SCIENTIFIC AMERICAN

APRIL 1992
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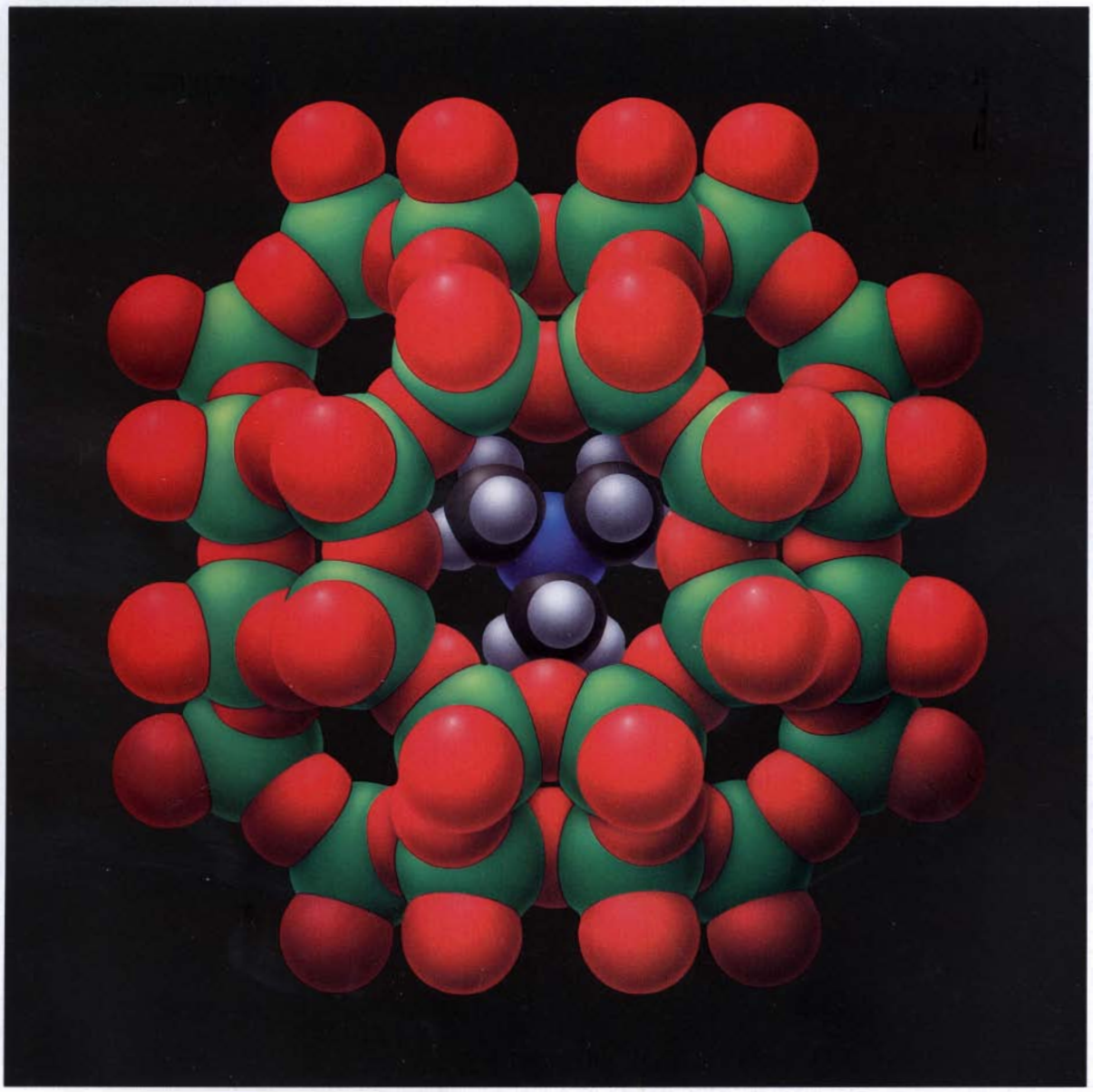
The life cycle of the drifting continents.

Debate: Is an African "Eve" the mother of us all?

The painful reality of phantom limbs.



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All it takes is some rapid eye movement around the cockpit to see what's new. For safety's sake, there's a *newly available front passenger-side air bag*. A driver-side air bag comes standard. Both supplemental restraint systems should be used with your safety belt.

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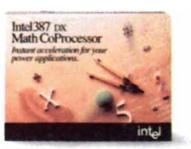

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SCIENTIFIC AMERICAN

April 1992 Volume 266 Number 4

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DEPARTMENTS

"The Earth/From Space" A Satellite Composite View of Earth ©Tom Van Sant/The GeoSphere Project, Santa Monica, CA 800 845-1522

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A Very Special Event in Scientific American

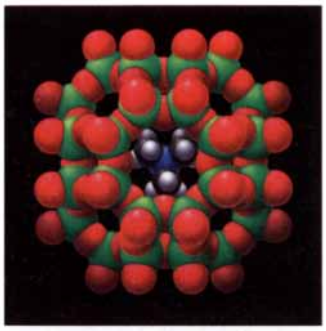
Appearing in the June 1992 issue of Scientific American will be *Meeting the Challenge of Sustainable Development*, a special advertising supplement produced in conjunction with the United Nations Conference on Environment and Development. The supplement will promote the 1992 Earth Summit in Rio de Janeiro and the emerging concept of sustainable development. It will open with a special introductory message from UNCED Secretary-General Maurice Strong, whose office is collaborating with the producers of the special supplement, World Communication Works, of Stamford, CT, and Chuck Wilhelm & Associates, of San Jose, CA.

Sponsoring firms will receive 50% of committed display ad space for executive commentaries to highlight how they are advancing corporate environmental responsibility and sustainable development. World Communication Works will assist sponsors to produce their executive commentaries.

Ad Closing Date: March 31, 1992

For more information, please contact Robert F. Gregory at Scientific American at 212-754-0522, or Ken Smalheiser, President of World Communication Works, at 203-356-1931.

SCIENTIFIC AMERICAN



THE COVER illustration is an atomic model of a solid acid catalyst called zeolite Rho. Such agents speed up chemical reactions and may obviate the production of certain environmentally adverse by-products (see "Solid Acid Catalysts," by Sir John Meurig Thomas, page 112). In this image the central compound, trimethylamine, which is unwanted, fits into a pore of Rho so tightly that it cannot escape. Only smaller, desired forms of methylamine are released. This model was provided by David R. Corbin, J. C. Calabrese and Eric Swanson of Du Pont.

THE ILLUSTRATIONS

Cover illustration by Tomo Narashima

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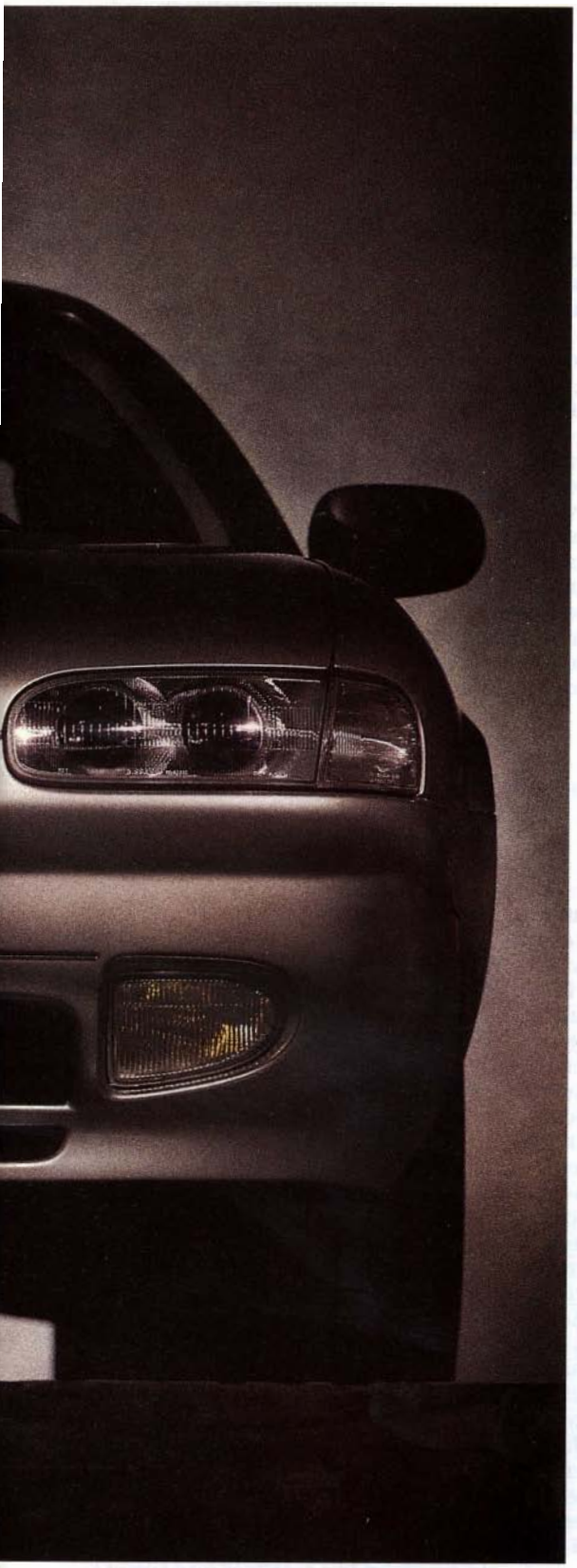

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Of course, the J30 is also equipped with a long list of impressive technological features. Like the variable valve timing system and the double isolated multi-link rear suspension. Three-sensor, three-channel ABS braking. And both driver's and passenger's side airbags.

But, in the end, what's really appealing about the new J30 is something far more than all its individual parts. Something indefinable. It's what happens when you cross sheet metal and desire.

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LETTERS TO THE EDITORS

Targeting Gun Control

In reference to "Firearms, Violence and Public Policy," by Franklin E. Zimring [SCIENTIFIC AMERICAN, November 1991], seldom have I seen such flawed, misleading and patently false propaganda passed off as a balanced study. Nowhere does Zimring mention current public policy regarding the private ownership of firearms, which is clearly stated in the Second and Fourteenth Amendments to the U.S. Constitution. Judicial research and Supreme Court decisions have established that the right to keep and bear arms is granted to each citizen.

Although Zimring states that areas in the Northeast with strict gun laws had lower handgun crime rates, just the opposite is true. Crime rates rose in areas with strict gun laws, particularly during the period after their adoption. Conversely, Florida adopted a law in 1988 that made it easier for citizens to obtain permits and carry concealed weapons. The state's homicide rate declined 6 percent between 1987 and 1990, even though Florida figures highly in the drug-trafficking problem.

JOHN E. KENNEY
Redwood City, Calif.

If scientific research on the firearms issue was the goal, it is unfortunate that *Scientific American* chose Franklin Zimring to write about it. His simplistic research efforts, fashioned with an open bias for handgun bans, ended in the mid-1970s, when he discovered that the federal gun laws weren't working. Since then, he has learned next to nothing from the ongoing research.

He may even have forgotten some of it. After all, in 1969 he asserted that there were 24 million handguns. Now he asserts that there are 35 million and that there may be as many as 50 million in 50 years. Leaving aside most estimates, which put the current figure at 60 to 65 million handguns, his figures assume that only about a net half-million handguns were added to the pool every year since 1969, even though about two million new handguns are produced every year.

Zimring states without evidence that more guns mean more deaths, thereby disregarding all the studies that show no relation between firearms availability and homicide. The charts of his cited source do not even pretend to show a relation between firearms ownership and homicide or other violent crimes, only between ownership and firearms-related crime—thereby ignoring three fourths of violent crime. His race- and age-group charts of mortality do not include data showing that the highest levels of mortality are among those males with the lowest levels of firearms ownership.

Had *Scientific American* waited a month, it could have reviewed *Point Blank: Guns and Violence in America,* by Gary Kleck, which summarizes his own and other research, all of which suggests that gun availability is not associated with higher rates of homicide or other violent crimes and that firearms represent the best means of protection from crime. It is unclear why *Scientific American* preferred Zimring's pseudoscientific assumptions rather than enlisting the aid of science.

PAUL H. BLACKMAN
National Rifle Association of America
Institute for Legislative Action
Washington, D.C.

Zimring replies:

Kenney believes the constitutional values to be found in his reading of the Second Amendment render any relation between guns and violence irrelevant to American public policy—a position widely held by those who object to gun control, which has been rejected in every major test of gun-control laws in the courts. If one believes the Second Amendment forbids regulation of firearms, data are of no consequence.

I did not stop publishing research in 1975; Blackman may have just stopped reading it. The basis for my present estimate of 35 million handguns extant is my analysis of the age distribution of confiscated handguns. The 1969 estimate of 24 million handguns was made by averaging 20th-century production with poll data on handgun ownership. What was then missing were any data from which to estimate the useful life of a handgun in the civilian inventory. An analysis of handguns confiscated by police during the 1970s showed that most were less than four years old when they were picked up.

The average risk-life of a handgun may therefore be less than a decade. If so, the two million handguns introduced every year would have enlarged the total inventory in the early 1970s by taking the place of a much smaller cohort of handguns introduced in the early 1960s. Now that the rates of introduction have been stable for a long period, however, the net increase should be small. The population of handguns in the U.S. probably expanded very rapidly in the late 1960s and early 1970s but much more modestly since then. The key issue is the average time that a handgun remains at risk. Perhaps Blackman should direct some of the National Rifle Association's research resources toward studying that question.

With Occam's Razor?

I was surprised to learn that the barber paradox described by Paul Wallich in "Silicon Babies" [SCIENTIFIC AMERICAN, December 1991] was a paradox at all. "The barber shaves every man who does not shave himself," the problem states. "Who shaves the barber?"

I'm inclined to think the barber shaves herself.

BARAK A. NELSON
Missoula, Mont.

A Mathematical Inequality

In her otherwise admirable article on the life of Sophie Germain [SCIENTIFIC AMERICAN, December 1991], Amy Dahan Dalmédico repeats the worn-out stereotype that "her charm [was] appreciated by all." Why is charm never ascribed to male mathematicians?

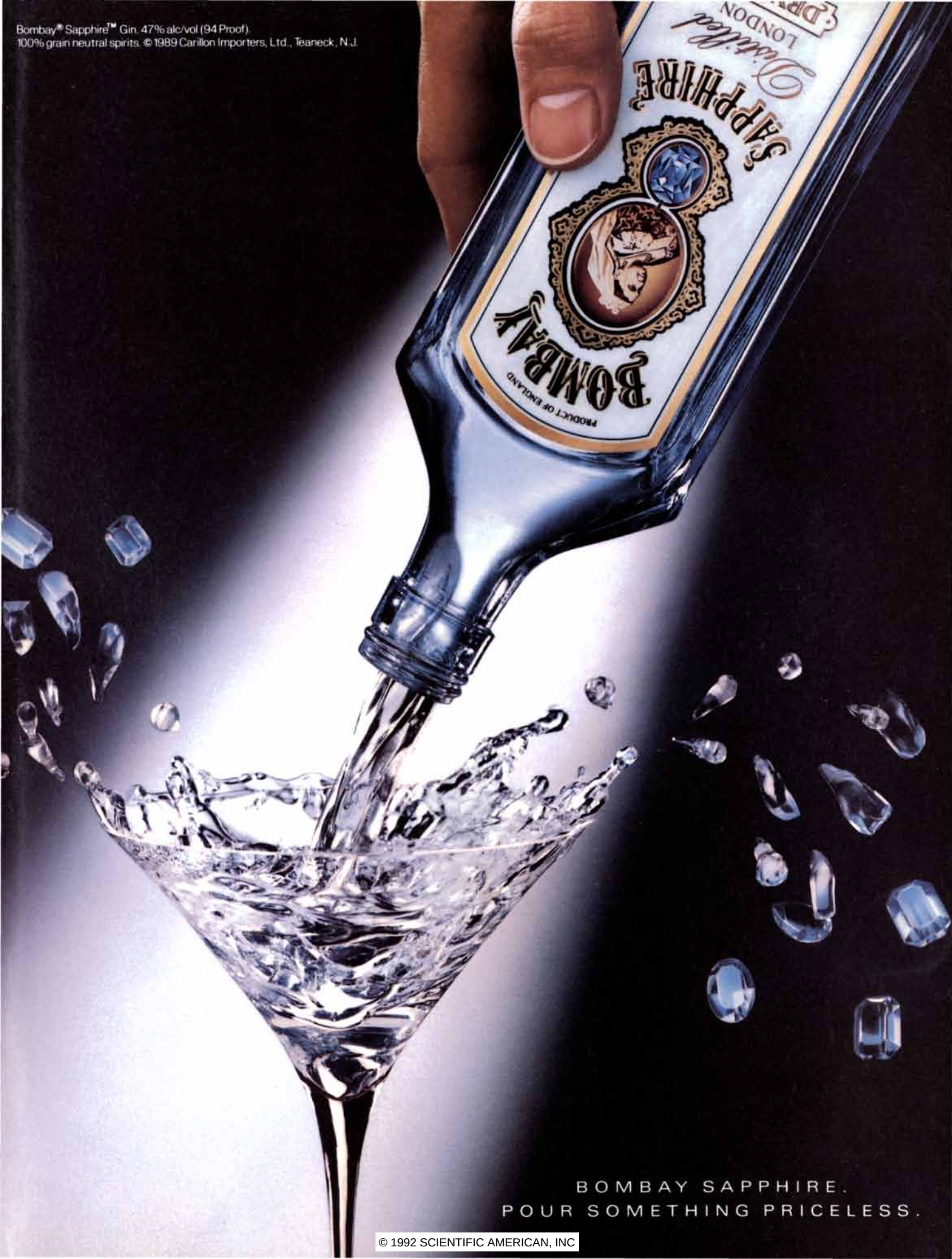
MORTON NADLER
Blacksburg, Va.

ERRATA

The sea turtles on the cover of the January issue are not hatchlings, as is stated on page 8; they are two or three years old.

The structure described as a nucleosome on page 131 of "Living Together," by John Rennie [January], is actually called a nucleomorph.

The engraving on page 118 of the December 1991 issue depicts the sociologist Charles Fourier, not mathematician Joseph Fourier as intended.



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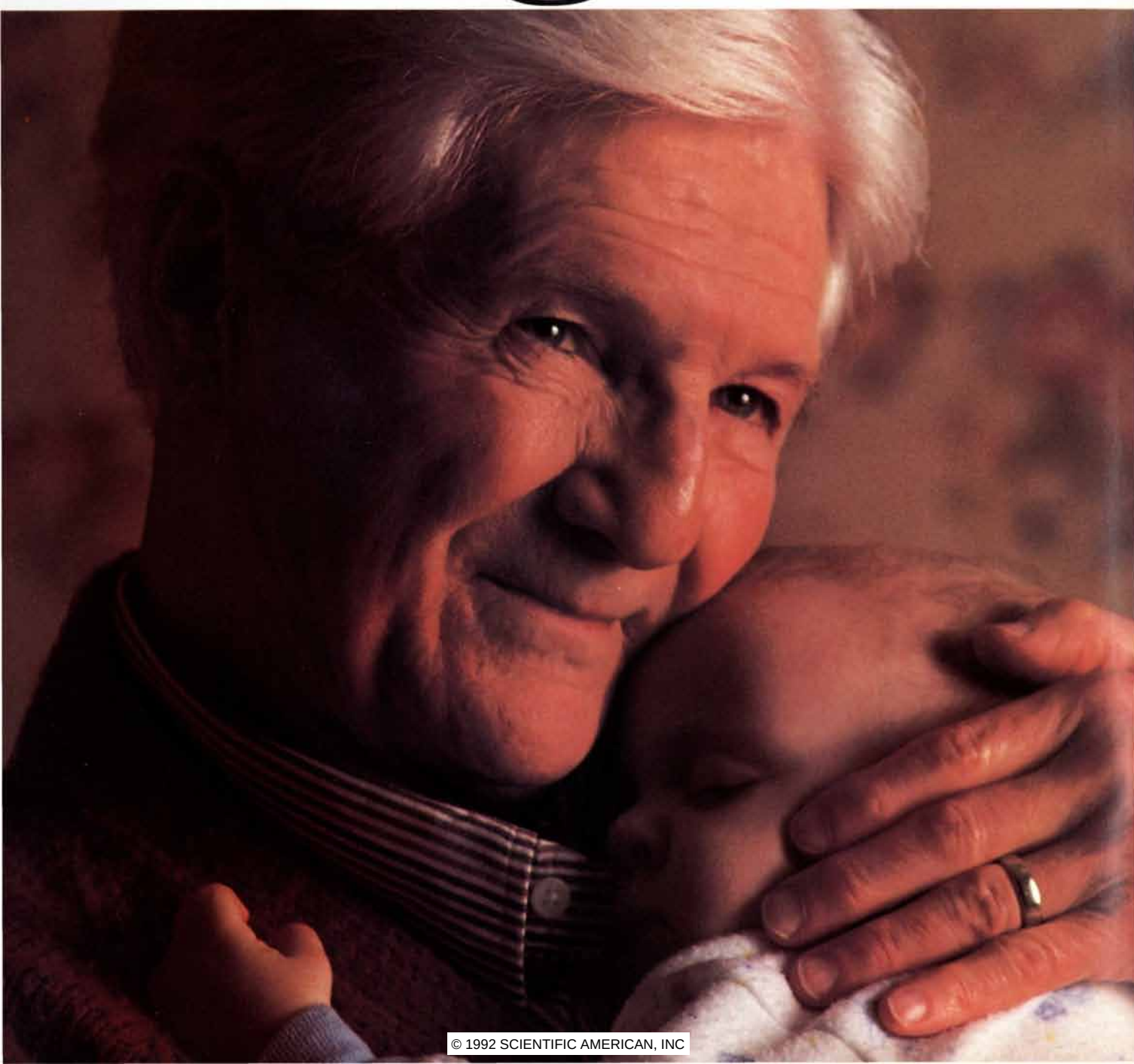

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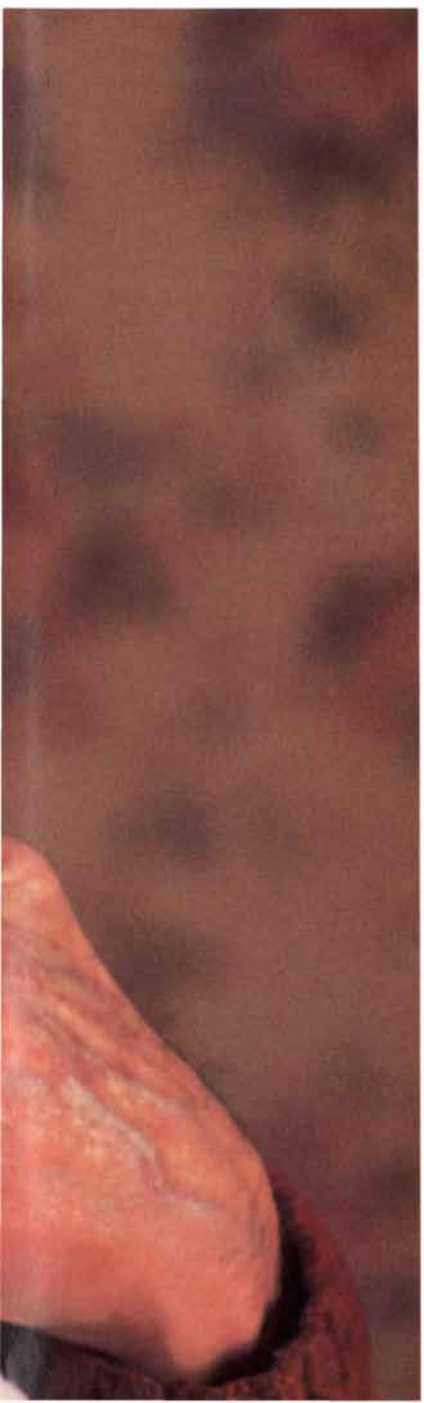

With each passing decade, people have been able to hold onto more of life's rich moments.

In 1950, the average life span of men was 65. Today it's approaching 80, due in many ways to advances in medicine. At the forefront are pharmaceutical companies who are making the nation's largest investment in drug research.

We now have 329 medicines in test for 45 diseases of aging. These efforts always hold hope for breakthroughs. Yet the process is slow and difficult, with only a few of the thousands of compounds developed ever achieving success.

This exhaustive, high risk research increases the industry's cost of doing business, and in turn affects the price of drugs. But it also contributes to saving lives, while saving millions in health costs by eliminating or reducing the need for surgery and shortening hospital stays.

To learn more about pharmaceutical research, and the critical role it plays in health care, call or write for our free booklet, "Good Medicine." The Pharmaceutical Manufacturers Association, 1100 15th St, NW, Box I, Wash., DC 20005. 1-800-538-2692.

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50 AND 100 YEARS AGO

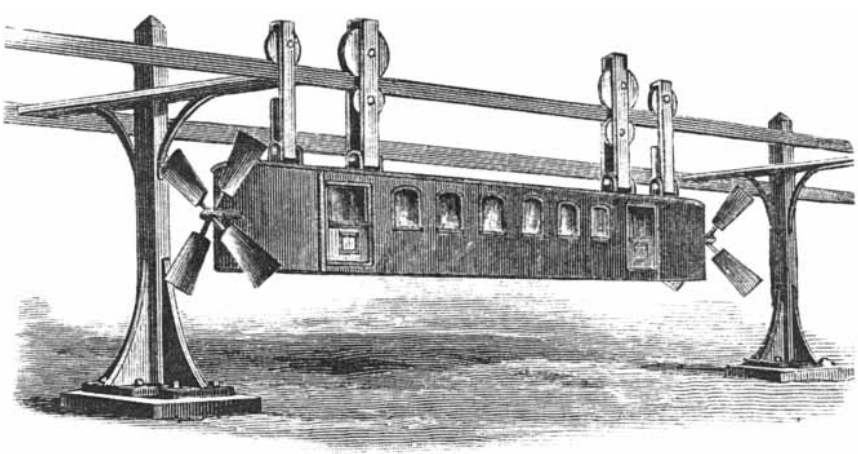
APRIL 1942

"We question whether any reputable publication has knowingly violated the code of honor voluntarily assumed by most editorial desks long before hostile action against the United States. So far as Scientific American is concerned, no illustrations or text pertaining to our national defense efforts prior to Pearl Harbor, or to our war activities since that date, have appeared within our pages which have not received the approval of the proper officials of the Army, the Navy, or the Marine Corps."

"Octane numbers are very deceptive; they do not mean what they say because the power goes up much faster than the numbers. Triptane, with a power output of 50 percent more than 100 octane fuel, would actually have an octane number of about 110. The best that Hitler can get today is 87 octane fuel and this is 30 percent less efficient than 100 octane variety. This means that Hitler's planes must be content with less speed, lower ceilings, smaller cruising ranges, longer times for climbing to a given altitude, and more wear and tear on the motors—all to the tune of some 30 percent less in efficiency. What could we do if we could utilize our now available 110 octane fuel which should give us some 80 percent more effective power than Hitler can now get?"

"The case against flies as the culprits that spread infantile paralysis is strengthened by a discovery reported by Dr. Albert B. Sabin and Dr. Robert Ward, of the Children's Hospital Research Foundation and the University of Cincinnati College of Medicine, in the current issue of *Science*. Previous discovery of the infantile paralysis virus in flies was made in rural areas. Flies caught in Cleveland and Atlanta in the neighborhoods of infantile paralysis patients were infected with the virus of the disease. Discovery of the virus in city flies is considered more significant, especially since the infected flies were found in modern neighborhoods with good plumbing and in which several children had mild illnesses that might have been abortive infantile paralysis."

"When a torpedo is discharged, an amazing number of things begin to happen inside it, in an incredibly short time. A starting lever, tripped by the missile's forward movement, opens a valve, and a blast of compressed air starts the main engine. Another unit provides a highly inflammable fuel spray. Two slow-burning cartridges explode, go on burning like candles, to ignite this spray. In the same split-second an ingenious self-starting, self-regulating water-pot begins spraying water on the flame. Only a few feet away, remember, is 600 pounds of high explosive. The water-pot supplies water to make steam and, by regulating the volume of its spray, keeps the temperature in the fire-box exactly at 1250 degrees—no higher. The steam-gas-compressed-air mixture slams into the main engines with such force that 400 horsepower is instantly generated, quickly driving the torpedo's speed up to nearly a mile a minute."



Anderson's elevated railway

SCIENTIFIC AMERICAN

APRIL 1892

"Our attention is called to an invention by which an ordinary clock is practically magnified to such a size as to permit of its being seen for a radius of fifty miles around. The invention employs a second train of clockwork which is controlled by the clock proper, and is put in motion every minute, when it whizzes around and actuates an electric flashing lens. The beam of light reflected into the sky goes through the movement of a striking hammer when the clock is indicating the even hour. Another symbol is used for every complete interval of five minutes, and yet another for odd minutes. The clock would not only permit of clocks being synchronized, but watches too, and for no charge."

"A sportsman engaged in hunting elephants had approached a large tusker, when he found to his chagrin that he had dropped his ammunition, so that he could only lie concealed and feast his eyes upon the huge animal. His disappointment was partly compensated for by observing the elephant informing the herd that danger was lurking near it. When the tusker recognized the presence of its enemy it stopped feeding, raised the tip of its trunk cautiously, and, in a low, suppressed, but penetrating tone, uttered with its lips the sound 'prut,' which it repeated so that it somewhat resembled the twittering of a bird. The sound was immediately understood by the herd, which moved quickly but silently away, followed by the sentinel."

"The illustration represents a form of elevated railway construction designed to permit of conveniently regulating the speed of the car, while the arrangement is such as to reduce friction to a minimum. The improvement has been patented by Mr. Anders Anderson, of Blossburg, Montana. It is designed that the car shall be driven by a motor in each end of the car, each motor rotating propeller wheels."

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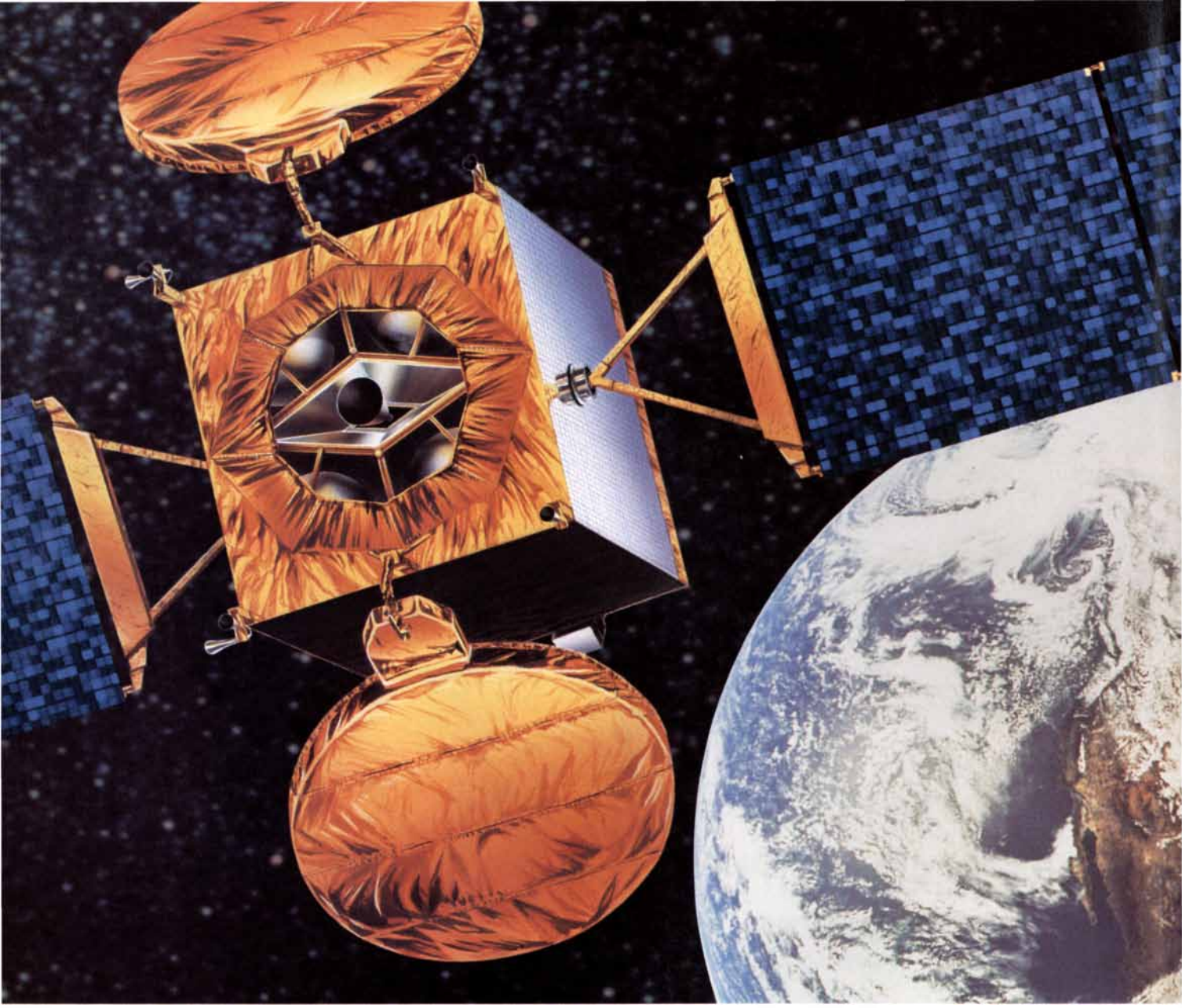

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By the end of 1993 we will be orbiting over one billion dollars in new spacecraft, upgrading our ground control facilities, and expanding our communications capabilities.

We're on a mission to maintain our renowned leadership in every aspect of satellite communications. The services we offer our customers will continue to be the most advanced, the most reliable, and the best managed available.

To realize that mission, we will continue to commit everything we have. There is no other way at Hughes Communications. That's why the future belongs to us and our customers. And that future is right on schedule.

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Brain Drain

Hard times for science in the former Soviet Union

RESEARCHERS at once top-secret military complexes, such as Cheliabinsk, are being courted by U.S. companies. Photo: V. Velengurin/Sovfoto.

The chaotic push in Russia and the other nations of the defunct Soviet Union to achieve prosperity through economic shock therapy has put a vital asset at risk: the fragmented empire's illustrious scientific establishment. Visiting Russian officials, émigrés and U.S. researchers who have recently returned from the Commonwealth of Independent States bring reports that add up to a picture of pervasive, rapid disintegration.

Many research institutions stopped paying salaries last December and have no hard currency to maintain Western equipment. "We haven't got an economic strategy," says Zhores I. Alferov, director of the Ioffe Physico-Technical Institute in St. Petersburg and a vice-president of the Russian Academy of Sciences, which supports most of the civilian research institutes in the C.I.S. "We receive funds month to month. Many institutes can't even pay for electricity and heating."

Alferov's institute is not alone, according to Paul R. Josephson, a science historian at Sarah Lawrence College, who returned early this year after three months spent studying the state of science in the C.I.S. Josephson reports that researchers at the Ukrainian Physico-Technical Institute in Kharkov idle away the hours because there is no power for their linear accelerator. Workers in defense research were hit particularly hard when the C.I.S. slashed its military research and development budget by 50 percent.

As funding dries to a trickle, outstanding obligations have become an acute problem. According to Glenn E. Schweitzer, director of the Office for Central Europe and Eurasia at the U.S. National Academy of Sciences, the new Russian Academy of Sciences inherited a foreign debt for publications from its Soviet predecessor. Alferov's institute has let all its subscriptions to Western journals lapse, and researchers are having difficulty maintaining working computers and photocopying machines. Biological laboratories lack vital reagents, notes Gerson S. Sher, senior manager of the Russia program at the U.S. National Science Foundation, and "research in these laboratories is coming to a halt."

Travel is another problem. Although official restrictions have disappeared, Alferov points out that a round-trip Aeroflot ticket from Moscow to New York until recently cost about 100,000 rubles—about 10 years' salary for many scientists. Prices of tickets have fallen threefold since January but are still out of reach for individuals.

The new government has been trying to help. Russian president Boris N. Yeltsin granted some institutes of the Russian academy tax-exempt status last November and allowed them to receive special hard-currency funds to maintain foreign equipment. The academy has prepared budget proposals that include large salary increases for scientists, Alferov says. A senior physics researcher in the C.I.S. now earns up to 1,500 rubles per month, less than a bus driver, according to Mikhail B. Voloshin, associate director of the Theoretical Physics Institute at the University of Minnesota. But even a bus driver's pay does not go very far: prices increased in Moscow by 350 percent during January alone.

Many researchers from the C.I.S. who have good contacts with foreign colleagues have chosen to weather the storm abroad. Sher says he was told seven out of the nine senior researchers at one laboratory at the Institute of Molecular Genetics in Moscow were working outside the country recently.

Such exits have aroused fears of a brain drain, one that could leave the C.I.S. lacking the research talent it needs to compete economically. Most of those working abroad intend to return when times are better, Alferov maintains. But he and Josephson agree that economic privations could tempt many demoralized young researchers to leave science and seek more lucrative endeavors.

Many obstacles thwart private and institutional efforts to help. Up to 40 percent of the value of foreign funds deposited in bank accounts in the C.I.S. are automatically converted into rubles at an unfavorable rate, Schweitzer notes. Some philanthropic organizations are therefore attempting to provide aid in kind. The MacArthur Foundation is planning an effort to underwrite for up to two years lapsed subscriptions to academic journals published by U.S. scientific organizations. The American Chemical Society estimates that its canceled

DIAMANTE.
THE APPRAISALS ARE IN.

Appraisals from experts are always enlightening. On the Diamante, they have been overwhelmingly glowing.

Motor Trend reported that "the Diamante's sharply defined performance enables a driver to feel eminently in control." Meanwhile, the interior design ensures that "driver and passengers are utterly pampered."

The Diamante is "a well-bred automobile," according to *Car and Driver*. "The ride is controlled, yet magic-carpet silky...the leather interior is a knockout...whisper-quiet."

And after road-testing the Diamante LS, with its 202-horsepower V6 engine, ABS brakes, exclusive TCL™ traction control,* driver-side air bag and numerous luxury amenities, *Road & Track* simply said, "We are mightily impressed."

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and unpaid C.I.S. subscriptions for 1991 are worth $177,000.

The Carnegie Corporation of New York has spent several hundred thousand dollars for each of the past several years to establish electronic mail links with the C.I.S. Carnegie is also making supplementary grants to U.S. researchers to support collaborations with investigators in the C.I.S. And the American Institute of Physics is donating subscriptions to editors of journals that it translates and distributes in the West.

In a display of entrepreneurial flair, Voloshin and Aferov are eyeing a potentially rich source of funds—those provided for basic research by the U.S. government itself. With labor costs in the C.I.S. at least 10 times lower than they are in the U.S., they argue, U.S. research dollars spent in the C.I.S. would go much farther than they do at home. Furthermore, Alferov asserts, the U.S. could learn from C.I.S. expertise in areas such as plasma physics, high-energy physics, spectroscopy and electronics research. The NSF does support some 40 collaborative basic research projects that involve C.I.S. researchers, according to Sher, and the National Institutes of Health has already awarded grants of more than half a million dollars for collaborative research with C.I.S. scientists. But the U.S. does not fund the foreign workers directly.

Nevertheless, Russian and other C.I.S. scientists may tap American and European bounty in other ways. Congressman George Brown of California, chairman of the Science, Space and Technology Committee, has proposed establishing a $200-million U.S.-Russian endowment fund to support collaborative research. French president François Mitterand has proposed an international fund to support science in the C.I.S.

The private sector has evinced interest, too. Several U.S. defense companies are already kicking the tires at former Soviet military research institutes. Among the browsers is TRW, Inc., in Redondo Beach, Calif. Lewis R. Franklin, TRW's vice president for space and defense, says on a recent visit he formed the impression that "they can declassify everything." TRW now has a provisional agreement on a joint civilian space venture with former Soviet military and space organizations, Franklin says, and is awaiting "a favorable nod" from the Pentagon.

Such a venture appears to fit well with the administration's concern that the likes of Saddam Hussein and Muammar Qadaffi will make work for idle C.I.S. scientific hands. Secretary of State James Baker has proposed establishing a clearing house to match up newly unemployed military researchers with vacancies in areas such as weapons disassembly. And Pentagon officials are considering buying into Soviet aerospace technology, such as space-based nuclear reactors and conventional as well as exotic propulsion systems.

Voloshin agrees that the danger posed by unemployed weapons scientists is real. But the U.S. should assume a larger role as well, he suggests. "In spite of the short-term benefits to the U.S. of a brain drain from the former U.S.S.R.," Voloshin says, "in the long run, it cannot be beneficial to allow the destruction of science there." *—Tim Beardsley*

The Plankton Stalkers

Plankton, plankton everywhere but not a patch of it to see" has been the lament of some oceanographers. These mite-size plants and animals form the basis of the marine food web, but little is known about their density or distribution—in particular, whether plankton occurs in small patches and clumps that allow marine organisms, including zooplankton, to graze on it.

A system called a video plankton recorder, or VPR, may help oceanographers answer those questions. Developed by researchers at Woods Hole Oceanographic Institution, the technology promises to revolutionize the study of plankton. "Even humans hanging out of a submarine can't see things as clearly as the VPR can," comments Peter H. Wiebe, chairman of the biology department at Woods Hole.

By towing the VPR behind a research vessel, scientists can view their subject matter in its natural environment. The device, invented by biologists Cabell S. Davis and Scott M. Gallager, consists of a red strobe light that is synchronized with the shutters of four video cameras, each set to a different high magnification. The strobe flashes 60 times a second, permitting the tracking of rapidly moving creatures. The VPR can record animals ranging in size from less than one millimeter to one centimeter, Davis says.

This view of plankton is not available from other technologies. Nets smear samples as well as picking up and mixing together creatures from different levels of the water column. Nets also obscure densities: everything caught becomes one messy mass. Even a more refined net system that is opened and closed electronically—called a mocness, or the "mocness lonster"—destroys fragile animals. Higher-tech systems also have shortcomings. Optical particle counters do not produce pictures. And for now at least, acoustic systems indicate density, but not composition.

UNIDENTIFIED CREATURE found with the video plankton recorder.

In its few trial runs, VPR has already surprised investigators. Davis was able to see the orientation of zooplankton, information lost in nets. And "we saw lots of organisms we couldn't identify," Davis notes. Of particular significance was the observation of planktonic micropatches. The existence of such small clusters has been hypothesized, but "these data show that microscale patchiness does, in fact, exist in the ocean," Davis reports.

One drawback to the VPR, Wiebe says, is that only small amounts of water are sampled. And, Davis adds, creatures are not caught, so they cannot be examined later. Davis and Gallager ultimately intend to preserve everything they photograph in a trap. Although their initial attempts to do so failed, they revealed a fascinating fact about zooplankton.

When Davis tested the equipment, he found that zooplankton easily avoided the trap. "The dexterity of these bugs was truly amazing," Davis describes. Imagine you have shrunk to one millimeter, he explains. A nozzle measuring 60 feet across comes at you at 2,000 miles an hour. When it is 60 feet away, you accelerate from a dead stop to more than 2,000 miles an hour in the opposite direction, in one sixtieth of a second. Creatures do not avoid the VPR, however. Says Davis, "I really think we have a 'Stealth' plankton recorder." *—Marguerite Holloway*

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New Orleans, LA 36857

May 15, 1992

Steve Sullivan
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Court C	3400	Y	Y	52nd	$1000

Word for Windows has an on-screen "Tables" function that lets you add rows almost instantly.

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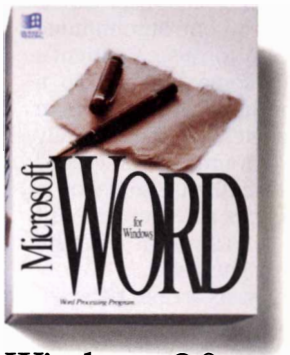

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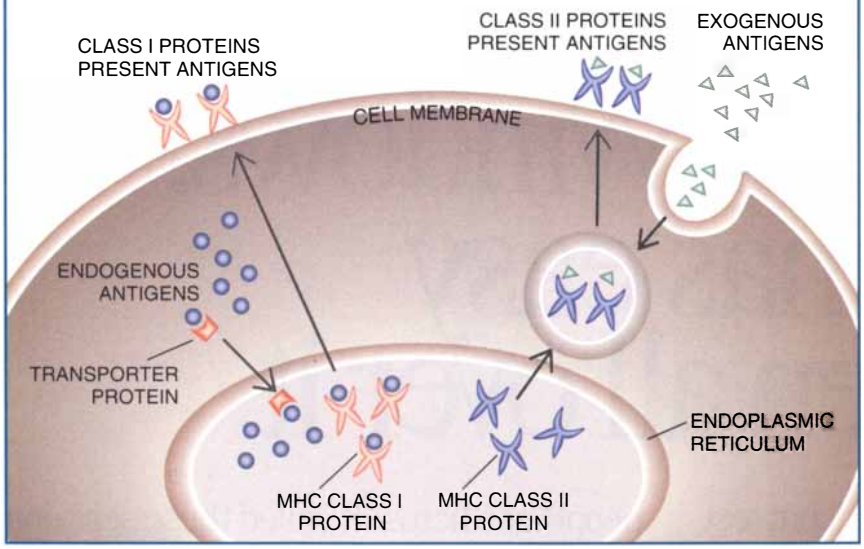
Pathways for MHC Proteins

MHC proteins, which regulate the immune system, must be linked to antigens to reach the cell surface. The class I proteins, unlike the class II proteins, rely on transporter molecules to bring them antigens. A new theory suggests that defective transporters and MHC class I deficiencies could cause autoimmune disorders.



First-Class Culprit

An autoimmunity theory meets with resistance

Immunologists do not know why the immune system turns against the body in diseases such as type I diabetes, multiple sclerosis and rheumatoid arthritis. Still, after years of molecular detective work, they have some dearly held suspicions.

That is why Denise Faustman of Harvard Medical School and a team of other immunologists have upset many of their colleagues with the claim that researchers have overlooked a prime suspect in the case of type I diabetes. If Faustman's group is right, its discovery calls into question some past assumptions about the mechanisms underlying many autoimmune diseases. Many experts contend, however, that Faustman's evidence is far from conclusive.

Type I diabetes seems to occur when disease-fighting cells called *T* lymphocytes destroy the islet cells of the pancreas that secrete insulin. In the absence of insulin, blood glucose levels can skyrocket with serious, even fatal consequences. No one fully understands why the immune system attacks the islet cells, but researchers have found clues. Human diabetics and nonobese diabetic (NOD) mice, a special laboratory strain that has a predisposition to develop the disease, appear to have abnormalities in their genes for MHC class II (major histocompatibility complex) proteins.

MHC class II proteins on certain cells present antigens, bits of molecular flotsam, that the cells encounter in the blood and tissues. In so doing, the proteins alert *T* cells to the presence of infections in the body. Immunologists now generally accept that a defect in MHC class II proteins can make mammals susceptible to diabetes by making it easier for the immune system to mistake healthy islet cells for diseased ones.

Faustman's study, which appeared last December in *Science,* is controversial because it shifts the blame for autoimmune diabetes from MHC class II proteins to different members of the same molecular family, MHC class I proteins. Like their siblings, MHC class I proteins appear on cell surfaces and regulate the immune system, but their job is to present antigens from a cell's own molecules. In the thymus gland, they seem to help teach young *T* cells to distinguish antigens that belong to the body from those that do not.

By incriminating class I MHC proteins, Faustman is proposing that *T* cells are not just tricked into attacking islet cells in diabetics. Instead, she suggests, the *T* cells may never properly learn to recognize antigens from the islet cells as normal parts of the body. Although the work of her group focused on diabetes, the same mechanism could play a part in other autoimmune diseases.

Faustman and her colleagues implicated MHC class I protein by showing it was unusually deficient in human diabetics and in people at extremely high risk for diabetes. When they looked at a strain of mouse that lacks MHC class I protein, they found that the animals had a mild tendency to develop diabetes.

Further studies on NOD mice, which also appeared deficient in MHC class I protein, suggested to the researchers that the animals had a mutation in a so-called transporter protein, which assists with the production of MHC class I molecules by linking them to antigens. Because MHC class I proteins are not stable unless attached to antigens, a defect in transporter proteins might be able to lower MHC class I production and cause immunologic problems.

The new findings raise many questions. MHC class I proteins present all the self-antigens in the body, not just those associated with diabetes. If they are in short supply, a broad range of autoimmune disorders would seem likely to strike type I diabetics. In fact, says George Eisenbarth of the Joslin Diabetes Center in Boston, a co-author of the Faustman study, clinicians have noted that susceptibility to one autoimmune disease does seem to raise a patient's susceptibility to some others. "To a large extent, both mice and men in whom type I diabetes develops actually have a series of autoimmune illnesses," he explains. "Which disease someone is going to express has a certain amount of randomness to it as well as a certain amount of genetic control."

