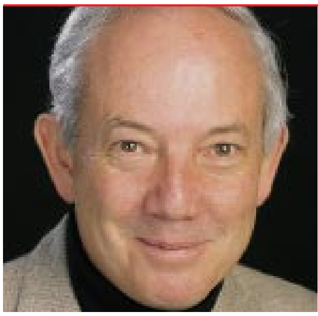
THE ILLUSTRATED PAGE

Taking Measures across the American Landscape
BY JAMES CORNER AND ALEX S. MACLEAN
Yale University Press, 1996 ($45)



ALEX S. MACLEAN

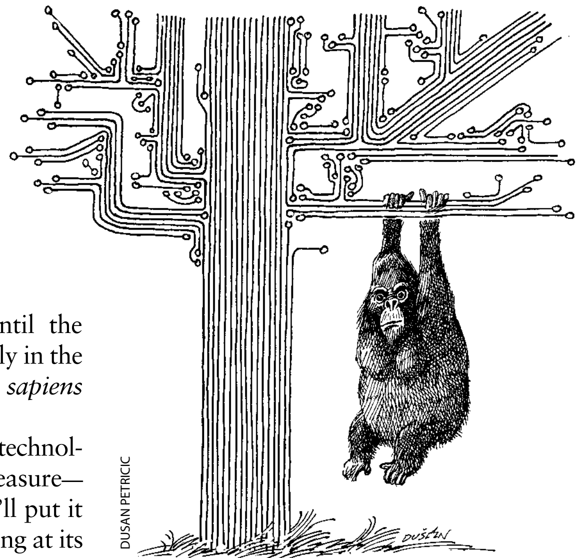
Staring down from the window of an airplane, one is struck by the incredible scales on which humans reshape the earth: even at altitudes where people are shrunken to microscopic dots, the signs of our activities are unmistakable. This book preserves that revelation in a series of outstanding aerial photographs from around the U.S. Some, such as a shot of a windmill field near Palm Springs, Calif., look like abstract art, betrayed only by their captions. An image of a railroad line cutting through the gridded fields of North Dakota (*above*), on the other hand, unambiguously chronicles the way life and land can be bent to the human will. Every page is a thought-provoking visual delight. —*Corey S. Powell*



WONDERS

by W. Brian Arthur

How Fast Is Technology Evolving?



DUSAN PETRICIC

My grandfather, for some reason, wore a hat to meals. Some evenings—also hatted—he would play the fiddle. He was born in Ireland in 1874, and he lived to see, in his long life, satellites, computers, jet airplanes and the Apollo space program. He went from a world where illiterate people footed their way on dirt roads, where one-room schools had peat fires in the corner, where stories were told at night in shadows and candlelight, to a world of motor cars and electricity and telephones and radio and x-ray machines and television. He never left Ireland, although late in life he wanted to go to England in an airplane to experience flying. But in his lifetime—one lifetime—he witnessed all these births of technology.

It is young, this new technology. It is recent. It has come fast. So fast, in fact, that speed of evolution is regarded as a signature of technology itself. But how fast? How quickly does technology evolve? It is hard to clock something as ill defined as technology's speed of evolution. But we can ask how fast we would have to speed up the natural, biological evolution of life on our planet to make it roughly match some particular technology's rate of change.

Let's imagine speeding up biological evolution in history by a factor of 10 million. This would mean that instead of life starting around 3,600 million years ago, in our fast-forwarded world the first, crude blue-green algae appear 360 years ago, about the year 1640. Multicellular organisms arise in Jane Austen's time, about 1810 or so, and the great Cambrian explosion that produced the ancestors of most of today's creatures happens in the early 1930s, the Depression era. Dinosaurs show up in the late 1960s, then lumber through the 1970s and into the 1980s. Birds and mammals appear in the mid-1970s but do not come fully into their own until the 1990s. Humankind emerges only in the past year or two—and as *Homo sapiens* only in the past month.