Many immunologists are not persuaded by Faustman's theory or evidence. Edward H. Leiter of Jackson Laboratory in Bar Harbor, Me., who has long studied the genetic causes of diabetes in NOD mice, notes that the transporter mutation cited by Faustman does not seem to induce any defects in the encoded transporter protein. It is therefore unclear why the mutation would reduce MHC class I levels. Indeed, some other investigators report that in their experience, NOD mice do not seem deficient in MHC class I protein at all.

Thomas Spies of the Dana-Farber Cancer Institute in Boston, an authority on transporter proteins, says although a few variant forms have been identified in humans, none has correlated significantly with diabetes. Such investigations are still in their infancy, he cautions, and no one has yet systematically searched for transporter protein defects in diabetics. Nevertheless, the strongest genetic indicators of a person's susceptibility to diabetes seem to be associated with MHC class II proteins.

The *Science* paper points out that in the mouse, the mutant transporter gene flanks the MHC class II gene region, and the work suggests this close association may have misled some researchers about the connection be-

tween MHC class II protein and diabetes susceptibility. Eisenbarth, however, does not dismiss the role of MHC class II protein. "There certainly is a lot of room in the MHC for multiple, different kinds of effects," he says. "I don't think an influence for class I in any way rules out or mitigates that class II can also be very important."

Eisenbarth believes a necessary next step is an investigation of what causes the lack of MHC class I protein in human diabetics—whether it is truly a malfunction of the transporter proteins or something else. Genes alone do not seem to govern the phenomenon: in some pairs of twins, only one is diabetic, and only the diabetic twin shows diminished levels of MHC class I protein. Some other influence apparently triggers the loss of the protein. The new study by Faustman's group may or may not bring researchers closer to solving the mystery of what causes type I diabetes and other autoimmune diseases, but it has certainly enlarged the circle of suspects. *—John Rennie*

A Census of Stranglers

Well-placed fig leaves are supposed to have protected the modesty of Adam and Eve, and now it seems they may have been keeping secrets of their own as well. James D. Thomson of the State University of New York at Stony Brook and a team of other ecologists have found that strangler figs, semiparasitic trees that grow throughout the tropics, are often colonies of individual plants that merge into a single entity.

Their discovery, which was reported in *Science,* highlights the difficulty of measuring biodiversity, let alone preserving it. Conservationists worry about the survival of the strangler fig because its life cycle is fragile and its fruit is a dietary staple of tropical mammals and birds.

The figs propagate from seeds in the animal droppings that collect in the crotches of trees. They extend roots that fuse into a woody lattice around the trunk of the host. Eventually the fig chokes off the tree's access to nutrients—hence, the fig's gruesome epithet. Thomson had wondered whether the roots from more than one fig seed ever fused in a mature fig tree. "It's the kind of question a lot of tropical biologists have undoubtedly speculated about over a beer," he says, but no one seemed to have tested the idea.

So Thomson and his collaborators went to Panama and checked for genetic differences among the branches in 14 fig trees. Only one of the trees proved to be a single individual—most were two or three fused plants, and one tree seemed to be eight individuals. "I had a feeling we probably could find the phenomenon if we looked long enough," Thomson recalls. "What was surprising and gratifying was that it seemed to be a basic feature of the way these plants grow."

Thomson realized that the mosaic nature of the strangler figs had implications for conservation efforts. Many strangler figs alternate between male and female phases, and they reproduce with the assistance of tiny symbiotic wasps. The male wasps spend their lives inside a female plant structure called the syconium, which houses the developing flowers and fruits; a female wasp leaves to lay eggs in a new syconium only after the male flowers bloom. In the process the wasps carry pollen from one fig to another.

A population of strangler figs cannot survive unless it simultaneously contains male and female plants within a distance that wasps can traverse in no more than a day or two. Unfortunately, Thomson says, no one has found a way to measure a wasp's range. E. A. Herre of the Smithsonian Tropical Research Institute in Panama, one of Thomson's collaborators, had proposed that the best way to determine whether a strangler fig population is large enough to be self-sustaining is to analyze the paternity of seeds. If many fig plants contribute to any one fruit crop, the population is probably stable.

Yet as Thomson points out, it is not enough to count trees: conservationists also need to consider the blooming schedules of each individual within a tree. If the branches bloom at different times, then few trees might be needed because they would act like many more. Conversely, if all the fused individuals in a tree bloom simultaneously, perhaps in response to some shared chemical cue, then more trees would be necessary to ensure that plants in the right stage of development were always available. Strangler figs would then be much more vulnerable to deforestation.

According to Thomson, preliminary reports often suggest that the branches of strangler fig trees do generally bloom in synchrony, which points to the more gloomy interpretation. He and other researchers are now planning more conclusive determinations. *—John Rennie*

***STRANGLER FIG** clings to the tree that is its host and victim. Photo: Walter H. Hodge/Peter Arnold.*

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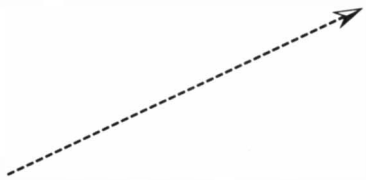

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Vexing Vortices

Why a magnetic field is the enemy of superconductivity

High-temperature superconductors are not always so super. True, the ceramic materials conduct current without resistance when they are cooled to 77 kelvins—a temperature only a physicist could consider warm. But superconductivity ceases if the material is overloaded with electric current or is placed in a strong magnetic field. Until researchers find a way to overcome such problems, they can only dream about such applications as superconducting magnets for levitating trains.

The first step consists of understanding how a magnetic field destroys superconductivity. A theory that explains the phenomenon has recently received substantial support from experiments conducted by two competing teams at the IBM Thomas J. Watson Research Center and AT&T Bell Laboratories. "It's fantastically interesting physics," says David J. Bishop of Bell Labs. "There is at least a potential that the theory will be relevant to some technology."

In 1988 Bishop suggested that whirlpools of electric current, known as flux vortices, can form in high-temperature superconductors and can arrange themselves in various configurations depending on the temperature of the material. Shortly thereafter, Matthew P. A. Fisher of IBM, his brother Daniel S. Fisher of Harvard University and David A. Huse of Bell Labs proposed a theory describing how vortices interact with one another and with imperfections in the material. In 1989 his colleague Roger H. Koch of IBM performed experiments that confirmed the theory, but critics maintained that Koch's results could be explained by applying conventional theories. During the past year, Bishop and his colleague Peter L. Gammel of AT&T have presented evidence that supports the work of Fisher and his collaborators and excludes competing ideas.

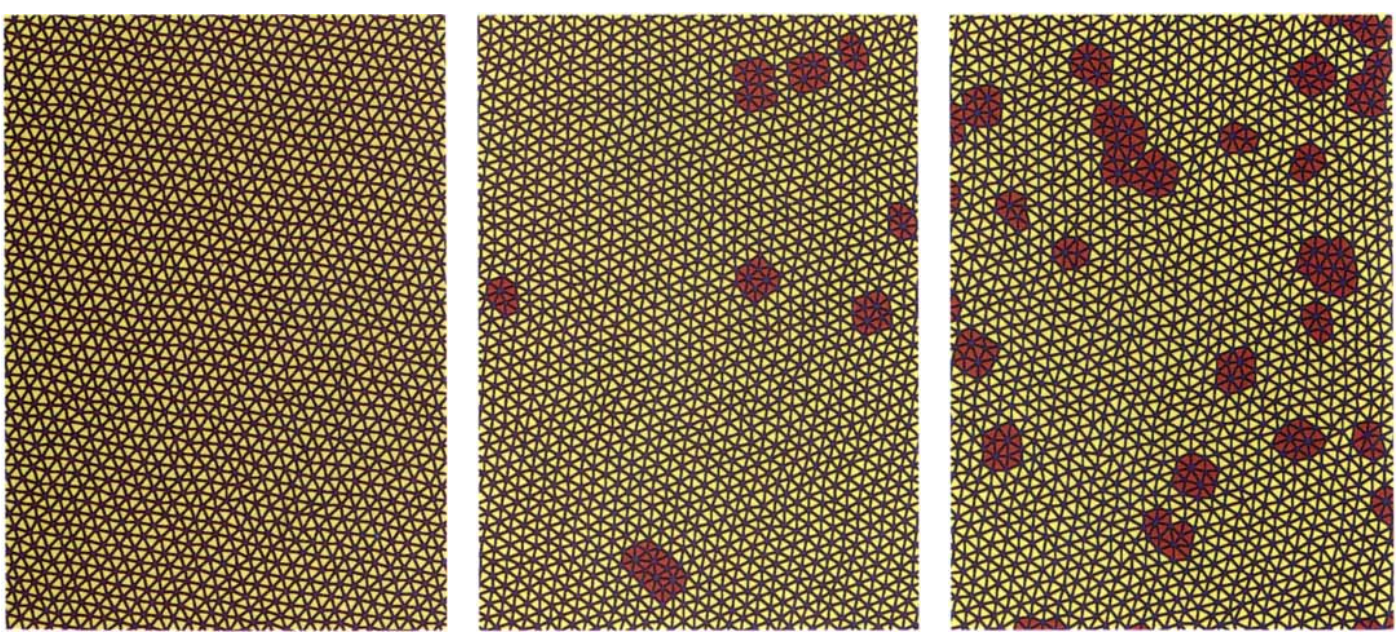
For decades, physicists have known that when a superconductor is cooled to temperatures very close to absolute zero, it shields itself from magnetic fields. It does so because the field induces electric currents at the surface of the material that prevent the field from entering the interior. At room temperature, magnetic fields can permeate a superconductor, and the material resists the flow of current. But somewhere between room temperature and absolute zero, some materials, including all high-temperature superconductors, neither completely shield nor readily admit magnetic fields.

As the field pushes its way into the material, it spawns vortices of electric current reminiscent of water swirling down a drain. The vortices in a superconductor extend from one surface of the material to the opposite side. The magnetic field, or more specifically magnetic flux, can enter the material through the vortices, but the remaining regions are shielded. The number of vortices is directly related to the strength of the magnetic field.

When a high-temperature superconductor is cooled in the presence of a magnetic field, vortices form and move about freely. Because this motion dissipates energy, the material still has electrical resistance. Yet some of the vortices will get stuck, or pinned, on defects and impurities in the material. (This effect is commonly known as flux pinning.)

The free vortices interact with pinned vortices and one another. If the temperature of the material falls to a critical value, the vortices freeze in an arrangement that has no apparent order. Fisher and his co-workers proposed that the vortices actually end up in a configuration that minimizes the interaction energy of the vortices in the material. Fisher calls such an arrangement a vortex glass because it is a disordered arrangement of vortices just as conventional glass is a disordered configuration of atoms.

Once the vortex glass forms, the resistance of the material drops to zero. According to the theory, a material will exhibit superconductivity as long as the vortex glass is stable. But the glass will "melt" if the material becomes warmer or the magnetic field becomes stronger. Equivalently, a strong current will generate a magnetic field that can destroy the glass. "Usually, imperfections are considered a real nuisance to physicists be-



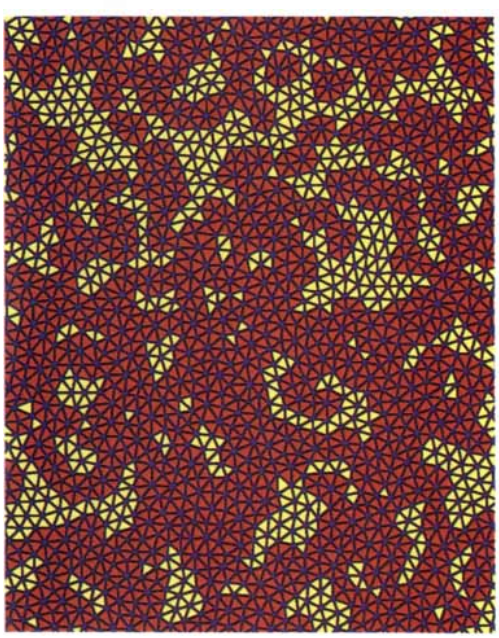
PATTERN OF TRIANGLES* (left) *is evidence for a vortex glass. Each vertex represents the position of a flux vortex as measured on the surface of a superconductor. The pattern of vortices is nonperiodic, similar to the arrangement of molecules in a conventional glass. The vortex glass "melts" as an applied magnetic field changes* (images from left to right). *The red triangles highlight irregularities in the pattern.

cause they make things harder to understand," Fisher explains. "But in this case, the only reason one has a superconducting phase in a magnetic field is because of the imperfections in the sample."

To test the vortex glass theory, Koch, Bishop, Gammel and their colleagues studied how the resistance of superconductors changes as they vary the temperature of the material and the strength of the magnetic field. The workers have performed such experiments on the superconducting ceramic yttrium-barium-2-copper-3-oxygen-7 and a few other high-temperature superconductors. The vortex glass theory accounts for the changes in resistance, whereas alternative theories do not provide satisfactory explanations.

The AT&T workers also found that images of the pattern of vortices produced at low temperatures were consistent with the theory. They apply a magnetic field to the material and allow tiny magnetic particles to fall on the surface. The particles are attracted to the top of each vortex and collect there. The researchers next turn off the magnetic field, warm the sample to room temperature and view the particles with an electron microscope. They can then see the arrangement of the vortices at the surface of the superconductor.

But can investigators produce a vortex glass that can withstand both high temperatures and a strong magnetic field? The key is to introduce certain types of defects and impurities in the material. Unfortunately, Fisher's ideas do not provide the tools to predict what kinds of imperfections would work best. "The vortex glass is going to be a tough thing to work with," Bishop sighs. —*Russell Ruthen*



D_2 or not D_2

A barroom brawl over an "alcoholism gene"

In April 1990 scientists claimed to have found a gene linked to one of the most devastating of all human scourges: alcoholism. The discovery was hailed on the front page of the *New York Times* and elsewhere as an important advance in the battle against a disorder that afflicts an estimated 20 million people in the U.S. alone.

Two years later the so-called alcoholism gene—more formally known as the D_2 gene—has become the focus of a bitter controversy. On one side are Kenneth Blum of the University of Texas at San Antonio and Ernest P. Noble of the University of California at Los Angeles, substance abuse experts who headed the team that wrote the 1990 report. They insist their finding has been amply corroborated by subsequent research. "There's a one in 10 million chance that we're wrong," Blum declares. He and Noble are taking steps toward marketing a test for alcoholism.

On the other side are skeptics such as Kenneth K. Kidd of Yale University, a veteran geneticist. He contends Blum and Noble's claim has been contradicted by other studies and is almost certainly invalid. "I believe there is a genetic component," Kidd says. "I just don't think the D_2 gene is that component."

Recently data related to race have added a volatile element to the debate. Kidd and other investigators have found that the gene's frequency varies widely among different races and even among ethnic groups within one race. Kidd thinks the failure to control for this variation may explain the results of Blum and Noble. They retort that the racial and ethnic data bolster their finding, since the D_2 gene seems to be most common among groups prone to alcoholism. "We love the ethnic data," Blum exclaims.

Few scientists dispute that heredity can create a susceptibility to alcoholism. As early as the 1970s, studies had shown that children of alcoholics—particularly sons of alcoholic fathers—who were adopted by nonalcoholics run a higher risk of becoming alcoholics than do their step-siblings. According to other experiments, sons of alcoholics have less intense brain-wave activity and a higher tolerance for alcohol than do control subjects.

Still, most investigators believed that environmental factors played a large if not predominant role and that the genetic contribution probably stemmed from a complex array of genes. Many were therefore startled when Blum and Noble announced in the April 18, 1990, *Journal of the American Medical Association* (*JAMA*) the discovery of a single gene that increased the risk of alcoholism by a factor of up to nine.

The gene, whose full name is the dopamine D_2 receptor gene, codes for one of several different dopamine receptors found on the surface of brain cells. Dopamine, one of the brain's most important neurotransmitters, helps to evoke pleasure and other sensations and has been implicated in various disorders, notably schizophrenia.

In previous experiments, the D_2 gene was shown to come in at least two variants, or alleles, designated A1 and A2. In their study, Blum and Noble compared genetic material from 35 deceased alcoholics with material from 35 deceased nonalcoholic controls. The workers found the A1 allele in 69 percent of the alcoholics and in only 20 percent of the controls.

Last July, in the *Archives of General Psychiatry,* Blum and Noble followed up their initial work with a report that the brains of corpses carrying the A1 allele had fewer dopamine D_2 receptors than did brains with the A2 marker. A1 carriers may ply themselves with alcohol or other drugs to compensate for a reduced ability to absorb pleasure-inducing dopamine, Blum and Noble hypothesized. Critics contended the reduction in dopamine receptors might have been an effect rather than a cause of alcoholism.

In October a group headed by David E. Comings and Steven D. Flanagan of the City of Hope National Medical Center in Duarte, Calif., announced in *JAMA* that the A1 allele was associated with a higher incidence not only of severe alcoholism but also of several other psychiatric disorders, including Tourette's syndrome, attention-deficit disorder and autism (but not schizophrenia). The group also found, but did not mention in its report, an association with "criminal aggression," according to Flanagan. The association with alcoholism, while only about two thirds as strong as the one reported by Blum and Noble, was still statistically significant.

Yet other published reports have challenged the alleged association between the A1 allele and alcoholism. Separate studies headed by Annabel M. Bolos of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and Joel Gelernter of Yale found incidences of the A1 allele among alcoholics not significantly higher than those among controls. Moreover, two investigations of families with high rates of alcoholism, one of which was done by C.

*1991 IMSA Firestone Firehawk Endurance Championship • ICY Racing/Saturn Coupe Results: Sebring—4th; Miami Grand Prix—4th;

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Anyway, when Dave and Peter tested our coupe, the Saturn SC, they loved it, and prepared a couple for racing in the IMSA Firestone Firehawk series* against Hondas, Nissans, and the like.

Our engineers were ecstatic, of course. The cars performed like crazy, and the ICY team drove to first place in the touring class. But to Dave, the key to their success was the performance of the kids. They'd not only beaten the pushers—they also beat professional pit crews at each and every race.

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The Case for and against the Alcoholism Gene

PRO **April 1990:** Blum, Noble and their co-workers find the A1 allele of the dopamine D_2 receptor gene in 69 percent of 35 deceased alcoholics and in only 20 percent of 35 deceased control subjects, according to an article in the *Journal of the American Medical Association* (*JAMA*).

CON **December 1990:** In *JAMA*, Bolos and her colleagues report no significant association between the A1 allele and alcoholism in two studies, one comparing 40 unrelated alcoholics and 127 control subjects and another examining two families with a history of alcoholism.

PRO **July 1991:** Carriers of the A1 allele have fewer dopamine D_2 receptors in their brains than do carriers of the A2 allele, according to a study by Noble and Blum involving 33 deceased alcoholics and 33 deceased nonalcoholics, described in the *Archives of General Psychiatry*.

CON **July 1991:** The A1 allele is not linked with alcoholism in a study of 17 families with a history of alcoholism, announce Parsian, Cloninger and others in the *Archives of General Psychiatry*.

CON **October 1991:** In *JAMA*, Gelernter and his co-workers report finding no significant association between the A1 allele and alcoholism in a study involving 44 alcoholics and 68 control subjects.

PRO **October 1991:** Comings's team finds the A1 allele is associated not only with alcoholism but also with autism, attention-deficit disorder, Tourette's syndrome and posttraumatic stress disorder. The paper in *JAMA* was based on data from several previous studies involving 853 subjects.

CON **October 1991:** A comparison of 45 German alcoholics with 69 ethnically matched control subjects finds fewer A1 carriers among the alcoholics, although the differences were not significant, according to an abstract by Schwab and his co-workers in the *American Journal of Human Genetics*.

Robert Cloninger of Washington University, a pioneer in alcoholism genetics, revealed no linkage to the A1 allele.

Recently, however, Cloninger reviewed the data from six published studies, both positive and negative, and became convinced that the association between the A1 allele and alcoholism—particularly the severest form of the disorder—is "highly significant." Cloninger argues that although the allele is neither "a necessary nor a sufficient cause of alcoholism," since some carriers are not alcoholics and some alcoholics are not carriers, it somehow exacerbates the course of the disorder.

Cloninger criticizes the negative studies of Bolos and Gelernter for excluding alcoholics with severe medical problems—the very group previous studies had suggested are most likely to carry the A1 allele—and for not screening alcoholics from their control group. These factors, Cloninger contends, biased the results toward a negative finding.

Gelernter replies that, according to the odds, at most only a few of his controls were alcoholic A1 carriers; such a small number, he says, would not significantly alter his results. He argues, moreover, that interviews are the best method for determining whether subjects are truly alcoholics. By emphasizing medical complications and even death as criteria for severe alcoholism, Gelernter adds, researchers such as Blum, Noble and Comings are more likely to discover a gene for predisposition to liver disease than alcoholism per se.

David Goldman of the NIAAA, who participated in the Bolos study, agrees. He suggests that Blum, Noble and Comings may not have controlled sufficiently for variation of the A1 allele among different ethnic groups. So far there have been two examinations of the A1 allele and alcoholism in an ethnically homogeneous population, Goldman notes. One study, which involved Germans and was described briefly in the *American Journal of Human Genetics* last October, found that alcoholics were less likely to have the A1 allele than were nonalcoholics. Goldman himself has unpublished data showing no significant association between the A1 allele and either alcoholism or dopamine metabolism variation in a population of Finns.

Yet Blum and Noble cite other ethnic data supporting their view. Unpublished findings from various researchers indicate that as many as 70 percent of Native Americans and 60 percent of the Irish, groups that have high rates of alcoholism, carry the A1 allele, Noble says. The allele seems to be relatively rare among Jews, he adds, who display low rates of alcoholism.

Noble even argues that data on Orientals, who have high A1 frequencies but low alcoholism rates, support his case. Many Orientals are prevented from becoming alcoholics because they lack an alcohol-metabolizing enzyme and so have a toxic reaction to alcohol, Noble explains. The "notorious" fondness of the Japanese for amphetamines and of the Chinese for opiates, he asserts, reveals their genetic susceptibility to addictive behavior. "They're also all big smokers," he adds.

The ethnic issue has been further complicated by George R. Uhl of the National Institute on Drug Abuse. He says blacks are almost twice as likely as whites to carry the A1 allele, yet black A1 carriers do not show significantly higher rates of alcoholism or related disorders than other blacks. Uhl's data show an association between the A1 allele and alcoholism in whites, but only when alcoholism is combined with the abuse of other drugs.

Other questions abound. For example, a persistent criticism of the A1 findings has been that, contrary to the impression left by many news accounts and peer-reviewed papers, the A1 allele is merely a marker for rather than an actual variant of the D_2 gene. In fact, Robert W. Karp of the NIAAA notes that the A1 allele lies some 10,000 base pairs from the "business end" of the D_2 gene, the region that generates the proteins for the D_2 receptor. According to Karp, no direct molecular evidence links the A1 alleles to any variation in the expression of the D_2 gene.

Blum and Noble respond that they and other researchers have recently identified two other markers that are closer to the coding region of the D_2 gene than are the A1 and A2 alleles. Preliminary data, they claim, suggest that alleles of these markers have an association with alcoholism at least as strong as that of the A1 allele.

Too impatient to wait for these issues to be resolved, Blum and Noble are discussing the possibility of developing a test for susceptibility to alcoholism with Pharmavene, Inc., a drug company in Gaithersburg, Md. Blum suggests the test could be given to job applicants, children and even fetuses. Blum is already the inventor of a nutrient drink, marketed under the name Supplemental Amino Acid Vitamin Enteral, or SAAVE, that he claims "facilitates recovery" of alcoholics.

—*John Horgan*

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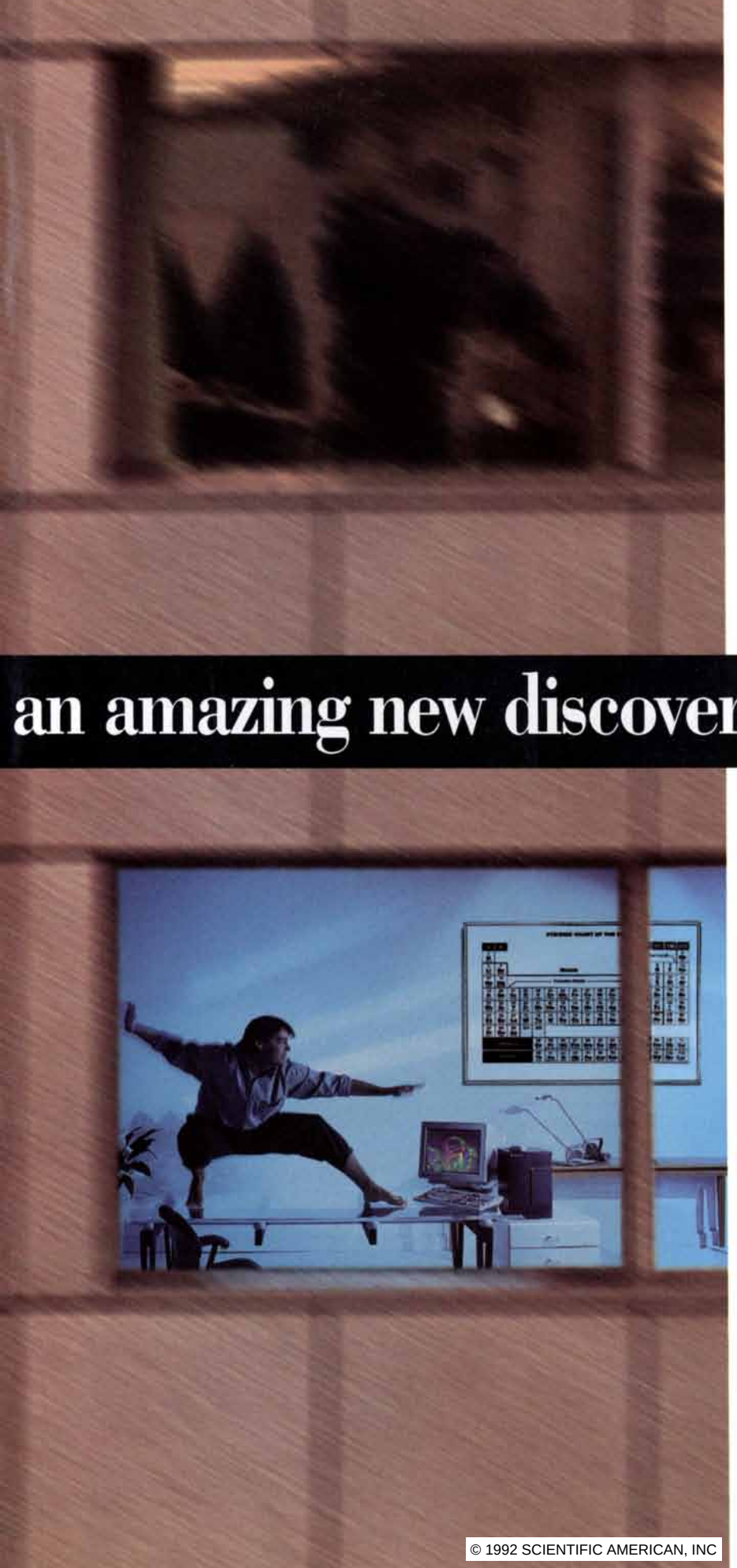

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A Second Glance

A dim class of galaxies offers unexpected fascination

Like cosmic wallflowers, a class of objects known as low surface-brightness (LSB) galaxies has been languishing from neglect. Until recently, all the known LSB galaxies were dwarfs. Loosely organized and small, they seemed minor members of the universe. Recently, however, astronomers have been giving them a whirl. With increased familiarity has come the recognition that the objects constitute a surprisingly diverse and intriguing group.

Interest in LSB galaxies picked up in 1987, when a group led by Gregory D. Bothun of the University of Oregon analyzed radio emissions from a previously identified dwarf galaxy in the constellation Virgo. The researchers realized the object is 10 times more distant than had been thought. Far from being a dwarf, the galaxy, dubbed Malin 1, is roughly a trillion times the mass of the sun and more than twice the diameter of our galaxy, the Milky Way. "It shows how biased our perceptions are," Bothun comments. "Here is this huge galaxy, and we discovered it totally by accident."

Now that astronomers know what to look for, they are discovering that such huge but hard-to-see LSB galaxies may actually be quite common. Last fall Bothun's group discovered another, similar galaxy, informally known as Malin 2. Stephen E. Schneider of the University of Massachusetts at Amherst, who is searching for radio emissions from these objects, reports that he is "seeing a lot more such things than people expected us to find."

Researchers trying to understand how galaxies form and evolve must come to grips with the fact that they may have overlooked a significant fraction of their subject matter. The biggest question is why these galaxies appear so different from "normal" galaxies, which have high surface brightness. Bothun thinks many of the dwarf LSB galaxies represent faded objects in which stars stopped forming long ago.

LSB giants, on the other hand, look more like galaxies that never formed many stars in the first place. Schneider notes that the disks of these galaxies appear very blue, implying that their stars are young and deficient in heavy elements. Old stars, in contrast, would impart a red color. Spectral analysis conducted by Stacy S. McGaugh of the University of Michigan, Bothun and others confirms that large LSB galaxies contain only slight traces of the elements created during stellar evolution.

The nuclei of giant LSB galaxies contain thick swarms of stars that closely resemble (in color and brightness) those in the nuclei of normal galaxies. In these dense central regions, stars evidently formed in the conventional fashion. Indeed, Malin 2 is not listed in any galaxy catalogue, in part because its bright nucleus resembles a star, whereas its faint outer disk shows up only under close examination. Recent observations show that large LSB galaxies appear increasingly blue farther from the nucleus, possibly hinting that the stellar formation process is slowly migrating outward.

Apparently, the outer disk regions of giant LSB galaxies have not developed the same way as the more familiar galaxies, such as our own. A number of researchers cite the low surface densities of these galaxies. Stars are known to form in clouds of molecular hydrogen. The density of objects like Malin 1 may be so low, however, that hydrogen tends to remain as single, unattached atoms. The diffuse hydrogen clouds in these galaxies might simply have been unable to fragment and collapse into stars. But some of the newfound galaxies seem to have normal densities.

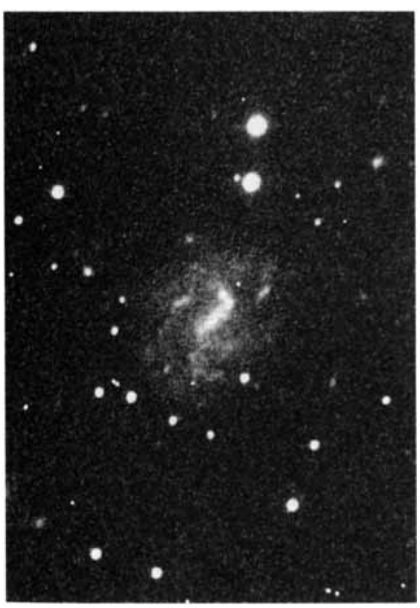
Giant LSB galaxies tend to reside well away from any others, Schneider reports. They are therefore insulated from gravitational tugs by neighboring galaxies. Such interactions are known to induce density waves that compress the hydrogen gas, setting off a burst of star formation. The absence of gravitational disruptions could explain why Malin 1 and its ilk remain relatively barren of stars.

Some stars seem to be forming in the outer regions of Malin 2, but in large, widely spaced clumps, each resembling in some ways a dwarf irregular galaxy—very different from the smaller, more evenly spaced star-forming regions distributed throughout the disk of the Milky Way. Indeed, Bothun speculates that the huge LSB galaxies may be "large objects that never fragmented," that is, cluster-size masses that never split into individual galaxies.

Giant LSB galaxies are clearly in a different evolutionary state than are the better studied bright ones. Schneider hesitates to call LSB galaxies more primitive, however. "We often think of humans as being more evolved than bacteria," he explains, "but in fact both are the product of billions of years of evolution." Similarly, the star-poor outer structures of giant LSB galaxies reflect a different, and heretofore ignored, pace of development.

Although they exist in relative isolation from other galaxies, LSB galaxies do not seem to fill the huge voids found in recent maps of the large-scale distribution of bright galaxies. The fact that LSB galaxies seem to reside only in low-density regions outside clusters does indicate, however, that such surveys have given a skewed picture of how galaxies are distributed. Patricia M. Knezek of the University of Massachusetts, who is working with Schneider to map out the population of LSB galaxies, reflects that "a large fraction of the matter in the universe could be hidden in these slowly evolving galaxies." Cosmologists, take note.

—Corey S. Powell



LOW SURFACE-BRIGHTNESS GALAXY **(left)** ***is about the same size and mass as a "normal" one*** **(right)** ***but contains far fewer stars. Images by Patricia Knezek.***

Fire in Water

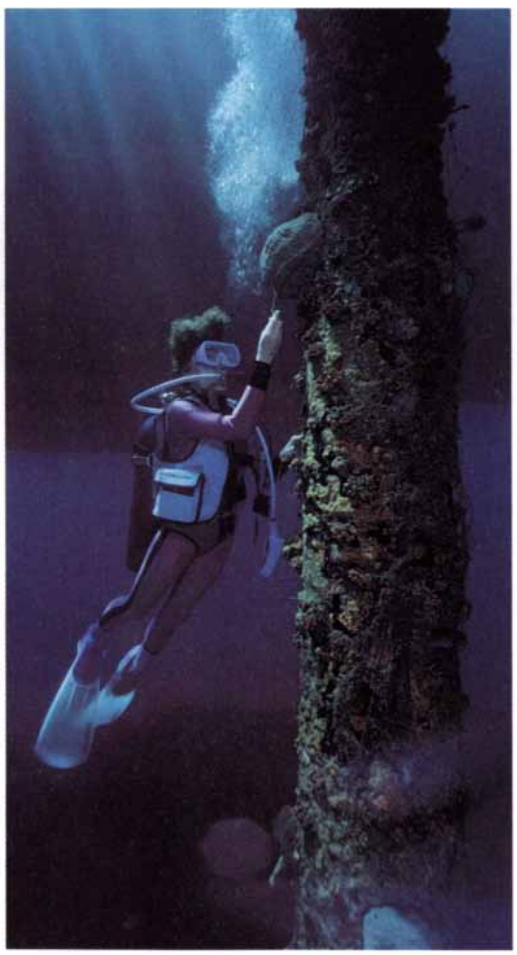
It is hard to pin down Sylvia A. Earle. Like a modern day Proteus, the mutable god of the sea, she moves with seeming ease from one project and one persona to another: marine botanist, deep-sea diver, explorer, businesswoman, conservationist, writer and, until recently, chief scientist at the National Oceanic and Atmospheric Administration (NOAA). Even in her manner, Earle is at once outspoken, soft-spoken, diplomatic, cagey, earnest, gracious and fiery.

The ability to be many things has allowed Earle to keep one foot in the water and one foot on the land, although she clearly prefers the ocean: "I am suffering from dry rot," she says. "I want to spend more time underwater." As a political appointee, Earle had the ear of a White House administration not known for its environmentalism. Yet she resigned in January, after little more than a year in the position. Earle was the first woman to serve as the lead scientist at NOAA, a $1.5-billion agency that oversees the weather service, conducts underwater research, manages fisheries and responds to marine spills of hazardous materials.

Earle denies reports that a clash with the White House precipitated her departure, but her position on several environmental issues clearly runs counter to prevailing policy. She seems almost desperate to tell journalists that she admires NOAA and the administration. Perhaps "you could toss a bouquet in their direction," she asks.

Even so, Earle says she can accomplish more by working independently. "I think I can be even more effective if I am on the loose," she notes. In this capacity, Earle will try to establish marine sanctuaries and to encourage deep-ocean engineering. But in her carefully worded comments—she will continue to work as an adviser at NOAA for at least a year—Earle admits some frustration.

"Every time I spoke, my words were likely to be interpreted as speaking for the administration and, therefore, as official policy," Earle explains, sitting in her NOAA office in Washington, which has been largely stripped of her aquatic mementos but which still houses a model moray eel draped around her computer. "You can easily get into trouble quite innocently," she says. Earle is not specific about any substantial trouble she might have found herself in, except to say that a statement she made last winter about not eating any fish "that I have known personally" was interpreted by the fishing industry as a sudden NOAA antipiscivorous policy.



6,000 HOURS underwater have made Sylvia Earle a strong conservationist. Photo: David Doubilet.

Being in the public eye is hardly new for Earle. In 1970 she and four other oceanographers spent two weeks living in an underwater habitat as part of a government-funded project called Tektite II. When the researchers surfaced, they found themselves dubbed "aquababes" and adorning the front page of the *Boston Globe*. Earle, who led the all-female team, was ambivalent about the attention at first. As a scientist, she explains, "if you fall into the league of the popularizers, you have somehow sullied your credentials forever."

Yet after reading an essay by the Victorian-era biologist Thomas Huxley, she says she felt a responsibility to educate the public—something she has done ever since and something that makes her the target of criticism. "I still get it from scientists who think I am a lightweight scientifically," Earle says matter-of-factly. "Scientists are put off by the difficulty of remaining precise and accurate while making it relevant to someone who doesn't know."

But even those peers who criticize Earle's scientific rigor laud her ability to communicate compellingly about marine life and the importance of studying the oceans. Although she has gone down under instead of up on high like an astronaut, Earle sees the planet as one blue, integrated system. And when she describes the insights gained in some 6,000 hours beneath the sea, her language, studded with phrases that she uses over and over again in her public speaking, becomes almost poetic. A squid is not merely a cephalopod, order Teuthoidea; it is a creature with "huge eyes that will likely inspect you. Some of them are like jewels," Earle says in a tone approaching awe.

Earle's love of the ocean began when she was young. Her family moved from New Jersey to the west coast of Florida, where her parents encouraged her interest in the out-of-doors. "I wasn't shown frogs with the attitude 'yuk,' but rather my mother would show my brothers and me how beautiful they are and how fascinating it was to look at their gorgeous golden eyes." At the same time as they supported her interest in biology, Earle adds, her parents made sure she got teaching credentials and learned to type, "just in case."

After attending Florida State University, Earle entered a graduate program at Duke University and specialized in botany. For her dissertation, she completed a classic study of the algae of

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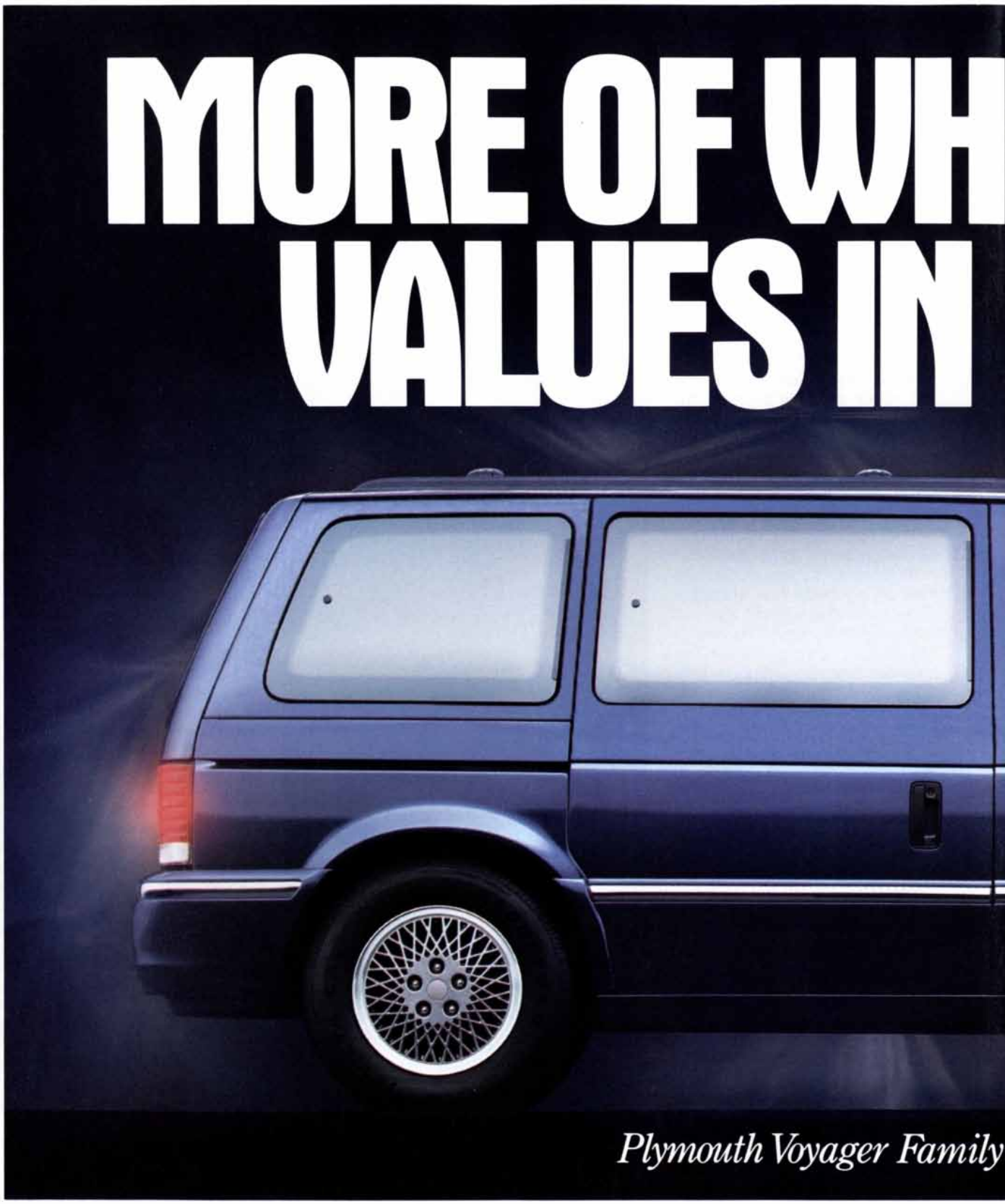

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the Gulf of Mexico. The project is one she continues today; she has more than 20,000 samples. "When I began making collections in the Gulf, it was a very different body of water than it is now—the habitats have changed. So I have a very interesting baseline."

Earle happened to be studying at a time when scuba equipment became widely available. Because the gear permitted direct observation, it changed the study of marine biology. As one of the first researchers to explore freely underwater, Earle was able to identify many new plants and organisms and even to discover some surprising geologic features, such as undersea "dunes" off of the Bahama Islands. "It was a simple Lewis and Clark kind of observation," she explains. But "the presence of dunes was a significant insight into the formation of the area."

She also happened to be one of the few female oceanographers. In some ways, Earle says, this distinction gave her a platform: "If I am the only woman in a crowd of 400 guys, all heads turn when I speak." On the other hand, she asserts she has been denied positions, including directing certain research vessels, because of her sex. Earle goes on to say, tactfully, that she is not complaining: "Elsewhere in the world it is infinitely more difficult."

Earle attributes some of her fierce independence to being a woman. Women are more self-reliant because they "are not as much in the network as men are; that is just a fact of life," says Earle, who was the first person to dive to 1,250 feet, untethered, in a rigid diving suit and one of the first pilots to take a submersible craft down 3,000 feet, alone. By leaving NOAA, Earle hopes to regain that independence. "Here, I am not really in control," she states.

Earle can also return to deep-ocean engineering. In 1981 Earle and her then-husband Graham Hawkes decided to build their own deep-sea vehicles. The two founded Deep Ocean Technology, Inc., and, shortly after, Deep Ocean Engineering, Inc., which is now the principal company. One of the first manned submersibles they designed, Deep Rover, took Earle 3,000 feet under the waves of the Pacific in 1985. The $5-million company has also produced robots for offshore oil and gas ventures.

The veteran diver is angry that less than 10 percent of the oceans have been explored and that technology does not allow any individual to go scouting about abyssal plains. "It is pathetic that we cannot go down in the sea," she exclaims, adding that of the five deep-sea manned submersibles in the world—those that can go to 20,000 feet or more—the U.S. has only one: *Sea Cliff*. "That's like having one jeep for all of North America," she says.

Paradoxically, Earle's commitment to deep-ocean exploration may have put her at odds with the administration over the very NOAA division that supports such research, the National Undersea Research Program (NURP). According to a congressional staff member, White House budget proposals have not included funding for NURP since 1983. The program, the staffer says, "has not been popular with the Republican administrations." Instead each year Congress has had to restore funding—currently a figure of about $17 million.

"If you fall into the league of the popularizers, you have somehow sullied your credentials forever."

Earle was invited to testify when the congressional Merchant Marine and Fisheries committee considered NURP's future last October. At the last moment she declined, and a NOAA official spoke against increased federal funding for NURP. "I could not testify as an individual, because it would have been contrary to NOAA's position," Earle comments.

Independently, she continues to find ways to visit oceanic depths. Earle is working with Japanese scientists who plan to send first a remotely operated and then a manned vehicle to 36,000 feet. "They have money from their government. They do what we do not: they really make a substantial commitment to ocean technology and science," she says. Earle also intends to lead Ocean Everest, a $10-million Deep Ocean Engineering project that would also take her to a similar depth and back.

As much as Earle woos technology, she abhors its misuse. "We have the technological capability to frightfully tip the scales off balance with any species," she frets, citing not only Saddam Hussein's destruction of Kuwait's oil wells and the purposeful oil spill in the Persian Gulf but drift nets and electronic fish finders used by some fishermen.

Indeed, the Persian Gulf War, which broke out a few months after Earle was appointed as chief scientist, not only shaped her focus at NOAA but, she says, was partly responsible for her sudden departure from the agency. Earle, who has worked with such organizations as World Wildlife Fund International, had intended to push for the creation of marine sanctuaries. She sees these ocean reserves, of which there are 10 in U.S. territorial waters, as the equivalents of national parks, each preserving wilderness, study sites and species diversity.

But the Gulf fires as well as a conflagration in Oakland, Calif., which nearly destroyed her home last fall, drove her back to the water, she explains. Those events "really instilled in me an even greater sense of urgency than I had already felt about doing the best you can with whatever time you have got."

Despite her brief tenure at NOAA, some colleagues credit Earle with bringing more prominence to the agency. "We never had a spokesperson before. No one really knew we were around," comments Joseph Bishop, a senior scientist at NOAA. And many specifically cite her efforts to ensure that the effects of the Persian Gulf crisis were studied. NOAA has sent a research vessel on a $6- to $8-million voyage that is scheduled to run through May. The expedition, involving some 130 scientists from all over the world, is expected to establish the basis for an ongoing monitoring program in the Gulf. Earle will act as coproject leader for one leg of the cruise, during which researchers will examine any effects of oil on the coral reefs.

"Her personal interest and enthusiasm were the key to the formulation of the current Gulf cruise," says Jacqueline Michel, an oil-spill expert at Research Planning, Inc., who has worked for NOAA in Prince William Sound, Alaska, and in the Persian Gulf. The cruise "wasn't a high priority in the agency or in the U.S. government, because they didn't want to be associated with the Gulf anymore."

Meanwhile Earle—in her many guises—is continuing to spread a message of environmental integrity, sustainable use and enhanced ocean research. As part of this effort, she recently spoke to students at Rutgers University. Earle, the political appointee, answered questions about her resignation: "It was hard to leave the government. I have new respect about what it takes to get something to work."

Earle, the poet, enchanted her listeners as she stood on the stage of a darkened auditorium under the image of a squid that had been projected, enormous and pinkish, on the wall above her. In an almost hypnotic tone, she described the 12-foot chunk of a tentacle that a colleague of hers had found in Monterey Bay, Calif. "Giant squid have never been seen," she told the rapt, silent audience. But it was Earle, the pragmatist, who finally drove the point home. "It says something about the magnitude of our ignorance that we have never seen something the size of a dinosaur." —*Marguerite Holloway*

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Dear Readers:

It is with great pride that I introduce this Scientific American feature, "Massachusetts: Advanced Technology for the Future." This report showcases the many innovations that Massachusetts is contributing to improve our future. It describes Massachusetts' historical emphasis on human intellect and skill for economic growth. Furthermore, it includes examples of recent technological breakthroughs in our laboratories and profiles of companies that are setting examples of how to adapt to a global economy in transition.

This report also illustrates how Massachusetts itself is setting an example of adaptation. We continue to move forward in our effort to create the best possible climate for new ideas to be conceived, gain support, and flourish in the commercial marketplace.

On behalf of the citizens of the Commonwealth of Massachusetts, I urge your close attention to this special feature. I think you will come to agree that for businesses which depend on a highly sophisticated workforce, there is no better environment for growth than Massachusetts.