Now let's lay this alongside a technology whose speed we want to measure—calculating machinery, say. We'll put it on the same timeline, but evolving at its actual rate. Early calculating machines—abacuses—trail back, of course, into antiquity. But the modern era of mechanical devices starts in the years surrounding the 1640s, when the first addition, subtraction and multiplication machines of Wilhelm Schickard, Blaise Pascal and Gottfried Wilhelm Leibniz begin to appear. These were rudimentary, perhaps, but early computational life nonetheless. The first successful multicellular devices (machines that use multiple instructions) are the Jacquard looms of Jane Austen's time. Calculators and difference engines of varying ingenuity arise and vanish throughout the 1800s. But not until the 1930s—the Cambrian time on our parallel scale—is there a true explosion. It's then that calculating machines become electrical, the government goes statistical, and accounting becomes mechanized. The 1960s see the arrival of large mainframe computers, our parallel to the dinosaurs, and their dominance lasts through the 1970s and 1980s. Personal computers show up, like birds and mammals in the mid-1970s, but do not take hold until the late 1980s and early 1990s.

Let's imagine speeding up biological evolution in history by a factor of 10 million.

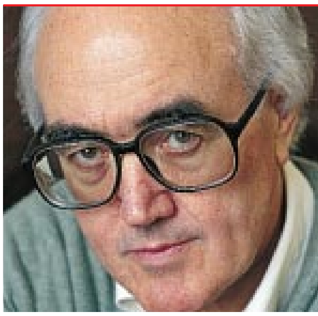
What then corresponds to humankind, evolution's most peculiar creation to date? My answer is the Internet or, more specifically, its offshoot, the World Wide Web. The Web? Well, what counts about the Web is not its technology. That's still primitive. What counts is that the Web provides access to the stored memories, the stored experiences of others. And that's what is also particular to humans: our ability not just to think and experience but to store our thoughts and experiences and share them with others as needed, in an interactive culture. What gives us power as humans is not our minds but the ability to share our minds, the ability to compute in parallel. And it's this sharing—this parallelism—that gives the Web its power. Like humans, the Web is new, although its roots are not. And its impact is barely two years old.

This correspondence between biology and technology is striking. And naturally, it's not perfect. Why should it be? This is fun, after all—more whimsy than science. But if we accept this correspondence, crude as it is, it tells us that technology is evolving at roughly 10 million times the speed of natural evolution. Hurricane speed. Warp speed.

From what I've said, it would seem that all the interesting things in technology or biology have occurred recently. But this is just appearance. In biological evolution, it is not the species markers that count but rather the new principles that are "discovered" at rare intervals. The miracles are not dinosaurs or mam-

Continued on page 107

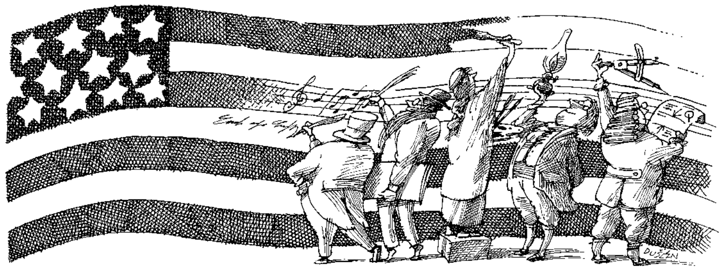
COMMENTARY



CONNECTIONS

by James Burke

Waving the Flag



DUSAN PETRICIC

I was gazing up at the Stars and Stripes during a ceremony recently in Washington, D.C., and thinking about how things might have been if Lord North, George III's prime minister, who fatally underestimated the American colonists, hadn't been off for the weekend when the Revolution (sorry: War of Independence) broke out. Probably nothing, because French financial backing for the rebels (sorry: patriots) had made sure, long before, that the U.S. would end up the U.S., as there was little the French wanted more than to cock a snook at the Brits. Some snook.

The whole incredible scam was masterminded by a character named Caron de Beaumarchais, who had made the flattest wristwatch anybody had ever seen for Madame de Pompadour and written a play (later snitched by Mozart) called *The Barber of Seville.* Beaumarchais was the CIA before the CIA. After 1773 he went on a spying mission to London and reported back that the British grip on America was weakening and that Louis XV would be well advised to take advantage of the situation. Louis put Beaumarchais in charge, leaving him to set up a fake firm (Roderigue, Hortales and Co.) for laundering funds and chartering a fleet to land nighttime shipments of arms, ammo and "technical advisers" on the American eastern seaboard. Right under the Brits' noses.

As I mentioned, it all worked rather too well. And also bankrupted France (as a result of which the economy gradually fell apart, and they had their own revolution, in 1789), despite the best efforts of Louis XVI's director general of finance, Jacques Necker, who cooked the books and *almost* convinced everyone the country wasn't going down the tubes. Not almost enough, though.

Earlier on in his career, in 1776, while running the department of Hérault in southern France, Necker had been approached by the young Swiss inventor of a new method of distilling. This fellow was Aimé Argand, and a few years later, he lit up the place with his next gadget, a kind of oil lamp with a round, hollow wick. A circulating current of air kept the flame bright, and a glass chimney kept it steady. Emitting the light of eight candles, the lamp got rapidly used for lifesaving purposes in lighthouses, to illuminate the night shift at the Boulton and Watt steam-engine factory in Birmingham and, in February 1785, to stupefy audiences at London's Drury Lane Theater.

The idea of footlights was pioneered by the theater's actor-manager, David Garrick, whose amazing Shakespeare-

January 1, 4713 B.C., was Scaliger's "Day One" in spades, from which all dates could now be calculated.

an portrayals had introduced the modern, realist style of acting. He quite impressed a newly arrived Swiss painter named Angelica Kauffmann, so much so that she possibly had an affair with Garrick and definitely painted his portrait (and that of almost anybody else of note in England). Kauffmann came from the hotbed of nouveau neoclassicism, the artists' colony in Rome, and she and her new style of painting, inspired by the recent excavations at Pompeii, took England by storm. Not quite storm enough, though. When in 1773 she applied for the commission to decorate Sir Christopher Wren's masterpiece, St. Paul's Cathedral, well, sorry, but she was foreign and Papist, and no thanks.

Wren himself wouldn't have cared. He was so High Anglican he was practically Catholic. He was also one of those Renaissance men of the kind people nowadays say never existed. Maybe not, but the breadth of his scholarship was nothing short of humongous. Apart from inventing pens that wrote in duplicate and odometers for carriages, he was expert in math, barometric studies, exploration, scientific illustration and city planning. Also, he wrote an algebraic work, when he was young, relating to something called the Julian period.

This was a great new chronological scheme, dreamed up in 1582 by Joseph Justus Scaliger, French scholar and peripatetic Protestant exile. The reasoning went that the intervals between historical events could be more accurately determined by a single chronological scheme for the whole of time, instead of pegging things to local chronologies based on coronations or battles and such, because such local chronologies didn't fit with anybody else's. Scaliger calculated his Julian period (named for his father, Julius Caesar Scaliger) by multiplying the 28-year solar cycle (when a date recurred on the same day of a seven-day week) by the 19-year lunar cycle (when the phases of the moon recurred on a specific day in the solar year) by the 15-year "indiction" cycle (based, for reasons best known to Scaliger, on Diocletian's tax census period).

The sum of 28 years × 19 years × 15 years gave a megacycle of 7,980 years. In this megacycle, any date would be pinpointed according to where it stood in each of the three minicycles. Scaliger reckoned the last time all three cycles had coincided (and therefore the last time his megacycle had begun and when the three dating references would have been 1:1:1) was January 1, 4713 B.C. This, then, was Scaliger's "Day One" in spades, from which all dates could now be calculated in a uniform three-cross-reference manner. Well, why not?