Sincerely,

Bill Weld

William F. Weld
Governor
Commonwealth of Massachusetts

THE COMMONWEALTH OF MASSACHUSETTS: ADVANCED TECHNOLOGY FOR THE FUTURE

A few decades after the United States became a nation, a flow of inventions and innovations began to build in Massachusetts. Progress in the social realm—in literature, theology and philosophy, and public affairs—helped forge the new nation's character. Meanwhile, Massachusetts' research and development climate in science, medicine, and mechanical engineering helped form new industries. Massachusetts' first century of contributions to America's industrial growth included the principle of interchangeable machine parts, the first American steam machinery, including the locomotive, the combustion engine, the electric transformer, as well as more storied inventions like the cotton gin and, of course, the telephone.

In this century, Massachusetts inventors hit upon the principle of frozen foods, designed and assembled the first analog and digital computers, launched the first liquid fuel rocket, created instant photography, initiated important innovations in computer design, and made a host of breakthroughs in robotics, biotechnology, and telecommunications. In a sense, Massachusetts has always stuck to one line of business: creating the future. Massachusetts has specialized in the incubation of the high technology of the time, whether it was clipper ships, CAD/CAM technology, or recombinant DNA.

The people of Massachusetts have created and passed on a culture of creativity, resourcefulness, and diligence which has transformed an outpost of rocky ground and cold weather into a wellspring of ideas and new applications. We have never relied upon the harvest of fossil fuels or farmland for our success; rather, as one commentator recently said, "We live by our wits."

Highly educated professionals provide Massachusetts with a uniquely competitive edge. The National Science Foundation's state profiles rank Massachusetts, which is 13th among states in population, second in the absolute number of science and engineering doctorates and fourth in the number of graduate students. Thanks to leading academic institutions such as Harvard and the Massachusetts Institute of Technology, Massachusetts bestows more advanced degrees per capita than any other state, and has the most college graduates per capita in the nation.

This superior level of training directly affects the constant evolution of the economy of Massachusetts. Graduates from MIT alone have founded more than 100 companies based in Massachusetts during the last five years. Furthermore, new Massachusetts companies consistently appear in lists such as the *Inc.* 500 and the *BusinessWeek* 100 in numbers far beyond the state's proportionate share.

As skillful entrepreneurs have churned out new ideas over the decades, Massachusetts has fueled them with a ready supply of financial expertise. Two Massachusetts-based corporate giants—Digital Equipment Corp. and the Raytheon Company—owe much of their present stature to consistent support from venture capitalists and banks during their earliest days. Today, startups that continue the tradition of leadership in emerging technologies enjoy the same financial treatment.

Since Governor William F. Weld took office in January 1991, the Massachusetts government has been working to re-orient the state's business climate to support the innovation engine which drives our economy. Massachusetts adopted the most generous research and development tax credit in the nation. We also repealed the sales tax on business services.

In addition, Governor Weld successfully fought for worker's compensation and health insurance reform so as to prevent premium increases for employers, and he proposed 139 legislative and administrative changes to clear out the regulatory underbrush that companies must overcome. In the face of a national trend, Massachusetts is decreasing the burden of government costs and regulations upon business.

These efforts were supplemented in 1991 by other cost-containment programs. Several Massachusetts utilities, for example, instituted economic development discount rates for new or expanding businesses to remediate some of New England's traditionally high energy costs.

1992 will be a year of building upon these achievements. In January, Govenor Weld announced his Economic Growth Plan, designed to maximize the strengths of the Massachussetts economy. Among other initiatives, it includes a phase-out of the state capital gains tax, a bonus one-year investment tax credit of 20%, and a reduction in the individual income tax. The intent is to marshall every potential resource within state government for the sake of economic growth and development.

As government-imposed expenses upon businesses are controlled, the Weld Administration is working to increase the value of Massachusetts' most important asset, its people. Proposals for needed reform in education and workforce development programs are designed to prepare workers for the high-skill, high-wage jobs of the next century. These reforms will establish competency standards for key subjects, hold school managers accountable to specific goals, and reshape educational programs to ensure that graduates have competent, marketable skills.

As the world struggles its way through the transition into its next phase of economic growth, it would do well to look to Massachusetts as one of its leaders. The people of Massachusetts have always believed in the power of innovation to create new prosperity. We are now retooling our state government to help in the task of unleashing it. This is a new day in Massachusetts.

—The Executive Office of Economic Affairs

DIGITAL EQUIPMENT CORPORATION

Digital Equipment Corporation, with headquarters in Maynard, ranks fifth in the US in corporate spending on research and development, allocating $1.65 billion to R&D in 1991. Projects at Digital's four-year old Cambridge Research Lab (one of the four research labs that DEC operates worldwide) concentrate on developing application technology for users of Digital systems. CRL's applications include data management, transactions processing, and visualization or display of information.

Some 35 software and computer architecture engineers at CRL work closely with Digital's development groups, according to Victor Vyssotsky, lab director. One current project involves work with a neurologist at Children's Hospital in Boston. The research physician's studies of physiological changes in the neurons in the hippocampus require construction of three-dimensional models of neurons. Digital's research lab has worked for two-and-a-half years to produce software that can construct such models; software has now been developed, and Digital is working to the day where it can be used by non-software professionals.

Inside DEC's semiconductor facility

Clearly, the most important customer of the lab is Digital itself. CRL has cooperated with various groups within the company to develop the first prototype system in Digital's new, open, 64-bit RISC computing architecture. Known internally as the Alpha project, the company expects to base its systems on the architecture for the next two decades. "We intend to make Alpha an industry standard," says Robert E. "Ed" Caldwell, vice president of semiconductor operations at the Hudson semiconductor plant. He directs the development of the Alpha architecture definition and the actual mircroprocessors themselves.

Alpha, explains Caldwell, is a family of microprocessors spanning the product range from mainframes to desktops to embedded systems that can be massively paralleled for supercomputing. Some 4,000 people in semiconductor operations have been involved in Alpha's design, development, manufacture, marketing, and sales of the microprocessors, and will continue to be involved as the chips enter production. "This is the first implementation of an internal RISC architecture to go to market," says Caldwell. The company believes that Alpha represents yet another example of Digital's leadership in performance, price, and architectural innovation, a position the company has held since its founding in 1957.

This special advertising section, under the direction of Special Reports Associates, was written by Beth McGoldrick and Sharon Kahn and designed by Frierson Mee + Herman.

Bay staters use one word to sum up the uniqueness of Massachusetts: Brainpower. "Our advantage is in our talent," says Stephen P. Tocco, State Secretary of Economic Affairs.

Massachusetts' pride is anchored in 120 institutions of higher education scattered throughout the Commonwealth and one of the most vital entrepreneurial hubs found anywhere—the "Brain Belt" of Route 128 ringing Boston. "Massachusetts enjoys a nearly unique pool of highly qualified professionals and highly skilled technicians," argues Professor Michael E. Porter of the Harvard Business School.

MECHANICAL MODELING

Pro/ENGINEER from Parametric Technology Corp., Waltham, provides a revolutionary approach to mechanical design automation. The parametric, feature-based solid modeling system offers a unique and powerful architecture which provides engineers with unprecedented ease and flexibility. Pro/ENGINEER is built on a single, underlying database, rather than many proprietary databases as is the case with older generation CAD/CAM systems. One database allows individuals from different departments to work concurrently, all from one product model or definition. Full associativity throughout the entire design-through-manufacturing process allows engineers to reconfigure product designs "on-the-fly" without incurring time and cost penalties in downstream applications such as manufacturing. This promotes design optimization, delivering higher quality products, faster, at lower costs. Circle No.1.

Regarding why Serono Laboratories located in Massachusetts, President Jules Musing quotes the company's chief executive officer, Fabio Bertarelli, who says, "When making wine, locate your wine-making where the grapes are growing." Musing elaborates: "The academic excellence for which Massachusetts is known, combined with the presence of world famous medical centers and other biotech companies, makes for an environment in which biotechnology thrives."

Massachusetts' unique "intelligence stew" continually nourishes technology companies of remarkable diversity, as well as a financial and service infrastructure to complement them. As a result, Massachusetts specializes in mid-sized-to-smaller companies. Often begun as spin-offs from university or corporate labs, many of the state's start-ups are funded through Massachusetts venture capitalists. "Massachusetts is like a big, applied research lab consistently turning out new products through new and rejuvenating companies," observes John Hodgman, president of Massachusetts Technology Development Corp., a quasi-public entity that helps launch and expand Massachusetts' companies through venture capital infusions. "It's a very fertile environment."

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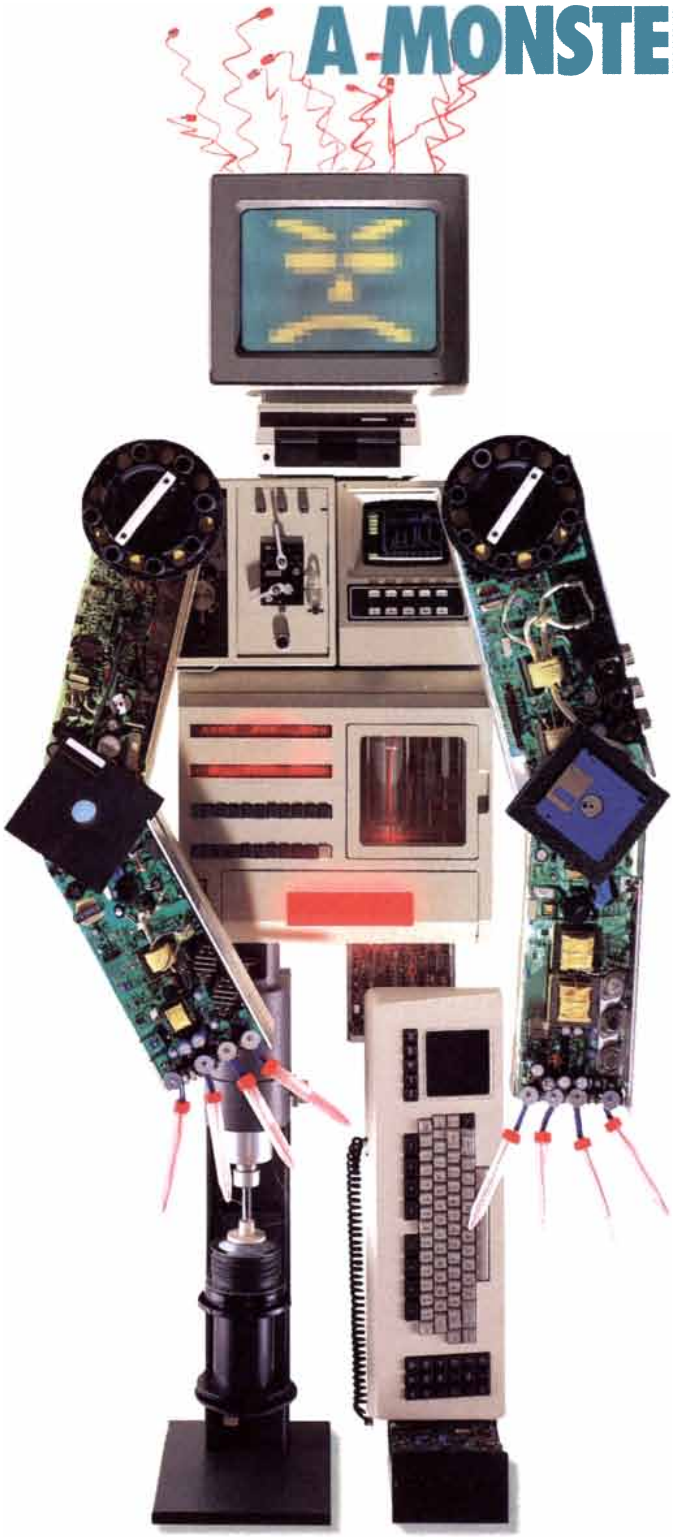
JOBS THAT ADD VALUE. Industries such as biotechnology and software that are invigorating Massachusetts—and vice versa—create higher value-added jobs than other

HAS YOUR LABORATORY CREATED A MONSTER?



It started out with the best of intentions. A PC here. A workstation there. A new spectrometer. Some chromatographs. But now it's grown into an amalgam of different computers, applications and laboratory instruments, none of which can work together or share information.

How do you integrate them to provide the right information at the right time to the right people? With the Open Advantage from Digital. A combination of industry standard products and services, powerful third-party relationships and an open attitude toward your particular needs, it allows you to finally unite all the elements of your laboratory. And create a solution of incredible power and flexibility.

With the Open Advantage, your lab can look forward to faster, more accurate reporting. Greater productivity with fewer resources. Easier compliance with regulatory agencies. Better response to customer needs.

Laboratory integration needn't be a nightmare. Talk to your Digital sales person. digital™

DIGITAL. THE OPEN ADVANTAGE.

RAYTHEON COMPANY

The Raytheon Company of Lexington is universally identified with Patriot missiles, used so effectively in the Persian Gulf conflict last year.

However, internally, Raytheon, a Fortune 100 corporation, identifies itself as a technology company, first and foremost. "Management is technology- and engineering-oriented," states Dr. Philip Cheney, vice president of engineering at Raytheon. With 1991 sales of more than $9 billion, the company is known worldwide for technological advances in its five major business segments—electronics, aircraft products, energy services, major appliances, and other lines, including publishing, highway equipment, and technical services. Raytheon operates more than 80 manufacturing plants and laboratories in 23 states, and employs 71,600 people worldwide.

Raytheon's Advanced Device Center

Government contracts account for 54.8% of Raytheon revenues. The research and development funds are similarly split. About half of Raytheon's $274 million annual R&D budget is reimbursed through contracts from the US government, with the balance met internally.

Raytheon's R&D challenge, as Dr. Cheney sees it, is to achieve research synergy throughout the company. For example, Seiscor, a Raytheon subsidiary engaged in the telephone switching business, needed assistance in making the transition from analog to digital switching. Seiscor engineers teamed with engineers from the company's Equipment Division, who primarily had worked on US Dept. of Defense projects.

Working together over two years, the research team produced a new product and an internal success story. "We want to judiciously use this synergistic team approach," says Dr. Cheney, who adds: "We're hopeful that in R&D, one plus one will equal three or more."

But Dr. Cheney emphasizes that research and development is not the only answer for technology-based companies. "R&D is too narrowly defined in this country," he says. "To achieve technological leadership, we need to work on a better transition to production."

Cheney argues that the task of engineering is not complete until a company manufactures its products at high quality and low cost. He contrasts the United States with Japan, which emphasizes engineering and production more than basic research. Raytheon expects an aggressive five year plan to yield technology innovations in both government and commercial areas, as well as improved quality and lower costs in manufacturing.

manufacturing industries. John T. Preston, director of the Massachusetts Institute of Technology Licensing Office, points out that "Our emphasis takes advantage of brain not brawn." Massachusetts' distinction involves innovation rather than following the practices of others.

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THE SILVER LINING. The country's general economic malaise has hit the Northeast, and particularly the minicomputer industry, hard. But Harvard's Prof. Porter notes that "Our current economic downturn is not a sign of structural problems in [the Massachusetts] economy, but of a cycle of over-building in local industries such as real estate and retailing. Over 70% of the job losses since 1987 have been in industries that do not compete outside the Commonwealth."

According to "The Competitive Advantage of Massachusetts," a study that Prof. Porter prepared in collaboration with the Monitor Co., the state's economy has outpaced much of America over the past 15 years. With an annual real growth rate of 2.4%, the Massachusetts per capita income of $22,400 in 1990 far exceeded the $16,000 that the US as a whole achieved that year.

POLLUTION PREVENTION

Molten Metal Technology, Cambridge, is a resource recovery and pollution prevention firm with a patented technology known as Catalytic Extraction Processing (CEP). CEP makes products from wastes, by-products, and co-products.

CEP, which destroys the toxic compounds in hazardous wastes and reconfigures the atoms to form raw materials that can be re-used by industry, is readily implemented using standard steel-making equipment. Typical capital and operating costs are one half or less than those of incineration. CEP processes a wide spectrum of non-hazardous wastes by injecting them into a high temperature (1500-1900°K) metallic solvent. Destruction of hazardous components often exceeds 99.99%, without generating any undesirable by-products, like dioxins or NOx. CEP's metal solvent dissociates compounds into their elemental constituents which are then reformulated through "elemental recycling" into metals, gases, and ceramics. These constituents can be used or sold to third parties, making the processing of waste streams profitable.

CEP envisions a potential of hundreds of full scale facilities in the US to commercially process waste from multiple generators. Dedicated units piped into a manufacturing process will process the residuals from one generator. Mobile units have been designed for shorter term projects, such as remediating soil. Circle No. 2.

Daniel Gregory, chairman of the Governor's Council on Economic Growth and Technology, points out that this is not the first time that the Massachusetts economy has had to refresh itself. "The hallmark of Massachusetts economic

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Raytheon technology is helping improve the safety of air travel in the U.S. and throughout the world.

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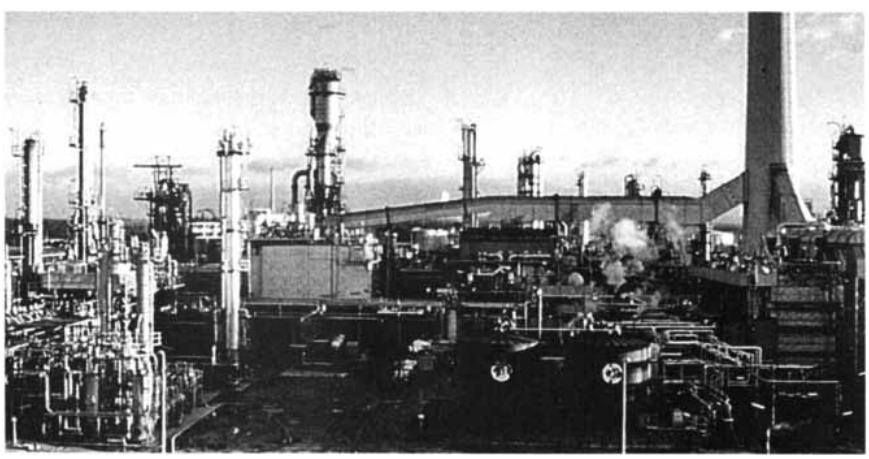

Raytheon's Badger Company helps oil companies make cleaner gasoline and build cleaner refineries.

The company is Raytheon. And many of the products and services we provide around the world are produced here in Massachusetts.

In Waltham, we build advanced air traffic control systems and weather radars that help air safety keep pace with air traffic.

In Cambridge, you'll find our Badger Company, a leader in the design and construction of refineries.

Massachusetts is also the home state for Raytheon divisions and subsidiaries that publish textbooks, produce electronic components and develop and manufacture sophisticated defense systems like the Patriot.

If you'd like more information about what we do in Massachusetts as well as around the world, write: Raytheon Company, 141 Spring Street, Lexington, MA 02173.

Raytheon

HAEMONETICS CORP.

Collaboration between Massachusetts' stellar medical community and technology companies is part of a Commonwealth tradition. "Haemonetics was started in Massachusetts because of Harvard Medical School," says Allen "Jack" Latham, who, in the 1950s, joined forces with Dr. Edwin Cohn of Harvard, who was the first to demonstrate how to fractionate the proteins in blood.

Haemonetics Corp., the company that Latham based on this technology just over 20 years ago, today is the world leader in the design, manufacture, and marketing of blood processing equipment and related disposables. The company's blood processing systems consist of a micro-processor-controlled centrifuge drive and pumps to deliver blood into and out of the system. Haemonetics has developed a cost-efficient process for making the processing chamber, as well as the tubing through which the blood passes, disposable. More than 600 employees work at the Braintree headquarters and manufacturing site, where Haemonetics also conducts research. R&D receives about 7% of sales each year; last year sales amounted to $157.3 million.

Dr. Jack Latham with the "Latham processing chamber"

The company concentrates in three major markets: surgical blood salvage, blood component therapy, and automated plasma collection. Haemonetics' Cell Saver® systems wash whole blood salvaged from surgical procedures, so that the red cells may be safely reinfused to the patient. "There has been a tremendous change in the attitude of the medical community due to AIDS," observes Latham, who continues to conduct research at age 83. "More surgeons are employing autologous transfusion, which uses a patient's own blood."

A negative side effect of today's aggressive cancer therapies is the depletion of platelets, which control bleeding. The V50 Plus, the Mobile Collection™ System and other Haemonetics systems efficiently harvest platelets and other essential blood components from donors on a large scale for use in component therapy. Haemonetics' equipment, which provides a superior platelet product, reduces the patient's exposure to a single donor.

Haemonetics has also improved plasma collection. Its automated systems—PCS® and the PCS Plus®, for use in donor centers, and the Ultralite®, a mobile system—collect larger volumes of plasma from single donors than can manual procedures.

Fifteen months ago, Navy ships anchored off the Persian Gulf carried blood supplies to treat casualties from Operation Desert Storm. The vital cargo for processing thousands of units of red blood cells came from Haemonetics. It was back to the future, in a sense; the solutions and machines were similar to those which helped launch the company.

history has been our adeptness at transforming ourselves to fit the times—and not just to survive, but to lead."

Even the state's current weak economy has a silver lining. The cost of living, notably housing, has leveled off during the past few years while living costs have risen in other technology areas. Lease rates for Massachusetts office and light manufacturing space are unusually attractive and research personnel are atypically available.

The Massachusetts ebullience of the 1970s and 1980s owed much to minicomputers and defense-based companies. The current wave of innovation from today's companies is broader, leading observers to predict a stronger, more diverse foundation in the long run. "Thriving industries are emerging in medical instrumentation and products, environmental technology, software, and new materials," says MIT's Preston. He points out that MIT alone creates six-to-eight new companies and 70-90 licenses each year. Preston doesn't rule out a resurgence in the Massachusetts computer hardware industry, either, particularly as advanced computer algorithms and electronic materials gain ground.

FOOD INGREDIENTS

Opta Food Ingredient's products can be used by processors to reduce the fat content, eliminate the need for sulfites, and provide protective edible coatings to various food systems. Opta food ingredients employ biochemical tools, especially protein chemistry and applied enzymology. Based on a fundamental understanding of structure-functionality correlation, Opta has developed a protein-based fat replacer called LITA®. Through physical manipulation of corn proteins, the quanternary structure of those proteins was altered to microspherical clusters of protein molecules. These protein microparticles form a stable suspension in water and possess certain physical characteristics and functionality similar to those of fat emulsions.

Opta has developed a family of potent polypherol oxidase inhibitors that functions in a variety of foods to inhibit enzymatic browning. One composition, EverFresh™, is available to the shrimp industry as a functional alternative to sulfiting agents. Circle No. 3.

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THE BUSINESS CLIMATE. During the last decade, Massachusetts has become a better place in which to do business and attract personnel. Between 1979 and 1988, the state's per capita tax burden fell from among the stiffest in the country to 43rd among all states. In fact, tax cuts under the Weld administration have led the press to label the state as "Slash-a-chusetts."

Also, evidence suggests that Massachusetts employers get more bang for their buck. In a report released by the Massachusetts Center for Technology Growth, the Bank of Boston found that average annual pay of communications equipment workers in Massachusetts was $44,207. While such salaries may seem high, the study found that communi-

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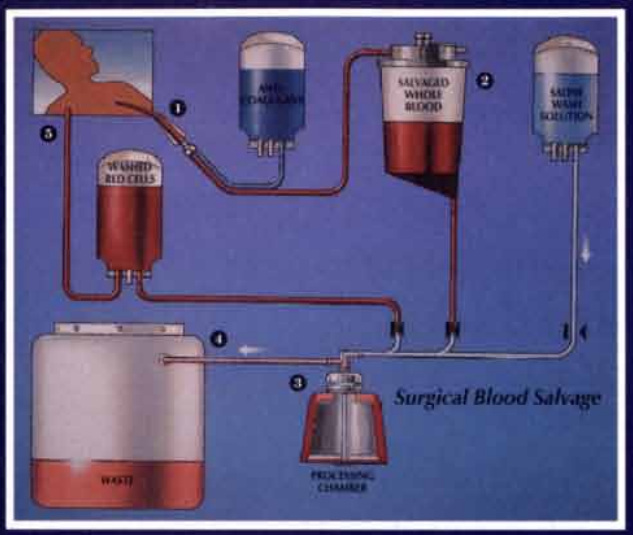
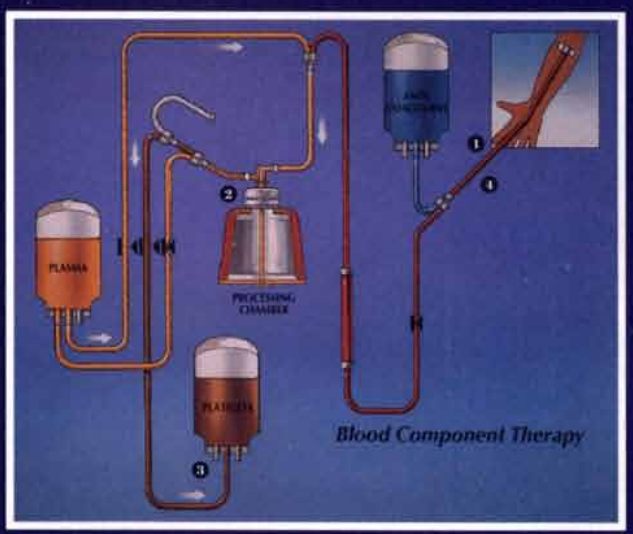


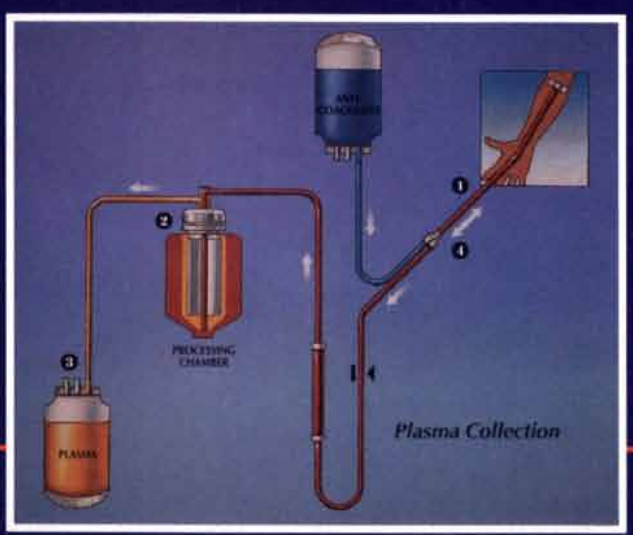
Surgical Blood Salvage

(1) Shed blood is collected from the surgical field and (2) stored in a reservoir. (3) Waste is separated from healthy red cells, (4) washed out and sent to a bag. (5) Washed red cells are returned to the patient.



Blood Component Therapy

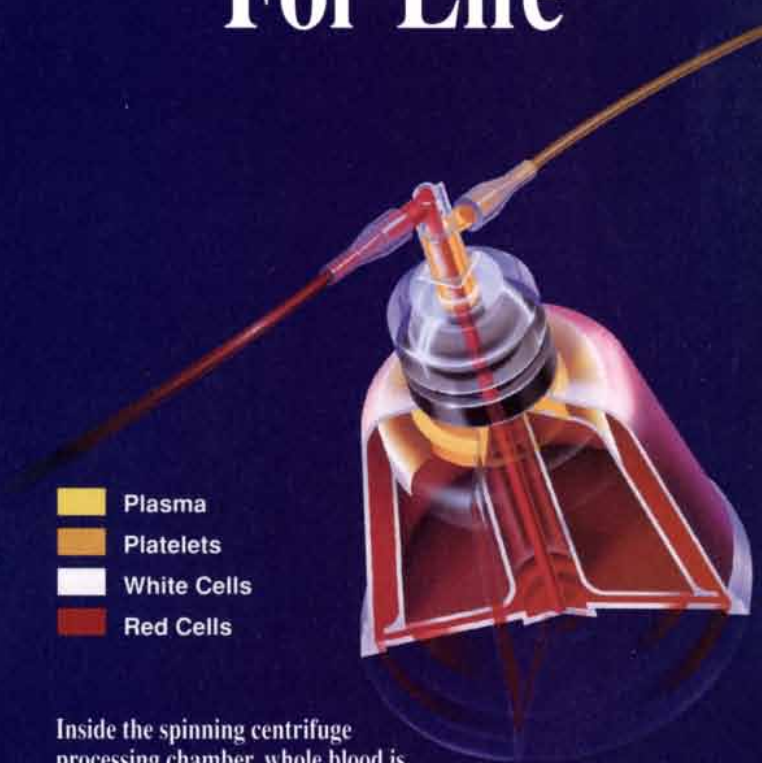
(1) Whole blood is collected from a healthy donor and (2) separated into its components. (3) Platelets are harvested and (4) remaining components are returned to the donor.



Plasma Collection

(1) Whole blood is collected from a healthy donor and (2) separated into its components. (3) Plasma is collected and (4) remaining components are returned to the donor.

Quality Blood For Life



Inside the spinning centrifuge processing chamber, whole blood is separated into its components (red cells, platelets, and plasma). The Latham processing chamber, invented by Haemonetics founder, Allen Latham, is used with a variety of Haemonetics processing systems to facilitate the processing of blood and to improve the quality of blood products.

In surgery, Haemonetics Cell Saver® Systems salvage shed red cells for reinfusion, eliminating or reducing the need for donated blood. In blood component therapy, platelets and plasma are collected for administration to cancer patients and others in need of specific blood components. In plasma collection, automated systems collect plasma to be fractionated into separate components.

HAEMONETICS®

BOSE CORPORATION

Dr. Amar G. Bose has strong opinions about quality sound. Chairman of the eponymous audio equipment manufacturer, Dr. Bose believes most stereo and audio products on the market today are unnecessarily complicated. Dr. Bose, whose component speakers are best-sellers in the US, Europe, and Japan, says there's usually no need for more than volume, dial selectors, and power switches on most stereo systems. "The saddest part is that if you ever turn all those knobs, the performance will actually deteriorate," he says. The same goes for loudspeakers. What really bothers Dr. Bose, an MIT-trained electrical engineer, is that people pay a lot of money for elaborately engineered specifications that they cannot detect by listening to music. "In a really good product, the technology should be on the inside, and simplicity on the outside," Dr. Bose insists.

That statement neatly sums up the philosophy of the company he founded nearly 30 years ago with one employee, his graduate school teaching assistant Sherwin Greenblatt, now president. Today, the privately held Bose® Corporation employs 2,800 people worldwide, and claims revenue of around $400 million, with over half of its sales from outside the US. In manufacturing products from car stereos to aviation headsets to the loudspeakers for the 1992 Olympic Games in Albertville, France, the philosophical foundation of Bose has never wavered. The company is dedicated to applying fundamental science to whatever project it undertakes.

Bose's noise-reducing headset helps prevent hearing loss for pilots

Bose backs up its commitment by reinvesting its profits in research and development. "Research," says Dr. Bose, who still teaches at MIT, "is what I would do 80 hours a week if I could." As his company's technical director, Dr. Bose clearly likes to keep close tabs on its scientific endeavor . The company's corporate headquarters building, dramatically located on a windswept hill-top in Framingham, also houses its research center. There, Bose's audio laboratory—considered by many the best-equipped in the country—is home to its acoustical engineering staff. The company's drive for excellence in engineering also led to the construction of a showcase manufacturing operation in nearby Westborough. Bose has seven other production facilities in Canada, Ireland, Mexico, and elsewhere in the US, but Westborough represents the culmination of years of studying the most advanced methods and adding refinements. "We disburse ideas from there to our other factories," says Greenblatt.

Secure in its successful track record and confident in the abilities of its research staff, Bose Corporation is comfortable with the long development times associated with building a breakthrough piece of audio equipment. At Bose, it is not unusual for a decade to elapse from the outset of a project to its manufacture. Some 14 years of research went into Acoustic Wave® Music System, a compact, portable stereo system introduced in 1984. Dr. Bose himself was involved in producing the mathematical formula enabling that technology, which cost some $14 million to develop. And back in 1979, based on a handshake agreement with General Motors Corp., Bose invested $13 million to design acoustically customized music systems for automobiles. The company, which didn't see its first dollar from that investment for three years, now is an acknowledged leader in factory-installed car stereo systems, also available on Japanese and European luxury autos.

When Bose research yields a product, it is often truly new and different, rather than a minor variation on last year's model. Recently, the company has reached out in new directions. Bose labs produced the revolutionary headset worn by pilots on the experimental around-the-world Voyager aircraft. The headset employs an active noise-reducing technology that helps prevent permanent hearing loss, an occupational hazard for pilots. The company is working to apply that concept to industrial and other environments where noise-reduction is a priority.

Bose Corporation considers its presence in the professional sound system market—the designing of sound systems for concert halls and other public spaces—full of future potential. Greenblatt notes a Bose computer design technique helps architects and designers "listen" to a hall before it is even built. Bose employed this technology when designing the sound systems for 16 different venues for the 1992 Winter Olympics.

Advanced technology for better sound...everywhere.

The 1988 and 1992 Winter Olympics selected Bose® as their professional sound system supplier.

NASA chose proprietary Bose speaker technology for its communication and alarm systems in the space shuttle.

The Bose 901® Direct/Reflecting® speaker system is the most highly acclaimed, regardless of size or price.

Founded by Professor Amar G. Bose of MIT, Bose Corporation is dedicated to advancing the quality of sound in all environments.

Bose research leads to innovative, award-winning products you'll hear in the most demanding places.

From airplane cockpits to the luxurious cruise ship Queen Elizabeth 2. From Bangkok's Royal Grand Palace to the Japan National Theatre. And other residential, commercial, and industrial applications worldwide.

If you're driving a leading luxury or sports car made in the USA, Europe, or Japan, and it features this logo BOSE it was delivered from the factory with a custom sound system designed and built by Bose. This system was developed specifically for the acoustics of your model. And you know the result.

When you want quality sound, contact Bose. For information and our all-product brochure, call toll free in the USA and Canada: **1-800-444-BOSE** Ext. 91. Elsewhere, call (508) 879-7330.

"If music is important in your life, sooner or later you will own a Bose system."

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Better sound through research.

SERONO LABORATORIES

Serono Laboratories Inc. was established in 1970 as the American distribution arm of The Ares-Serono Group of Geneva, Switzerland, an international pharmaceutical and diagnostic company with 1991 worldwide sales of $751 million. Since then, the Norwell-based operation has grown from $1 million in sales into a fully integrated, research-based pharmaceutical house with 1991 sales of over $130 million. Today, the largest biotechnology company in Massachusetts, Serono has become one of the few to advance to the product-manufacturing stage and enjoys dominant patent positions for all its recombinant products currently in development. "We have been a company that sells naturally derived products," observes president Jules Musing. "But we have expanded into a true biotechnology company, and next year we hope to start selling our first recombinant infertility product."

Ares-Serono harvests recombinant human growth hormone from roller bottles

Serono is considered the world leader in infertility products. Along with its parent, Serono is the largest maker of gonadotropins, or human fertility hormones, in the world. Musing says that within the next four years, Serono will be the first biotechnology company to make its trademarked drugs—Pergonal® (menotropin), Metrodin® (urofollotropin), and Profasi® (human chorionic gonadotropin)—as recombinant products.

In its second key therapeutic area, immunology and oncology, Serono produces drug therapies for patients with impaired natural defenses. Frone®, also known as native beta interferon, fights viral infections by strengthening cell resistance to viruses, and is used to treat genital herpes and breast cancers. TP-1® is used in a broad range of cancer treatment protocols. Again, Serono has a recombinant beta interferon product in its biotech pipeline.

The company's interleukin-six, also under development, shows promise in the treatment of severe side-effects of cancer therapies as well as treating certain cancers.

Serono's third principal area is human growth, specifically pediatric endocrinology. Its Randolph biotech manufacturing facility produces for export Saizen® (somatropin), a recombinant growth hormone used to treat children who suffer from dwarfism.

Sister company Ares Advanced Technology's $12 million, state-of-the-art research laboratory in Randolph serves as a worldwide biotechnology R&D center for the parent company. Its two major research interests are human fertility and the development of new interferons, proteins the body produces in response to viral infections. The facility is notable for its mammalian cell-based technology, considered to produce complex molecules, physiologically closer to human cells than other biotech methods using bacterial or yeast cells.

continued from page MA 8

cations equipment produced in the state has 32% more "value-added" per worker than the national average.

The latest analysis of productivity showed output per Massachusetts employee was three times the national average between 1979-1986. "We located our new, state-of-the-art manufacturing facility in Massachusetts because there is a complex technological component involved in our manufacturing, and we've found workers here to master it," says Sherwin Greenblatt, president of Bose Corporation.

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MASSACHUSETTS LIFESTYLE. When discussing lifestyle in Massachusetts, the emphasis is on cultural pursuits found in Boston, the nation's seventh largest city: the Boston Symphony, the Boston Ballet, the Theater District, and the history rediscovered by millions each year who march the Freedom Trail. "And there is my personal favorite," says Dr. Paul Hoffman, president of Textron Specialty Materials, "the Boston Red Sox."

AUTOIMMUNE DISEASE

In the early 1980s, multiple sclerosis expert Howard Weiner, M.D., of Brigham and Women's Hospital and Harvard Medical School began animal studies to determine whether the phenomenon of oral tolerance in which specific immune suppression occurs following the ingestion of proteins might be applied to patients. In concert with AutoImmune Inc., Boston, Weiner has conducted a series of experiments using the animal model of MS that shows feeding the autoantigen myelin basic protein protected them against disease. Extensive animal research has demonstrated the efficacy of oral tolerance to autoantigens in a variety of animal disease models.

Results of a clinical trial initiated by Weiner and David Hafler, M.D., in which patients with early MS ingest specially prepared myelin proteins, will be available in late 1992. Also, collaboration with AutoImmune and the Brigham group has led to oral tolerance human trials in rheumatoid arthritis by David Trentham, M.D., at the Beth Israel Hospital in Boston, and by Robert Nussenblatt, M.D., in uveitis at the NIH. This approach could provide a nontoxic, easy to administer therapy for autoimmune diseases. Circle No. 4.

Boston also abounds in museums, including the Museum of Fine Arts and the world's only Computer Museum. The Museum of Science holds 400-plus permanent exhibits dedicated to "improving science literacy by making basic and cutting-edge science understandable and approachable." Steven L. Solomon, vice president of resources, says that the Science Museum "wouldn't be the same without the intellectual horsepower of the high-tech companies and institutions like MIT and Harvard that are our neighbors."

Massachusetts has 351 cities and towns, but "One major reason we're here is we can live in an area of low population density," says Alain Hanover, chairman of Viewlogic Systems Inc., Marlborough, and co-chair of the Massachusetts Center

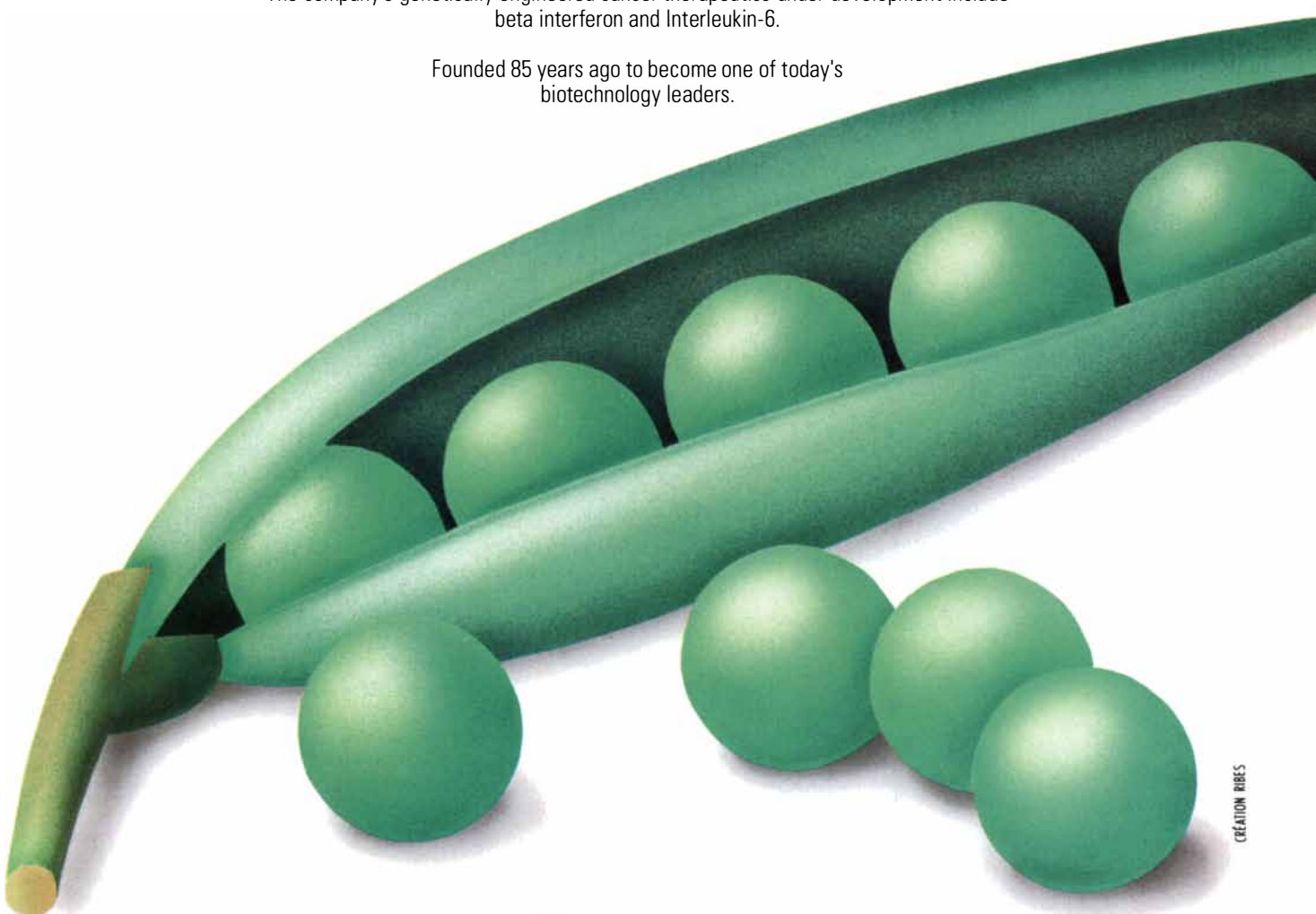
FROM PEAS TO SUCCESS, THANK YOU GREGOR J. MENDEL

Thanks to Gregor Mendel's very early work in plant genetics,
our scientists, today, are applying recombinant DNA technology to treat a wide array of human disorders.

Ares-Serono's current biotechnology pipeline is rich with six recombinant products in the company's main therapeutic specialties - obstetrics/gynecology, pediatric endocrinology and immunology/oncology.

As the world leader in the treatment of infertility,
Ares-Serono is now developing recombinant gonadotropins (fertility hormones) to offer new perspectives in infertility treatment.
The company's genetically engineered cancer therapeutics under development include beta interferon and Interleukin-6.

Founded 85 years ago to become one of today's
biotechnology leaders.



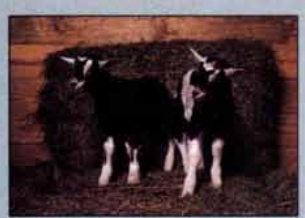
Serono

TUFTS VET SCHOOL

Massachusetts is not only home to the country's oldest institute of higher education, Harvard University, but also one of the newest. Tufts University Veterinary School, still the only vet school in New England, first accepted students in 1979. "Our little vet school doesn't have the biggest endowment," says Dean Franklin M. Loew, "so we've had to be more strategic than our neighbors."

The North Grafton school developed an aggressive industry collaboration program to fund its future. This decision meshed beautifully with another of its decrees: to make biotechnology one of the school's "signature programs." Says Dean Loew: "My colleagues and I decided that biotechnology would be one of the industries of the future. We wanted Tufts to be part of that."

More than 40 companies throughout Massachusetts and the world have approached Tufts with specific research proposals. An early collaboration began five years ago when Tufts signed research contracts with Integrated Genetics, a Framingham company that has since become a Genzyme Corp. subsidiary. Last fall the corporation and university announced they had engineered a "transgenic goat." The genetically modified goat produces a pharmaceutical in its milk used to treat heart disease.



Tuft's researchers engineered transgenic goats

Scientists obtain transgenic animals by implanting a genetic material into the germ cells or already fertilized ovum of a female animal. When the introduced DNA is integrated into the chromosome of her offspring, both that animal and successive generations carry the new gene. Genes for a certain trait can come from other species. Rat hormones inserted into mice yield a superior growth hormone, for example. Other Tufts collaborations could lead to decreased cholesterol in chicken eggs, disease-resistant farm animals, and pharmaceuticals that tackle both human and animal health concerns.

"The high and noble reason we enter industry collaborations is to further our mission of creating knowledge and improving the health of humans and animals," says Dean Loew. But he acknowledges the importance of other reasons. The school has received well over $10 million in research contracts and grants from biotechnology companies to date. This money goes to further research and provide financial aid to students. Licensing and royalty fees could represent a substantially larger bounty in the future, as products of research are commercialized.

Also, nobody doubts that biotechnology is a core technology of the future. "If my school can be part of the biotech industry and lead us into a healthier economy, we will be involved in job creation," says Dean Loew. "Biotech is one successor technology to microelectronics."

for Technology Growth, a non-profit group of high-tech CEOs, venture capitalists, management consultants, and government officials who focus on attracting technology employers to Massachusetts. Viewlogic is situated on Route 495, the second high-tech belt around Boston after famed Route 128. The Commonwealth's small size means it's possible to drive from one corner of the state to the other in three hours. That puts Cape Cod, the Berkshires, and the islands of Martha's Vineyard or Nantucket within easy reach.

TRANSGENIC GOATS

Researchers at Tufts University School of Veterinary Medicine and Genzyme Corp. have announced the first genetically modified (transgenic) goats to produce a human pharmaceutical in their milk. The goats lactate a protein, tissue plasminogen activator (t-PA), which is used to treat heart attacks. The breakthrough demonstrates the feasibility of producing pharmaceuticals from livestock and could lead to lower drug manufacturing and production costs, as well as a new "value-added" agriculture.

As part of the veterinary school, a New England Regional Biotechnology Transfer Center will be developed with $1.5 million in federal funding, enhancing Tufts' plans to develop a biotechnology research park on its 634-acre North Grafton campus. The proposed park is envisioned as an integral part of a biotechnology corridor extending from Worcester County to Boston, where Tufts University Development Corporation is the designated developer of "Technopolis," the $600 million Tufts International Research Center for biomedicine at Boston's South Station. Circle No. 5.

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MONEY OF THE COMMONWEALTH. Among the many Massachusetts inventions is the concept of risk capital. "Boston used to finance clipper ships and textile mills when they were the high-tech businesses of the day," says David Redlick, a partner at Hale and Dorr, a Boston legal firm that specializes in representing high-tech companies. Financial returns from those early successes helped make Boston a repository of "old money" and the mutual fund capital of America.

"Today, Boston has probably the largest concentration of venture capital in the US," says Michael E. Lytton, a partner and co-chairman of the biotechnology and health care practice group at Hale and Dorr. American Research & Development, formed in the 1940s, is often cited as the first significant venture capital fund in the country. Its $70,000 investment in Digital Equipment in the 1950s remains one of America's shining venture capital success stories.

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BUSINESS INFRASTRUCTURE. Despite assurances from astronomers, business people insist that the earth is spinning at an ever increasing rate, giving innovations an increasingly

continued on page MA 18

Pioneers in Biotechnology

Collaborations are the Future.

Tufts University School of Veterinary Medicine has the scientific, clinical, biomedical and diagnostic laboratory expertise to aid you in your quest to discover and develop biotechnology products. Located on a 634-acre campus, between Boston and Worcester, the School has the land, personnel and state-of-the-art facilities available for successful collaborative ventures in biotechnology. The school has developed collaborative relationships with over 50 emerging and established biotechnology companies. These ventures span a spectrum of activities that range from R&D to the evaluation of new therapeutic agents and biomaterials. A recent collaboration with Genzyme Corporation of Cambridge has led to the development of genetically modified goats that produce tpA in their milk. This innovative approach demonstrates the feasibility of producing commercially available pharmaceuticals from livestock which could lower manufacturing and production costs for certain drugs and other compounds.

Partners in Biotechnology

Let us show you what Tufts can do for you.
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TEXTRON SPECIALTY MATERIALS

As the world's most diversified materials developer and supplier, Textron Specialty Materials strives to meet current market demands for materials with high-performance applications. At the same time, the Lowell-based company attempts to anticipate product needs and markets that will emerge decades in the future. This dedication to strategic planning and R&D, notes Textron Specialty Materials President Dr. Paul Hoffman, has resulted in the company's diversification, a key to its average 20% growth rate over the past 10 years.

A division of Textron Inc., Textron Specialty Materials is a fully integrated material supplier with emphasis on high-temperature applications. From the Apollo capsule heatshield to F-15 fighter jets to offshore oil rigs, Textron has developed unique materials to meet specific needs. Its 400 employees develop high-performance materials for applications that require exceptional strength, stiffness, light weight, and heat resistance. A pioneer in advanced materials, Textron invented 3D carbon-carbon composites, is the world's only commercial producer of boron fiber, and is the largest producer of chemically vapor deposited fibers. The company also developed the first outdoor fireproofing material to receive an Underwriters Laboratory listing.

Advanced turbine engines use Textron's silicon carbide filament reinforced titanium composite materials

Textron remains in the forefront of materials science by attracting top scientists and engineers. The way the company works with customers is also essential. "Because our products are so new, we do a lot of concurrent engineering," says Dr. Hoffman. That means, for example, working with the designer of a gas turbine engine on a part at the same time that Textron develops its manufacturing process.

Textron Specialty Materials has been particularly adept at the transfer of technologies from one industry to another, as well as from one generation of material to another. A product's life cycle that begins with in-house R&D typically finds support from government R&D programs. After the products move into military applications, they eventually reach the commercial arena. For example, the boron fiber used in F-15 fighters is also found in high-performance sporting goods.

One project on Textron's roster is a silicon carbide fiber reinforced titanium composite, the baseline material for a futuristic experimental aircraft, the National Aerospace Plane (NASP). The single-stage-to-orbit hypersonic vehicle is meant to fly at mach 25, more than 10 times faster than the Concorde. "The plane will take off from a runway, and will fly into orbit," says Dr. Hoffman. As the NASP plane flies increasingly faster, intense heat will build on its surface. That is where Textron's heat-resistant metal matrix composites come in. Together, the US government and a national project team of leading aerospace companies (McDonnell Douglas, Rockwell, General Dynamics, Pratt & Whitney, Rocketdyne) has awarded Textron over $20 million to develop materials and manufacturing techniques and to make test components for the project.

Textron Specialty Materials is establishing a new manufacturing facility near its Lowell headquarters to support the NASP—the first plant ever dedicated to producing continuous metal matrix composites. The company also is developing its metal matrix composites for high-performance advanced turbine engine programs like the High Speed Civil Transport and the Integrated High Performance Turbine Engine Technology initiative. As yet, these projects remain in the R&D stage, but, as with the NASP, growth potentials lie ahead.

Textron's catalog of military-to-commercial technology transfers is about to expand. For 20 years the military has reinforced and repaired stresses and cracks in its aircraft with boron/epoxy doublers. The material stops the spread of cracks caused by impact, corrosion, and fatigue. Because it is adhesively bonded rather than mechanically fastened to the aircraft, the boron/epoxy doubler minimizes additional stress caused by bolting or riveting. Says Dr. Hoffman: "We are working to have the boron/epoxy process approved by the FAA for commercial aircraft."

Moving new material from the lab to the market sometimes requires decades. But that kind of commitment has been Textron's strength. "Seventy-five percent of our revenues are for fixed-price material for delivery," notes Dr. Hoffman. But the rest represents R&D sales for government contract work ike the NASP project. "That means 25% of our sales are for the future." The company now has efforts underway to develop intermetallic composites, advanced silicon nitride-based ceramic composites, rapid densification methods for carbon-carbon composites, and super-high temperature fibers. Applications for such materials will occur in the next century.

MATERIALS THAT REDEFINE THE LIMITS

HIGH TEMPERATURE COMPOSITES

Textron Specialty Materials' metal and ceramic matrix composites are used in applications such as advanced turbine engines and aircraft structure. Textron's continuous silicon carbide reinforced titanium has been selected as the baseline structural material for the National Aerospace Plane.

BORON FIBERS

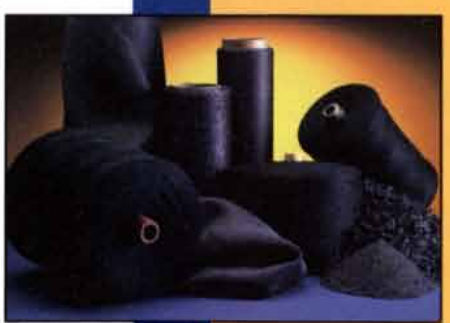
Textron's boron fibers are used worldwide for the structure of U.S. military aircraft including F-14 and F-15 fighters, B-1 bombers and the Space Shuttle. It is also used to reinforce and repair military and commercial aircraft and to enhance high-performance sporting goods.

CARBON-CARBON COMPOSITES

Textron Specialty Materials' three dimensional Carbon-Carbon composites comprise the rocket nozzles on Peacekeeper, Trident and SICBM missile systems. Textron's specialized facilities produce rocket components as large as 8 feet in diameter with temperature resistance in excess of 5000° F.

FIRE PROTECTION MATERIALS

Based upon thermal protection capabilities developed for the Apollo capsule's heatshield, Textron offers an array of outdoor fire protection systems including spray-on intumescent coatings and prefabricated panel systems for chemical plants, oil refineries and offshore platforms worldwide.



CARBON FIBERS

Textron's Carbon Fibers include stabilized acrylic and carbonized yarns and fabrics. These fibers' unique mechanical properties are tailorable to customer requirements and have applications in aircraft brakes, ablation, stealth and reinforcement of high-temperature bushings and bearings.

TEXTRON Specialty Materials

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continued from page MA 14

short shelf-life before competitors enter the fray. Massachusetts companies say that the superior business, university, and workforce infrastructure at their doorstep allows them to bring products to market in record time. "Look at the product cycle," says Gregory Sheldon, director of the Massachusetts Center for Technology Growth, "It's all here. The secret ingredient today is bringing high quality products to market quickly at a reasonable price." Adds Allan Jennings,vice president of AViiON development at Data General: "Massachusetts retains one of the best technical infrastructures in the nation."

SPEECH RECOGNITION

Dragon Systems Inc., Newton, is world-renowned for DragonDictate-30K, the first large vocabulary, general purpose, speech recognition available for personal computers. DragonDictate-30K combines a dynamic 30,000-word vocabulary with a unique speaker adaptation feature that learns your voice as you speak. The user interface features voice-driven menus and error correction.

Dragon is now developing large vocabulary speech recognizers in numerous languages, and has demonstrated high-performance continuous speech capabilities with vocabularies over 5,000 words. Partnerships with companies such as Apricot Ltd., IBM, and Lanier Voice Products have extended Dragon's technology to applications in areas such as medicine, law, and general business. Circle No. 6.

DIAMOND FILMS

Synthetic diamond products made from methane and hydrogen gases are in the early stages of commercialization by the Norton Diamond Film group in Northboro. Norton's Diamond Film group and its associates have developed two proprietary chemical vapor deposition (CVD) manufacturing processes which create high quality diamonds at low pressures and moderate temperatures.

Using a patented DC arc jet plasma CVD process, Norton makes freestanding diamond thick film wafers up to 150 millimeters in diameter and up to one millimeter in thickness. Fine-grained diamond film coatings five to 25 microns thick are made using a microwave plasma CVD process. Deposition parameters can be varied to optimize thermal, mechanical, and optical properties. These breakthroughs make the synthetic diamond available for a wider range of tribological, optical, and thermal management applications. Circle No. 7.

Financial, legal, communicatons, data, and marketing networks are also at the beck-and-call of the Commonwealth's smaller technology companies. "A variety

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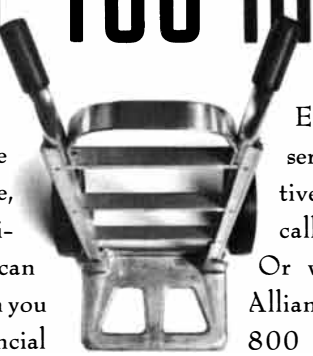

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Massachusetts Utility Alliance for Economic Development

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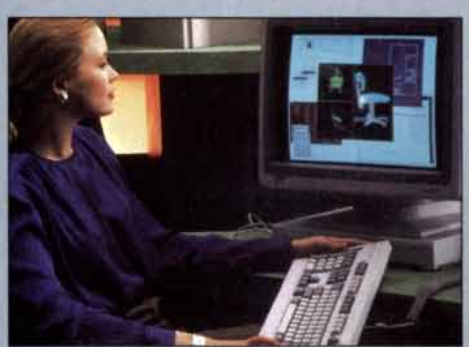
DATA GENERAL

Westborough-based Data General has essentially re-made itself over the past two years. Known until recently as a dominant factor in the minicomputer market, the company overhauled its product strategy and is now a leading proponent of "open systems," based on high-performance RISC (reduced instruction set computing) microprocessor chips and industry standard software. Data General's open systems approach allows businesses to integrate their existing desktop personal computer systems and networks, regardless of manufacturer, and thus make their different networks act as one. "This represents the next generation of enterprise computing," says Allan Jennings, vice president and head of AViiON development. The company's new AViiON server products, he adds, represent the future of Data General.

Servers, explains Jennings, are the computing systems that sit behind the desktop computers, linking them together, and enabling them to participate in corporate networks and access corporate data banks. The powerful server computing products under the AViiON umbrella, says Jennings, are helping Data General customers achieve the full organizational productivity that has long eluded many PC and desktop system users. Data General's technology is based on symmetric multiprocessing, which allows its systems to deliver up to 120 million instructions per second, by knitting together multiple low-cost RISC microcomputers. Since introducing AVjiON just over two years ago, sales in that product area have doubled to $200 million in 1991. Data General as a whole posted sales of $1.23 billion last year.



AViiON computer products offer low-cost alternatives to mainframes

The company's transformation over the last few years has been dramatic. It halved its workforce, for instance, from 17,000 employees to 8,500 and reduced its manufacturing plants from 11 to 4. And the new direction required a totally new and different mindset and organizational profile at Data General from what prevailed in its proprietary minicomputer business.

To be sure, the open systems field is crowded with competitors, but Jennings points out that most other companies treat the trend as simply one of many businesses they're in. What's unique about Data General's approach, says Jennings, is that "our commitment is complete and total."

of assembly operations, providers, and suppliers make it feasible for small companies to manufacture without incurring enormous capital costs," agrees Hodgman. "Innovative companies often have a tight connection between the design and manufacturing of their products."

CULTURED TISSUE GRAFTS

Based on its patented technology for growing epithelial tissue, BioSurface Technology has established a business in culturing burn victims' own undamaged skin, called AUTOgrafts. BioSurface is extending the application of its technology to chronic wound healing through the development of ALLOgrafts, biologically active bandages consisting of cultured, living skin. ALLOgrafts are currently undergoing initial clinical trials for five major wound healing indications.

BioSurface's procedure expands a postage stamp-sized piece of skin into two square meters in three weeks. BioSurface is also experimenting with the culturing of other types of cells, and has initiated clinical trials with cultured autologous oral tissue in periodontal and maxillofacial surgery. Circle No. 8.

BIODEGRADABLE PLASTICS

At the University of Massachusetts, Amherst, a joint research program of the Polymer Science and Engineering Department (R.Lenz) and the Biochemistry Department (R.C.Fuller) has generated many new biodegradable plastics and elastomers by utilizing different bacteria grown with different substrates. An especially promising product is the family of strong, tough thermoplastic elastomers, which are totally biodegradable. These elastomers are produced by a common aerobic bacterium grown with aliphatic acids such as octanoic and nonanoic acid. The physical and mechanical properties of these elastomers can be readily controlled by selection of the growth medium, and large quantities are produced in short growth cycles. Currently, the University has fully automated fermentation facilities capable of carrying out up to 80 liter batch culture processes, and the research group can provide either new biodegradable polymers or can participate in cooperative programs for the development and evaluation of bacterial polymers. Circle No. 9.

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21ST CENTURY PIONEERS. Hodgman, referring to many Bay State companies as "21st Century Pioneers," speculates that "present day Massachusetts companies are

QUANTITATIVE ULTRASOUND

New ultrasound technology from Hewlett-Packard Medical Products Group in Andover adds valuable quantitative measurements of heart function to the traditionally qualitative echocardiography examination. Using the quantitative information provide by HP Acoustic Quantification (AQ) technology, physicians can track a cardiac patient's condition more accurately and consistently over time. The efficacy of drug therapy or other interventions can be measured immediately and noninvasively. During open-heart surgery, HP AQ provides an objective measure of how well the heart is recovering from cardio-pulmonary bypass. More clinical applications of HP AQ technology are under investigation. Circle No. 10.

precursors of what successful businesses will look like in the 21st century." The state's pioneering products command premium prices and hefty profit margins because "they are equipped with very high value-added components." Such an edge allows small companies to compete on the global level.

By the next century, Hodgman suggests large bureaucratic corporations will play a less vital role in

GENSYM CORPORATION

Quick, what do the aerospace and bread baking industries have in common? Gensym Corp., Cambridge, points out that each requires intelligent monitoring and control of hundreds of dynamically changing variables. Gensym's G2 real-time expert system helps deploy an organization's operational expertise. With more than 1,000 copies of G2 installed, the company is "the leading real-time expert systems product company in the world—if not the leading expert systems company period," says Chairman and CEO Lowell Hawkinson.

G2 applications are typically developed by the client's experts using everyday language: "Whenever X happens, do Y." G2 provide early detection of safety and quality deviations.

Founded just six years ago, Gensym is marketing the third-generation of G2. Products layered on G2 include the Dynamic Scheduler, which automates the scheduling function for made-to-order manufacturers with highly responsive operations, and the Diagnostic Assistant, which identifies faults in complex situations. Meanwhile, an Energy Manager prototype helps large process plants optimize energy usage.

REAL-TIME RESULTS, REAL-WORLD BENEFITS

Companies around the world are beginning to use expert system technology as a strategic weapon in their bid to improve their competitive positions. The technology is allowing them to improve their plant productivity while dramatically reducing costs--thereby increasing their market share.

Gensym Corporation, of Cambridge, Mass., is leading the effort to advance the application of this technology and move it into the mainstream of industrial production. In 1988, Gensym introduced the G2 Real-Time Expert System, a powerful, but easy-to-use decision support tool. Today, there are over 1,000 installations of G2 in 30 industries around the world.

G2 makes "expert knowledge" available to people working in time-critical environments so they can make faster, more reliable decisions. This is especially crucial in places like manufacturing plants, petroleum refineries, and chemical plants.

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FLEXIBLE CONDUCTORS

The new family of ceramic oxide high temperature superconductors (HTS) has become increasingly more useful due to advanced manufacturing processes from American Superconductor Corp. Applying standard metal-working methodologies, ASC refined a patented fabrication technique that yields superconducting ceramic wires in flexible form. The "metallic precursor" process results in wires that have the flexibility and durability to withstand the physical handling they typically undergo during incorporation into electromagnetic coils and other components.

Since its founding in 1987, ASC has developed other proprietary manufacturing processes. American Superconductor can produce lengths of wires or tapes with consistent electrical and magnetic properties spanning up to 50 meters that are among the best reported in the literature. ASC is proceeding with research to further improve the superconducting properties of HTS wires, while preserving their robust qualities. Circle No. 11.

LIQUID SOLAR CELLS

Chemist Stuart Licht of Clark University in Worcester is developing a liquid solar cell capable of converting more of the sun's energy to electricity and of producing a voltage twice as high as that of conventional photovoltaic cells. Liquid solar cells can be adapted to store energy for use when there is no sunlight and also can generate valuable chemical byproducts, such as hydrogen, which can be used to run cars without pollution.

Licht's liquid solar cell is compact enough to hold in the hand. It consists of two electrodes immersed in a chemical solution. Energy is generated when a semiconductor is hit by sunlight, generating a stream of both electrons and chemicals. The electrons then flow through a wire, from which a current can be tapped. After the energy is tapped, the electrons flow back into the solution and return to the semiconductor, insuring continued energy. Circle No. 12.

international and local economies, while more fleet-footed companies in the $50 million to $500 million revenue range will have an advantage. Strategies of even very large companies, like Raytheon, stress decentralization in marketing, R&D, and decision making. "The economies of scale that drove companies to mass markets won't be so crucial next century," Hodgman explains. ■

SEPTAGE TREATMENT

Ecological Engineering Associates in Marion has developed a technology for treating septage, the concentrated waste pumped periodically from septic tanks. Using aquaculture systems and artificial wetlands in a greenhouse, the process functions year-round with enhanced organic decomposition, nutrient removal, and pathogen deactivation.

A 21-month pilot project treating septage for Harwich, Massachusetts indicates the technology meets the most stringent Advanced Wastewater Standards. The technology concentrates the natural processes by managing the structure of the ecosystems through the choice and encouragement of appropriate organisms and by controlling environmental variables. Research on the process, invented by John Todd, has been done by John Teal and associates at Woods Hole Oceanographic Institution. The process produces cleaner water and lower volumes of well-stabilized solids than conventional technologies in a physically attractive, pleasant smelling facility. Circle No. 13.

Throughout the report, short, special narratives have focused on technology developments within the universities and corporations of Massachusetts. Using the reader response facility following the report, you can learn more about any of the intellectual properties in this report. Or, write: SCIENTIFIC AMERICAN April 1992, P.O. Box 5147, Pittsfield, MA. 01203-9827.

The Massachusetts Executive Office of Economic Affairs joins SCIENTIFIC AMERICAN in thanking The Technology Review Board: Allan Ferguson, J. Michael Greata, G. Felda Hardymon, Dr. Ronald Newbower, John Preston, Dr. Alison Taunton-Rigby, Stephanie K. Marrus.

Research organizations featured in the tech briefs include: American Superconductor Corp., AutoImmune Inc., Beth Israel Hospital, BioSurface Technology, Brigham and Women's Hospital, Clark University, Dragon Systems Inc., Ecological Engineering Associates, Genzyme Corp., Harvard Medical School, Hewlett-Packard Medical Products Group, Molten Metal Technology, Norton Diamond Film, Opta Food Ingredients, Parametric Technology Corp., Tufts University School of Veterinary Medicine, University of Massachusetts, Woods Hole Oceanographic Institution.

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MASSACHUSETTS UTILITY ALLIANCE

The Massachusetts Utility Alliance for Economic Development, in its partnership with Massachusetts state government, reflects a new "can-do" attitude in Massachusetts. Its mission is to maintain a vital state economy. Comprised of the seven leading utilities in the state (Boston Edison, Commonwealth Electric, Eastern Utility Associates, Fitchburg Gas & Electric, Massachusetts Electric, New England Telephone, and Western Massachusetts Electric), the group provides a comprehensive site finder function to companies thinking about locating in Massachusetts. Members also offer special incentive rates on power.

The Utility Alliance initiated the program because its members recognize that the encouragement of business development is itself a competitive business in the US and around the world. The alliance will offer prospective Massachusetts companies a host of services: on-line information about sites, complete with photographs; videos describing specific sites and communities; information on workforce educational level, age and prevailing wage rates, as well as local and state taxes and other financial considerations.

Additionally, each member of the alliance plans to offer businesses its own special incentive rates on electric power and other utility services. Moreover, members will demonstrate a number of energy-saving options that will save money for new customers.

The Massachusetts Utility Alliance may well expand, possibly inviting gas and municipal electric companies to join. An investment in growth today—like the efforts of the Alliance—goes a long way in assuring the future of the Massachusetts economy.

THERMO ELECTRON

Thermo Electron Corp., Waltham, controls seven high-tech subsidiaries, prompting one financial analyst to describe it as a "perpetual idea machine." Founded by chief executive George Hatsopoulos, the 36-year-old company now employs 6,000 people. Thermo Electron focuses on developing socially relevant technology, including: small power plants that burn agricultural waste, trucks that incinerate petroleum-soaked soil, instruments to monitor environmental contamination, and gas-fired air conditioners. Some projects—including its artificial heart program—encompass 25 years of research.

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Where Did Modern Humans Originate?

A million or more years ago primitive humans we now label Homo erectus *walked out of Africa into an uninhabited world. Were their descendants—the Neanderthal of Europe, the Beijing Man of China, the Java Man of Indonesia and others—really our ancestors? Or were they only distant cousins on dead branches of the human family tree? These questions now divide paleoanthropologists.*

In this showdown of ideas the traditional fossil evidence has been joined by a new trove of information: molecular biologists are now extrapolating the evolutionary history of living organisms from changes in their genes. The inferences are not accepted universally. In the following pages, two geneticists, the late Allan C. Wilson and his colleague Rebecca L. Cann, suggest that modern humans descended from people who lived in Africa only 200,000 years ago and supplanted early humans elsewhere. Anthropologists Alan G. Thorne and Milford H. Wolpoff advocate instead that modern Homo sapiens *emerged gradually throughout the world. The insights offered by both sides reveal the power—and the limitations—of the tools available for peering into prehistory.*

Neanderthal

Homo erectus

Homo erectus

Neanderthal

PREHISTORIC HUMANS have been reconstructed for the new Hall of Human Biology and Evolution at the American Museum of Natural History, scheduled to open in 1993. Their heads are based on fossil skulls. The bodies are modifications of casts from living people whose physical builds generally match those that the early humans are believed to have had.

The Recent African Genesis of Humans

Genetic studies reveal that an African woman of 200,000 years ago was our common ancestor

by Allan C. Wilson and Rebecca L. Cann

In the quest for the facts about human evolution, we molecular geneticists have engaged in two major debates with the paleontologists. Arguing from their fossils, most paleontologists had claimed the evolutionary split between humans and the great apes occurred as long as 25 million years ago. We maintained human and ape genes were too similar for the schism to be more than a few million years old. After 15 years of disagreement, we won that argument, when the paleontologists admitted we had been right and they had been wrong.

Once again we are engaged in a debate, this time over the latest phase of human evolution. The paleontologists say modern humans evolved from their archaic forebears around the world over the past million years. Conversely, our genetic comparisons convince us that all humans today can be traced along maternal lines of descent to a woman who lived about 200,000 years ago, probably in Africa. Modern humans arose in one place and spread elsewhere.

Neither the genetic information of living subjects nor the fossilized remains of dead ones can explain in isolation how, when and where populations originated. But the former evidence has a crucial advantage in determining the structure of family trees: living genes must have ancestors, whereas dead fossils may not have descendants. Molecular biologists know the genes they are examining must have been passed through lineages that survived to the present; paleontologists cannot be sure that the fossils they examine do not lead down an evolutionary blind alley.

The molecular approach is free from several other limitations of paleontology. It does not require well-dated fossils or tools from each part of the family tree it hopes to describe. It is not vitiated by doubts about whether tools found near fossil remains were in fact made and used by the population those remains represent. Finally, it concerns itself with a set of characteristics that is complete and objective.

A genome, or full set of genes, is complete because it holds all the inherited biological information of an individual. Moreover, all the variants on it that appear within a population—a group of individuals who breed only with one another—can be studied as well, so specific peculiarities need not distort the interpretation of the data. Genomes are objective sources of data because they present evidence that has not been defined, at the outset, by any particular evolutionary model. Gene sequences are empirically verifiable and not shaped by theoretical prejudices.

The fossil record, on the other hand, is infamously spotty because a handful of surviving bones may not represent the majority of organisms that left no trace of themselves. Fossils cannot, in principle, be interpreted objectively: the physical characteristics by which they are classified necessarily reflect the models the paleontologists wish to test. If one classifies, say, a pelvis as human because it supported an upright posture, then one is presupposing that bipedalism distinguished early hominids from apes. Such reasoning tends to circularity. The paleontologist's perspective therefore contains a built-in bias that limits its power of observation.

As such, biologists trained in modern evolutionary theory must reject the notion that the fossils provide the most direct evidence of how human evolution actually proceeded. Fossils help to fill in the knowledge of how biological processes worked in the past, but they should not blind us to new lines of evidence or new interpretations of poorly understood and provisionally dated archaeological materials.

All the advantages of our field stood revealed in 1967, when Vincent M. Sarich, working in Wilson's laboratory at the University of California at Berkeley, challenged a fossil primate called *Ramapithecus.* Paleontologists had dated its fossils to about 25 million years ago. On the basis of the enamel thickness of the molars and other skeletal characteristics, they believed that *Ramapithecus* appeared after the divergence of the human and ape lineages and that it was directly ancestral to humans.

Sarich measured the evolutionary distance between humans and chimpanzees by studying their blood proteins, knowing the differences reflected mutations that have accumulated since the species diverged. (At the time, it was much easier to compare proteins for subtle differences than to compare the genetic sequences that encode the proteins.) To check that mutations had occurred equally fast in both lineages, he compared humans and chimpanzees against a reference species and found that all the genetic distances tallied.

Sarich now had a molecular clock; the next step was to calibrate it. He did so by calculating the mutation rate in other species whose divergences could be reliably dated from fossils. Finally, he applied the clock to the chimpanzee-human split, dating it to between five and seven million years ago—far later than anyone had imagined.

At first, most paleontologists clung to the much earlier date. But new fossil finds undermined the human status of *Ramapithecus:* it is now clear *Ramapithecus* is actually *Sivapithecus,* a creature ancestral to orangutans and not to

The late ALLAN C. WILSON and REBECCA L. CANN applied the tools of genetics to paleontology during many of their collaborations. Until his death in 1991, Wilson was professor of biochemistry at the University of California, Berkeley. A native of New Zealand, he received his undergraduate degree from the University of Otago in 1955, his master's from Washington State University and his doctorate from Berkeley. Wilson also worked at the Weizmann Institute of Science, the University of Nairobi and Harvard University. Cann is associate professor of genetics and molecular biology at the John A. Burns School of Medicine of the University of Hawaii at Manoa. She received both her bachelor's degree in genetics and her Ph.D. in anthropology from Berkeley. As a postdoctoral fellow, she worked at Berkeley with Wilson and at the University of California, San Francisco. As one of her current projects, Cann is using mitochondrial DNA to assay the genetic diversity of birds in the Hawaiian Islands.

any of the African apes at all. Moreover, the age of some sivapithecine fossils was downgraded to only about six million years. By the early 1980s almost all paleontologists came to accept Sarich's more recent date for the separation of the human and ape lines. Those who continue to reject his methods have been reduced to arguing that Sarich arrived at the right answer purely by chance.

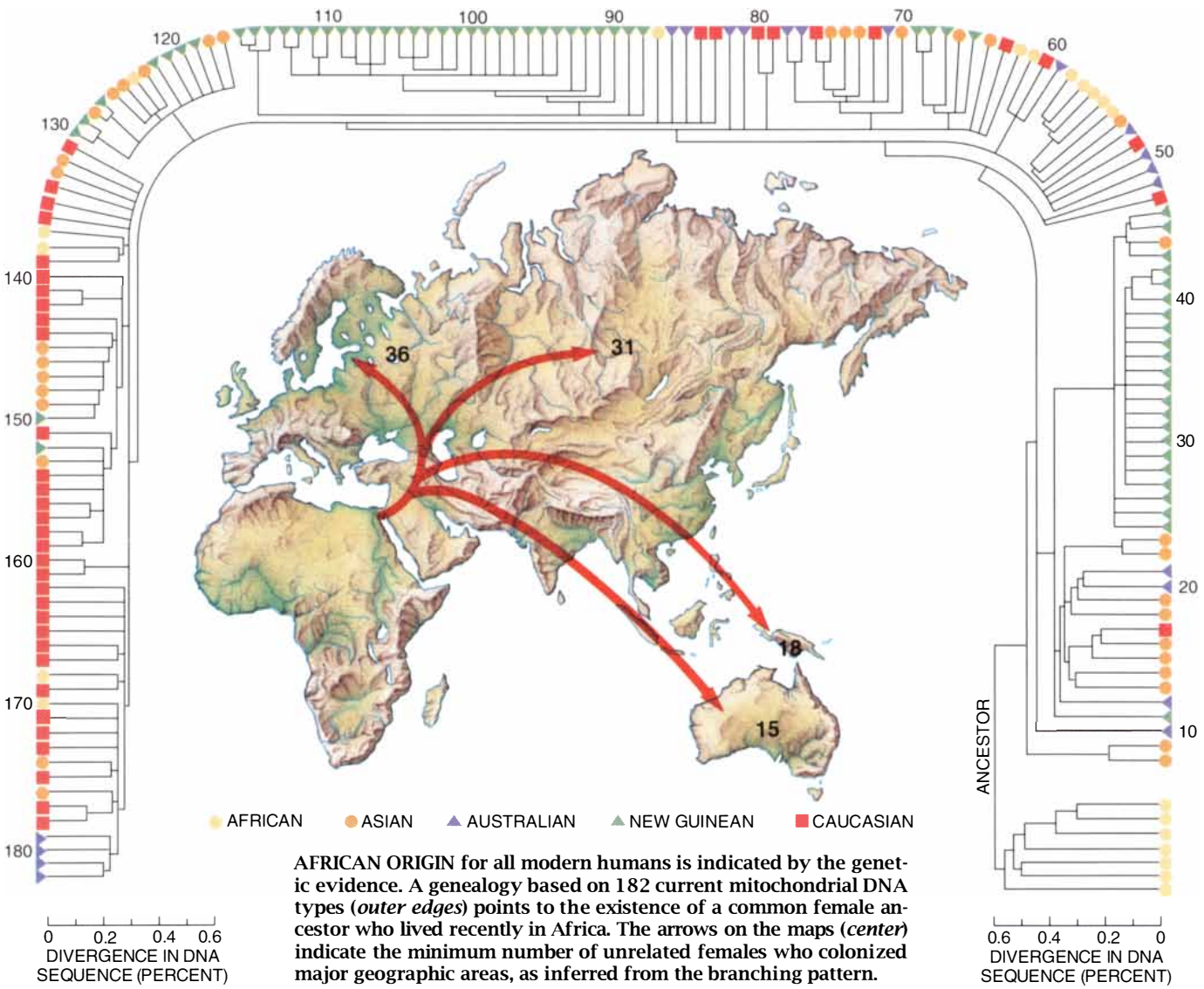
Two novel concepts emerged from the early comparisons of proteins from different species. One was the concept of inconsequential, or neutral, mutations. Molecular evolution appears to be dominated by such mutations, and they accumulate at surprisingly steady rates in surviving lineages. In other words, evolution at the gene level results mainly from the relentless accumulation of mutations that seem to be neither harmful nor beneficial. The second concept, molecular clocks, stemmed from the observation that rates of genetic change from point mutations (changes in individual DNA base pairs) were so steady over long periods that one could use them to time divergences from a common stock.

We could begin to apply these methods to the reconstruction of later stages in human evolution only after 1980, when DNA restriction analysis made it possible to explore genetic differences with high resolution. Workers at Berkeley, including Wes Brown, Mark Stoneking and us, applied the technique to trace the maternal lineages of people sampled from around the world.

The DNA we studied resides in the mitochondria, cellular organelles that convert food into a form of energy the rest of the cell can use. Unlike the DNA of the nucleus, which forms bundles of long fibers, each consisting of a protein-coated double helix, the mitochondrial DNA comes in small, two-strand rings. Whereas nuclear DNA encodes an estimated 100,000 genes—most of the information needed to make a human being—mitochondrial DNA encodes only 37. In this handful of genes, every one is essential: a single adverse mutation in any of them is known to cause some severe neurological diseases.

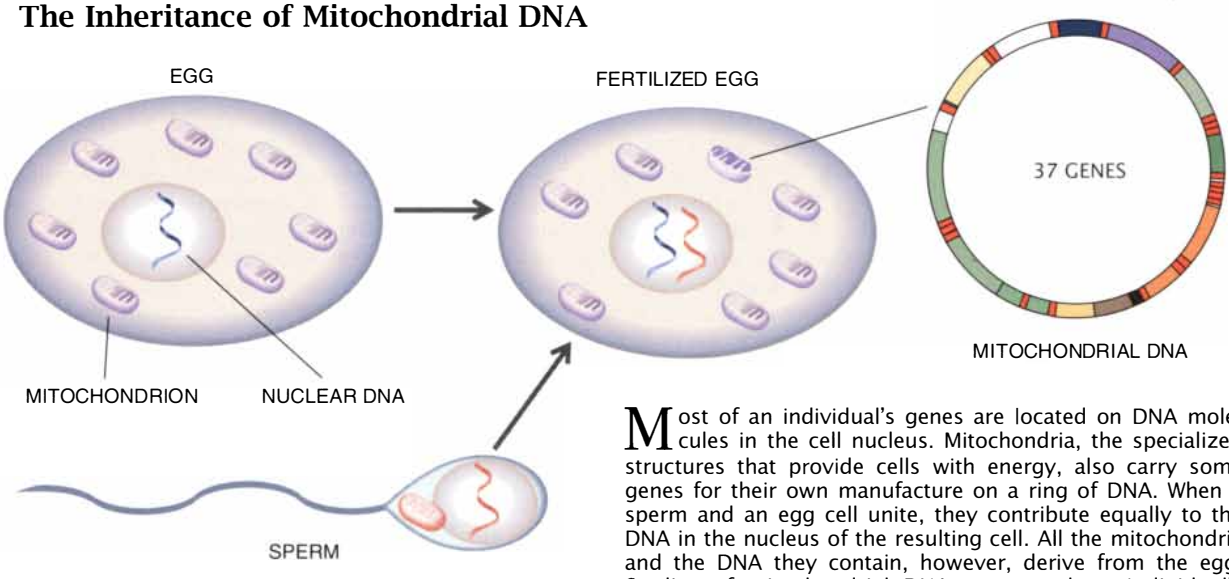
For the purpose of scientists studying when lineages diverged, mitochondrial DNA has two advantages over nuclear DNA. First, the sequences in mitochondrial DNA that interest us accumulate mutations rapidly and steadily, according to empirical observations. Because many mutations do not alter the mitochondrion's function, they are effectively neutral, and natural selection does not eliminate them.

This mitochondrial DNA therefore behaves like a fast-ticking clock, which is essential for identifying recent genet-



AFRICAN ORIGIN for all modern humans is indicated by the genetic evidence. A genealogy based on 182 current mitochondrial DNA types (*outer edges*) points to the existence of a common female ancestor who lived recently in Africa. The arrows on the maps (*center*) indicate the minimum number of unrelated females who colonized major geographic areas, as inferred from the branching pattern.

The Inheritance of Mitochondrial DNA



Most of an individual's genes are located on DNA molecules in the cell nucleus. Mitochondria, the specialized structures that provide cells with energy, also carry some genes for their own manufacture on a ring of DNA. When a sperm and an egg cell unite, they contribute equally to the DNA in the nucleus of the resulting cell. All the mitochondria and the DNA they contain, however, derive from the egg. Studies of mitochondrial DNA can reveal an individual's maternal ancestry.

ic changes. Any two humans chosen randomly from anywhere on the planet are so alike in most of their DNA sequences that we can measure evolution in our species only by concentrating on the genes that mutate fastest. Genes controlling skeletal characters do not fall within this group.

Second, unlike nuclear DNA, mitochondrial DNA is inherited from the mother alone, unchanged except for chance mutations. The father's contribution ends up on the cutting-room floor, as it were. The nuclear genes, to which the father does contribute, descend in what we may call ordinary lineages, which are of course important to the transmission of physical characteristics. For our studies of modern human origins, however, we focus on the mitochondrial, maternal lineages.

Maternal lineages are closest among siblings because their mitochondrial DNA has had only one generation in which to accumulate mutations. The degree of relatedness declines step by step as one moves along the pedigree, from first cousins descended from the maternal grandmother, to second cousins descended from a common maternal great-grandmother and so on. The farther back the genealogy goes, the larger the circle of maternal relatives becomes, until at last it embraces everyone alive.

Logically, then, all human mitochondrial DNA must have had an ultimate common female ancestor. But it is easy to show she did not necessarily live in a small population or constitute the only woman of her generation. Imagine a static population that always contains 15 mothers. Every new generation must contain 15 daughters, but some mothers will fail to produce a daughter, whereas others will produce two or more. Because maternal lineages die out whenever there is no daughter to carry on, it is only a matter of time before all but one lineage disappears. In a stable population the time for this fixation of the maternal lineage to occur is the length of a generation multiplied by twice the population size.

One might refer to the lucky woman whose lineage survives as Eve. Bear in mind, however, that other women were living in Eve's generation and that Eve did not occupy a specially favored place in the breeding pattern. She is purely the beneficiary of chance. Moreover, if we were to reconstruct the ordinary lineages for the population, they would trace back to many of the men and women who lived at the same time as Eve. Population geneticists Daniel L. Hartl of Washington University School of Medicine and Andrew G. Clark of Pennsylvania State University estimate that as many as 10,000 people could have lived then. The name "Eve" can therefore be misleading—she is not the ultimate source of all the ordinary lineages, as the biblical Eve was.

From mitochondrial DNA data, it is possible to define the maternal lineages of living individuals all the way back to a common ancestor. In theory, a great number of different genealogical trees could give rise to any set of genetic data. To recognize the one that is most probably correct, one must apply the parsimony principle, which requires that subjects be connected in the simplest possible way. The most efficient hypothetical tree must be tested by comparison with other data to see whether it is consistent with them. If the tree holds up, it is analyzed for evidence of the geographic history inherent in elements.

In 1988 Thomas D. Kocher of Berkeley (now at the University of New Hampshire) applied just such a parsimonious interpretation to the interrelatedness of the mitochondrial DNA of 14 humans from around the world. He determined 13 branching points were the fewest that could account for the differences he found. Taking the geographic considerations into account, he then concluded that Africa was the ultimate human homeland: the global distribution of mitochondrial DNA types he saw could then be explained most easily as the result of no more than three migration events to other continents.

A crucial assumption in this analysis is that all the mitochondrial lineages evolve at the same rate. For that reason, when Kocher conducted his comparison of the human mitochondrial DNAs, he also included analogous sequences from four chimpanzees. If the human lineages had differed in the rate at which they accumulated mutations, then some of the 14 human sequences would be significantly closer or farther away from the chimpanzee sequences

than others. In fact, all 14 human sequences are nearly equidistant from the chimpanzee sequences, which implies the rates of change among humans are fairly uniform.

The chimpanzee data also illustrated how remarkably homogeneous humans are at the genetic level: chimpanzees commonly show as much as 10 times the genetic variation as humans. That fact alone suggests that all of modern humanity sprang from a relatively small stock of common ancestors.

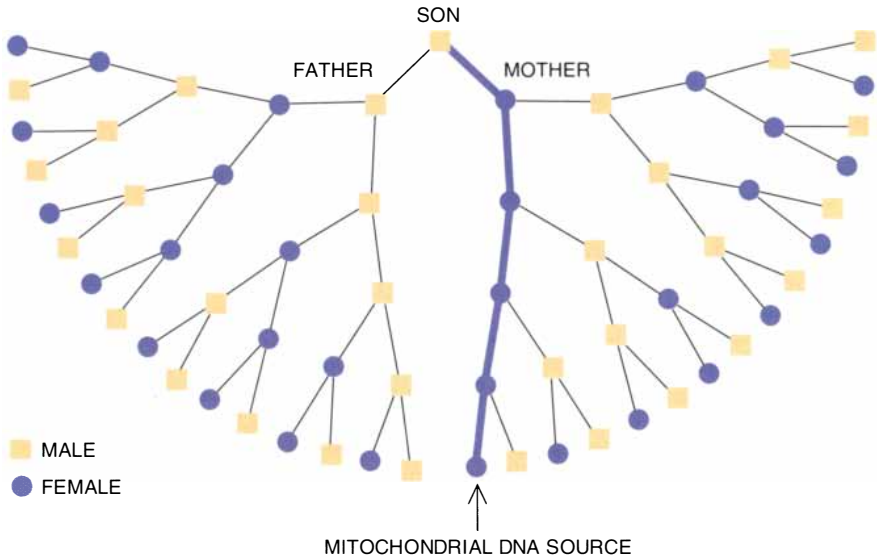
Working at Berkeley with Stoneking, we expanded on Kocher's work by examining a larger genealogical tree made up from 182 distinct types of mitochondrial DNA from 241 individuals. The multiple occurrences of mitochondrial DNA types were always found among people from the same continent and usually in persons who lived within 100 miles of one another. Because the tree we constructed had two main branches, both of which led back to Africa, it, too, supported the hypothesis that Africa was the place of origin for modern humans.

One point that jumps out of our study is that although geographic barriers do influence a population's mitochondrial DNA, people from a given continent do not generally all belong to the same maternal lineage. The New Guineans are typical in this respect. Their genetic diversity had been suspected from linguistic analyses of the remarkable variety of language families—generally classified as Papuan—spoken on this one island [see "The Austronesian Dispersal and the Origin of Languages," by Peter Bellwood; SCIENTIFIC AMERICAN, July 1991]. On our genealogical tree, New Guineans showed up on several different branches, which proved that the common female ancestor of all New Guineans was not someone in New Guinea. The population of New Guinea must have been founded by many mothers whose maternal lineages were most closely related to those in Asia.

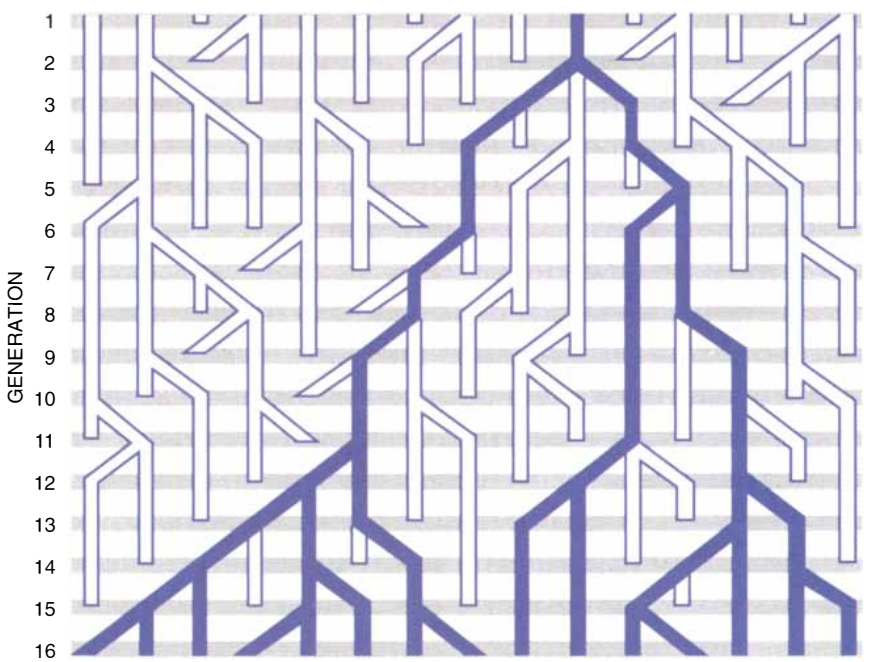
That finding is what one would expect if the African origin hypothesis were true: as people walked east out of Africa, they would have passed through Asia. Travel was probably slow, and during the time it took to reach New Guinea, mutations accumulated both in the lineages that stayed in Asia and in those that moved on.

Thus, people who are apparently related by membership in a common geographic race need not be very closely related in their mitochondrial DNA. Mitochondrially speaking, races are not like biological species. We propose that the anatomic characteristics uniting New Guineans were not inherited from the first settlers. They evolved after people colonized the island, chiefly as the result of mutations in nuclear genes spread by sex and recombination throughout New Guinea. Similarly, the light skin color of many whites is probably a late development that occurred in Europe after that continent was colonized by Africans.

During the early 1980s, when we were constructing our genealogical tree, we had to rely on black Americans as substitutes for Africans, whose mitochon-



PEDIGREE of one individual illustrates the difference between the patterns of nuclear and mitochondrial inheritance. All 32 ancestors from five generations ago contributed equally to his nuclear DNA. His mitochondrial lineage (*blue line*) leads back to only one person in every generation.



UNIVERSAL MATERNAL ANCESTOR can be found for all the members of any population. The example traces the lineages of 15 females in a stable population. In each generation, some maternal lineages proliferate and others become extinct. Eventually, by chance, one maternal lineage replaces all the others.

drial DNA was difficult to obtain in the required quantities. Fortunately, the recent development of a technique called the polymerase chain reaction has eliminated that constraint. The reaction makes it possible to duplicate DNA sequences easily, ad infinitum; a small starting sample of DNA can expand into an endless supply [see "The Unusual Origin of the Polymerase Chain Reaction," by Kary B. Mullis; SCIENTIFIC AMERICAN, April 1990].

The polymerase chain reaction enabled Linda Vigilant, now at Pennsylvania State University, to redo our study using mitochondrial DNA data from 120 Africans, representing six diverse parts of the sub-Saharan region. Vigilant traced a genealogical tree whose 14 deepest branches lead exclusively to Africans and whose 15th branch leads to both Africans and non-Africans. The non-Africans lie on shallow secondary branches stemming from the 15th branch. Considering the number of African and non-African mitochondrial DNAs surveyed, the probability that the 14 deepest branches would be exclusively African is one in 10,000 for a tree with this branching order.

Satoshi Horai and Kenji Hayasaka of the National Institute of Genetics in Japan analogously surveyed population samples that included many more Asians and individuals from fewer parts of Africa; they, too, found that the mitochondrial lineages led back to Africa. We estimate the odds of their arriving at that conclusion accidentally were only four in 100. Although these statistical evaluations are not strong or rigorous tests, they do make it seem likely that the theory of an African origin for human mitochondrial DNA is now fairly secure.

Because our comparisons with the chimpanzee data showed the human mitochondrial DNA clock has ticked steadily for millions of years, we knew it should be possible to calculate when the common mother of humanity lived. We assumed the human and chimpanzee lineages diverged five million years ago, as Sarich's work had shown. We then calculated how much humans had diverged from one another relative to how much they had diverged from chimpanzees—that is, we found the ratio of mitochondrial DNA divergence among humans to that between humans and chimpanzees.

Using two different sets of data, we determined the ratio was less than 1:25. Human maternal lineages therefore grew apart in a period less than $^1/_{25}$th as long as five million years, or less than 200,000 years. With a third set of data on changes in a section of the mitochondrial DNA called the control region, we arrived at a more ancient date for the common mother. That date is less certain, however, because questions remain about how to correct for multiple mutations that occur within the control region.

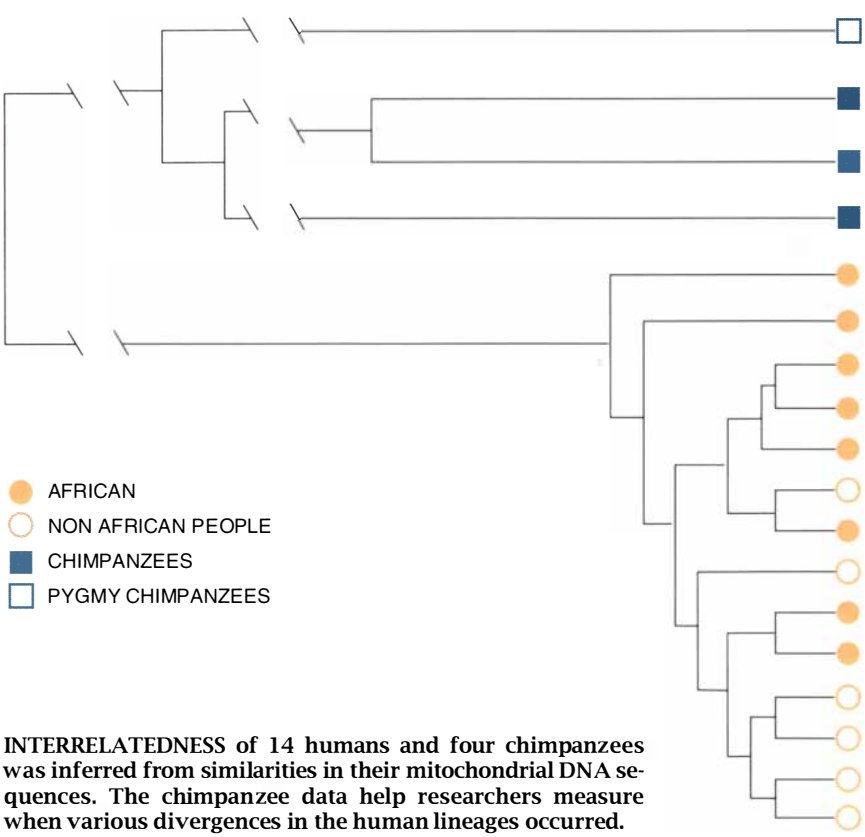
One might object that a molecular clock known to be accurate over five million years could still be unreliable for shorter periods. It is conceivable, for example, that intervals of genetic stagnation might be interrupted by short bursts of change when, say, a new mutagen enters the environment, or a virus infects the germ-line cells, or intense natural selection affects all segments of the DNA. To rule out the possibility that the clock might run by fits and starts, we ran a test to measure how much mitochondrial DNA has evolved in populations founded at a known time.

The aboriginal populations of New Guinea and Australia are estimated to have been founded less than 50,000 to 60,000 years ago. The amount of evolution that has since occurred in each of those places seems about one third of that shown by the whole human species. Accordingly, we can infer that Eve lived three times 50,000 to 60,000 years ago, or roughly 150,000 to 180,000 years ago. All our estimates thus agree the split happened not far from 200,000 years ago.