Scaliger had learned his stuff at the Calvinist Geneva Academy, and though while there he never managed to meet Isaac Casaubon, they did later strike up an undying scholarly friendship (via more than 1,000 letters) on the subject of Greek and Latin manuscripts and everything else academic. While in Geneva, Casaubon married (and had 18 children by) Florence, daughter of one of Europe's most esteemed editors, Henri Estienne, whose family had been in printing almost since the start, when his grandfather had opened a shop in Paris in 1502. Estienne's greatest claim to fame was that he discovered, translated and, in 1554, printed the work of a sixth-century B.C. Greek poet called Anacreon, who mainly wrote erotic poetry and drinking songs.

Estienne's translation caught on all over Europe, and by the 18th century Anacreon's poetry was so enjoyed in London by well-heeled fun-lovers that in 1776 they formed the Anacreon Society. Aim: meet once every two weeks, get drunk, sing songs. (Forerunner of modern glee clubs.) One of the society's members was a now long-forgotten singer and composer who went by the memorable name of John Smith. When it was decided that the group should have a signature tune, Smith whistled one up, entitled "To Anacreon in Heaven." The song was soon on the lips of everybody, from tipsy clubmen who had survived a night out in London to nervous young American lawyers who had hazarded a night out in Baltimore.

Well, September 13, 1814, *had* been quite a night, during which the British fired 1,800 shells at Fort McHenry. One of the young American lawyers in question, watching from an offshore boat, was so taken with events that he dashed off a commemorative song on the back of an envelope and set it to John Smith's tune dedicated to Anacreon. Today it's better known in the version I was listening to while I watched Old Glory waving aloft in the District of Columbia. Because Francis Scott Key gave the composition a new title: "The Star-Spangled Banner."

Inspiration is flagging, so I'll stop.

Wonders, continued from page 105

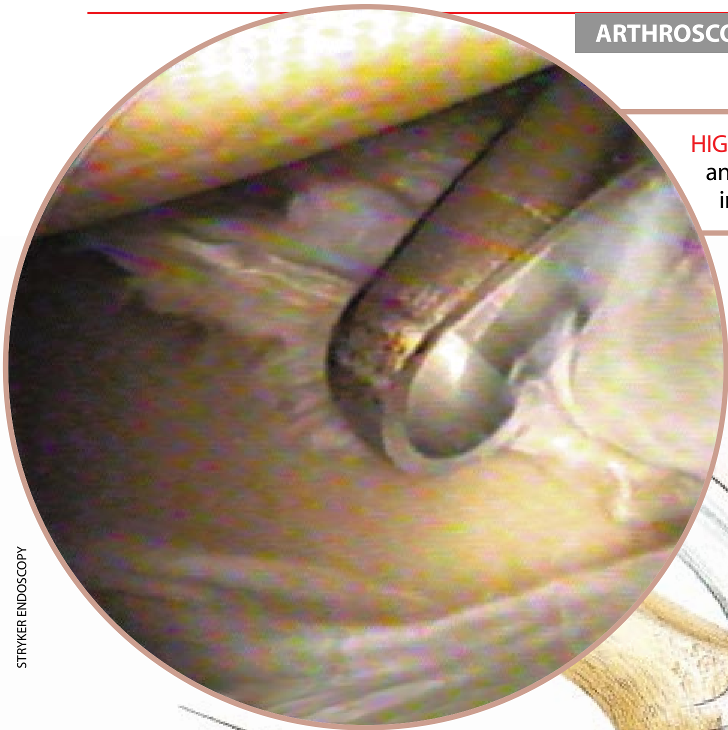
mals or humans but are the "inventions" of nucleotide-protein coding, cellular compartmentation, multicelled organisms with differentiated cells, networks of on-off regulatory genes. So it is with technology. The miracles are not computers or the Net; they are the original ideas that human reckoning can be rendered into movements of cogs and sprockets, that sequences of instructions can be used to weave silk patterns, that networks of electrical on-off switches can be used to pinpoint the zeroes of the Riemann zeta function. The miracles are these new principles, and they arrive infrequently. Evolution merely kludges them together to make new species or new machines in continually novel ways.