Those estimates fit with at least one line of fossil evidence. The remains of anatomically modern people appear first in Africa, then in the Middle East and later in Europe and east Asia. Anthropologists have speculated that in east Africa the transition from anatomically archaic to modern people took place as recently as 130,000 years ago [see "The Emergence of Modern Humans," by Christopher B. Stringer; SCIENTIFIC AMERICAN, December 1990].

On the other hand, a second line of evidence appears to conflict with this view. The fossil record shows clearly that the southern parts of Eurasia were occupied by archaic people who had migrated from Africa to Asia nearly a million years ago. Such famous fossils as Java Man and Beijing Man are of this type. This finding and the hypothesis that the archaic Eurasian population underwent anatomic changes that made them resemble more modern people led to the multiregional evolution model: similar evolutionary changes in separate geographic regions converted the inhabitants from archaic small-brained to modern big-brained types.

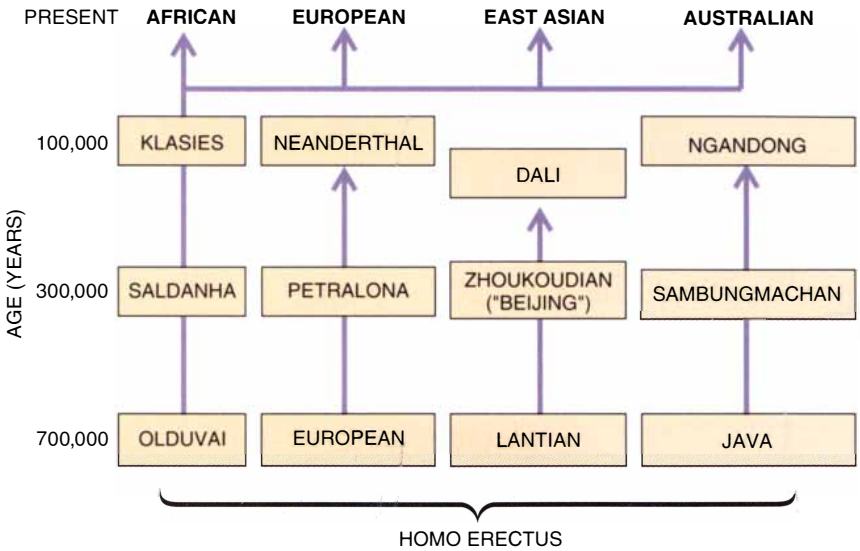
Huge levels of gene flow between continents, however, would be neces-



INTERRELATEDNESS of 14 humans and four chimpanzees was inferred from similarities in their mitochondrial DNA sequences. The chimpanzee data help researchers measure when various divergences in the human lineages occurred.

sary to maintain human populations as one biological species. The multiregional evolution model also predicts that at least some genes in the modern east Asian population would be linked more closely to those of their archaic Asian predecessors than to those of modern Africans. We would expect to find deep lineages in Eurasia, especially in the Far East. Yet surveys in our laboratories and in others, involving more than 1,000 people from Eurasia and its mitochondrial DNA satellites (Australia, Oceania and the Americas), have given no hint of that result.

It therefore seems very unlikely that any truly ancient lineages survive undetected in Eurasia. We simply do not see the result predicted by the regional model. Moreover, geneticists such as Masatoshi Nei of Pennsylvania State University, Kenneth K. Kidd of Yale University, James Wainscoat of the University of Oxford and Luigi L. Cavalli-Sforza of Stanford University have found support for an African origin model in their studies of nuclear genes.



HUMAN GROUPS WERE REPLACED throughout the Old World by modern humans from Africa. Archaic females do not seem to have contributed mitochondrial genes to the modern people of Europe, east Asia and Australia.

Proponents of the multiregional evolution model emphasize they have documented a continuity of anatomic morphologies between the archaic and modern residents of different regions; they insist these morphologies would be unlikely to evolve independently in any invading people. For that argument to hold true, it must also be shown that the cranial features in question are truly independent of one another—that is, that natural selection would not tend to favor certain constellations of functionally related features. Yet we know powerful jaw muscles may impose changes on the mandible, the browridge and other points on the skull; circumstances that promoted the evolution of these features in one population might do so again in a related population.

Other paleontologists also dispute the evidence for continuity. They argue modern populations are not linked to past ones by morphological characteristics that evolved uniquely in the fossil record. Instead fossils and modern populations are united by their shared retention of still older ancestral characteristics. The continuity seen by believers in multiregional evolution may be an illusion.

The idea that modern humans could cohabit a region with archaic ones and replace them completely without any mixture may sound unlikely. Nevertheless, some fossil finds do support the idea. Discoveries in the caves at Qafzeh in Israel suggest Neanderthals and modern humans lived side by side for 40,000 years, yet they left little evidence of interbreeding.

How one human population might have replaced archaic humans without any detectable genetic mixing is still a mystery. One of us (Cann) suspects infectious diseases could have contributed to the process by helping to eliminate one group. Cavalli-Sforza has speculated the ancestors of modern humans may have developed some modern trait, such as advanced language skills, that effectively cut them off from breeding with other hominids. This and related questions may yield as molecular biologists learn how to link specific genetic sequences to the physical and behavioral traits those sequences influence.

Even before then, further studies of both nuclear and mitochondrial DNA will render more informative genetic trees. Particularly enticing are the sequences on the Y chromosome that determine maleness and that are therefore inherited from the father alone. Gerad Lucotte's laboratory at Collège de France has indirectly compared such sequences in an effort to trace paternal lineages to a single progenitor—"Adam," if you will. Those preliminary results also point to an African homeland, and with further refinements this work on paternal lineages may be able to provide an invaluable check on our results for maternal lineages. Unfortunately, base changes accumulate slowly on useful regions of the Y chromosome, making it technically difficult to conduct a detailed genealogical analysis.

Still more progress can be expected in the immediate future, as molecular biologists learn to apply their techniques to materials uncovered by our friendly rivals, the paleontologists. Preliminary molecular studies have already been conducted on DNA from mummified tissues found in a Florida bog and dated to 7,500 years ago. Improved methods of extracting DNA from still older fossilized bone now appear close at hand. With them, we may begin building the family tree from a root that was alive when the human family was young.

FURTHER READING

MITOCHONDRIAL DNA AND HUMAN EVOLUTION. Rebecca L. Cann, Mark Stoneking and Allan C. Wilson in *Nature,* Vol. 325, No. 6099, pages 31–36; January 1–7, 1987.

MITOCHONDRIAL DNA. M. Stoneking and A. C. Wilson in *The Colonization of the Pacific: A Genetic Trail.* Edited by Adrian V. S. Hill and Susan W. Serjeantson. Oxford University Press, 1989.

MITOCHONDRIAL DNA SEQUENCES IN SINGLE HAIRS FROM A SOUTHERN AFRICAN POPULATION. Linda Vigilant, Renee Pennington, Henry Harpending, Thomas D. Kocher and Allan C. Wilson in *Proceedings of the National Academy of Sciences,* Vol. 86, No. 23, pages 9350–9354; December 1989.

SEQUENCE EVOLUTION OF MITOCHONDRIAL DNA IN HUMANS AND CHIMPANZEES. T. D. Kocher and A. C. Wilson in *Evolution of Life.* Edited by S. Osawa and T. Honjo. Springer-Verlag, Tokyo, 1991.

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The Multiregional Evolution of Humans

Both fossil and genetic evidence argues that various human groups arose where they are found today

by Alan G. Thorne and Milford H. Wolpoff

Two decades ago paleoanthropologists were locked in a debate about the origin of the earliest humans. The disagreement centered on whether the fossil *Ramapithecus* was an early human ancestor or ancestral to both human and ape lineages. Molecular biologists entered that discussion and supported the minority position held by one of us (Wolpoff) and his students that *Ramapithecus* was not a fossil human, as was then commonly believed. Their evidence, however, depended on a date for the chimpanzee-human divergence that was based on a flawed "molecular clock." We therefore had to reject their support.

Today the paleoanthropological community is again engaged in a debate, this time about how, when and where modern humans originated. On one side stand some researchers, such as ourselves, who maintain there is no single home for modern humanity—humans originated in Africa and then slowly developed their modern forms in every area of the Old World. On the other side are workers who claim that Africa alone gave birth to modern humans within the past 200,000 years. Once again the molecular geneticists have entered the fray, attempting to resolve it in favor of the African hypothesis with a molecular clock. Once again their help must be rejected because their reasoning is flawed.

Genetic research has undeniably provided one of the great insights of 20th-century biology: that all living people are extremely closely related. Our DNA similarities are far greater than the disparate anatomic variations of humanity might suggest. Studies of the DNA carried by the cell organelles called mitochondria, which are inherited exclusively from one's mother and are markers for maternal lineages, now play a role in the development of theories about the origin of modern human races.

Nevertheless, mitochondrial DNA is not the only source of information we have on the subject. Fossil remains and artifacts also represent a monumental body of evidence—and, we maintain, a much more reliable one. The singular importance of the mitochondrial DNA studies is that they show one of the origin theories discussed by paleontologists must be incorrect.

With Wu Xinzhi of the Institute of Vertebrate Paleontology and Paleoanthropology in Beijing, we developed an explanation for the pattern of human evolution that we described as multiregional evolution. We learned that some of the features that distinguish major human groups, such as Asians, Australian Aborigines and Europeans, evolved over a long period, roughly where these peoples are found today.

Multiregional evolution traces all modern populations back to when humans first left Africa at least a million years ago, through an interconnected web of ancient lineages in which the genetic contributions to all living peoples varied regionally and temporally. Today distinctive populations maintain their physical differences despite interbreeding and population movements; this situation has existed ever since humans first colonized Europe and Asia. Modern humanity originated within these widespread populations, and the modernization of our ancestors was an ongoing process.

An alternative theory, developed by the paleontologist William W. Howells of Harvard University as the "Noah's ark" model, posited that modern people arose recently in a single place and that they subsequently spread around the world, replacing other human groups. That replacement, recent proponents of the theory believe, must have been complete. From their genetic analyses, the late Allan C. Wilson and his colleagues at the University of California at Berkeley concluded that the evolutionary record of mitochondrial DNA could be traced back to a single female, dubbed "Eve" in one of his first publications on the issue, who lived in Africa approximately 200,000 years ago. Only mitochondrial DNA that can be traced to Eve, these theorists claim, is found among living people.

How could this be? If Eve's descendants mixed with other peoples as their population expanded, we would expect to find other mitochondrial DNA lines present today, especially outside Africa, where Eve's descendants were invaders. The most credible explanation for the current absence of other mitochondrial DNA lineages is that none of the local women mixed with the invading modern men from Africa—which means that Eve founded a new species. Wilson's reconstruction of the past demands that over a period of no more than 150,000 years there was a complete replacement of all the preexisting hunter-gatherers in Africa and the rest of the then inhabited world; later, the original African features of the invading human species presumably gave way to the modern racial features we see in other regions.

An analogy can highlight the difference between our multiregional evolution theory and Wilson's Eve theory. According to multiregional evolution, the pattern of modern human origins is like several individuals paddling in separate corners of a pool; although they maintain their individuality over time, they influence one another with the spreading ripples they raise (which are the equivalent of genes flowing between populations). In contrast, the total replacement requirement of the Eve theory dictates that a new swimmer must jump into the pool with such a splash that it drowns all the other swimmers. One of these two views of our origin must be incorrect.

ALAN G. THORNE and MILFORD H. WOLPOFF have extensively studied the original fossil material on the origins of *Homo sapiens*. Thorne is head of the department of prehistory in the Institute of Advanced Studies at the Australian National University. He graduated in anthropology and zoology from the University of Sydney in 1963 and later taught human anatomy at the medical school there. Thorne's excavations at Kow Swamp and Lake Mungo produced most of the Pleistocene human remains in Australia. Among his documentaries is the television series *Man on the Rim*. Wolpoff is professor of anthropology at the University of Michigan at Ann Arbor, where he directs the paleoanthropology laboratory. He received his Ph.D. in 1969 from the University of Illinois at Urbana-Champaign. Wolpoff has written widely on paleoanthropology, including an introductory textbook.

Mitochondrial DNA is useful for guiding the development of theories, but only fossils provide the basis for refuting one idea or the other. At best, the genetic information explains how modern humans might have originated if the assumptions used in interpreting the genes are correct, but one theory cannot be used to test another. The fossil record is the real evidence for human evolution, and it is rich in both human remains and archaeological sites stretching back for a million years. Unlike the genetic data, fossils can be matched to the predictions of theories about the past without relying on a long list of assumptions.

The power of a theory is measured by how much it can explain; the scientific method requires that we try to incorporate all sources of data in an explanatory theory. Our goal is to describe a theory that synthesizes everything known about modern human fossils, archaeology and genes. The Eve theory cannot do so.

The Eve theory makes five predictions that the fossil evidence should corroborate. The first and major premise is that modern humans from Africa must have completely replaced all other human groups. Second, implicit within this idea is that the earliest modern humans appeared in Africa. Third, it also follows that the earliest modern humans in other areas should have African features. Fourth, modern humans and the people they replaced should never have mixed or interbred. Fifth, an anatomic discontinuity should be evident between the human fossils before and after the replacement.

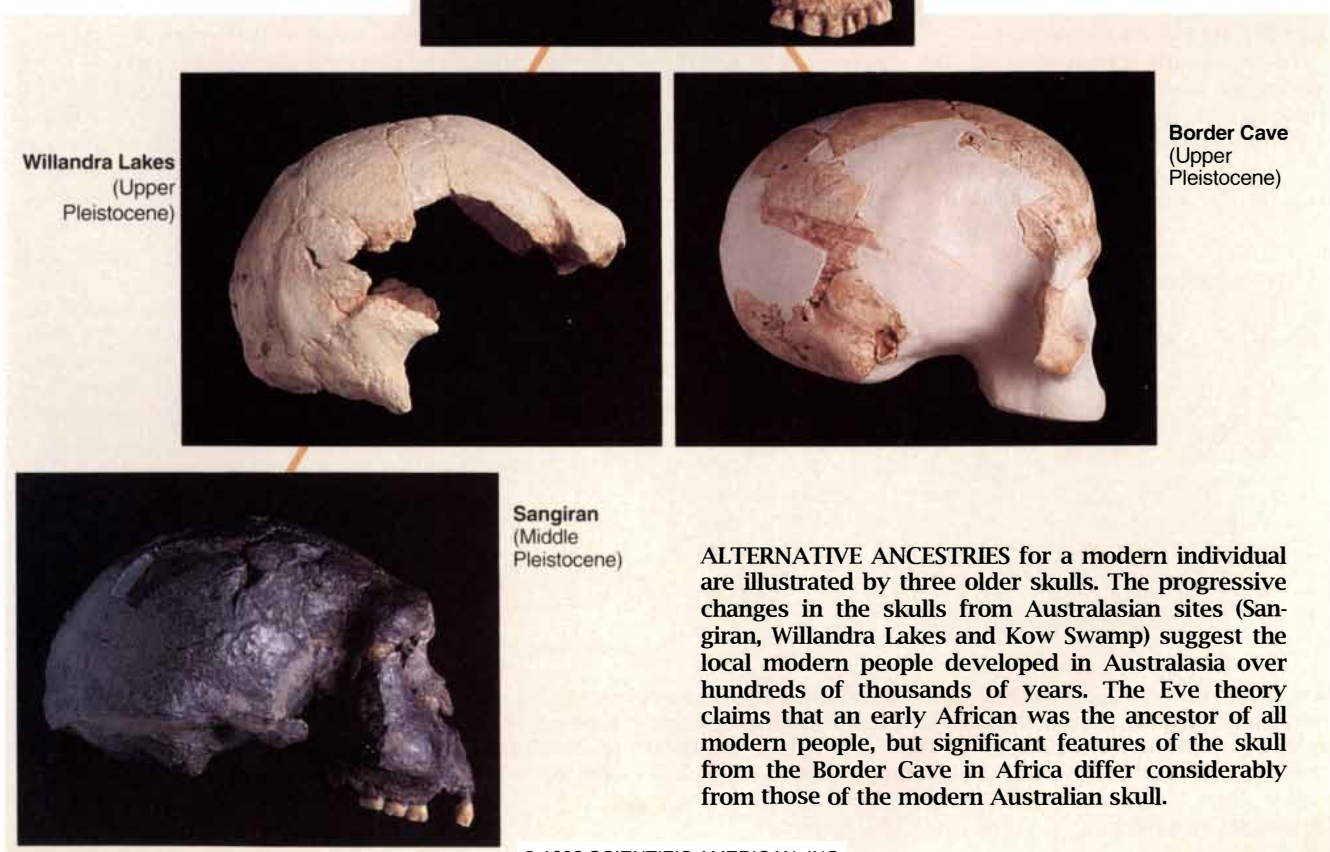
We are troubled by the allegations that beginning about 200,000 years ago one group of hunter-gatherers totally replaced all others worldwide. Although it is not uncommon for one animal species to replace another locally in a fairly short time, the claim that a replacement could occur rapidly in every climate and environment is unprecedented.

We would expect native populations to have an adaptive and demographic advantage over newcomers. Yet according to the Eve theory, it was the newcomers who had the upper hand. How much of an advantage is necessary for replacement can be measured by the survival of many hunter-gatherer groups in Australia and the Americas; they have persisted despite invasions by Europeans, who during the past 500 years arrived in large numbers with vastly more complex and destructive technologies.

If a worldwide invasion and complete replacement of all native peoples by Eve's descendants actually took place, we would expect to find at least some archaeological traces of the behaviors that made them successful. Yet examining the archaeology of Asia, we can find none. For instance, whereas the hand ax was a very common artifact in Africa, the technologies of eastern Asia did not include that tool either before or after the Eve period. There is no evidence for the introduction of a novel technology.

Geoffrey G. Pope of the University of Illinois has pointed out that six decades of research on the Asian Paleolithic record have failed to unearth any indication of intrusive cultures or technologies. Types of artifacts found in the earliest Asian Paleolithic assemblages continue to appear into the very late Pleistocene. If invading Africans replaced the local Asian populations, they must have adopted the cultures and technologies of the people they replaced and allowed their own to vanish without a trace.

Archaeological evidence for an invasion is also lacking in western Asia, where Christopher B. Stringer



ALTERNATIVE ANCESTRIES for a modern individual are illustrated by three older skulls. The progressive changes in the skulls from Australasian sites (Sangiran, Willandra Lakes and Kow Swamp) suggest the local modern people developed in Australasia over hundreds of thousands of years. The Eve theory claims that an early African was the ancestor of all modern people, but significant features of the skull from the Border Cave in Africa differ considerably from those of the modern Australian skull.

SERIES OF CHINESE SKULLS shows continuity in form without evidence of an influx of African characteristics. From left to right, the male skulls are from the Zhoukoudian Lower Cave (Middle Pleistocene period), Dali site (early Upper Pleistocene period) and Zhoukoudian Upper Cave (late Upper Pleistocene).

of the Natural History Museum in London and a few other researchers believe the earliest modern humans outside of Africa can be found at the Skhūl and Qafzeh sites in Israel. The superb record at Qafzeh shows, however, that these "modern" people had a culture identical to that of their local Neanderthal contemporaries: they made the same types of stone tools with the same technologies and at the same frequencies; they had the same stylized burial customs, hunted the same game and even used the same butchering procedures. Moreover, no evidence from the time when Eve's descendants are supposed to have left Africa suggests that any new African technology emerged or spread to other continents. All in all, as we understand them, the Asian data refute the archaeological predictions implied by the Eve theory.

Perhaps that refutation explains why Wilson turned to a different advantage, asserting that the invasion was successful because Eve's descendants carried a mitochondrial gene that conferred language ability. This proposal is yet to be widely accepted. Not only does it conflict with paleoneurology about the language abilities of archaic humans, but if it were true, it would violate the assumption of Wilson's clock that mitochondrial mutations are neutral.

The remaining predictions of the Eve theory relate to abrupt anatomic changes and whether the earliest recognizably modern humans resembled earlier regional populations or Africans. With the fossil evidence known at this time, these questions can be unambiguously resolved in at least two and possibly three regions of the world. The most convincing data are from southern and northern Asia.

The hominid fossils from Australasia (Indonesia, New Guinea and Australia) show a continuous anatomic sequence during the Pleistocene that is uninterrupted by African migrants at any time. The distinguishing features of the earliest of these Javan remains, dated to about one million years ago, show they had developed when the region was first inhabited.

Compared with human fossils from other areas, the Javan people have thick skull bones, with strong continuous browridges forming an almost straight bar of bone across their eye sockets and a second well-developed shelf of bone at the back of the skull for the neck muscles. Above and behind the brows, the forehead is flat and retreating. These early Indonesians also have large projecting faces with massive rounded cheekbones. Their teeth are the largest known in archaic humans from that time.

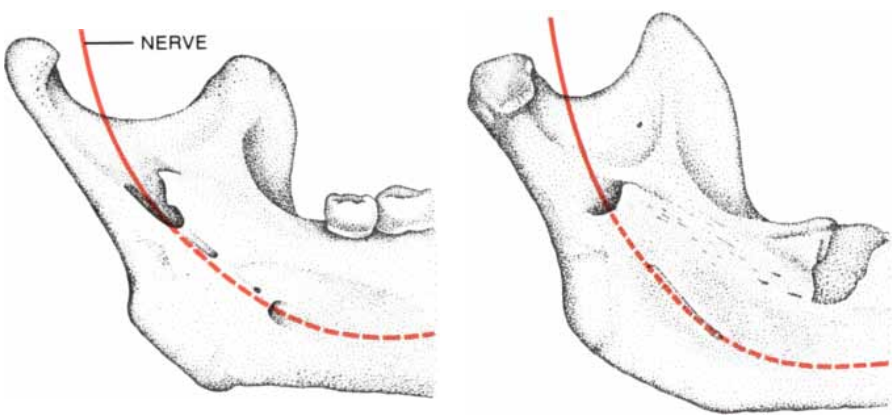
A series of small but important features can be found on the most complete face and on other facial fragments that are preserved. These include such things as a rolled ridge on the lower edge of the eye sockets, a distinctive ridge on the cheekbone and a nasal floor that blends smoothly into the face.

This unique morphology was stable for at least 700,000 years while other modern characteristics continued to evolve in the Javan people. For example, the large fossil series from Ngandong, which recent evidence suggests may be about 100,000 years old, offers striking proof that the Javans of that time had brain sizes in the modern range but were otherwise remarkably similar to much earlier individuals in the region.

The first inhabitants of Australia arrived more than 60,000 years ago, and their behavior and anatomy were clearly those of modern human beings. Their skeletons show the Javan complex of features, along with further braincase expansions and other modernizations. Several dozen well-preserved fossils from the late Pleistocene and early Holocene demonstrate that the same combination of features that distinguished those Indonesian people from their contemporaries distinguishes modern Australian Aborigines from other living peoples.

If the earliest Australians were descendants of Africans, as the Eve theory requires, the continuity of fossil features would have to be no more than apparent. All the features of the early Javans would need to have evolved a second time in the population of invaders. The repeated evolution of an individual feature would be conceivable but rare; the duplication of an entire set of unrelated features would be unprecedentedly improbable.

Northern Asia also harbors evidence linking its modern and ancient inhabitants. Moreover, because the similarities involve features different from those significant in Australasia, they compound the improbability of the Eve



JAW MORPHOLOGY distinguishes many Neanderthal skeletons. In most living and fossil people the rim around the mandibular nerve canal opening is grooved (*left*), but in many Neanderthals, it was surrounded by a bony bridge (*right*). Some later Europeans also had this Neanderthal feature, although it was less common.

theory by requiring that a second complete set of features was duplicated in a different population.

The very earliest Chinese fossils, about one million years old, differ from their Javan counterparts in many ways that parallel the differences between north Asians and Australians today. Our research with Wu Xinzhi and independent research by Pope demonstrated that the Chinese fossils are less robust, have smaller and more delicately built flat faces, smaller teeth and rounder foreheads separated from their arched browridges. Their noses are less prominent and more flattened at the top. Perhaps the most telling indication of morphological continuity concerns a peculiarity of tooth shapes. Prominently "shoveled" maxillary incisors, which curl inward along their internal edges, are found with unusually high frequency in living east Asians and in all the earlier human remains from that area. Studies by Tracey L. Crummett of the University of Michigan show that the form of prehistoric and living Asian incisors is unique.

This combination of traits is also exhibited at the Zhoukoudian cave area in northern China, where fully a third of all known human remains from the Middle Pleistocene have been found. As Wu Rukang of the Chinese Academy of Sciences has pointed out, even within the 150,000 or more years spanned by the Zhoukoudian individuals, evolutionary changes in the modern direction, including increases in brain size, can be seen. Our examinations of the Chinese specimens found no anatomic evidence that typically African features ever replaced those of the ancient Chinese in these regions. Instead there is a smooth transformation of the ancient populations into the living peoples of east Asia.

Paleontologists have long thought Europe would be the best source of evidence for the replacement of one group, Neanderthals, by more modern humans. Even there, however, the fossil record shows that any influx of new people was neither complete nor without mixture. In fact, the most recent known Neanderthal, from Saint-Césaire in France, apparently had the behavioral characteristics of the people who succeeded the Neanderthals in Europe. The earliest post-Neanderthal Europeans did not have a pattern of either modern or archaic African features. Clearly, the European Neanderthals were not completely replaced by Africans or by people from any other region.

Instead the evidence suggests that Neanderthals either evolved into later humans or interbred with them, or both. David W. Frayer of the University of Kansas and Fred H. Smith of Northern Illinois University have discovered that many allegedly unique Neanderthal features are found in the Europeans who followed the Neanderthals—the Upper Paleolithic, Mesolithic and later peoples. In fact, only a few Neanderthal features completely disappear from the later European skeletal record.

Features that persist range from highly visible structures, such as the prominent shape and size of the nose of Neanderthals and later Europeans, to much more minute traits, such as the form of the back of the skull and the details of its surface. A good example is the shape of the opening in the mandibular nerve canal, a spot on the inside of the lower jaw where dentists often give a pain-blocking injection. The upper part of the opening is covered by a broad bony bridge in many Neanderthals, but in others the bridge is absent. In European fossils, 53 percent of the known Neanderthals have the bridged form; 44 percent of their earliest Upper Paleolithic successors do, too, but in later Upper Paleolithic, Mesolithic and recent groups, the incidence drops to less than 6 percent.

In contrast, the bridged form is seen only rarely in fossil or modern people from Asia and Australia. In Africa the few jaws that date from the suggested Eve period do not have it. This mandibular trait and a number of others like it on the skull and the rest of the skeleton must have evolved twice in Europe for the Eve theory to be correct.

In sum, the evolutionary patterns of three different regions—Australasia, China and Europe—show that their earliest modern inhabitants do not have the complex of features that characterize Africans. There is no evidence that Africans completely replaced local groups. Contrary to the Eve theory predictions, the evidence points indisputably toward the continuity of various skeletal features between the earliest human populations and living peoples in different regions.

If Africa really were the "Garden of Eden" from which all living people emerged, one would expect to find evidence for the transition from archaic to modern forms there—and only there. Following the lead of the German worker Reiner Protsch of Goethe University in Frankfurt, some paleontologists did argue that modern *Homo sapiens* originated in Africa because they believed the earliest modern-looking humans were found there and that modern African racial features can be seen in these fossils. But the African evidence is sparse, fragmentary and for the most part poorly dated; it includes materials that do not seem to fit the Eve theory.

WE CAN'T PROVE T ARE BETTER DRIVERS, MAYBE THER

Ask the owners of one of the current crop of new luxury automobiles why he or she bought the car he or she bought, and you'll no doubt get a variety of answers.

Some will probably cite the image and prestige of the automaker. Others may wax poetic about the car's quiet operation and fine craftsmanship. Still others may offer up the concept that a car is just a car, so why not buy the one that costs less?

"You sit up high in a BMW, there's glass all around. It's easy to see, you've got lots of visibility to take in what's going on around you I like that." Don Orman, Owner 1969 BMW 2000A

While these are all sound reasons for buying a home appliance, BMW believes that a car is not just a car, and a car with a premium price should do more than simply improve the driver's image.

It should improve nothing less than the driver's ability.

Our owners seem to agree.

"When I took the car for a test drive, I knew the difference. I could feel it in the steering wheel…we were one." Dr. Jim Dacey, Owner 1980 BMW 320i

"The BMW brakes, accelerates and handles so well, it will correct your mistakes much quicker than a lot of other vehicles." Victor Bruno, owner BMW 850i Coupe.

And when you consider that from the beginning BMW has looked upon the driver as an integral, fully functioning part of the car itself, the human part of the equation which completes the car's mechanical system, it becomes clear rather quickly why a BMW owner confronted with the same question of why this car versus that car would say, "When I get into the car, it's like putting on a leather glove. I become united with the car and it becomes an extension of myself." Howard Rogers, owner 1991 BMW M5.

"The car gives you a fair understanding of where it's at, at all times. It constantly gives you feedback through the steering wheel and other controls. It's very predictable." Jeff Parks, Owner 1988 BMW M6

Improving the driver's ability means that every BMW design begins not with a clean sheet of paper, but instead, with the driver.

Research conducted at the University of Freiburg, for example, gives dramatic importance to the kind of steering response that should be designed into your car.

"The car feels strong. It handles well. It doesn't slip and slide. It's easy to drive. It's enjoyable to drive." Monica Dragul, Owner 1987 BMW 325es

This research concludes that typical emergency corrections are made not with a conscious thought but by automatic, subconscious

HAT BMW OWNERS BUT IF THEY BELIEVE IT, E'S A REASON.

reflexes. And therefore that the single most meaningful source of information for the driver concerning the behav-

"In a BMW, you drive the car. It does not drive you." Victor Bruno, Owner 1991 BMW 735i/850i

ior of his automobile, and the condition of the road surface is not, as generally supposed, his eyes, but rather, his steering wheel.

So rather than deprive the driver of road feel — as do the "dead" steering systems found in many of today's

"No matter how good a driver you are, it's hard to be 100% focused on driving all of the time…having a car that can react when you demand it is critical in the traffic I drive in." Melissa Hilton-Silver, Owner 1992 BMW 325i

passive, auto-piloted luxury sedans — BMW's are designed with a positive offset steering geometry to better connect the driver to the functioning parts of the suspension system through the steering wheel itself.

Thus providing him with all of the information needed to react instantly and confidently whenever the occasion happens to arise.

In other words, "The car is so connected to you that it barely needs any stimulus beyond your own thoughts to respond in the correct manner. That leaves more of your conscious energy available to apply to other areas of safety when you're driving." Jeff Parks, owner 1988 BMW M6.

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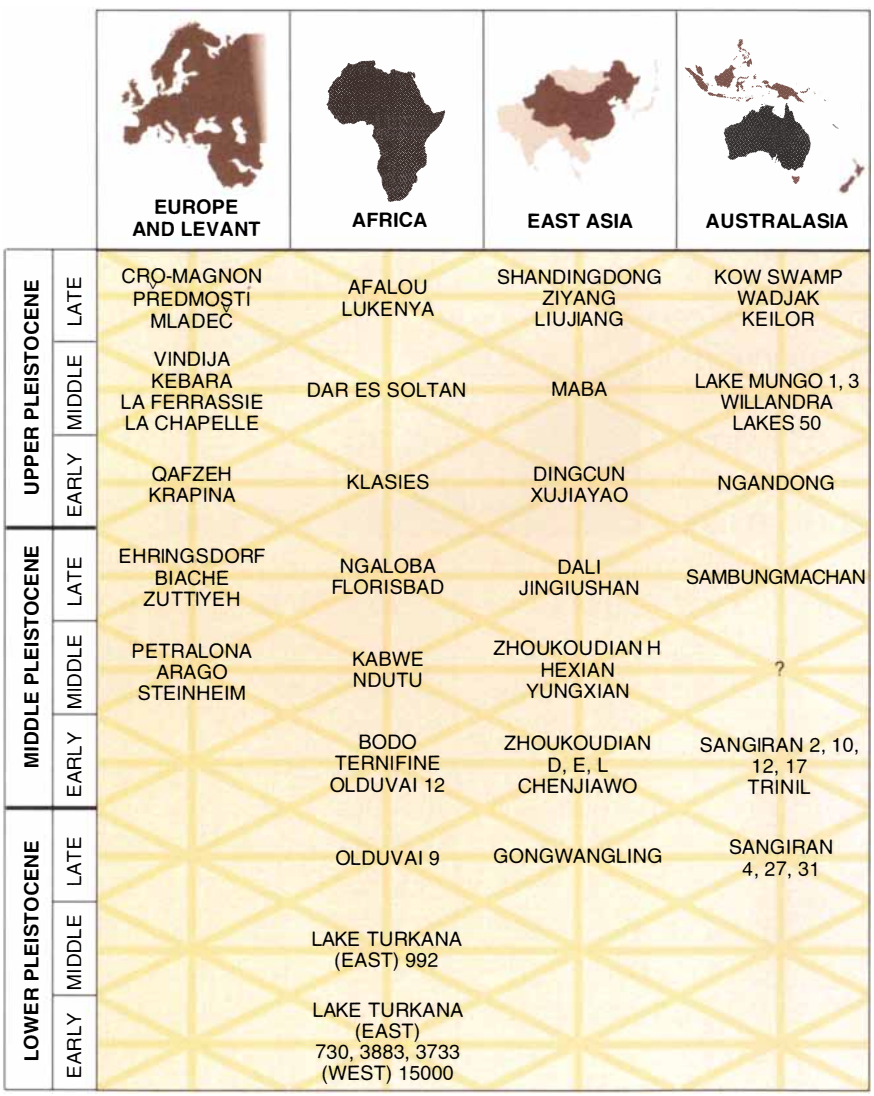
Early human remains from Africa, such as the Kabwe skull from Zambia, are extremely rare and are presumed to be at least 150,000 years old. Later transitional fossils from Morocco, Ethiopia, Kenya and South Africa confirm the expectation that local modernization occurred in Africa, as it did everywhere else. No pattern in the fossils, however, indicates the previous emergence of skeletal features that uniquely characterize modern humans generally or even modern Africans in particular.

The evidence for a great antiquity of modern-looking people is based primarily on the interpretation of bones from three sites: the Omo site in Ethiopia and the Klasies River and Border Cave sites in South Africa. Some of the Omo and Border Cave individuals resemble modern humans, but all the remains are fragmentary. Most of the Omo remains were found on the surface, not in datable strata. The estimate of their age, which is based on inappropriate dating techniques, is widely considered to be unreliable. Some of the Border Cave bones, including the most complete cranium, were dug out by local workmen looking for fertilizer and are of unknown antiquity. Other human bones found at a 90,000-year-old level are chemically different from animal bones found there. They may actually be more recent burials dug into the cave.

The best excavated remains are from the Klasies River Mouth Cave and are securely dated to between 80,000 and 100,000 years ago. Some of the skull fragments are small and delicate and are said to "prove" that modern humans were present. Yet a comparative analysis of the entire sample by Rachel Caspari of Albion College showed that others are not modern-looking at all. Two of the four lower jaws do not have chins, so thorough proof of a modern jaw is lacking. The single cheekbone from the site is not only larger than those of living Africans but also larger and more robust than those of both the earlier transitional humans and the archaic humans found in Africa. The claim that this sample contains modern Africans is highly dubious and does not justify the proposal that the earliest modern humans arose in Africa.



WELL-DATED FOSSILS point to the continuous, linked evolution of modern humans at sites around the world. Modern human groups in different regions developed distinct anatomic identities. Nevertheless, gene flow between the groups through interbreeding was sufficient to maintain humans as a single species.

With the disproof of the unique African ancestry theory for the living people of most areas and the lack of evidence showing that modern people first appeared in Africa, we conclude that the predictions of the Eve theory cannot be substantiated. We must wonder why the analysis of mitochondrial DNA suggested a theory so contrary to the facts. Perhaps the mitochondrial DNA has been misinterpreted.

The basic difficulty with using mitochondrial DNA to interpret recent evolutionary history stems from the very source of its other advantages: in reproduction, the mitochondrial DNA clones itself instead of recombining. Because mitochondrial DNA is transmitted only through the maternal line, the potential for genetic drift—the accidental loss of lines—is great: some mitochondrial DNA disappears every time a generation fails to have daughters.

The problem is analogous to the way in which family surnames are lost whenever there is a generation without sons. Imagine an immigrant neighborhood in a large city where all the families share a surname. An observer might assume that all these families were descended from a single successful immigrant family that completely replaced its neighbors (just as Eve's descendants are supposed to have replaced all other humans). An alternative explanation is that many families immigrated to the neighborhood and intermarried; over time, all the surnames but one were randomly eliminated through the occasional appearance of families that had no sons to carry on their names. The surviving family name would have come from a single immigrant, but all the immigrants would have contributed to the genes of the modern population. In the same way, generations without daughters could have extinguished some lines of mitochondrial DNA from Eve's descendants and her contemporaries.

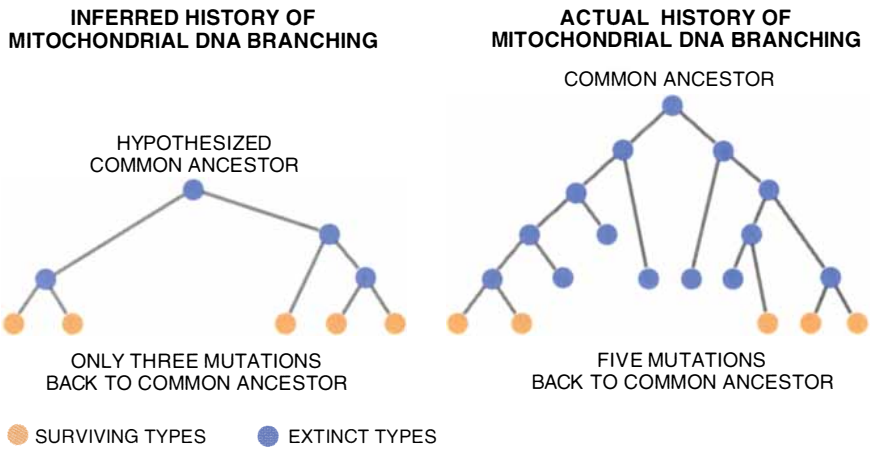
Any interpretation of the surviving mitochondrial DNA mutations in populations consequently depends on a knowledge of how the size of the populations has changed over time and how

many maternal lines may have vanished. Random losses from genetic drift alter a reconstruction of the tree of human mitochondrial DNA branching by pruning off signs of past divergences. Each uncounted branch is a mutation never taken into account when determining how long ago Eve lived.

Changes in population sizes have been dramatic. In parts of the Northern Hemisphere, some human populations shrank because of climate fluctuations during the Ice Ages. Archaeological evidence from both Africa and Australia suggests that similar population reductions may have taken place there as well. These reductions could have exacerbated genetic drift and the loss of mitochondrial DNA types.

At the end of the Ice Ages, along with the first domestication of animals and plants, some populations expanded explosively throughout a wide band of territory from the Mediterranean to the Pacific coast of Asia. Although the number of people expanded, the number of surviving mitochondrial DNA lines could not—those lost were gone forever.

Human populations with dissimilar demographic histories can therefore be expected to preserve different numbers of mutations since their last common mitochondrial DNA ancestor. They cannot be used together in a model that assumes the lengths of mitochondrial lineages reflect the age of their divergence. One cannot assume, as Wilson does, that all the variation in a population's mitochondrial DNA stems solely from mutations: the history of the population is also important.



MATERNAL LINEAGE RECONSTRUCTIONS based solely on the mitochondrial DNA types found today are inherently flawed. A hypothetical tree inferred from only five surviving types (*left*) leaves out the branches and mutational histories of extinct lines (*right*). Consequently, it sets the date for a common ancestor much too recently by presenting evidence of too few mutations.

A major problem with the Eve theory, therefore, is that it depends on an accurate molecular clock. Its accuracy must be based on mutation rates at many different loci, or gene positions. Yet genes in the mitochondrial DNA cannot recombine as genes in the nucleus do. All the mitochondrial DNA genes are the equivalent of a single locus. The molecular clock based on mitochondrial DNA is consequently unreliable.

Mitochondrial DNA may not be neutral enough to serve as the basis for a molecular clock, because some data suggest that it plays a role in several diseases. Because of random loss and natural selection some vertebrate groups —cichlid fish in Lake Victoria in Africa, American eels, hardhead catfish and redwing blackbirds, for example—have rates of mitochondrial DNA evolution that are dramatically slower than Wilson and his colleagues have claimed for humans. A number of molecular geneticists disagree with Wilson's interpretation of the mitochondrial genetic data.

The molecular clock of Wilson and his colleagues has, we believe, major problems: its rate of ticking has probably been overestimated in some cases and underestimated in others. Rebecca L. Cann of the University of Hawaii at Manoa and Mark Stoneking of Pennsylvania State University, two of Wilson's students, admitted recently that their clock was able to date Eve only to between 50,000 and 500,000 years ago. Because of the uncertainty, we believe that for the past half a million years or more of human evolution, for all intents and purposes, there is no molecular clock.

Putting aside the idea of a clock, one can interpret the genetic data in a much more reasonable way: Eve, the ultimate mitochondrial ancestor of all living humans, lived before the first human migrations from Africa at least one million years ago. The spread of mitochondria would then mark the migration of some early human ancestors into Eurasia when it contained no other hominids. Such an interpretation can fully reconcile the fossil record with the genetic data. We propose that future research might more productively focus on attempts to disprove this hypothesis than on attempts to recalibrate a clock that clearly does not work.

The dramatic genetic similarities across the entire human race do not reflect a recent common ancestry for all living people. They show the consequences of linkages between people that extend to when our ancestors first populated the Old World, more than a million years ago. They are the results of an ancient history of population connections and mate exchanges that has characterized the human race since its inception. Human evolution happened everywhere because every area was always part of the whole.

Neither anatomic nor genetic analyses provide a basis for the Eve theory. Instead the fossil record and the interpretation of mitochondrial DNA variation can be synthesized to form a view of human origins that does fit all the currently known data. This synthetic view combines the best sources of evidence about human evolution by making sense of the archaeological and fossil record and the information locked up in the genetic variation of living people all over the world. The richness of human diversity, which contrasts with the closeness of human genetic relationships, is a direct consequence of evolution. We are literally most alike where it matters, under the skin.

FURTHER READING

MODERN HOMO SAPIENS ORIGINS: A GENERAL THEORY OF HOMINID EVOLUTION INVOLVING THE FOSSIL EVIDENCE FROM EAST ASIA. Milford H. Wolpoff, Wu Xin Zhi and Alan G. Thorne in *The Origins of Modern Humans: A World Survey of the Fossil Evidence.* Edited by Fred H. Smith and Frank Spencer. Alan R. Liss, 1984.

EVOLUTION OF MITOCHONDRIAL DNA IN MONKEYS, APES, AND HUMANS. J. N. Spuhler in *American Journal of Physical Anthropology,* Vol. 77, Supplement 9: *Yearbook,* Vol. 31, pages 15–48; 1988.

THE SEARCH FOR EVE. Michael H. Brown. Harper & Row, 1990.

THE CASE AGAINST EVE. Milford Wolpoff and Alan Thorne in *New Scientist,* Vol. 130, No. 1774, pages 37–41; June 22, 1991.

Mountain Belts and the Supercontinent Cycle

Every 500 million years the continents assemble into a single landmass. The tectonic interactions associated with the formation and breakup of such supercontinents provide a new way to view the origin of mountain belts

by J. Brendan Murphy and R. Damian Nance

In recent years, we and several colleagues have come to the surprising conclusion that the motion of the crust of the earth follows an orderly pattern: every few hundred million years, all the continents congregate into a single landmass, or supercontinent. A particular virtue of this theory is its ability to explain the diverse kinds of mountain building observed around the globe. Our theory also will aid geologists in their attempts to reconstruct the ancient geographic positions of continents.

Present understanding of supercontinents grows out of the theory of plate tectonics, advanced some 25 years ago. This theory provided the first unified explanation of the origin of mountain chains, of the development and destruction of ocean basins, and of the global distribution of earthquakes and volcanoes. The lithosphere—the rigid outer layer of the earth containing both ocean floors and elevated continental masses—is divided into seven major sections, or plates. The plates ride atop a hot, pliable layer of the earth's mantle, called the asthenosphere. Radioactive elements within the earth release heat that drives convection currents deep inside the earth; these currents ferry the plates across the surface at the rate of a few centimeters a year.

Tracing the present motions backward implies that the continents bounding the Atlantic Ocean were all part of a single landmass that broke up roughly 180 million years ago. The German meteorologist Alfred L. Wegener, who first proposed the theory of continental drift in 1912, called the continental progenitor Pangaea, meaning "all lands." Support for his supposition has come from geologists who have found that features more than 180 million years old match up across continental boundaries. Evidence of the distribution of ancient species and climate zones also supports the theory.

Researchers have increasingly come to realize that Pangaea was not the first such supercontinent. In the early 1970s J. Tuzo Wilson, then at the University of Toronto, suggested that thermal effects within the earth might cause a continent to disperse and then to reassemble as oceans periodically open and close. More recently one of us (Nance), along with Thomas R. Worsley and Judith B. Moody of Ohio University, expanded on Wilson's ideas. We have proposed the existence of a supercontinental cycle having a period of about 500 million years [see "The Supercontinent Cycle," by R. Damian Nance, Thomas R. Worsley and Judith B. Moody; SCIENTIFIC AMERICAN, July 1988].

A major clue to the existence of such a cycle is the intense episodes of mountain building and continental rifting that appear to have occurred at roughly 500-million-year intervals. We first tested our ideas by looking at the geologic effects of the most recent supercontinent, Pangaea. We then applied our model to a critical period in the earth's history, roughly 700 million to 500 million years ago. At that time, a succession of geologic events, thought to be associated with the assembly of an earlier supercontinent, resulted in profound environmental changes, including alterations in the composition of seawater, in the global climate and in worldwide sea level. Such changes may have had a great influence on the evolution of life; they coincided with the appearance of the first complex, multicellular organisms. These creatures paved the way for the development of modern life-forms, including human beings.

What could have caused Pangaea (or any of the past supercontinents) to break apart? Two complementary theories have been proposed to answer this question. Don L. Anderson of the California Institute of Technology posits that supercontinents disassemble because continental rocks are poor conductors of heat compared with the thinner, denser (basaltic) ocean floors. Large continents or supercontinents therefore act like insulating blankets that block the escape of heat from the mantle. Temperatures rise beneath the supercontinent in much the way they do under a book lying on an electric blanket. As the heat accumulates, material at the base of the lithosphere

PANGAEA SUPERCONTINENT is shown as it appeared 290 million years ago. Continental collisions created folded, interior mountains (*purple*). Ocean floor that sank into the hot interior at the periphery of the supercontinent produced volcanoes and related uplift (*orange*). Through these processes, supercontinent formation and breakup can account for the great diversity of mountain belts.

J. BRENDAN MURPHY and R. DAMIAN NANCE began collaborating in 1985 because of their shared interest in the origin of ancient mountain belts preserved in the Canadian Appalachians. They soon realized that the evolution of these belts reflected global-scale plate tectonic processes. A native of Birr in the Republic of Ireland, Murphy moved to Canada in 1975. He received a Ph.D. in geological sciences at McGill University in 1982. At that time, Murphy joined St. Francis Xavier University in Antigonish, Nova Scotia, where he is now chairman of the department of geology. Nance is from Cornwall, England; he completed his Ph.D. at the University of Cambridge in 1978. He relocated to Canada and taught at St. Francis Xavier until 1980. Nance then moved to Ohio University, where he is now a professor of geology.

becomes less dense, causing the overlying supercontinent to dome upward and crack. Molten rock from the overheated asthenosphere rapidly fills the resulting fractures, which continually widen as pieces of the fragmented supercontinent are driven apart.

A second model of supercontinent dispersal, proposed by Andrew Hynes of McGill University, attributes the breakup to effects connected with the rotation of the earth. Supercontinents possess high angular momentum because they consist of an elevated mass that makes the earth's surface lopsided. This momentum produces long-lived stresses within the supercontinent that eventually cause it to tear itself apart.

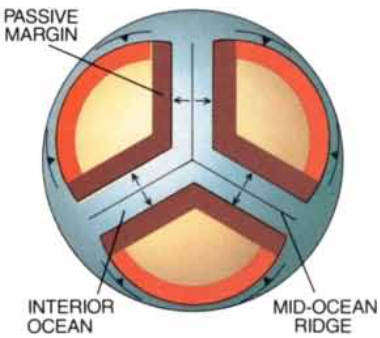
Both models probably play a role in the breakup of a supercontinent. In either case, the supercontinent sows the seeds of its own destruction even as it forms. The material from the asthenosphere that fills the spaces between the continental fragments is inherently denser than the continental crust because the mantle is richer in elements such as iron and magnesium. When the injected magma cools and solidifies, it therefore subsides, creating a low-lying area that ultimately floods with water to become the floor of a new ocean. The rift where the hot material rose becomes a spreading center, technically known as a mid-ocean ridge. As hot material continues to ascend at the ridge, the ocean spreads and the continents drift apart. This process is happening now in the middle of the Atlantic Ocean, where new crust forms as the Americas drift away from Europe and Africa.

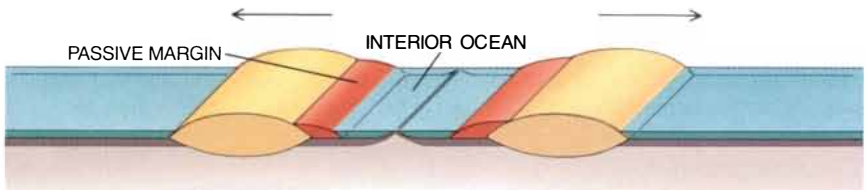
The scattering of the continents cannot continue indefinitely. Oceanic crust grows colder and denser the longer it is exposed to the surface; the seafloor therefore subsides as it migrates away from the ridge. Indeed, scientists examining the floor of the Atlantic find that it grows older and deeper the farther it lies from the Mid-Atlantic Ridge. The

oldest Atlantic seafloor rocks sit at the margins of the Central Atlantic. These rocks are about 180 million years old. Eventually the oldest ocean floor along the margin of the ocean grows denser than the asthenosphere below. Deep trenches, such as the Mariana Trench in the modern Pacific Ocean, identify the locations where cold oceanic crust sinks back into the earth's interior, a process known as subduction.

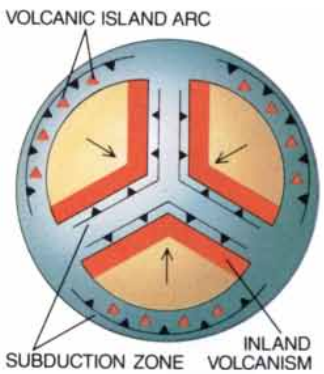
Calculations by Hynes suggest that increasing density overcomes resistance to subduction when the ocean floor reaches an age of about 200 million years. In fact, scientists do not observe any crust in today's oceans more than 200 million years old. The Atlantic Ocean presumably is approaching its maximum age and width. Within a few tens of millions of years, subduction

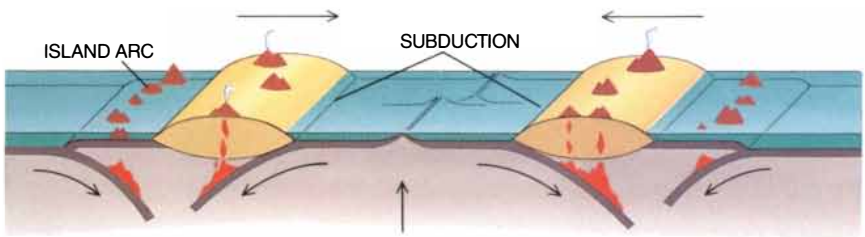
How the Supercontinent Cycle Works



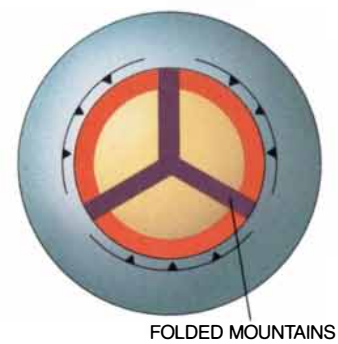


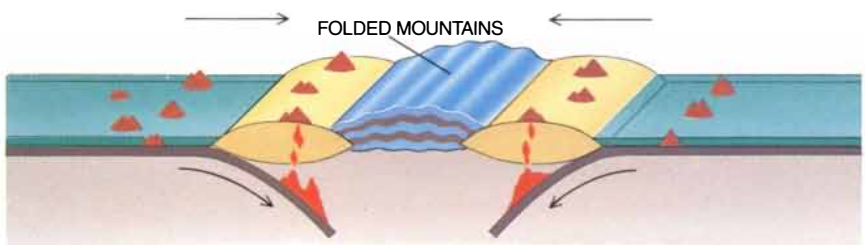
BREAKUP OF A SUPERCONTINENT results in the birth of interior oceans like the present Atlantic (*left*). Inward-facing margins of the separating continents are tectonically stable; undisturbed sediments collect along the margins, recording this period of relative placidity (*above*). Passive margin sediments continue to collect until the continents reach their maximum dispersal.



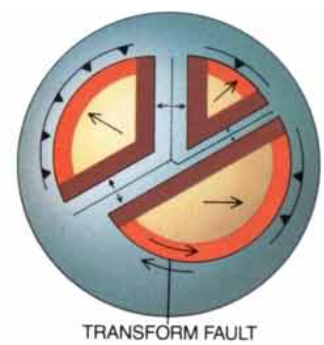


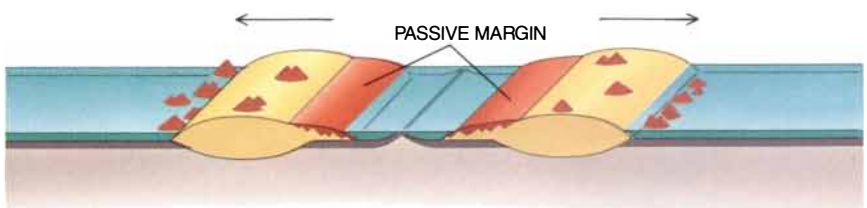
MAXIMUM DISPERSAL of the continents occurs when the interior oceans are about 200 million years old. Then the oldest parts of the interior oceans begin to sink, or subduct, into the earth (*left*). Subduction generates magma that fuels volcanoes in the overlying continent. Subduction can take place in the exterior ocean at the same time, forming island arcs that lag behind the continental plates (*above*).





CONTINENTAL COLLISIONS happen after the interior oceans are consumed. Collisions create interior mountain belts and broad areas of intense deformation, uplift and erosion (*left*). Subduction zones occur around the margin of the supercontinent, leading to widespread peripheral volcanism. Island arcs may be swept in from the exterior ocean and accreted onto the edges of the supercontinent (*above*).





NEXT SUPERCONTINENT BREAKUP results from thermal and rotational forces. Exterior subduction continues where the continental margin is roughly perpendicular to the direction of its motion (*left figure, top*). Transform, or sideways, faults appear where the motion of the plate is nearly parallel to the orientation of the margin (*left figure, bottom*). Passive margin sediments resume collecting (*above*).

should begin in those areas of the Atlantic where the seafloor is oldest, at the margins of the continents. When that happens, the rim of the Atlantic will become geologically active, and the present outward drift of the continents should cease.

Thermal changes deeper within the earth help to direct this subduction into a net inward pull on the continents. The heat that originally accumulated beneath the supercontinent, culminating in the development of a mid-ocean ridge, escapes easily through the thin ocean floor. Pieces of the supercontinent therefore subside as they separate, and the convective currents driving them apart draw to a halt. Hence, subduction at the edges of the ocean effectively reels in the dispersed continents. Finally, the oceans that stretched between the continents vanish entirely, and the continents collide, creating a new supercontinent and setting the stage for the next cycle.

Based on the deduced history of Pangaea, the life expectancy of a supercontinent is about 100 million years. The oceans that form when the supercontinent breaks up cannot last more than 400 million years if they close at about the same rate that they open.

By combining concepts from the supercontinent cycle and from plate tectonics, we have developed an all-encompassing model that accounts for the great diversity of the mountain chains around the earth. We realized that the assembly and breakup of supercontinents should create two distinct types of mountain belts, or orogens (from *oros,* the Greek word for mountain). Collisions between continents fold and buckle the crust; the resulting mountain belts are called interior orogens because they lie within the supercontinent after its amalgamation. The Himalaya Mountains reflect the current collision between India and Asia. Subduction of oceanic crust at the edge of a continent or supercontinent elevates the overlying crust and triggers volcanic activity, producing very different kinds of mountainous zones, called peripheral orogens. The Rocky Mountains reflect the subduction of oceanic Pacific plates under western North America.

Pangaea serves as a test case of how well our model of interior and peripheral orogenies fits with the known movements of the continents. Researchers reconstruct the past locations of the continents using various techniques. Some iron-rich volcanic and sedimentary rocks record the orientation of the earth's magnetic field when they form; these rocks act like compasses, reporting the local latitude at that time. Measurements of radioactive isotopes, in turn, reveal the ages of these rocks. Geologists also infer the relative positions of the continents at remote times by attempting to unite large geologic features that have been split up by more recent plate motions.

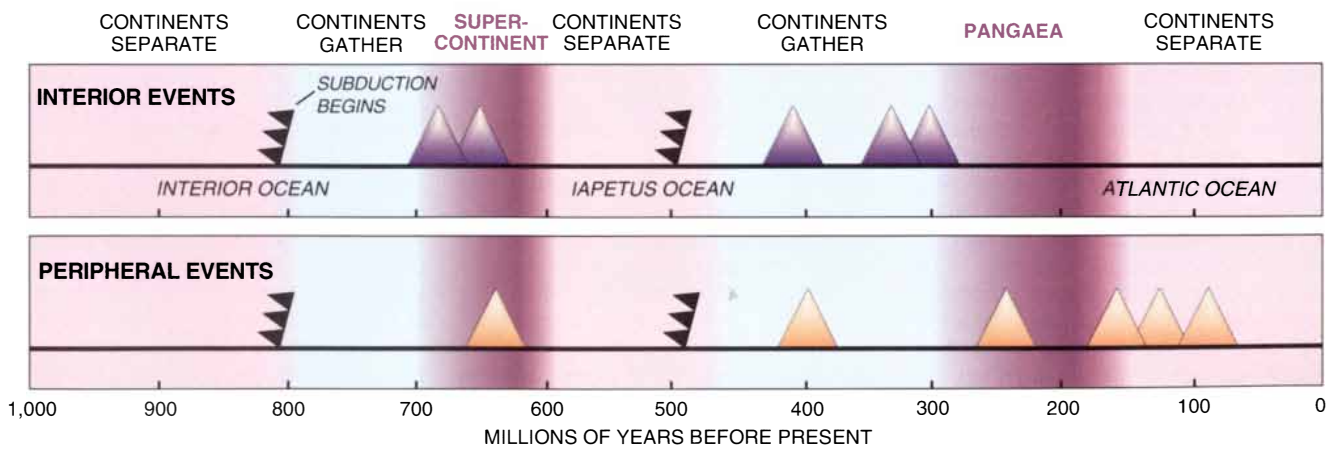
The formation of the supercontinent Pangaea involved multiple collisions that took place over many millions of years. Roughly 420 million to 380 million years ago, the continental mass called Laurentia (which included much of modern North America) crashed into Baltica (Europe). The two masses fused to become Laurasia. Then, between 360 million and 270 million years ago, Laurasia collided with Gondwana (consisting of pieces of present-day Africa, India, South America, Australia and Antarctica) and with Siberia, thereby giving birth to Pangaea.

Such encounters between continents dismember the continental shelves of the colliding plates. The edge of one continent is thrust on top of another, causing widespread buckling or folding of rock layers that were originally horizontal. As a consequence, the continental lithosphere grows markedly thicker in the collision zone. Compressional forces uplift the overriding continental plate to form high mountains.

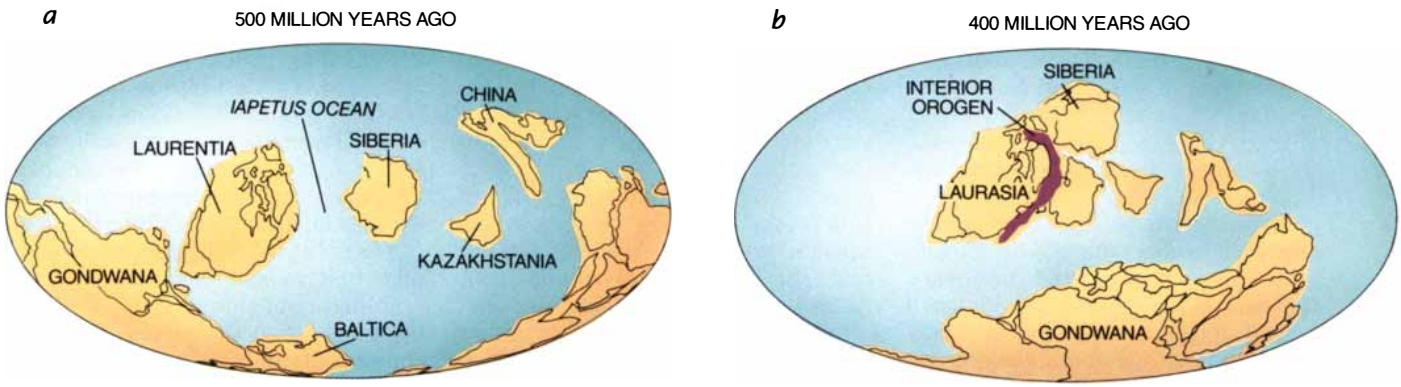
Eroded remnants of uplifted mountains appear in the places where the components of Pangaea collided. The encounter between Laurentia and Baltica gave rise to the Caledonian orogenic belt, a large deformed region that marks an eroded mountain range running from Ireland to northern Scandinavia and Greenland. Folded mountain belts and faults appeared in the southern U.S. (the Ouachita orogeny) and the eastern U.S. (the Appalachian Mountains) when Laurasia crashed into Gondwana; similar features arose in eastern Europe (creating the Urals) when Laurasia fused with Siberia.

Interior orogenies leave several characteristic signs that geologists can recognize. Collisional forces push the overridden plate into the deeper, hotter regions of the earth's crust. Minerals formed near the surface become unstable when they are exposed to greater temperatures and pressures. These minerals melt and rise to the surface. In some cases, they react with one another, or metamorphose, to form new, stable mineral assemblages. The resulting metamorphic rocks are described as high grade because they crystallize only at the high temperatures and pressures found near the base of the crust.

When the compressional forces cease within the zone of collision between continents, the depressed but still buoyant crust rapidly rebounds, just as a



GEOLOGIC TIMELINE shows mountain building associated with the formation and breakup of the most recent two supercontinents, during the past one billion years. Two kinds of events, interior and exterior, produce mountains. Interior events (*top line*) occur when continents collide, building folded mountains (*purple cones*). Interior oceans open when continents separate and start to close as subduction begins. Peripheral events (*bottom line*) involve the emergence of volcanic mountains (*orange cones*) at the margins of landmasses, where oceanic crust subducts under a continental plate.



HISTORY OF PANGAEA began about 500 million years ago, when the continents were dispersed around the Iapetus Ocean (*a*). Laurentia (North America) collided with Baltica (Europe) to form Laurasia (*b*). The Iapetus vanished when Laurasia

wooden block held under water bobs up once the downward force is removed. Over millions of years, erosion wears away the resulting uplifted crust until the formerly depressed, high-grade continental crust is exposed at the surface.

Because of this massive uplift and the enormous amount of erosion that results from it, the near-surface record of interior orogenies is commonly not preserved. Instead huge thicknesses of new sediments may be deposited on the older, high-grade rocks. In places where the strata are exposed, however, geologists can readily distinguish the telltale signs of a continental collision.

Sediments that accumulate after the period of mountain building are not subjected to the compressive stresses of their predecessors. They therefore consist of minerals that originated at low temperatures and pressures and form undisturbed, parallel layers, in sharp contrast to the underlying, distorted or tilted high-grade rocks. The interior orogenies mentioned above all display these expected mineral, sedimentary and structural signatures.

The geologic record shows little or no evidence of mountain building at the continental margins before Pangaea began to assemble. The perimeter of today's Atlantic Ocean is similarly sedate. Deposits that accumulate on these stable areas are called passive margin sediments. Such sediments collected along the stable eastern edge of North America between about 600 million and 480 million years ago, for example. When the continents reached their maximum, separation and subduction of the interior ocean commenced (roughly 480 million years ago for North America), tectonic conditions altered radically. The thrusting of the ocean floor beneath the continents disrupted formerly calm margins and initiated a period of mountain formation.

When the down-going ocean crust enters the asthenosphere, it brings along volatile compounds (primarily water) that lower the melting point of the surrounding minerals. This effect, combined with the high temperature of the asthenosphere, causes material to melt within and above the slab. The resulting molten minerals, generically known as melts, rise toward the surface, carrying with them their heat and their distinctive chemistry. These melts acquire a so-called calc-alkalic composition as a result of their interaction with the oxygen and water that travel down in the subducted slab.

Some melts reach the surface and emerge in volcanoes. Material that cools and solidifies at depth in chambers forms plutonic rocks (named after Pluto, the Roman god of the underworld), such as granite. The heat and buoyant materials rising from the subducting slab lift up the margin of the overlying continent, leading to the appearance of a mountain belt.

Subduction and associated mountain building along the periphery of a continent may commence at any time, depending on the age of the neighboring ocean floor. Obviously, subduction takes place at the margins of an interior ocean as the continents move inward toward a future rendezvous. But even as the interior oceans are closing, oceanic crust may also be sinking at the edges of the exterior ocean that surrounds the assembling supercontinent. In this case, the continent is actually retreating from the subduction zone. Melted rock produced by subduction of the exterior ocean therefore rises mostly through oceanic crust. Melt from interior subduction zones, in contrast, rises predominantly through the oncoming continental crust.

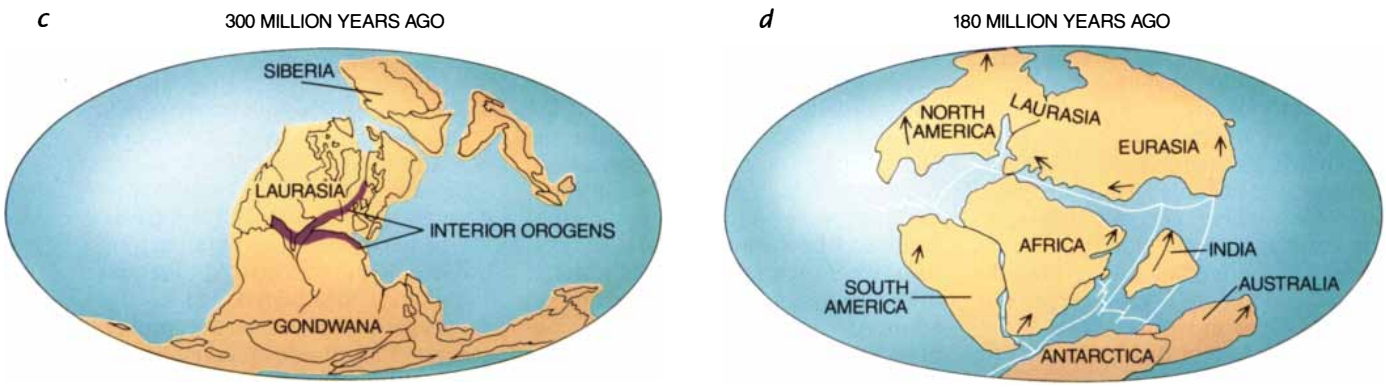
The contrasting geometries of interior and exterior subduction show up in the chemistry of the igneous material that reaches the surface: melts that rise through oceanic crust tend to be richer in iron and magnesium and poorer in silicon than melts that move through continental crust. This compositional disparity results in significant differences in the mineral content of the resulting rocks, which enables geologists to infer the timing and geometry of ancient mountain-building episodes.

Material from exterior subduction zones surfaces through the ocean floor, some distance behind the inward-moving continent. This material creates volcanic island chains called island arcs. A series of such island arcs is thought to have formed approximately 470 million years ago off the west coast of North America. These eruptions document subduction of the exterior ocean. Exterior subduction may also pull off small continental blocks, or microcontinents, from the retreating continents. The islands of Japan are a modern example of such ruptured continental fragments.

Peripheral mountain building continues after the amalgamation of the supercontinent is complete, but under very different conditions. Once the continents collide, oceanic crust is consumed preferentially at the exterior subduction zones. Exterior subduction zones (some of which previously may have been in the middle of the ocean) tend to relocate to the periphery of the supercontinent.

Because the continents can no longer move away from the exterior subduction zones, nearly all the melts pass through continental rather than oceanic crust. Here also, hot, buoyant material elevates the crust and gives rise to volcanoes and volcanic mountains. The resulting mountain belts resemble those that developed when the interior ocean was likewise subducting beneath the continents. The precise location where these thermal effects appear at the surface depends on the angle of the descending oceanic plate.

As the exterior subduction zones mi-



fused with Gondwana (all the other continents), creating Pangaea (*c*). Each collision yielded an episode of mountain building. Plate motions changed as Pangaea dispersed. North America moved north, then west away from Eurasia (*d*).

grate to the edge of the supercontinent, the ocean floor becomes like a conveyer belt that carries island arc chains and microcontinents back to the continental edge. Paul F. Hoffman of the University of Victoria described the resulting interactions as "bump and grind" collisions. Small landmasses may either fuse with or deflect off one another and the supercontinent. These collisions have much different effects than do interactions between continents. Bump and grind motions are far more erratic, and microcontinents create only local regions of tectonic activity at their margins. As a result, microcontinental collisions and the resulting deformation may be episodic, although the volcanic activity associated with subduction can remain fairly continuous.

When Laurentia united with Baltica, about 420 million to 380 million years ago, exterior island arcs began to collide with the western margin of what is now North America. These collisions led to the observed local but occasionally intense deformation of rocks in the region from the California-Nevada border to Idaho (the Antler orogeny). As Pangaea came together, continued subduction at the periphery produced more volcanic island arcs. These islands apparently rammed into North America about 250 million years ago. The resulting episode of mountain building in northwest Nevada, known as the Sonoma orogeny, coincides with the completion of the assembly of Pangaea. The subsequent formation of the Rockies and the Sierra Nevadas has obscured much of the surface evidence of these early orogenies.

About 180 million years ago Pangaea rifted, and a new interior ocean—the Atlantic—opened up. The effect of the dispersal of the supercontinent depends on the relative orientation of the external subduction zones and the direction of dispersal of the continents. If these features are approximately parallel, subduction and pulses of deformation may continue as the interior oceans open. Because of the outward motion of the continents, melt from these exterior subduction zones rises through continental rock, in much the way the melt did from interior subduction zones when the continents were drifting inward.

During the first stage of the breakup of Pangaea, 180 million to 140 million years ago, Laurasia separated from Gondwana, causing what would become North America to move northward. The change in direction may have forced oceanic crust to subduct under western North America. Indeed, the geologic record at this time shows a surge of volcanic and plutonic activity, one aspect of the Nevadan orogeny in eastern California. The associated rocks have the calc-alkalic composition typical of melt rising from a subducted slab.

The second stage of the breakup happened some 140 million years ago. Gondwana split, and Laurasia rifted apart into North America and Eurasia. The splintering of Laurasia changed the motion of the North American plate from northward to westward. This change in motion would have compressed continental rocks as oceanic crust was forced far under North America. These events coincided with a series of pulses of mountain building throughout western North America, including the Sevier and Laramide orogenies that initiated the formation of the Rocky Mountains.

If the external subduction zone lies parallel to the direction of outward movement of the continent, subduction will give way to a sideways movement, becoming a transverse (strike-slip) fault. Microcontinents and volcanic arc islands situated oceanward of these faults may be transported sideways far from their original positions. Alaska was built by this process: a collage of crustal blocks swept in from the exterior ocean (today's Pacific Ocean) during the formation and breakup of Pangaea. These blocks slid northward along the western margin of North America until they were trapped in a corner in the Pacific subduction zones.

Peripheral mountain building does not involve collisions between continental blocks, so there is little thickening of the crust and hence little uplift and erosion. Consequently, the remnants of volcanic activity, along with contemporaneous sediments derived from the erosion of the volcanic mountains, remain well preserved. The preservation of these rocks over a large region clearly distinguishes peripheral orogenies from internal ones. Where collisions do occur, they usually involve microcontinental blocks such as volcanic islands. The resulting deformation varies greatly from region to region. Interior orogenies, in comparison, result from collisions between continents that yield widespread, more uniform deformation.

Our analysis of the history of Pangaea unites disparate information about mountain-building processes into a coherent picture. It therefore seemed reasonable to ask whether our model could make sense of orogenies associated with earlier supercontinents. In other words, do the remains of mountain belts 600 million to 800 million years old show signs of the same kind of interior and peripheral processes that shaped Pangaea 500 million years later?

Many obstacles stand in the way of answering that question. There is a severe paucity of exposed rocks that predate the Pangaea cycle. Measurements of paleomagnetism become increasingly uncertain in older rocks. And many ancient geologic formations have been severed and recombined multiple times. Nevertheless, we think many seemingly confusing characteristics of such an-

cient mountain belts can be explained by looking for signs of interior and peripheral mountain building.

The story of the earlier supercontinent begins roughly one billion years ago, when passive margin sediments accumulated at the edges of the separated continents. Then, about 820 million years ago, subduction commenced more or less simultaneously in both the exterior and interior oceans (earlier subduction zones must have been situated in the middle of the exterior ocean, where they left no evidence). Island arcs, which later fused with the edges of the continents, record this beginning of subduction. Subduction of the shrinking interior oceans unleashed volcanic eruptions primarily along the continental margins. Remnants of this volcanic activity still exist in strata in Brazil and in western Africa, dating from 820 million to 800 million years ago. When the interior oceans had been completely consumed, about 650 million years ago, the continents collided, completing the assembly of the supercontinent.

The evidence for these interactions resides between large blocks of ancient (more than a billion years old) continental crust, known as cratons. Cratons are essentially the stable nuclei of present-day continents. Between the cratons lie the scars of huge interior orogenies, as much as 1,000 kilometers across, which attest to the powerful collisions that occurred as the older supercontinent amalgamated.

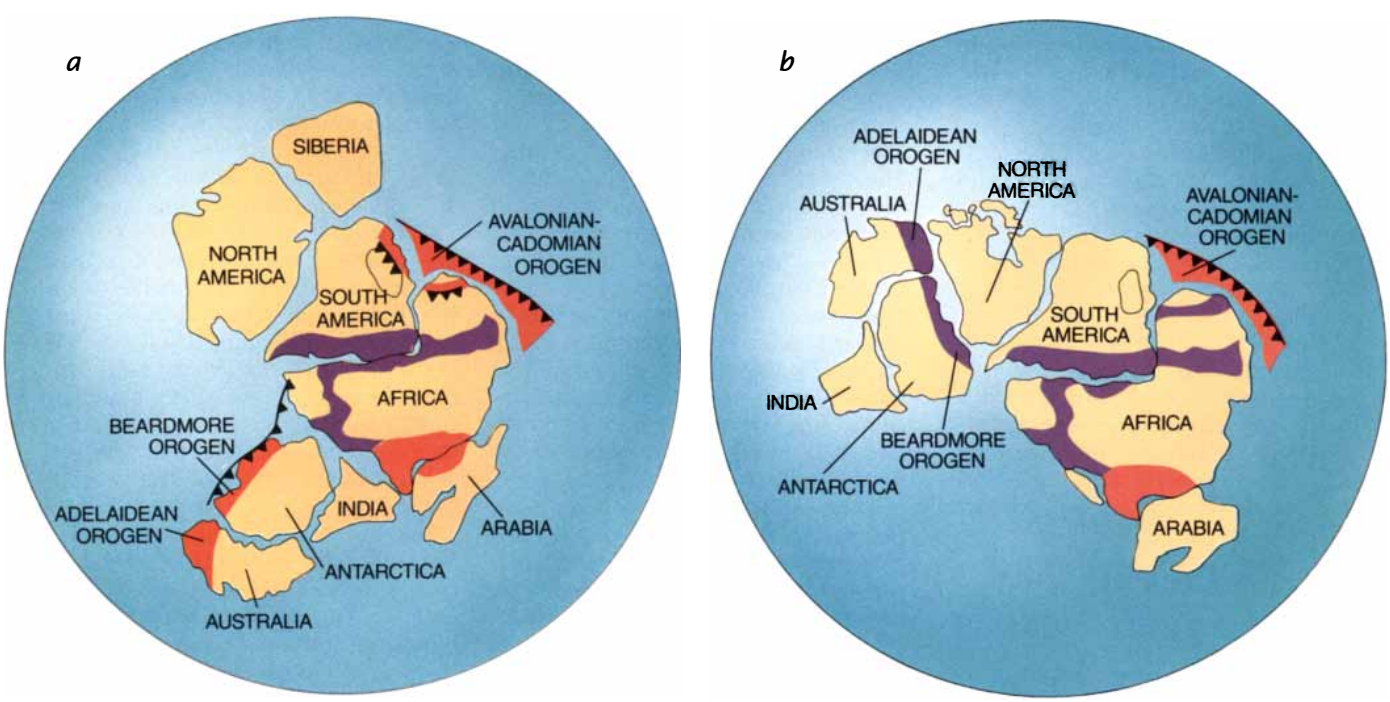
For example, continental motions brought together the cratons of west Africa and Guyana some 675 million to 650 million years ago. The result of the impact can be seen in west Africa (the Mauritanide-Bassaride-Rokelide orogeny). Exposed high-grade rocks attest to the presence of folded mountains that have since been mostly worn away. Collisions between other cratons resulted in the Trans-Saharan and Damaride (in South Africa) mountain belts. Collisional events of similar age also are seen in eastern South America, in eastern Australia and in Antarctica.

Each of these belts shows signs of widespread deformation, thrusting and crustal thickening indicative of interior orogenies, where continents collide. Both calc-alkalic igneous rocks (from the subduction of the interior ocean) and high-grade metamorphic rocks (from the subsequent compression of the cratons) are abundant in west Africa and eastern South America. More recent sediments having a relatively simple, tabular geometry rest on contorted orogenic rocks, indicating that severe uplift occurred, followed by substantial erosion. These features collectively confirm that collisions between continents (interior orogenies) affected large areas of the globe between 675 million and 600 million years ago.

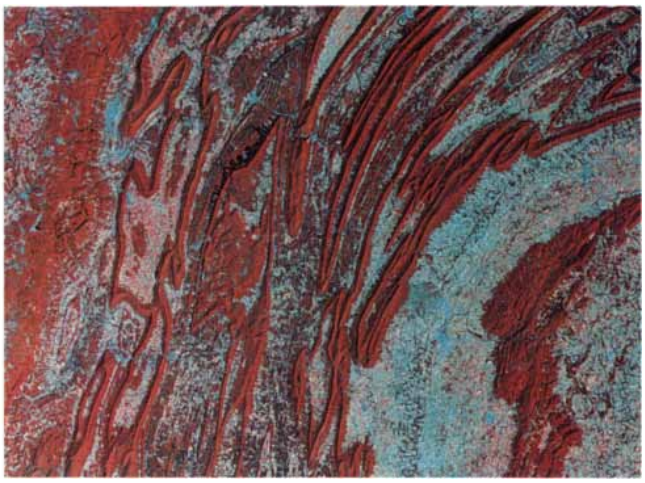
Other features record widespread peripheral orogenies. As the interior oceans closed, the continents retreated from the expanding exterior ocean, generating many volcanic islands along the exterior subduction zone. These islands later collided with northern South America and with western and northern Africa; the characteristic variable styles and intensities of deformations from these collisions are still preserved. The fusion of the supercontinent roughly 650 million years ago led to renewed and intensified subduction at its edges.

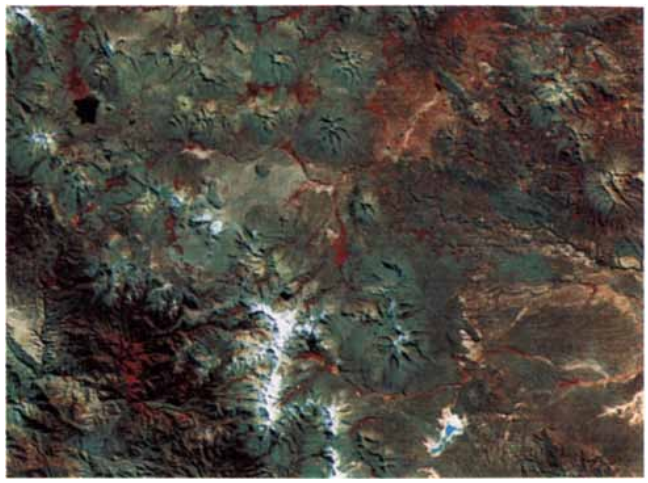
This peripheral subduction probably generated the Avalonian-Cadomian belt, an eroded range of mountains that now occupies the eastern seaboard of North America and parts of western Europe. Geologic and paleomagnetic evidence suggests that 600 million years ago this belt was situated off South America and northwest Africa at the edge of the ancient supercontinent.

The Avalonian-Cadomian belt encompasses a great volume of low-grade volcanic and related sedimentary rocks 650 million to 600 million years old. The rocks in this region are, for the most part, only mildly deformed. In many instances, they conform closely with the overlying strata. The absence of widespread deformation and the preservation of the low-grade volcanic and sedimentary rocks imply that the crust in these regions was only minimally disturbed. Such traits are consistent with the expected appearance of a peripheral orogeny. The presence of some local, intense deformation can be explained by collisions with island arcs



ONE SUPERCONTINENT RECONSTRUCTION implies that the Adelaidean and Beardmore mountain belts resulted from peripheral subduction (*a*). Another reconstruction holds that continental collisions created those belts (*b*). Our model of supercontinent-related orogenies will help distinguish between these reconstructions and provide a test for others.





LANDSAT IMAGE of the Appalachian Mountains in Pennsylvania (*left*) shows a regular pattern of folded mountains, characteristic of an interior orogeny. An equivalent view of the Andes in Peru (*right*) reveals more randomly distributed volcanic mountains, a result of peripheral subduction of oceanic crust beneath western South America.

and microcontinents. The signature of subduction vanished and was replaced by strike-slip faulting about 550 million years ago, coinciding with the breakup of the supercontinent.

The present Arabian peninsula probably formed as a result of peripheral orogenic activity during the same era. This region consists of a mosaic of microcontinental blocks in which abundant volcanic and associated plutonic rocks—the telltale signs of island arc eruptions—date from 820 million to 740 million years ago. Screens of ancient ocean crust are sandwiched between the blocks. Above these rocks lies a younger sequence of strata 640 million to 600 million years old.

We infer from this collage of material that the Arabian peninsula is an ancient analogue of Alaska, a patchwork quilt of volcanic island arcs that originated in the ocean around the supercontinent. After the supercontinent fragmented, transverse plate motions swept the pieces into northeast Africa, where they fused to become the modern Arabian shield.

Thick, passive margin sediment layers appeared nearly simultaneously in many parts of the world about 575 million to 550 million years ago, signifying the beginning of the breakup of the supercontinent. As the continents dispersed, they cooled and subsided. Seawater flooded the sinking continents, creating large continental shelves. This event is consistent with the geologic record at that time. Vast accumulations of sedimentary layers are found in many areas, indicating a global rise in sea level and deposition of sediments in many relatively undisturbed settings. These passive margin sediments represent the stratigraphic background on which geologists have read the later episode of tectonic activity and mountain building associated with the formation of Pangaea.

Many parts of the picture of the pre-Pangaea supercontinent remain fuzzy. Researchers disagree on the ancient latitudes of many parts of the supercontinent (North and South America, for example). A reconstruction worked out by Ian W. D. Dalziel of the University of Texas at Austin (and a similar one by Hoffman) implies that peripheral subduction was responsible for an old mountain belt in Mozambique, at the same time suggesting that interior encounters between continents led to the formation of the Adelaidean (Australia) and Beardmore (Antarctica) belts.

An alternative continental reconstruction by Gerard Bond and his colleagues at Lamont-Doherty Geological Observatory predicts exactly opposite styles of orogeny. In the future, improved paleomagnetic data may settle this dispute, but our model of interior and exterior orogens can also help. A closer examination of the style of orogenic activity in these belts should make it possible to decide between the two reconstructions.

Attempting to reconstruct even earlier supercontinents is exceedingly difficult. Nevertheless, it is possible to deduce the ages of the most extensive interior orogenies (indicating the fusion of a supercontinent) and pulses of rifting (associated with breakup). Continental collisions followed by major rifting episodes seem to have occurred in pulses approximately 2,700 million to 2,500 million, 2,100 million to 2,000 million, 1,700 million to 1,500 million and 1,100 million to 1,000 million years ago. Although these ages are somewhat uncertain, they strongly suggest that the supercontinent cycle has been a long-standing feature of the evolution of the earth's surface.

The orogenic belts described in this article have been known for many years; our work attempts to organize and explain them in a global context. The recognition of contrasting peripheral and interior orogenic processes and the identification of the locations corresponding to each are creating a framework in which to view the development of mountain systems. Our model should assist geoscientists as they attempt to reconstruct the ancient configuration of the continents and identify the tectonic forces that have shaped our planet's past.

FURTHER READING

THE GROWTH OF WESTERN NORTH AMERICA. David L. Jones, Allan Cox, Peter Coney and Myrl Beck in *Scientific American,* Vol. 247, No. 5, pages 70–84; November 1982.

PALEOZOIC PALEOGEOGRAPHY OF NORTH AMERICA, GONDWANA, AND INTERVENING DISPLACED TERRANES: COMPARISONS OF PALEOMAGNETISM WITH PALEOCLIMATOLOGY AND BIOGEOGRAPHICAL PATTERNS. Rob Van der Voo in *Geological Society of America Bulletin,* Vol. 100, No. 3, pages 311–324; March 1988.

SUPERCONTINENT MODEL FOR THE CONTRASTING CHARACTER OF LATE PROTEROZOIC OROGENIC BELTS. J. Brendan Murphy and R. Damian Nance in *Geology,* Vol. 19, No. 5, pages 469–472; May 1991.

DID THE BREAKOUT OF LAURENTIA TURN GONDWANALAND INSIDE-OUT? Paul F. Hoffman in *Science,* Vol. 252, pages 1409–1412; June 7, 1991.

Superantigens in Human Disease

These proteins cause food poisoning and toxic shock. They may also contribute to arthritis and AIDS. Investigators are learning how superantigens overstimulate the immune system and induce disease

by Howard M. Johnson, Jeffry K. Russell and Carol H. Pontzer

Normally, when a person's immune system encounters a protein made by a virus or other microbe, fewer than one in 10,000 of the white blood cells known as *T* lymphocytes react. Although their number is small, the cells orchestrate an attack that specifically targets the alien protein, or antigen, erasing the invader without harming healthy tissue. In contrast, proteins called superantigens whip the immune system into an unproductive, even destructive frenzy.

These astonishing substances can arouse as many as one in five *T* cells, most of which are useless for fighting a current infection. What is worse, certain of the activated cells may unleash an autoimmune attack and hurt the individual they should protect, like a pit bull turning against its master. At times, superantigens may even have the opposite effect: they somehow trigger the death of the cells they excite. They thus punch holes in the body's defensive shield.

Recent studies have identified the steps by which superantigens stimulate excessive numbers of *T* cells. The work is helping to explain such medical mysteries as how certain toxins cause the symptoms of food poisoning and of the toxic shock syndrome. At the same time, the research is opening up new avenues of investigation into causes and possible treatments of a number of diseases, including arthritis, AIDS and cancer. There is even reason to hope that the immune-stimulating and immune-depressing properties of superantigens can be turned to advantage and harnessed for therapeutic applications.

HOWARD M. JOHNSON, JEFFRY K. RUSSELL and CAROL H. PONTZER are colleagues at the University of Florida at Gainesville. Johnson is a graduate research professor in the department of microbiology and cell science. Russell is an assistant research scientist and Pontzer is a postdoctoral associate in that same department.

Scientists have gleaned much of what they understand about superantigens from studying the earliest known examples: a group of structurally related proteins called staphylococcal enterotoxins. One of us (Johnson) helped show in the 1970s that the enterotoxins were superantigens, although that term was not coined until many years later.

Johnson and his colleagues at the University of Texas Medical Branch in Galveston uncovered the proteins' remarkable potency while attempting to discern how the toxins, which account for as much as 45 percent of all cases of food poisoning, make people sick. By 1970 physicians knew that when strains of the bacterium *Staphylococcus aureus* colonize food, they secrete one or more enterotoxins, which are now named alphabetically as A, B, C, D and E. Within hours after people ingest badly contaminated, toxin-laden food, they begin to feel weak, feverish and nauseated and to vomit or suffer diarrhea. Physicians also were aware that symptoms abate within a day or two because intestinal enzymes degrade the toxins in that time. There were few clues, however, to exactly how enterotoxins cause discomfort in the first place.

Indeed, investigators had noted that intestinal tissue of affected patients looks virtually normal under the microscope. The proteins apparently did not damage the most obvious target of an intestinal invader: the specialized cells that regulate the passage of nutrients and water between the gut and the bloodstream. The only obvious abnormality was the presence of white cells in the tissue. Such infiltration was an expected response to any infection, and so there was little reason to think the cells were doing something unusual.

Soon, however, there would be plenty of reason to think the cells were causing harm. First, in 1970, Duane L. Peavy and his associates at the University of Florida at Gainesville observed that introduction of enterotoxin B to blood cells triggers the proliferation of lymphocytes. Five years later Johnson, with his co-workers at the Cincinnati branch of the Food and Drug Administration, demonstrated that the affected lymphocytes were *T* cells. They determined that toxin A stimulated *T* cell growth as well.

Curious as to how readily enterotoxins cause *T* cell replication, Johnson initiated the studies that ultimately revealed the proteins' profound effect on the immune system. After moving to the University of Texas, he, together with Marlyn P. Langford and G. John Stanton, measured the minimal concentrations of toxin A that would generate proliferation.

Amazingly, they found that only minuscule amounts were needed. Just a few hundred molecules of toxin triggered a degree of replication that surpassed what could be achieved by a billion copies of a conventional antigen—for example, a protein on the influenza virus. Certain plant and microbial proteins had earlier been found to stimulate prodigious lymphocyte multiplication, but no protein was as strong as the enterotoxin.

A small amount of toxin A also yielded extraordinarily high production of gamma interferon, one of several cytokines, or chemical messengers, pro-

BACTERIAL CELLS (*spheres*) belong to the species *Staphylococcus aureus*. Strains of *S. aureus* cause food poisoning and the toxic shock syndrome by releasing superantigens, which activate abnormally high numbers of the immune system cells known as helper *T* lymphocytes. The cell at the top right is in the midst of decaying because it has been bombarded by an antibiotic.

duced by the subset of *T* lymphocytes called helper cells. These cells direct much of the immune response. They do not attack microbes themselves; instead they rely on cytokines to activate both cytotoxic *T* lymphocytes, which kill infected cells, and *B* lymphocytes, which secrete antibodies against antigens. The interferon data implied that helper cells were among the targets of staphylococcal enterotoxins.

How could massive helper cell activity lead to the miseries of food poisoning? An early tip came from Kendall A. Smith of Dartmouth Medical School, who had other matters on his mind.

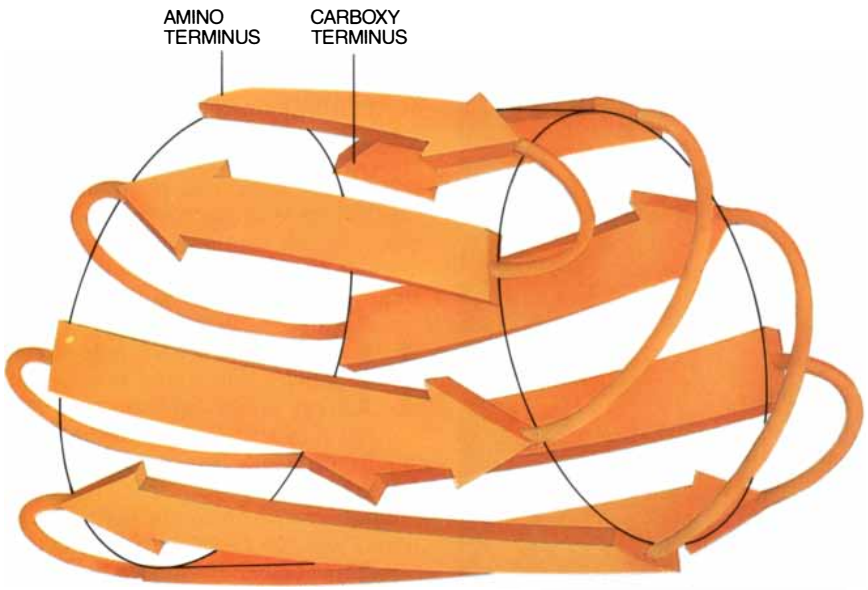
While studying how normal antigens spur *T* cells to replicate, Smith determined that helper *T* cells must produce interleukin-2, another cytokine, in order to respond to the antigens [see "Interleukin-2," by Kendall A. Smith; SCIENTIFIC AMERICAN, March 1990]. This discovery suggested to Johnson that interleukin-2 probably also mediated the effect of superantigens on *T* cells. Conceivably, though, the toxins could activate *T* cells by other means.

In 1985 Roland Carlsson and his colleagues at the University of Lund in Sweden found evidence supporting a central role for interleukin-2. They showed that when a tiny amount of enterotoxin A was mixed with *T* lymphocytes, the collection of cells produced a huge quantity of the cytokine. A few years later Johnson and his graduate student Harold I. Magazine confirmed that interleukin-2 mediates enterotoxin-induced *T* cell multiplication; the toxins do not bypass the interleukin pathway.

At about the same time, Steven A. Rosenberg of the National Institutes of Health observed that infusion of high doses of interleukin-2 into the circulation of cancer patients (as part of an experimental therapy) caused disturbing side effects. The patients suffered from fever, malaise, nausea, vomiting and diarrhea—the very symptoms that bedevil victims of food poisoning.

These varied data indicated that the enterotoxins make people ill by stimulating production of high levels of interleukin-2. The fact that infusion of this cytokine leads to the same symptoms seen in food poisoning further implied that excess interleukin-2 does not cause trouble by acting locally. Instead it makes its way into the bloodstream and then travels, or sends signals, to brain centers that give rise to nausea, fever and gastric distress.

By implication, one can speculate that excess interleukin-2 also causes the



CYLINDRICAL SHAPE common to several proteins is thought to occur in *S. aureus* enterotoxins, the superantigens responsible for food poisoning. Arrows represent beta structures, areas in which the backbone of a protein is extended rather than folded into coils known as alpha helices. Enterotoxins do include a few helices, but their locations in three-dimensional space have yet to be identified. The predominance of beta structures suggests that much of the protein is exposed to its environment, ready to interact with other molecules.

symptoms of the toxic shock syndrome. The superantigen responsible for this disorder is produced by a strain of *S. aureus* and is structurally similar to the *S. aureus* enterotoxins. Patients stricken with toxic shock initially display signs of food poisoning, but later they suffer a dangerous slowing of the circulation. Presumably the illness becomes more severe because, unlike the bacteria that bring on food poisoning, the strain causing toxic shock reproduces in the body. As a result, people are exposed to more toxin and hence to higher or sustained levels of interleukin-2.

As of 1988, then, scientists understood that stimulation of many millions of *T* cells leading to an overabundance of interleukin-2 was the link between enterotoxins and the symptoms of food poisoning. The accumulated data, though, failed to explain just how enterotoxins flip the "switch" that turns on so many *T* cells. Recent work is now filling in that blank.

An analysis of structure is a first step when one is trying to understand how a given molecule communicates with cells in the body. Accordingly, much new research builds on the pioneering studies of Merlin S. Bergdoll. With his colleagues at the University of Wisconsin, Bergdoll determined the amino acid sequence of enterotoxin B in 1970. Since then, that group and others have uncovered the sequences of all the enterotoxins and of the toxin responsible for the toxic shock syndrome.

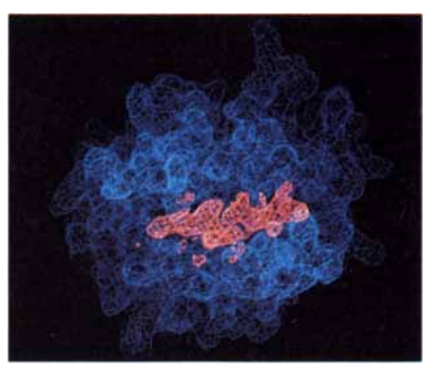
Related analyses have established that the poisons are all medium-size proteins rich in hydrophilic, or water-loving, amino acids. Each molecule also consists mainly of beta structures (conformations in which the backbone of the protein is extended rather than folded in on itself), although the proteins also include a few alpha helices (conformations in which the backbone forms a tight coil) [see "The Protein Folding Problem," by Frederic M. Richards; SCIENTIFIC AMERICAN, January 1991]. In other words, the enterotoxins are relatively noncompact; much of their surface is exposed to the body's aqueous environment and is thus available for interaction with other molecules.