If technology is indeed evolving at something like 10 million times biology's rate, perhaps this is too fast. Perhaps we are careening into the future in a bobsled with no controls. Or being rocketed into orbit with no reentry possible. This is frightening, maybe. Until we realize that we use all the complicated, sleek, metallic, interwired, souped-up gizmos at our disposal for simple, primate social purposes. We use jet planes to come home to our loved ones at Thanksgiving. We use the Net to hang out with others in chat rooms and to exchange e-mail. We use quadraphonic-sound movies to tell ourselves stories in the dark about other people's lives. We use high-tech sports cars to preen, and attract mates. For all its glitz and swagger, technology, and the whole interactive revved-up economy that goes with it, is merely an outer casing for our inner selves. And these inner selves, these primate souls of ours with their ancient social ways, change slowly. Or not at all.

My grandfather died in 1968, the year before human beings landed on the moon. He never did realize his ambition to fly in an airplane. At 90, they told him he was too old. The world of his childhood no longer exists. It has all changed. Our world is changing, too, and rapidly. And yet nothing really is changing. For some of us at least, even lovers of technology like me, this is a comfort.

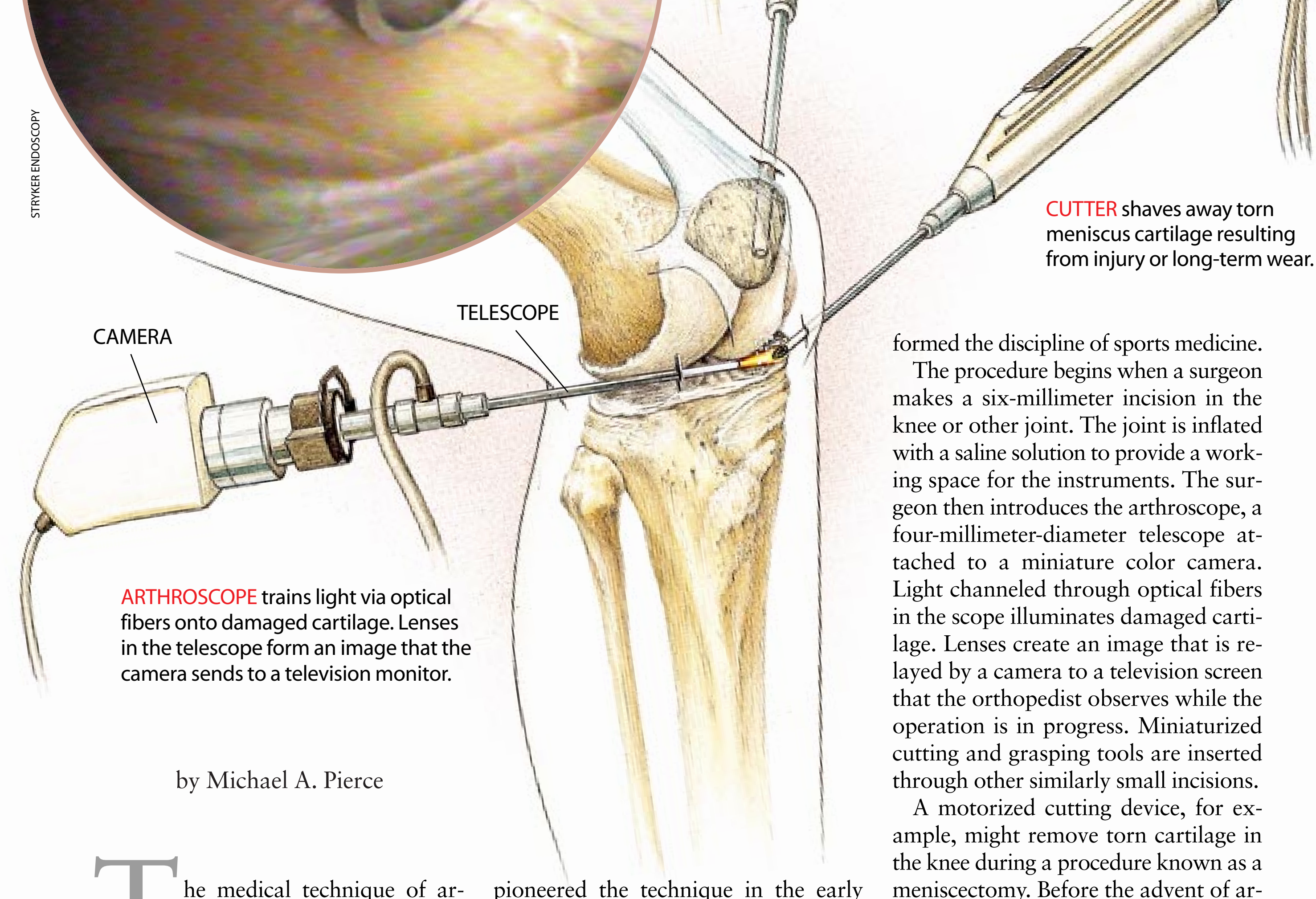
W. BRIAN ARTHUR is Citibank Professor at the Santa Fe Institute in New Mexico. Philip Morrison returns to "Wonders" next month.