Further clues to how superantigens activate *T* cells came from studies by Carlsson in Sweden and Bernhard Fleischer and Hubert Schrezenmeier of the University of Ulm in Germany showing that the toxins behave like conventional antigens in some ways but exhibit critical differences in others. Before helper *T* cells can recognize conventional protein antigens, the proteins must first undergo processing by macrophages or other antigen-presenting cells. These cells essentially swallow antigens and chop them into peptides, or small chains of amino acids. The presenters then display the peptide antigens at the cell surface in combination with what are called major histocompatibility complex (MHC) class II molecules. A peptide fits in a cleft on an MHC molecule much as a gem fits in a setting on a ring or as a hot dog fits in a hot dog bun. Once an antigen is displayed, the few helper cells in the body that bear receptors for the particular peptide link up with it. (Each *T* cell is specific for one kind of peptide antigen.)

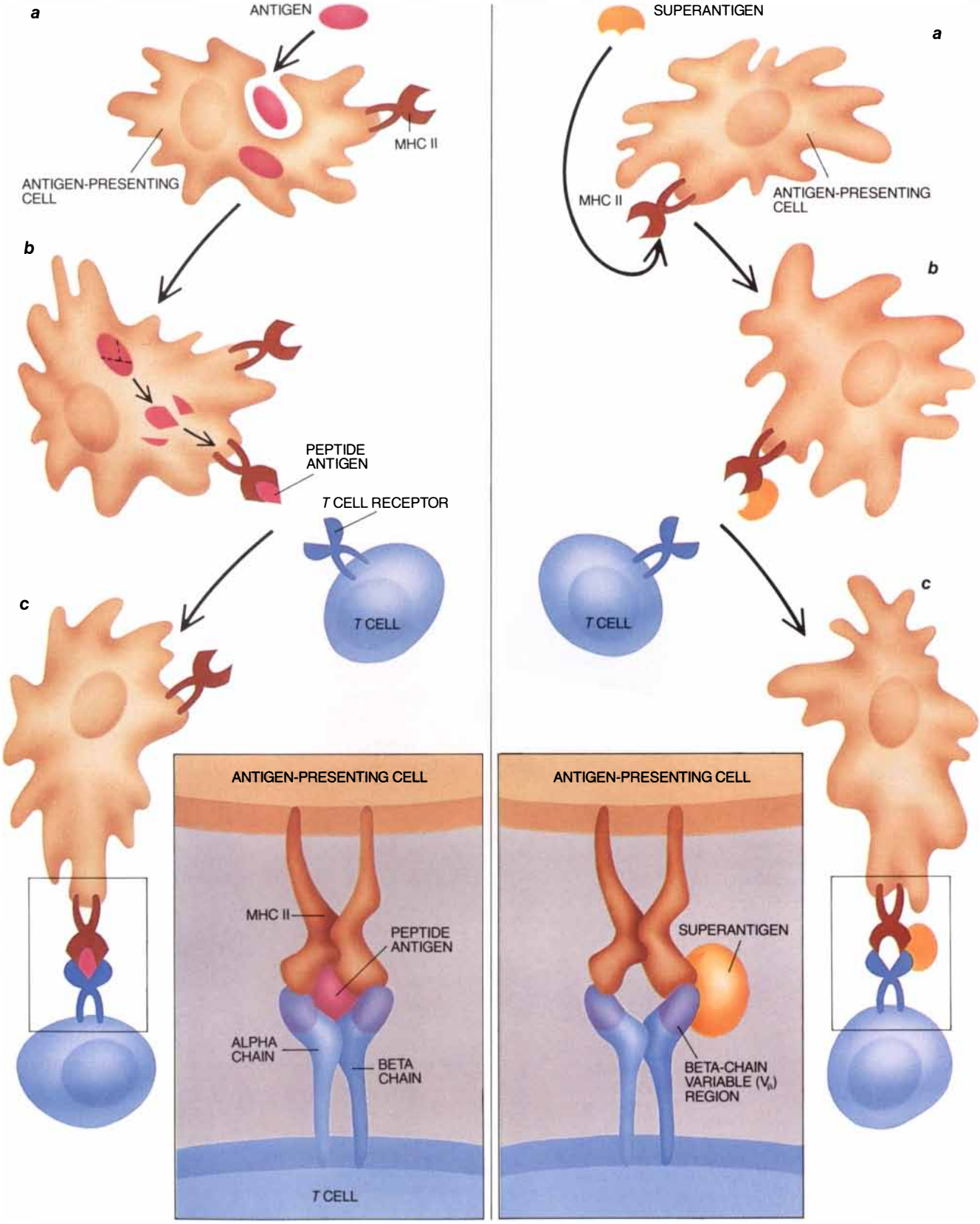
In 1988 the Swedish and German groups independently demonstrated that, as is true of garden-variety antigens, enterotoxin superantigens can arouse helper cells only if antigen-presenting cells display the proteins to the *T* cells. Moreover, it is MHC class II molecules that do the presenting.

Yet, unlike typical antigens, the enterotoxins bind MHC molecules directly; they do not require uptake and processing. This strange behavior meant that *T* cells, too, respond to intact toxins. Such oddities suggested that elucidation of the enterotoxin-binding sites on MHC molecules and *T* cells might reveal why more *T* cells react to superantigens than to conventional antigens.

Today it is clear that enterotoxins bypass the inner surface of the peptide-recognizing pocket of the MHC molecule, attaching instead to its outer surface. Then the MHC-superantigen unit contacts the *T* cell receptor at a site distinct from the surface that envelops conventional antigens. To be more precise, *T* cell receptors consist of two protein chains, alpha and beta. Both chains include structurally invariant and variable regions that participate in the binding of conventional peptide antigens. The enterotoxins are thought to link up with the beta-chain variable—or V-beta (V_β)—region, at a part not involved in the binding of typical antigens.



PEPTIDE (*pink*) held in the binding cleft of an MHC molecule (*blue*) is often likened to a hot dog in a bun. The image, made by Don C. Wiley of Harvard University and his co-workers, is based on an MHC class I molecule but presumably resembles MHC class II molecules.



BINDING TO *T* CELLS is accomplished differently by conventional antigens and superantigens. Conventional antigens (*left side*) must first be engulfed by antigen-presenting cells (*a*), chopped and displayed as protein fragments, or peptides, in the peptide-binding cleft on MHC class II molecules (*b*). Then the antigens attract *T* cells bearing antigen-specific receptors (*c*). The receptors' alpha and beta chains both touch the antigen (*detail*). Superantigens bind directly to the outside of MHC molecules (*right side, a* and *b*) and then to the outside of *T* cell receptors (*c*), attaching at a structurally variable part of the beta chain (*detail*). Linkage to the variable (V_β) region accounts for the powerful effect of superantigens on *T* cells.

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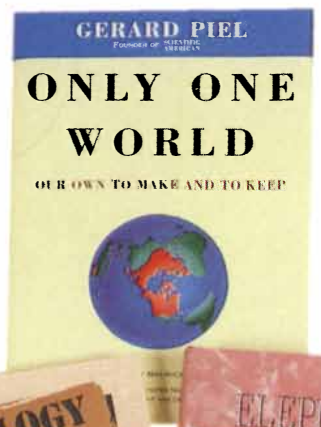

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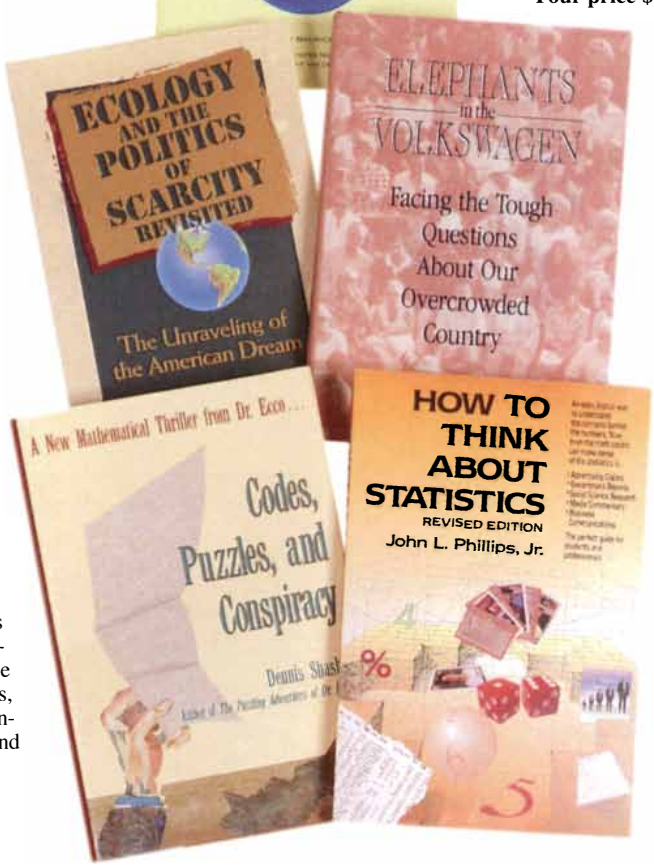

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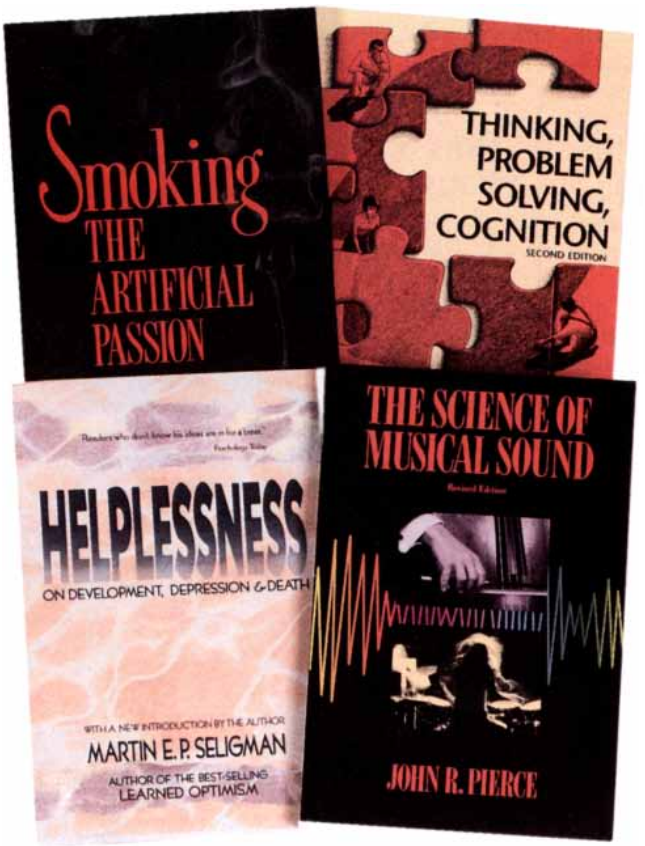

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It is also clear that each enterotoxin attracts particular V_β types. For instance, one enterotoxin may be recognized by the types numbered 5 and 12, whereas another might be recognized by types 12, 15 and 18. Investigators estimate that every human being has fewer than 30 V_β types, although the fraction of helper *T* cells carrying any given type can differ from person to person. Hence, a conventional antigen can activate only the relatively few helper cells specific for that antigen. A given enterotoxin, however, can activate many times that number of helpers (having a huge variety of peptide-antigen specificities) as long as the *T* cells bear selected V_β types.

This tidy picture, which did not emerge easily, is a testament to the perseverance of several research groups. We and other teams concentrated on the unusual binding to the MHC class II molecule. In the meantime Philippa Marrack and John Kappler of the National Jewish Center for Immunology and Respiratory Medicine in Denver and Charles A. Janeway, Jr., and colleagues at Yale University directed much of the initial research on the interaction of superantigens and *T* cells.

Don C. Wiley of Harvard University paved the way for our studies of the interaction between enterotoxins and MHC molecules, when he and his coworkers deduced the probable three-dimensional structure of MHC class II molecules. As is true of the *T* cell receptor, cells fashion MHC class II molecules from two intersecting protein chains, called alpha and beta. The region that forms the binding cleft, or hot dog bun, for conventional antigens consists of a helix donated by the alpha chain (one half of the bun), a helix donated by the beta chain (the other half of the bun) and a nonhelical connector at the floor of the cleft (where the halves join), constructed from segments of both chains.

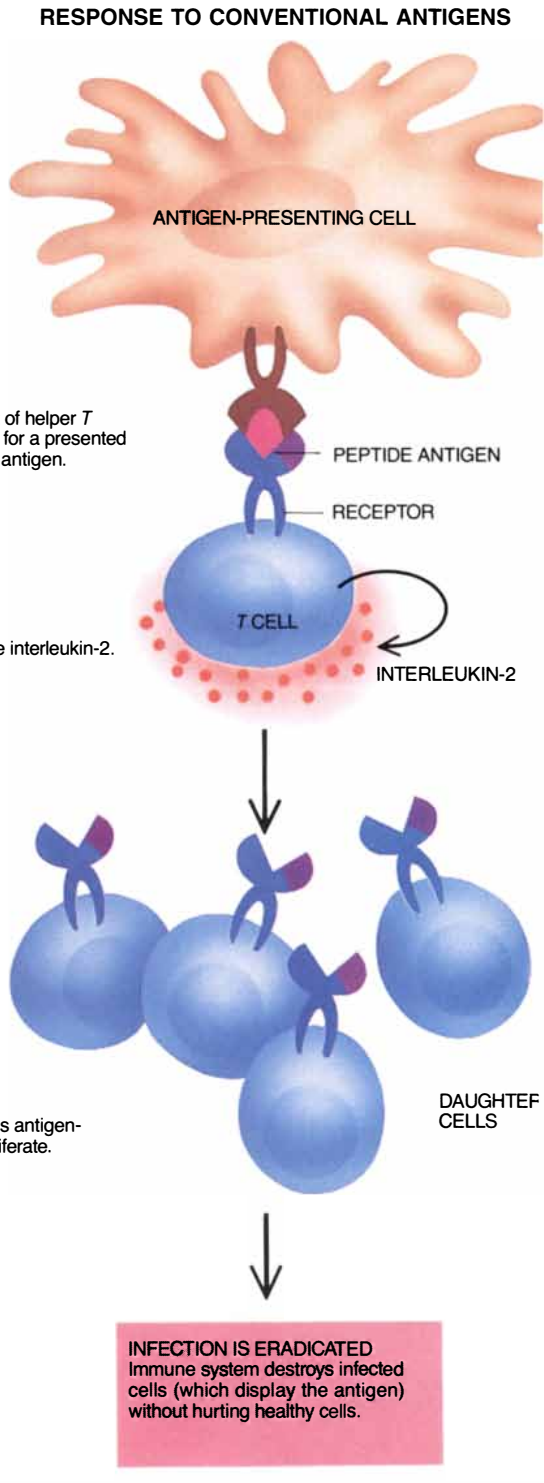
To identify where enterotoxins might bind the MHC molecule, we took advantage of the finding by other investigators that a peptide having a well-defined structure within a larger protein will generally adopt that same structure or a similar one if it is synthesized solely as a peptide. When we produced the three major components of the MHC molecule's antigen-binding region and then exposed each of them separately to enterotoxin A, a definite pattern emerged.

The toxin bound only those peptides corresponding to the sides of the antigen-binding domain, not to the floor. When we then made beta-chain helices in which the amino acid alanine substituted for native amino acids at selected sites, we found that only substitutions on a surface away from the one that binds conventional antigens decreased binding by toxin A. Together these findings established that, in common with conventional antigens, enterotoxin superantigens attach to the peptide-antigen binding region of the MHC class II molecule, but they lodge at the outside surface and not at the surface that contacts typical antigens.

More recently we have identified several segments of enterotoxin A that can interact with MHC molecules. We did this by mixing fragments of the entero-

How Superantigens Cause Disease

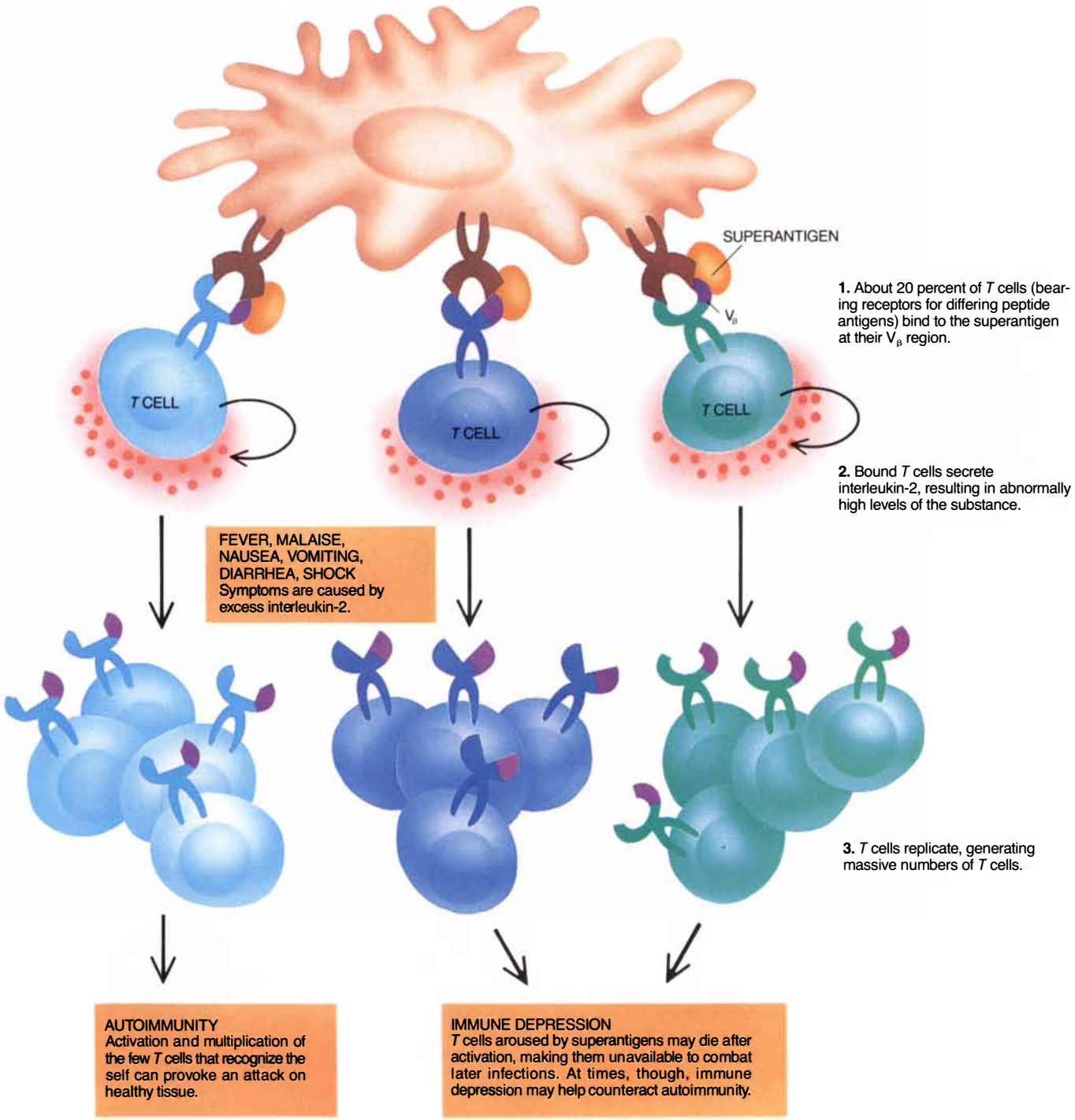
Conventional foreign antigens (*left*) arouse only those helper *T* cells whose receptors can bind the antigens snugly—that is, exactly the *T* cells needed to fight an existing infection. Superantigens (*right*) indiscriminately activate any *T* cells whose receptors include selected V_β segments. They thereby arouse millions of helper cells, sometimes with dire consequences (*gold boxes*).



toxin with MHC molecules on cells and determining which of the pieces combined with the MHC molecules. Most of the reactive parts came from one end of the enterotoxin, the region called the amino terminus.

During this study, we made a discovery that could have therapeutic significance. We found that amino terminal peptides bind so readily to the MHC molecule that they essentially bar the intact enterotoxin from binding. The peptides thereby block the enterotoxin from stimulating lymphocytes. Such reactive fragments might eventually serve as medications to ease food poisoning, toxic shock and other disorders.

Work on the other half of the story, interaction of superantigens with *T* cells, gained prominence in 1989. That was the year two different teams concluded that MHC-bound enterotoxins can activate *T* cells simply by linking up with the V_β region of the *T* cell receptor. Marrack and Kappler and their co-workers in Colorado formed one of the teams. And Janeway and his group



at Yale made the discovery with Steve Buxser of the Upjohn Company.

Marrack and Kappler's group then proposed the term "superantigen" to describe such molecules. The word specifically refers to a protein that activates many different *T* cell clones (each with its own peptide-antigen specificity) by binding to selected V_β structures.

Since then, Nicholas R. J. Gascoigne and Kristina T. Ames of the Scripps Clinic in La Jolla, Calif., found the first direct evidence that superantigens must be attached to MHC molecules in order to link up with the V_β part of a *T* cell receptor. When enterotoxin A was associated with an MHC class II molecule, it bound to a particular V_β segment on a synthetic beta chain. Free superantigen by itself, however, could not attach to the chain. Linkage to the MHC molecule may change the shape of enterotoxins in a way that makes the site responsible for V_β binding accessible to *T* cells, or such linkage may increase the site's affinity for the V_β region.

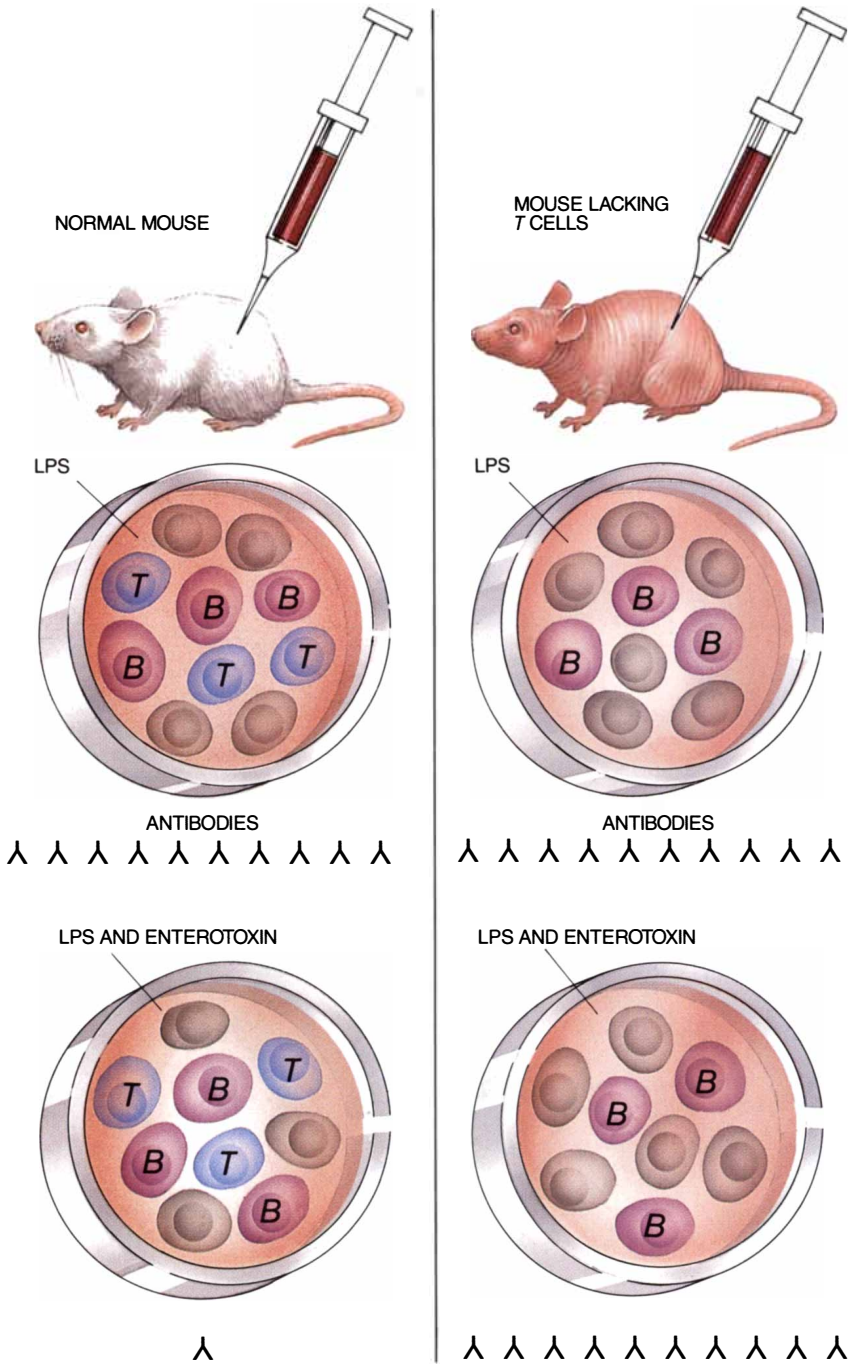
Growing evidence indicates that several microbial superantigens, including proteins made by streptococcal bacteria and mycoplasmas, arouse *T* cells in much the way enterotoxins do—that is, by docking with particular V_β types. Substances called minor lymphocyte-stimulating (Mls) antigens, which are found in mice, behave similarly.

The Mls proteins were once thought to be native to the rodents, and so they were referred to as self-superantigens. Now, however, the Mls antigens are known to derive from the mouse mammary tumor virus (MMTV). The organism is a retrovirus; it incorporates its genes into the DNA of mice, who then synthesize the viral Mls antigens as if the proteins were their own.

Certain of these or other superantigens may well contribute to autoimmune diseases, in which components of the immune system attack normal tissue. After all, it seems reasonable to guess that arousal of 20 percent of a person's *T* cell repertoire could lead to the undesirable replication of the few circulating *T* cells that recognize the self. (The immune system normally deletes or inactivates self-reactive *T* cells, but occasionally a few escape the surveillance mechanism.)

Consistent with this notion, *T* cells bearing certain V_β types have been implicated in various autoimmune conditions, including arthritis and multiple sclerosis. These findings imply that the destructive cells might be activated by a superantigen that binds to the identified V_β types. Moreover, research led by Barry C. Cole of the University of Utah has shown that a superantigen produced by *Mycoplasma arthriditis* may cause arthritis in rats.

On the other hand, some evidence suggests that superantigens occasionally depress the immune system. *T* cell clones aroused by superantigens often disappear or become inactive after being stimulated. And several groups reported last year that at least one Mls superantigen leads to the destruction of several subsets of *T* cells in mice.



MOUSE EXPERIMENTS suggest that superantigens can impair immunity by activating suppressor *T* cells. When LPS, a conventional antigen, was added to blood from normal mice (*top left*) and from those that lack *T* cells (*top right*), the expected occurred: LPS stimulated *B* lymphocytes, the body's antibody makers, to release anti-LPS antibodies. When both LPS and an enterotoxin were added to fresh samples, the enterotoxin inhibited antibody production in the normal blood (*bottom left*) but not in the samples lacking *T* cells (*bottom right*). Because the blood differed only in *T* cells, the data indicated that *T* cells had suppressed the antibodies.

One consequence might be cancer. After a large fraction of *T* cells was destroyed, the immune system would presumably have difficulty detecting and eliminating cancer cells. Indeed, deletion of *T* cells could explain in part why the mouse mammary tumor virus—carrying genes that encode Mls superantigens—gives rise to tumors.

Some researchers have also proposed that superantigens might contribute to the immunodeficiency of AIDS. For reasons that are still mysterious, the number of helper *T* cells in people infected with the AIDS-causing human immunodeficiency virus (HIV) declines dramatically, leaving patients vulnerable to severe infections that eventually prove fatal. Last year Luisa Imberti and Daniele Primi of the University of Brescia in Italy reported that *T* cells with certain V_β types were notably absent in a group of HIV-positive patients—a "footprint" that investigators would expect to find if one or more superantigens were at work. The notion, one of several reasonable explanations for the *T* cell death associated with HIV, is speculative, of course, but intriguing.

So far this article has concentrated on the link between superantigen-induced immune disorders and helper *T* cell activity. But the possible deranging effects of superantigens on *B* cells should not be ignored. In studies conducted in the 1970s Johnson found that staphylococcal enterotoxins sometimes enhance antibody production by *B* cells and sometimes inhibit it, depending on the initial state of immune arousal. Johnson's studies also indicated that inhibition of antibody production is mediated by suppressor *T* cells.

Enhancement and suppression may each be destructive. Inhibition of antibody production can depress immune functioning. Overzealous production can lead to immune complex disorders, in which antibodies attract various components of the immune system to healthy tissues, clogging them and impeding normal functioning.

Research on superantigens is doing more than clarifying the causes of disease. It is generating ideas for treatment. As we suggested above, synthetic peptides might help inhibit superantigens, by competing for binding sites on helper *T* cells or MHC molecules.

Strangely enough, controlled delivery of selected superantigens might prove therapeutic for some diseases. For instance, studies in rodents suggest it may be possible for certain superantigens to knock out undesirable *T* cell populations and thereby quiet autoimmune attacks on normal tissue. By administering enterotoxin B to mice, Caius Kim and others at the University of Toronto have reduced the severity of lupus nephritis, an autoimmune disorder. Similarly, by giving the same toxin to mice, our group, in collaboration with Joel Schiffenbauer and Jeanne M. Soos at Gainesville, has protected animals against experimental multiple sclerosis. Conversely, superantigens could be delivered to shore up a depressed immune system by stimulating *T* cell proliferation—that is, if the tendency of superantigens themselves to delete *T* cells could be checked.

In support of such treatment scenarios, Nathan D. Griggs, also at Gainesville, has made the surprising discovery that a small fragment of toxin A, like toxin A itself, can activate human *T* cells. Studies of other proteins have shown that fragments often block the activity of a full protein (usually by competitively occupying the binding site on a target molecule) but that they rarely mimic the intact protein. Griggs's finding suggests that researchers may well be able to design superantigenic drugs by mixing and matching fragments with selected properties.

The prospect of both treating superantigen-induced diseases and enlisting superantigens to correct immune disorders serves as a continuous spur to further research. These studies are sure to identify still other superantigens and should offer important insights into the causes of and therapies for heretofore incurable immune diseases.

CHILD WITH AIDS is being given AZT by his adoptive mother. Some evidence suggests that one or more superantigens on the AIDS virus may contribute to the lethal depletion of helper *T* cells in infected individuals.

FURTHER READING

ENTEROTOXINS. Merlin S. Bergdoll in *Staphylococci and Staphylococcal Infections,* Vol. 2. Edited by C.S.F. Easmon and C. Adlam. Academic Press, 1983.

THE STAPHYLOCOCCAL ENTEROTOXINS AND THEIR RELATIVES. Philippa Marrack and John Kappler in *Science,* Vol. 248, pages 705–711; May 11, 1990.

STRUCTURAL BASIS FOR DIFFERENTIAL BINDING OF STAPHYLOCOCCAL ENTEROTOXIN A AND TOXIC SHOCK SYNDROME TOXIN 1 TO CLASS II MAJOR HISTOCOMPATIBILITY MOLECULES. Carol H. Pontzer, Jeffry K. Russell and Howard M. Johnson in *Proceedings of the National Academy of Sciences,* Vol. 88, No. 1, pages 125–128; January 1, 1991.

BOTH α-HELICES ALONG THE MAJOR HISTOCOMPATIBILITY COMPLEX BINDING CLEFT ARE REQUIRED FOR STAPHYLOCOCCAL ENTEROTOXIN A FUNCTION. Jeffry K. Russell, Carol H. Pontzer and Howard M. Johnson in *Proceedings of the National Academy of Sciences,* Vol. 88, No. 16, pages 7228–7232; August 15, 1991.

STAPHYLOCOCCAL ENTEROTOXIN MICROBIAL SUPERANTIGENS. Howard M. Johnson, Jeffry K. Russell and Carol H. Pontzer in *FASEB Journal,* Vol. 5, No. 12, pages 2706–2712; September 1991.

The International Thermonuclear Experimental Reactor

This tokamak fusion reactor, sponsored by four industrial powers, will be the most powerful ever built. By fusing deuterium and tritium, ITER should generate more energy than it consumes

by Robert W. Conn, Valery A. Chuyanov, Nobuyuki Inoue and Donald R. Sweetman

At their Geneva summit of November 1985, Mikhail S. Gorbachev and Ronald Reagan discussed several topics of worldwide concern: strategic defense, arms control and human rights, among others. Unknown to many was a statement in the final communiqué that has led to a project without precedent in the history of international cooperation in science and technology. The two leaders called for joint work to develop fusion energy "for the benefit of all mankind." In response to this summit call, scientists and engineers at the world's major fusion research programs—conducted by the European Community, Japan, the Commonwealth of Independent States (the former Soviet Union) and the U.S.—agreed in 1987 to embark on a joint venture to design a fusion experimental device. They named it the International Thermonuclear Experimental Reactor—ITER, for short.

ITER is now about 13 years away from completion. Its ability to generate more than 1,000 times the power of current fusion reactors will make ITER the penultimate experiment in the quest for a practical device of this kind. The scientific and engineering knowledge gained from ITER should lead to the demonstration of a fusion reactor power station, perhaps within the next three decades.

Indeed, the promise of harnessing fusion has led to substantial commitments of the four powers involved. Last July the participants agreed to embark on a six-year effort to produce the final engineering design of the ITER reactor. Design centers will be located at the University of California at San Diego, the Max Planck Institute for Plasma Physics in Garching and the Naka Fusion Research Establishment of the Japan Atomic Energy Research Institute. An ITER council, centered in Moscow, will provide general oversight. Each group has pledged to spend about $40 million annually to support the design team and the required research, development and testing.

In the spirit of cooperation (and in a bow to diplomacy), the four parties agreed to name a European to head the central design team, a Japanese to act as the principal deputy, a Russian to head the San Diego center, an American to direct the Garching center, a European to lead the Naka center and a Russian to chair the ITER council. The fact that these complex appointments were made in a relatively brief period of less than nine months demonstrates the seriousness of all concerned.

Why the seriousness, why fusion, why now? And what might the ITER machine look like, and what will it accomplish? We focused on these issues when we served on the ITER Scientific and Technical Advisory Committee during the first phase of the conceptual design. The answers we describe in this article are the fruits of the international team's efforts. They are also the result of scientific research that has persisted for more than 40 years [see "The Engineering of Magnetic Fusion Reactors," by Robert W. Conn; SCIENTIFIC AMERICAN, October 1983].

The quest for a practical reactor continues because fusion liberates a tremendous amount of energy from a small amount of fuel. The process powers the sun and stars; it was first elucidated by Hans A. Bethe of Cornell University in the late 1930s. To produce energy, fusion reactors will rely on two isotopes of hydrogen: deuterium, which has an extra neutron and is sometimes called heavy hydrogen, and tritium, which has two extra neutrons. These nuclei fuse together far more efficiently than any other combination of light nuclei. Ordinary hydrogen, which the sun burns, fuses much too slowly (thank goodness, for otherwise the life of the sun and the universe would be altogether too short).

PLASMA CHAMBER interior of tokamaks, such as this one of the JT-60 machine in Naka, Japan, is lined with carbon-fiber composite tiles to protect against the tremendous heat generated by the plasma. The sides are sometimes referred to as the first wall. The ports hold equipment that heats as well as controls the plasma.

ROBERT W. CONN, VALERY A. CHUYANOV, NOBUYUKI INOUE and DONALD R. SWEETMAN were ITER advisory committee members during the conceptual design phase. Conn, who received his Ph.D. from the California Institute of Technology, is professor of nuclear engineering and director of the Institute of Plasma and Fusion Research at the University of California, Los Angeles. He has served on science and policy committees for the U.S. Department of Energy and is a member of the National Academy of Engineering. Chuyanov has led several tokamak projects in Russia. He received his doctorate from Moscow University and heads the physical engineering department at the I. V. Kurchatov Institute of Atomic Energy. Inoue received his Ph.D. from Kyoto University and is now professor of nuclear engineering at the University of Tokyo. He has served on several technical and policy review committees for the Japanese government. Sweetman, a plasma physicist at Culham Laboratory in Abingdon, U.K., is also chief executive of fusion research of Britain's Atomic Energy Authority. He completed his Ph.D. at the University of Birmingham in England.

Equally important, the fuel for fusion reactors is readily available. Deuterium occurs naturally in water: about one of every 6,700 hydrogen atoms has a deuterium nucleus. Tritium is less prevalent. It is radioactive and has a half-life of 12.3 years, so it does not occur naturally in large amounts. The isotope, however, can be produced from an abundant natural stockpile, the geologic deposits of the metal lithium.

Nuclear fusion reactors also promise to be environmentally benign. An accidental, runaway reaction cannot occur, because the amount of deuterium and tritium in the machine at any given time is small. Any uncontrolled burning will quickly consume all the available fuel and then sputter out. Furthermore, the fusion of deuterium and tritium generates only energetic neutrons and alpha particles (helium nuclei), which are not themselves radioactive. The main concern about radiation comes from a secondary process. Energetic neutrons can transmute the nuclei of the materials that make up the reactor structure and components. The materials then become radioactive. Fortunately, research has shown that the proper selection of construction materials should be able to keep the level of this induced radioactivity very low.

Despite the years of work on fusion, combining the positively charged nuclei to produce useful amounts of energy has proved elusive. To overcome the natural electrical repulsion, the nuclei must become highly energetic. The deuterium and tritium must reach at least 50 million kelvins (in contrast, the center of the sun is about 15 million kelvins). Measured in electron volts (eV), this temperature equals 4,500 eV and represents the fuel ignition temperature.

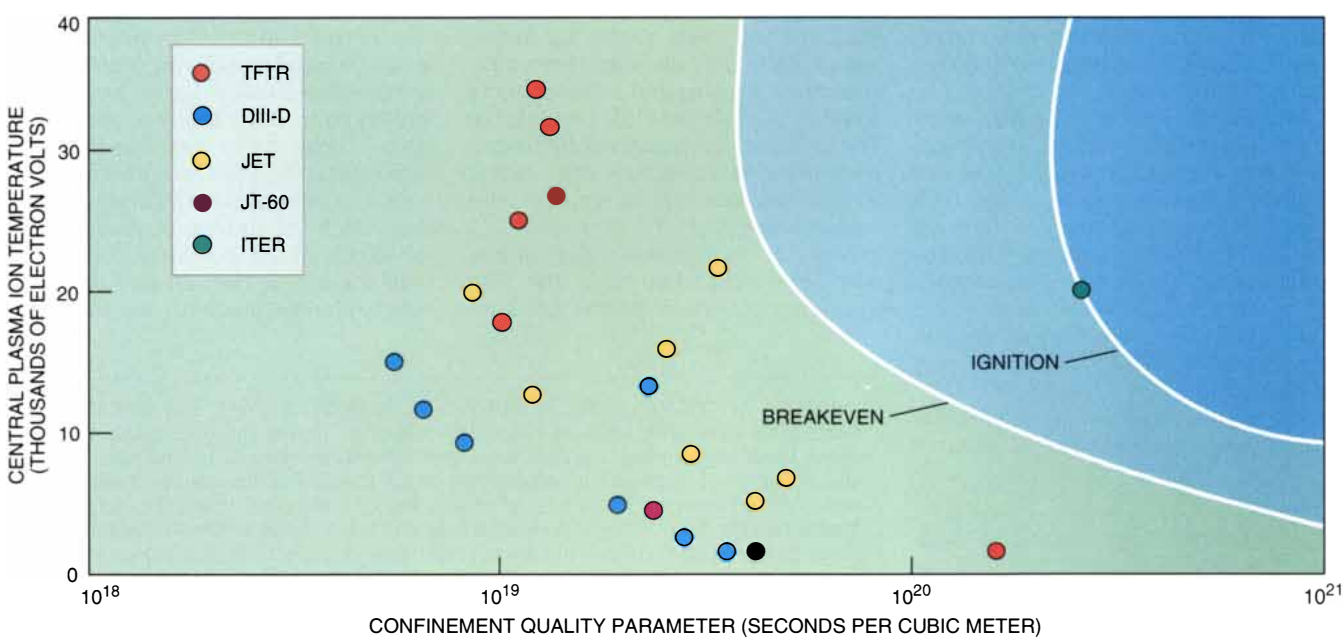
At such temperatures the electrons are stripped from the nuclei (in fact, only 13.56 eV are needed to ionize hydrogen). The collection of deuterium and tritium, then, is more properly referred to as a plasma, an electrically neutral assemblage of positively charged nuclei and negatively charged electrons.

Maintaining the high plasma temperature has been one of the crucial tasks in fusion research. Energy is lost through several processes. For instance, the charged particles in the plasma radiate electromagnetic energy when they interact with one another. Fusion produces tremendous amounts of energetic neutrons, which easily escape the plasma. Radiation, heat conduction and the turbulent convection of plasma particles are just some of the other processes that lower the plasma temperature over time.

Of course, one can continually stoke the plasma fire by injecting energy from the outside, using radio-frequency waves or beams of high-energy neutral particles. There is, however, an efficient, self-sustaining source of additional heat: the energetic alpha particles that are produced. These helium nuclei are the primary ash of fusion reactions. They have about 3.5 million eV of energy, and because they are twice positively charged they are easily confined by magnetic fields. The alpha particles would give up their energy as heat if they were to collide with the plasma particles. So far no experiment has been able to generate a sufficient number of energetic alpha particles to compensate completely for the heat energy lost.

Investigators refer to the overall mean time for heat to escape the plasma as the energy confinement time. This time is represented by the Greek letter tau, τ. The product of the confinement time and the plasma density, n, indicates the ability of the plasma to retain its heat and is called the confinement quality. Practically speaking, for a fusion reaction both to sustain itself and to provide usable energy, $n\tau$ must be greater than 2×10^{20}, in units of seconds and particles per cubic meter, at a temperature, T, of 10,000 eV (about 100 million kelvins). The objective of fusion research, then, is to achieve the triple product of n, τ and T of about 2×10^{24} second-eV per cubic meter.

The design concept that has come the closest by far to achieving these conditions is the tokamak. Conceived in the early 1950s by the Russian physicists Andrei D. Sakharov and Igor Y. Tamm, the tokamak derives its name from the Russian words for toroidal magnetic chamber. The principles behind the device are relatively simple. Plasma is first produced in a vacuum chamber shaped like a torus, or doughnut. A set of electromagnets



BREAKEVEN is being approached by current tokamak reactors: TFTR, DIII-D, JET and JT-60. To reach this state, the confinement quality—that is, the product of the plasma density and the average time for energy to escape—must be at least 5×10^{19} seconds per cubic meter. ITER is designed to exceed this value by a factor of 10 at a central plasma temperature of about 20,000 eV. It thus should reach ignition, in which the energy produced by fusion sustains the plasma burn.

outside the chamber produces a toroidal magnetic field along the axis of the doughnut. The field acts like a sleeve that maintains the pressure within the plasma and keeps the plasma away from the chamber walls.

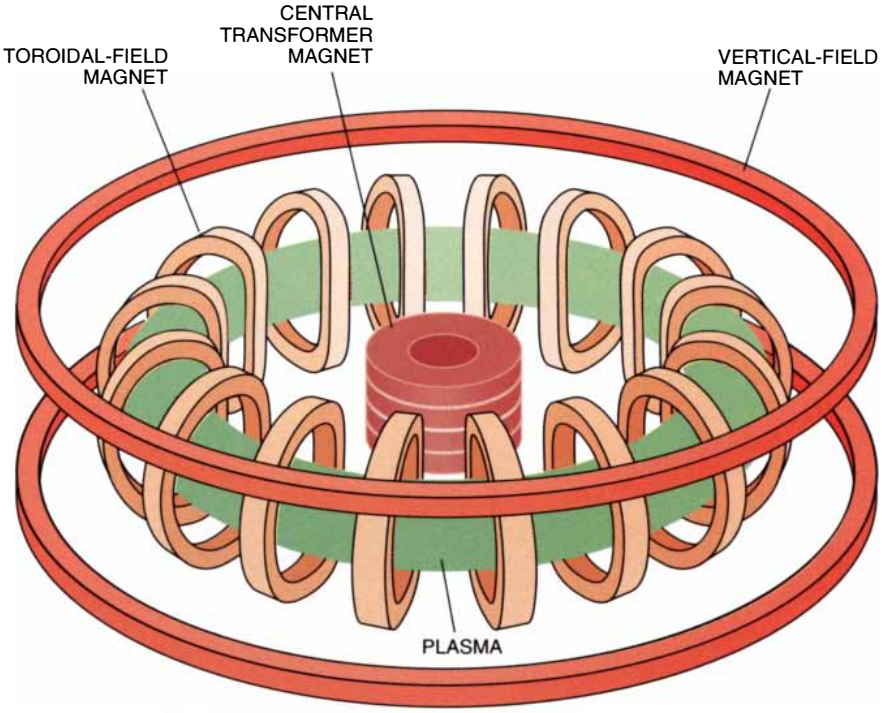
Another set of external electromagnets located at the center of the torus (the doughnut hole) is used to induce current in the plasma that flows in the toroidal direction. The current heats the plasma to a temperature of about 1,000 eV. The plasma current produces a magnetic field that loops around the toroid. This field prevents the plasma particles from drifting out of the main magnetic confinement region. Finally, external conductors generate a vertical magnetic field to keep the plasma from moving up and down, or in and out, within the chamber.

The former Soviet Union was the only country to pursue the tokamak concept seriously, until the mid-1960s. Then, Lev A. Artsimovich and his colleagues at the I.V. Kurchatov Institute of Atomic Energy in Moscow were able to lengthen the energy confinement time and increase the plasma temperature significantly. Their achievements led to worldwide research in tokamaks.

As a result, the design has advanced substantially. In the mid-1970s tokamak devices reached a temperature of 3,000 eV and a confinement quality value of about 10^{18} seconds per cubic meter. Today the most powerful tokamak experiments—the Joint European Torus (JET), the JT-60 tokamak in Japan, and the Tokamak Fusion Test Reactor (TFTR) and DIII-D tokamaks in the U.S.—have achieved plasma temperatures of 30,000 eV and confinement quality values of 2×10^{19} seconds per cubic meter. Overall the triple product of density, confinement time and temperature has increased by more than a factor of 100 during the past 20 years.

Last October the team at JET took fusion research another major step forward. Using deuterium and tritium, JET produced more than one million watts of fusion power for two seconds. This energy exceeds by two orders of magnitude the energy produced by previous controlled-fusion experiments. Significantly as well, the outcome confirmed the predicted performance. More impressive results may come after the summer of 1993, when TFTR will begin its own deuterium-tritium experiments. Researchers hope those reactions will generate 30 million watts of fusion power. That amount approximately equals the power needed to maintain the plasma, a state called breakeven.

Two other, more subtle indicators of progress must also be considered. First, there is beta. It is the ratio of the plasma pressure to the pressure exerted by the external magnetic field that holds the plasma. Essentially, it is a measure of the efficiency by which the magnets confine the plasma. For a given plasma pressure, the higher the value of beta, the smaller the magnetic field—and hence the smaller and more economical the magnets can be. In the mid-1970s experiments had beta values of about 1 percent, which is about 2 to 6 percent less than what is considered desirable for practical tokamaks. Researchers have been able to increase beta through several techniques, such as reshaping the plasma cross section from a circle into a vertical ellipse. The DIII-D tokamak at the General Atomics in San Diego has achieved the highest tokamak beta value, about 10 percent. This value exceeds the desired beta substantially and demonstrates an important aspect of the economic practicality of these magnetic confinement schemes.



TOKAMAK PRINCIPLE relies on three sets of electromagnets. One series of magnets produces a toroidal field that acts as a sleeve to confine the plasma. The central transformer magnets are used to induce an electric current in the plasma. That current, which flows toroidally, heats the plasma. The vertical-field magnets act to keep the plasma centered and in stable equilibrium.

Second, there is the matter of maintaining current flow in the plasma. Recall that this current is induced by external electromagnets. The laws of electrodynamics state that an induced direct current can be sustained only by a magnetic field that grows increasingly strong. No current will flow if the magnetic field remains constant. The external magnets that induce the plasma current must therefore generate a field that increases indefinitely—a practical impossibility. Instead workers must shut down the plasma after a certain time and then reset the amount of current flowing through the magnets to the original level. Only an external, noninductive means of sustaining the plasma current can result in a steady plasma operation.

In 1971 Roy J. Bickerton, Jack W. Conner and J. Bryan Taylor of the Culham Laboratory in Abingdon, U.K., suggested a way to maintain the current. They predicted the radial pressure gradient and viscous forces running parallel to the field would combine in sufficiently hot plasmas to produce a self-driven, toroidal current. Researchers call this self-driven electrical flow the bootstrap current. Here, finally, seemed to be something nature might provide free of cost to enable tokamaks to operate steadily. Experiments to confirm the existence of the bootstrap current proved futile until 1989, when TFTR, and then JET and JT-60, finally discovered it.