ARTHROSCOPIC SURGERY



HIGH-RESOLUTION IMAGERY from an arthroscope gives an orthopedist a clear view of the meniscus cartilage inside a knee so that a cutter can remove tissue.

STRYKER ENDOSCOPY



CANNULA, a type of drainage tube, infuses a saline solution into the knee. The solution expands the joint to provide more working space.

CUTTER shaves away torn meniscus cartilage resulting from injury or long-term wear.

ARTHROSCOPE trains light via optical fibers onto damaged cartilage. Lenses in the telescope form an image that the camera sends to a television monitor.

TOMO NARASHIMA

by Michael A. Pierce

The medical technique of arthroscopy produces a clear image of tissue located inside skeletal joints. The arthroscope, derived from Greek roots meaning "to look at joints," allows a surgeon to see within a damaged knee, shoulder or other joint so that repairs can be made with miniature surgical tools. Its advantages include reduced discomfort for the patient, a shorter postoperative recovery and often a better surgical outcome.

A Japanese physician, Kenji Takagi, pioneered the technique in the early 1930s, but it remained a curiosity until one of Takagi's students, Masaki Watanabe, developed the first modern arthroscope more than 35 years ago. Although crude by current standards, it still produced a good image of knee joints. Orthopedists began to take up the procedure widely in the 1970s, when optical fibers made the use of scopes more practical. Today surgeons perform more than 1.5 million arthroscopies every year in the U.S.—and the technique has transformed the discipline of sports medicine.

The procedure begins when a surgeon makes a six-millimeter incision in the knee or other joint. The joint is inflated with a saline solution to provide a working space for the instruments. The surgeon then introduces the arthroscope, a four-millimeter-diameter telescope attached to a miniature color camera. Light channeled through optical fibers in the scope illuminates damaged cartilage. Lenses create an image that is relayed by a camera to a television screen that the orthopedist observes while the operation is in progress. Miniaturized cutting and grasping tools are inserted through other similarly small incisions.

A motorized cutting device, for example, might remove torn cartilage in the knee during a procedure known as a meniscectomy. Before the advent of arthroscopic surgery, a meniscectomy involved a many-centimeter-long incision along the side of the knee, with a recovery period that could last months. An arthroscopic operation requires a recovery period of only a few days. The technique has given meaning to the notion of minimally invasive surgery.

MICHAEL A. PIERCE is vice president of business development for Stryker Endoscopy in Santa Clara, Calif.