The results obtained with the bootstrap current in JT-60 are particularly important for practical fusion. In certain cases, up to 80 percent of the 500,000 amperes of plasma current came from the free bootstrap current. In separate experiments, workers suc-

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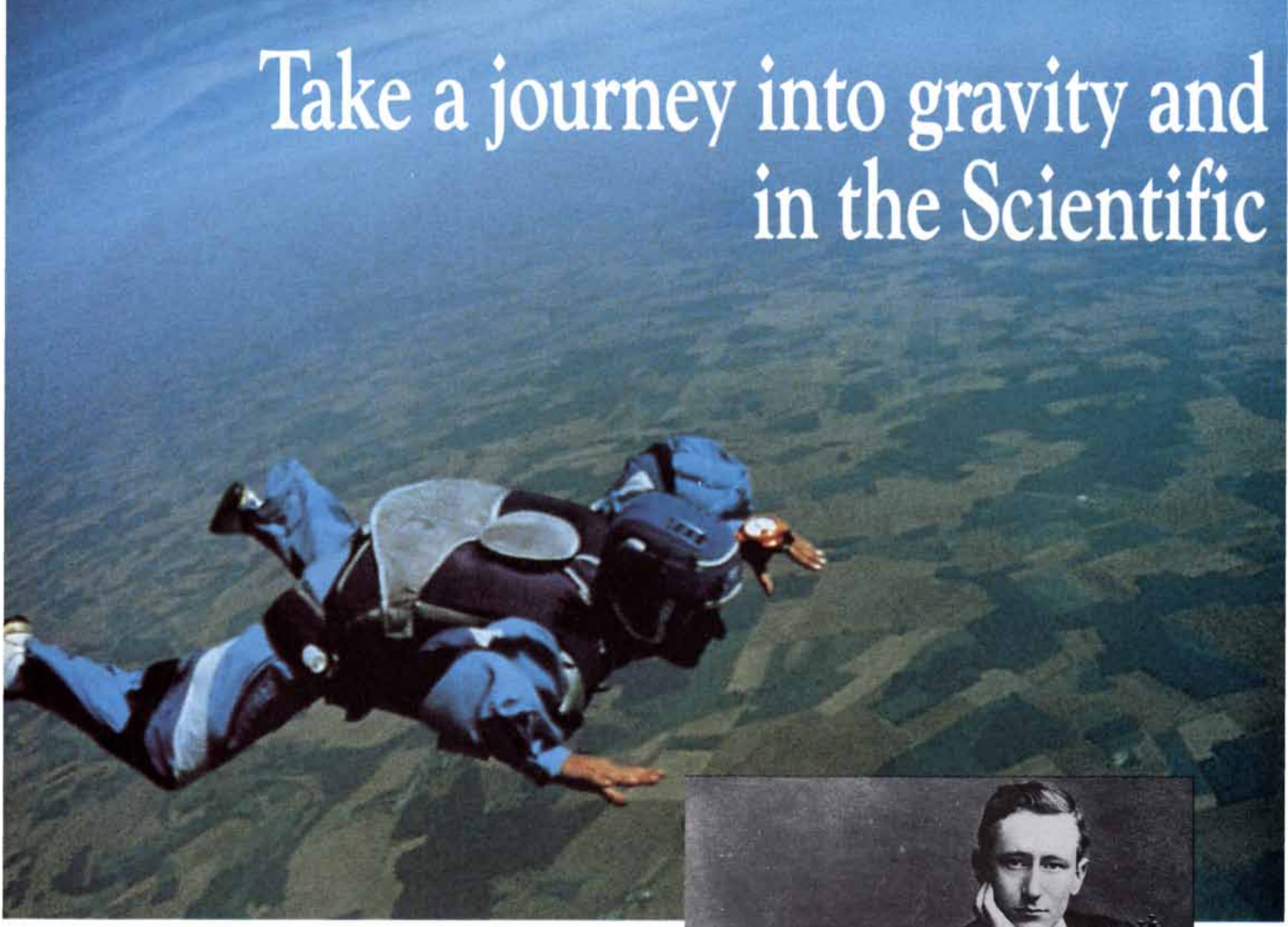

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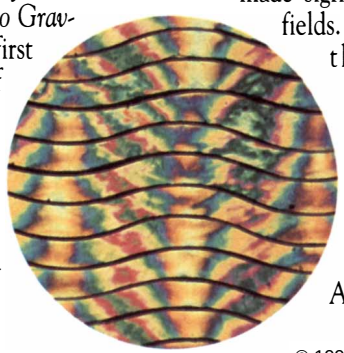

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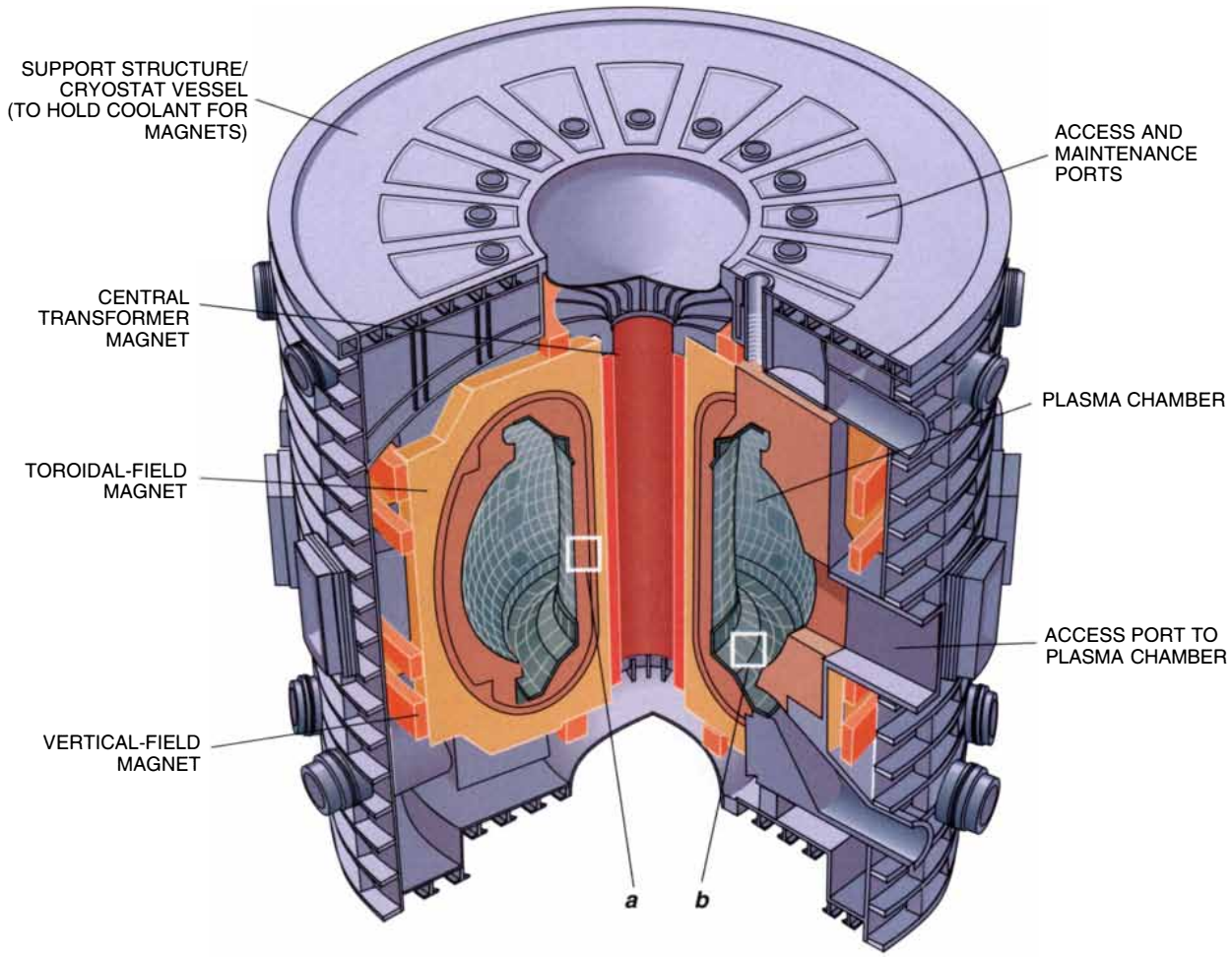
The ITER Tokamak

This experimental reactor will be the largest tokamak ever built, about 25 meters high. The plasma chamber itself will measure 4.3 by 8.4 meters. The cutaway view (*below*) shows the essential features of the machine. Among the most important are the components for heat protection, many of which are now only conceptual designs. One such structure (*a*) would consist of three main parts: the first wall, the blanket and the shield. It not only insulates but also might produce tritium. Heat from the plasma initially encounters the first wall, which consists of carbon-fiber composite tiles mounted on water-cooled pipes. The blanket would absorb the neutrons



ceeded in sustaining two million amperes of toroidal plasma current.

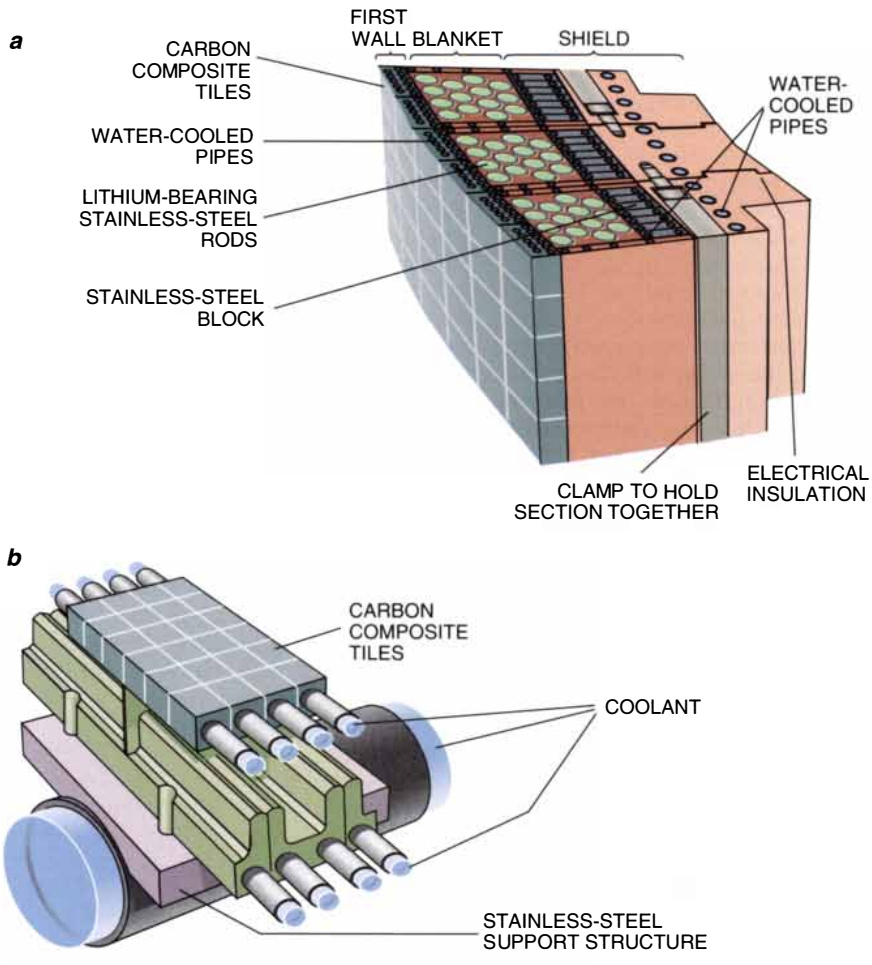
Despite the progress in tokamak research, several issues remain. Investigators still do not understand the fundamental nature of the turbulent transport of particles and heat across the lines of magnetic force, a process that reduces the temperature of the plasma. Knowledge of the physics of ignition and sustained fusion burning is incomplete as well. ITER will address these issues. Its principal objectives are to achieve ignited, burning plasma conditions that would be typical in a true fusion reactor and to test and demonstrate the technologies required for practical fusion.

Goals for the ITER program were established by an international collaboration of 40 to 60 professionals, including us and our colleagues who served on the advisory committee. The team worked together for extended periods at the Max Planck Institute for Plasma Physics, from 1987 to 1990, and the members met frequently with the advisory committee at the International Atomic Energy Agency in Vienna, the official host agency for the program. After the team defined the technical characteristics of the ITER tokamak machine, it proceeded to produce a conceptual design for the facility. It then developed a plan for the operation and research program, an important matter because the machine will operate for at least 15 years.

The team also settled on the schedule for ITER. Construction will take place from 1997 to 2004; the device will be commissioned in 2005. Of course, the schedule depends on the continued agreement of the participants. Political factors make a guarantee difficult. We expect, however, that the countries should be able to decide on the construction site within four years, although they will still have another year before rendering a final decision to proceed.

We estimate $1 billion will be spent to complete the engineering design and perform related research and development. That cost is to be divided equally among the four powers involved and spread over the six-year design period. The construction cost is estimated to be about $5.8 billion during the six to

produced in the reaction. To breed tritium, the blanket might contain lithium and perhaps beryllium in stainless-steel rods. The shield might consist of stainless-steel structures cooled by water and would absorb radiation as well as heat. Another important component is the divertor target plate (*b*), which would absorb the energy of the charged particles from the plasma. It might be constructed of carbon-fiber composite tiles mounted on water-cooling tubes.



seven years needed to build ITER. Whether the construction cost will be evenly divided among the participants or whether the country hosting the project will pay more so as to counterbalance the benefits to its local economy remains to be determined. During construction, an additional $500 million is required for research and development. Summing these figures gives a total design and construction cost of about $7.5 billion over 13 years.

After construction, the ITER program will consist of two principal stages. The first, called the physics stage, will last six to eight years. During this phase, workers will attempt to achieve ignited, burning plasma conditions similar to those in a working fusion reactor. After initial start-up and full testing, the research effort will focus on the steady operation of the plasma and on the technical requirements for deuterium and tritium fusion. Researchers will also investigate the effects of alpha-particle heating of the plasma, the dynamics and control of the plasma burn, and the diffusion and removal of the helium after it has given up all its energy.

The next stage will be a multiyear program focusing on technology and engineering. Many technologies will have already been demonstrated in the physics phase—most notably, the operation of the superconducting magnets, the plasma heating and current maintenance systems, the refueling and ash exhaust devices, the remote maintenance tools and the external support systems. As such, the technology phase will test the integrated performance and durability of the equipment as well as alternative materials and designs.

The design and engineering should yield an ITER reactor that can generate 1,000 megawatts from the fusion of deuterium and tritium. The achievement will be a considerable one. The projected fusion power output is three orders of magnitude greater than that achieved by JET, the most powerful fusion reactor today. The plasma system will operate initially in a pulsed mode, sustaining the operation for more than three minutes before the current in the transformer magnets needs to be reset. Eventually the plasma should be able to function steadily, using some combination of the naturally occurring bootstrap current and a supplementary system to drive the current. Such a system is now being studied by JT-60 and TFTR. The plasma current should reach about 25 million amperes, exceeding the current used in JET by 20 million amperes. The dimensions of the ITER tokamak will be roughly twice that of the largest now operating: the elliptical cross section of the torus will be 4.3 meters wide and 8.4 meters high, and the major radius will be somewhat more than six meters.

To confine the plasma, 16 D-shaped, superconducting magnets will generate the strong toroidal magnetic field. At 14.8 meters high and 7.1 meters wide, these superconducting magnets will be the largest in the world. Liquid helium will keep the superconducting wire, made of a niobium-tin alloy embedded in copper, at about 4.5 kelvins. The superconductor will be able to carry 35,000 amperes of current. Each magnet will have 240 turns of this wire.

The system will thus be able to generate a magnetic field of 4.85 tesla at the center of the plasma. But because of the toroidal nature of the confinement, the maximum field produced on the vertical inner leg of the D is 11.2 tesla. This field, which is 200,000 times the average magnetic field of the earth, stores more than eight times the energy of today's tokamak magnets. Other superconducting magnets will produce the transformer flux and shape the plasma cross section.

The superconducting magnets must be kept insulated from the nearby plasma. The immense amount of heat from the fusion reactions would make refrigeration of the magnets impractical. More important, the energetic neutrons released in the reaction would damage the magnet materials. These neutrons make up 80 percent of the heat released by each fusion reaction. The remaining 20 percent is deposited in the plasma by the alpha particles. The plas-

ma heat escapes in the form of electromagnetic radiation (primarily x-rays) and charged particles that have managed to diffuse away from the main body of the plasma.

The torus chamber facing the plasma is the first layer of heat protection. Called the first wall, it will be constructed of stainless-steel panels cooled by water. Armor tiles of carbon-fiber composite material will protect the panels against melting and fatigue. This arrangement is similar to an existing structure that operates in an extreme environment: the underbelly tiles of the space shuttle, which protect the craft during reentry. These tiles, which can be removed for maintenance, should be able to operate at temperatures above 1,800 kelvins and will radiate most of the heat they absorb.

The heat escaping as charged particles will follow the lines of magnetic force to the top and bottom of the plasma chamber. There a special system of plates known as the divertor will absorb about 100 megawatts. The divertor is one of the most critical parts of the ITER machine, for the power loading can approach 25 million watts per square meter. In contrast, the average solar radiation reaching the earth's outer atmosphere is about 1,300 watts per square meter. Again, carbon-fiber composite tiles bonded to a cooled heat sink have been proposed for the divertor, but much research and development remains.

Behind the first wall will be a 1.5-meter-thick system called the blanket and shield. This system is the centerpiece of the ITER technology phase and is the only main system that has never been tested. Researchers have proposed several designs. The final one will be decided sometime in the next six years, during the engineering design phase.

One proposal illustrates the essential features of the system. It calls for the blanket to consist of hollow, stainless-steel rods. Inside these rods would be spheres, one millimeter in diameter, of a lithium ceramic, such as lithium oxide or lithium aluminate. (Alternatively, the lithium could take the form of layers of sintered material.) Water coolant would pass outside the rods to remove the heat, keeping the spheres inside between 670 and 870 kelvins.

Structured this way, the blanket should be able to remove most of the energy of the neutrons (in the form of heat). The neutrons will be slowed enough to be efficiently absorbed by the blanket. The absorption is actually a means to generate, or breed, more fuel. Natural isotopes of lithium, especially lithium 6, readily take in energetic neutrons and disintegrate into helium and tritium. In fact, more tritium can be produced than is consumed if researchers incorporate some beryllium in the blanket. When beryllium absorbs a high-energy neutron, it produces two additional, secondary neutrons that can be captured by the lithium.

The tritium produced in the rods will diffuse from the lithium ceramic spheres. Low-pressure helium gas passes inside the steel tubes, purging them and carrying the tritium to a recovery and recycling system. The gas also serves to promote transfer of heat from the pack of lithium spheres to the walls of the container tube.

Behind this zone of tritium breeding and heat removal is the final barrier to the magnets: the water-cooled shield. Although primarily constructed of stainless steel, the shield will also contain lead and boron carbide. That combination is effective in attenuating the neutrons that escape the blanket. For each watt of neutron power that crosses the first wall, less than 60 microwatts of heat reach the magnet system. Furthermore, the shield blocks the gamma rays that are generated when neutrons interact with the atoms of the blanket. It thus serves to protect workers and the public from exposure to the radiation.

Many other systems will have to be developed for a fully functional ITER reactor. For instance, a means to inject deuterium and tritium is needed to replenish the plasma. An exhaust system must be able to remove helium and maintain a vacuum in the torus. The radioactivity of the torus means robots are necessary for maintenance.

A true fusion power plant, one that produces electricity, will ultimately require a way to recover the heat generated by the reaction. The coolant of the blanket and shield would serve this purpose. It would be used to carry the approximately 2,500 megawatts of heat energy produced by the reactor. The coolant would give up its heat via a steam generator. The steam would then drive a turbine to produce about 1,000 megawatts of electric power.

Although the ITER reactor itself will be built to test the integrated components of a tokamak, it will not produce electricity. The requirements for an electricity-generating reactor will be tested in the second part of the ITER operating program, which may mean the materials and designs in the basic ITER machinery must be modified.

This second part of the ITER program will therefore be devoted to studying new materials and concepts that may be more suited to a power plant. For the blanket and shield, investigators will test materials such as vanadium alloys and fiber-reinforced ceramics made of silicon carbide, which do not become nearly so radioactive as stainless steel. Researchers have also proposed using lithium or a lithium-lead alloy in liquid form to generate the tritium. As a liquid, the lithium would also act as a coolant.

To test the appropriateness of the designs, one must fix the intensity of the neutron flux high enough so that the results are scalable to a power station. In ITER the flux of primary fusion neutrons will be 1.2 megawatts per square meter—sufficient to observe how effectively a particular blanket and shield design will perform. Changes in thermal and physical properties of the ceramics will be observable in about one month of continuous exposure, or its equivalent. After one to three years, the changes in the properties of metal structures can be explored.

Because of the length of these property-change tests, they may be carried out in a separate, much smaller fusion machine rather than in ITER itself. Tests performed in ITER will require the device to function continuously for one week or more at any given time. When one combines the number of tests with the time for each and the variety of designs, it becomes apparent why a program covering many years is necessary. The program also demonstrates the importance of the ITER technology mission as a pilot fusion power station.

The ITER program may also be breaking new ground in another sense. "Big science" projects, such as the Superconducting Supercollider and the Human Genome Project, now push at the limit of U.S. resources. In contrast, ITER has been fully international from its conception. It may be demonstrating a new paradigm for large-scale scientific projects. But even if it does not, we can be assured ITER will take us to the next frontier of fusion research.

FURTHER READING

MAGNETIC FUSION REACTORS. Robert W. Conn in *Fusion,* Vol. 1: *Magnetic Confinement,* Part B. Edited by Edward Teller. Academic Press, 1981.

ITER CONCEPTUAL DESIGN. K. Tomabechi et al. in *Nuclear Fusion,* Vol. 31, No. 6, pages 1135–1224; June 1991.

THE ITER TOKAMAK DEVICE: ITER DOCUMENTATION SERIES, No. 25. International Atomic Energy Agency, 1991.

PLASMA PHYSICS AND CONTROLLED FUSION RESEARCH: 1990. International Atomic Energy Agency, 1991.

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Solid Acid Catalysts

Great progress has been made in the design of these important industrial materials. Some novel solid acid catalysts can reduce the emission of environmentally harmful products

by Sir John Meurig Thomas

Hidden among the tiny galleries, pores and cavities of solid acid catalysts is the basis for much of the manufacturing industry. Within their internal pathways and chambers, these agents—like other catalysts—speed up reactions that would occur at much slower rates in their absence. But, unlike other catalysts, solid acids offer the potential for superior effectiveness and environmental integrity.

Every year more than a trillion dollars' worth of goods is manufactured with the aid of man-made catalysts. Without them, fertilizers, pharmaceuticals, fuels, synthetic fibers, solvents and surfactants would be in short supply. Indeed, 90 percent of all manufactured items entail catalysis at some stage of production. Because these agents play such a pivotal role in petrochemical and other industries, chemists and materials scientists are forever searching for novel catalysts and seeking to improve those already in use.

This quest has now assumed fresh urgency. New and pending industrial legislation in the U.S., Europe and other countries requires more stringent environmental protection. For instance, it will soon become illegal to release into the atmosphere such products as the carcinogen benzene, which is a component of gasoline. Other substances subject to regulation include poisonous carbon monoxide, corrosive and reactive oxides of sulfur and nitrogen, as well as carbon dioxide and volatile hydrocarbons, which contribute to the greenhouse effect.

As ingredients of important industrial processes, catalysts have a crucial part to play in suppressing or altogether eliminating the generation of these environmentally detrimental products. Thanks to continuing research, it is becoming feasible for some catalysts to yield transport fuels that are essentially free of benzene. Other catalysts can produce gasoline components that boost octane ratings, thereby enhancing engine performance and diminishing the need for lead [see "Bimetallic Catalysts," by John H. Sinfelt; SCIENTIFIC AMERICAN, September 1985].

Yet many of the effective catalysts, including those that could be used to limit toxic by-products, have drawbacks. Often they themselves are highly toxic or corrosive acids in liquid form, such as hydrogen flouride. In 1989, for instance, 44 million tons of sulfuric acid and 12 million tons of phosphoric acid were used industrially in the U.S.—albeit not all for catalysis. These acids corrode storage and disposal containers and can be dangerous to transport and handle. In addition, because the reagents are mixed into the acids, separating the products of the reaction from the liquid is often a difficult and energy-consuming process.

Apart from making it easy to harvest the reaction products, solid acid catalysts can also allay concerns about safety and environmentally hazardous emissions. Because these solids hold their acidity internally, they are easy to handle—they can even be held safely in the palm of one's hand. Moreover, they are very effective: some of them exceed the acidity of concentrated sulfuric acid by a factor of more than 10 million. Roughly half the catalytic reactions involved in manufacturing use them as the vital agents of change.

Superior solid acid catalysts are needed for existing industrial processes and for environmental considerations. Work on designing more effective, innovative solid acid catalysts has been advancing steadily over the past few decades. Recently the refined techniques of solid state chemistry and computer modeling have allowed researchers, myself included, to tailor several different forms of solid acid catalysts.

Although they differ in structure from liquid acids, solid acid catalysts work on the same principle. Acids are characterized by their ability to give up hydrogen ions, or protons: H^+. Strong acids readily give up large numbers of these ions. Protons are often released from such entities as ionizable hydroxyl groups in which the bond between oxygen and hydrogen is severed to yield O^- and H^+. Protons may also be released from hydrated ions, such as H_3O^+ or $H_5O_2^+$.

The ability to lend protons makes acids valuable as catalysts. When a reactant receives and incorporates protons from an acid, it forms what is called a reactive intermediate. This positively charged intermediate changes shape and configuration. Then it may follow one of two courses. The intermediate may simply shed a proton (returning it to the catalyst), thereby forming an isomer—a compound having the same molecular composition as its parent but a different molecular structure. Or the intermediate may undergo further reaction, which culminates in the creation of a new molecule. Again, the proton is returned to the catalyst.

Among the first kinds of solid acid catalysts to be used industrially were silica-alumina gels. These agents catalyze the cracking of hydrocarbons—the process by which the complicated, bulky molecules that make oil viscous are converted into smaller molecules with high

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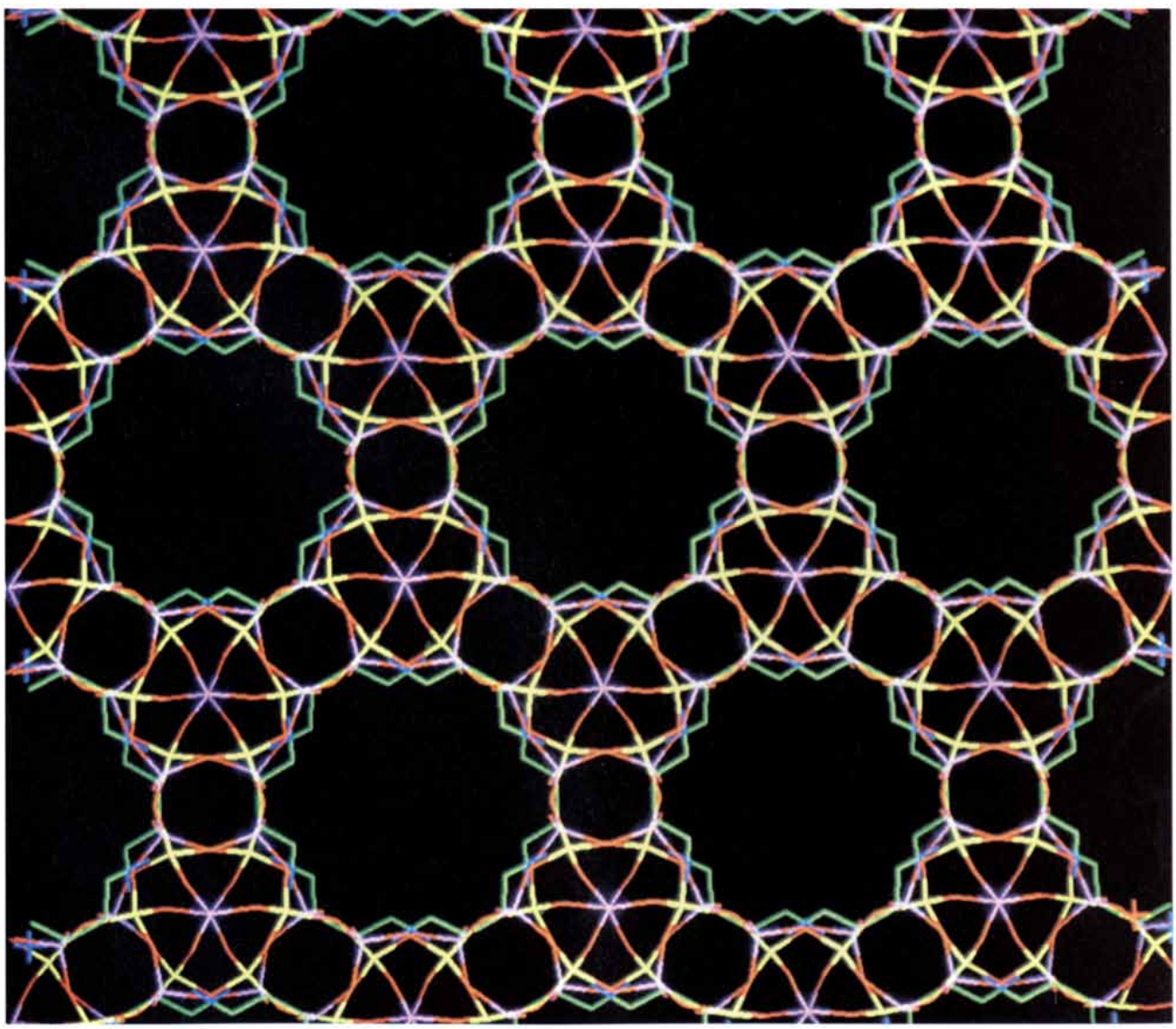
volatility, like those of gasoline. Silica-alumina gels have no defined structure and contain many micropores, which range in diameter from a few to a few hundred angstroms (10 millionths of a millimeter). Lining each micropore are loosely attached protons that provide the acidic catalytic activity of the gel.

Some characteristics of silica-alumina gels—especially their highly variable pore size and their amorphous quality—make them less than ideal catalysts. These compounds tend to lose their activity during hydrocarbon cracking because large carbonaceous products, created by the polymerization of some of the initial products of catalysis, form in their cavities. As a result, many unwanted side reactions occur, until the products accumulate and clog the pores. In addition, because the gels, unlike crystals, have no regular structure, their protons are unevenly distributed, and it is therefore difficult to control catalysis precisely.

In the mid-1960s silica-alumina gels were for the most part replaced by more effective solid acid catalysts called zeolites. These "boiling stones" (from the Greek *zeo,* to boil, and *lithos,* stone) are highly porous crystals laced with minute channels that range in diameter from three to eight angstroms [see "Synthetic Zeolites," by George T. Kerr; SCIENTIFIC AMERICAN, July 1989]. Zeolites do not share the disadvantages of silica-alumina gels. The pores inside these remarkable crystalline structures are so small that the creation of large molecules leading to carbonaceous buildup is greatly suppressed.

Depending on a zeolite's precise atomic architecture, as much as 50 percent of its volume may be composed of pores. Essentially all the atoms that constitute its framework structure are accessible to any molecule small enough to enter the internal network of channels. In other words, most atoms in a zeolite are surface atoms. If a spoonful of an acid zeolitic catalyst were spread out to a thickness of one molecule, it would have an area larger than that of a baseball field.

In addition to the extensive surface area, a well-defined, regular microenvironment surrounds the detachable protons in the cavities of zeolites. The protons, or active sites, are therefore evenly distributed through the entire internal structure. Although it is extremely difficult to determine the number and nature of active sites in many other types



POROUS SHEETS of aluminophosphates—like this one—soon may be adapted to serve as solid acid catalysts, if hydrogen ions can be introduced so as to make the pores in these sheets acidic. The different colors mark the bonds between various atoms: aluminum (*yellow*), phosphorus (*purple*), oxygen (*red*), carbon (*green*) and nitrogen (*blue*).

of solid catalysts, such determinations are easily made for zeolites. We know that some of them, for example, have as many as 10 million trillion active sites per gram lining their pores.

Indeed, the realization that measurements from the realms of surface science and solid state science were one and the same with regard to zeolites led to a greater understanding of these materials. In 1980 my students at the University of Cambridge and I embarked on a series of solid state chemical adventures that brought to light many facts about a range of new zeolitic catalysts. For instance, in collaboration with Anthony K. Cheetham of the University of Oxford, we used the scattering of neutrons, or neutron diffraction, to determine precisely the nature of the site of the detachable proton in the hydrocarbon-cracking catalyst lanthanum ion–exchanged zeolite-Y, or La Y.

In inorganic catalysts, just as in enzyme catalysts, a knowledge of the detailed structure of the active site provides the beginning of wisdom. Such understanding is the basis for the rational design of improved catalysts. Because protons scatter neutrons more intensely than they do x-rays, protons are rendered more visible when exposed to beams of neutrons. We have, however, also used x-ray diffraction, magnetic resonance spectroscopy, high-resolution microscopy and many other techniques to reveal the secrets of the composition and framework structure of these catalysts.

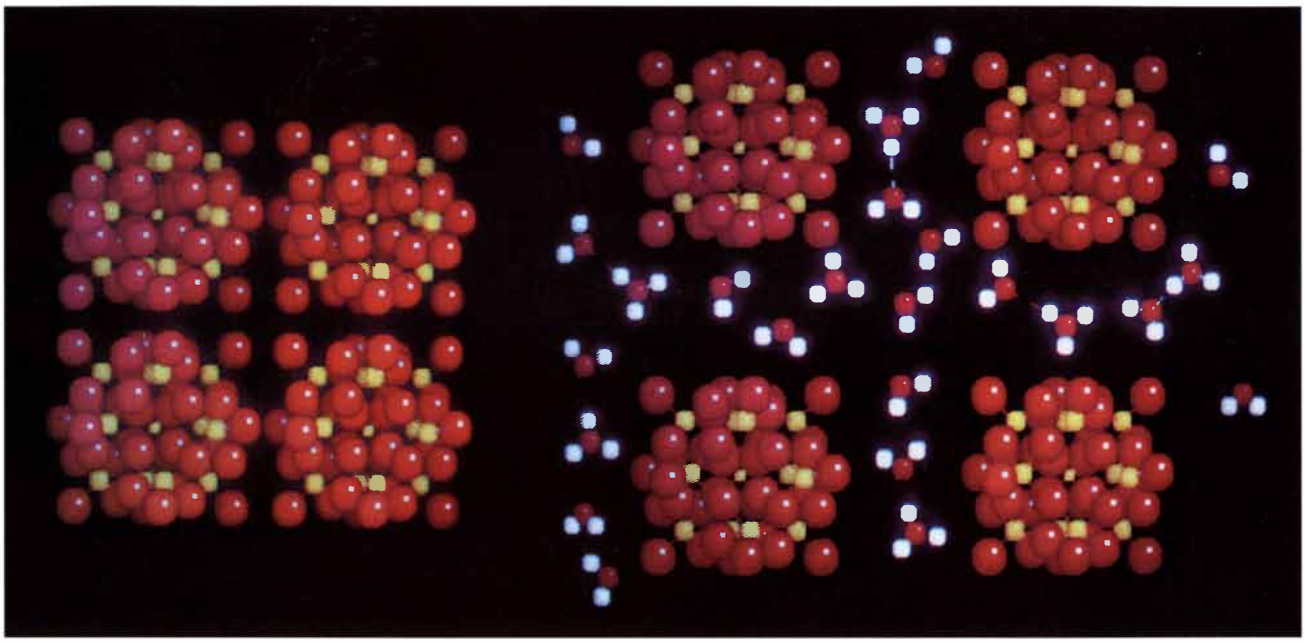
One of the most important qualities of zeolites that has become more apparent, partly through electron microscope imaging techniques, is their ability to exhibit shape-selective catalysis. This principle, the study of which was initiated in the early 1960s by Paul B. Weisz and his colleagues at Mobil Research and Development Corporation, is quite simple. When reactions take place within the tiny pores of a particular zeolite, only those product molecules that readily fit into and migrate along the channels will emerge. In other words, the shape of the cavities can control the shape of the product of the catalyzed reaction.

Many industrially important reactions are catalyzed by a solid acid catalyst called ZSM-5, which operates using the concept of shape selectivity. A good example is the synthesis of *para*-xylene, the precursor of nylon. When molecules of the chemical toluene combine with methyl alcohol in a ZSM-5 catalyst, only the commercially desirable, rod-shaped molecules of *para*-xylene are released—not the less desirable, boomerang-shaped molecules of *ortho*-xylene. This catalyst also yields ethylbenzene when ethylene is added to benzene—without the use of aluminum trichloride, a chemically unpleasant and environmentally harmful catalyst. Ethylbenzene is the precursor of styrene.

David R. Corbin and his associates at Du Pont have ingeniously extended the strategy of shape-selective catalysis by using an acid zeolite called Rho. Rho, which was first synthesized by Richard Barrer of Imperial College in London, brings about the production of methylamines from methanol and ammonia. A standard acid catalyst, like a silica-alumina gel, yields three progressive-

Some Important Reactions That Use Solid Acid Catalysts

PROCESS	EXAMPLE
HYDROCARBON CRACKING Large viscous molecules are converted into a series of smaller, more volatile ones.	$n(C_{12}H_{18})$ (OIL) $\xrightarrow[\text{La Y}]{\text{CATALYST}}$ $n(C_2H_4) + n(C_6H_6) + n(C_4H_8)$ (ETHYLENE BENZENE BUTENE)
DISPROPORTIONATION OF AROMATIC COMPOUNDS Two molecules of one compound are catalytically rearranged into two different compounds.	$2(C_6H_5CH_3)$ (TWO TOLUENES) $\xrightarrow[\text{ZSM-5}]{}$ $C_6H_6 + C_8H_{10}$ (BENZENE XYLENE)
ALKYLATION A hydrocarbon fragment is added to an organic compound through the use of an alkene such as ethylene or 2-methylpropene. The process is regarded as the reverse of cracking.	$C_6H_6 + C_2H_4$ (BENZENE ETHYLENE) $\xrightarrow[\text{ZSM-5}]{}$ $C_6H_5C_2H_5$ (ETHYLBENZENE (PRECURSOR OF STYRENE))
	$CH_2C(CH_3)_2 + (CH_3)_3CH$ (2-METHYLPROPENE ISOBUTANE) $\xrightarrow[\text{ACIDIC CLAY}]{}$ $(CH_3)_3CCH_2CH(CH_3)_2$ (ISOOCTANE)
CONVERSION OF METHANOL TO GASOLINE Methanol, a relatively abundant chemical compound, is readily transformed into a source of fuel.	$n(CH_3OH)$ (METHANOL) $\xrightarrow[\text{ZSM-5}]{}$ $n(CH_2) + n(H_2O)$ (GASOLINE WATER)
SYNTHESIS OF METHYL TERTIARY BUTYL ETHER (MTBE) This valuable gasoline component, which boosts octane ratings and thereby engine performance, is formed through acid catalysis.	$CH_3OH + CH_2C(CH_3)_2$ (METHANOL 2-METHYLPROPENE) $\xrightarrow[\text{ACIDIC CLAY}]{}$ $CH_3OC(CH_3)_3$ (MTBE)
FORMATION OF ETHYL ACETATE This important solvent and component of perfumes and flavorings can be made from ethylene and acetic acid.	$C_2H_4 + CH_3COOH$ (ETHYLENE ACETIC ACID) $\xrightarrow[\text{ACIDIC CLAY}]{}$ $CH_3COOC_2H_5$ (ETHYL ACETATE)



FOUR KEGGIN IONS (*left*) are composed of a central atom of silicon or phosphorus (*tiny yellow*), surrounded by oxygen (*red*) and molybdenum or tungsten (*larger yellow*). Structures made up of Keggin ions absorb polar molecules (*red and white*), which have a slight electrical charge, to become swollen quasiliquids (*right*) with a large surface area and high acidity.

ly more bulky types of methylamines—let us call them *a, b* and *c*—in the thermodynamically predicted proportions 15:23:62. The methylamines are produced in those proportions because the pores of the catalyst permit the free movement of each product.

In acid zeolite Rho, however, the pore size is restricted, so that little of the bulkiest methylamine (*c,* or trimethylamine) can migrate out. The product ratio therefore becomes 14:86:04. Dimethylamine, or *b,* is an important chemical building block for synthetic resins, fibers, dyes and pharmaceuticals. It is obviously favored in high yield. By taking advantage of the cavities of Rho, a more desirable product can be generated.

The large surface area and the many active sites of zeolites make them very effective catalysts. Yet whereas zeolites provide a more or less rigid three-dimensional network of interconnecting channels for catalysis, some inorganic solids offer two-dimensional access to their interiors. The two-dimensional solid acid catalysts can be almost as effective as zeolites for certain reactions.

Indeed, high-area solid acids that are entirely different from zeolites can be designed and manipulated so as to create microenvironments conducive for controlled catalysis. Studies that my colleagues and I started 20 years ago at the University College of Wales in Aberystwyth have led to the development of such a series of novel solid acid catalysts, called modified clays.

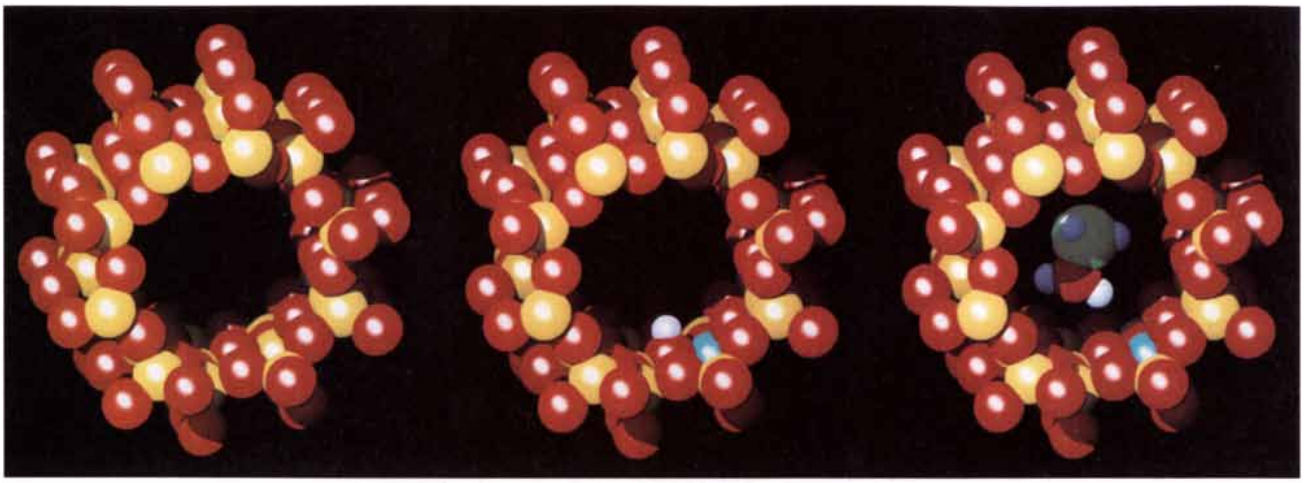
My work on the catalytic properties of solid acids began almost by accident. As a physical chemist, I wanted to investigate the dynamics of the sandwichlike compounds that form when molecules are incorporated, or intercalated, into the spaces between the individual sheets of clays. Clays are some of the most abundant, porous and benign materials on the earth. They are composed of layers of atoms, almost invariably silicon, oxygen, aluminum or magnesium in crystalline form. In most clays the layers themselves have a negative charge and are held together by the positive charge of sodium and calcium ions that reside in the interlamellar spaces between the layers [see "The First Organisms," by A. G. Cairns-Smith; SCIENTIFIC AMERICAN, June 1985].

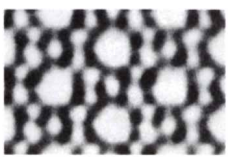
My colleagues and I were particularly interested in understanding the phenomenon of intercalation, and we also wanted to improve the characterization of clays using new techniques based on x-rays, neutrons and electrons. In collaboration with Howard Purnell and James A. Ballantine of the University College of Swansea, my students and I made two modest discoveries that later proved exceptionally useful in the formation of solid acid catalysts.

First, we established it was easy to replace the sodium, calcium or other alkaline earth ions in the interlamellar spaces with hydrated protons in the form H_3O^+. In particular, we studied this process in a clay called montmorillonite, which is composed of aluminosilicate layers. Such substitution of ions did not change the integrity of the clay. By altering the ions in the interlamellar spaces, we had simply changed a salt clay into an acidic one.

Second, we discovered the remarkable facility with which these clays catalyzed certain reactions. For example, alkenes such as hexene, an unsaturated hydrocarbon, could be combined with water in the interlamellar spaces to produce dihexyl ethers—important solvents. The protons stationed in the interlamellar space successfully served as catalytic agents. It soon became apparent that the acidic clays we had created could catalyze many commercial reactions, some of which have now taken on environmental significance.

A particularly exciting discovery was the ease with which our acidic clay catalyzed the formation of ethyl acetate, an important industrial solvent and an essential ingredient of perfumes and flavorings. More than 100,000 tons of this fragrant, colorless liquid are manufactured every year, normally by two separate catalytic steps. The first step uses concentrated sulfuric acid as a catalyst to hydrate ethylene into ethanol. The second uses sulfuric acid to accelerate the joining of ethanol with acetic acid to yield water and ethyl acetate. But these steps are less than ideal. Not only do they use a liquid corrosive acid, but the water eliminated during the second process dilutes the acid, weakening





PORES OF ZEOLITE ZSM-5, which measure 5.5 angstroms in diameter, are seen as regular white patches in an electron micrograph (*bottom left*). A model of a single pore (*upper left*) shows the atomic arrangement of silicon (*yellow*) and oxygen (*red*). If a silicon atom is chemically replaced by an aluminum atom (*blue*), a hydrogen ion (*white*) attaches to an oxygen atom to preserve the structure's electroneutrality (*center*). This proton gives the pore its catalytic acidity. When a reagent such as methanol incorporates the proton (*right*), it becoms a reactive intermediate.

it so that great quantities are required.

But our acidic clay could form ethyl acetate in one step, obviating the need for the potent liquid sulfuric acid. The solid acid catalyst also circumvents the problem of dilution because no water is produced when intercalated acetic acid is combined with ethylene to form ethyl acetate.

Not all clays make effective catalysts, however. Some have impurities that render them unstable. Clays from certain geologic provenances—montmorillonite from Wyoming, for example—have small amounts of transition-metal impurities in their layers. Despite their low abundance, these impurities induce side reactions that interfere with the main reaction to be catalyzed.

Clays that are free of such impurities make valuable catalysts, ones that can curb the production of environmentally adverse compounds. One of the fastest-growing additives for gasoline is methyl tertiary butyl ether (MTBE). This compound is a favored octane booster in the new generation of lead-free gasolines. MTBE also diminishes the vapor pressure of the fuel, so that liberation of greenhouse gases is reduced when an engine idles. It has the added advantage of contributing oxygen to the fuel, facilitating more complete combustion. As a result, the fuel releases less carbon monoxide and other pollutants.

Our acid montmorillonite, which is free of transition-metal impurities, proves very efficient in catalyzing the formation of MTBE from methyl alcohol and 2-methylpropene at temperatures less than 100 degrees Celsius. The currently favored catalysts for this process are sulfonated resins, which contain sulfur that ultimately contributes to soil pollution when the catalysts are discarded. The clay catalyst, however, exists in harmony with the environment, and disposed quantities of it may be safely used as landfill.

Work carried out recently in Japan on a totally different kind of solid acid, called a heteropoly acid, had its origins in a discovery made in 1834 by the Swedish chemist Jöns Jakob Berzelius. Berzelius, apart from coining the term "catalysis," found a new kind of acid; 100 years later x-ray crystallographer J.D.F. Keggin determined the structure of this class of acid. He found that these oxygen-rich compounds include a central atom—either phosphorus, arsenic, silicon or germanium—and atoms of molybdenum or tungsten as well as high concentrations of detachable protons. The heteropoly acids were subsequently named Keggin ion systems.

Just as clays swell when they take up water and organic molecules, so do heteropoly acids. These compounds can incorporate ample quantities of water and a range of other polar molecules—those that have no overall electrical charge but have one slightly negative end and one slightly positive end.

The resulting swollen solid is a quasi-liquid in which hydrated protons and other incorporated molecules have great mobility, just as they do in the interlamellar spaces of other acid catalysts. Reactants have access to many protons in such a swollen system because the surface area is large, just as it is in three-dimensional catalysts, such as zeolites. The precise molecular details of the swelling process remain a mystery.

Yoshio Ino and Makoto Misono and their colleagues at the Tokyo Institute of Technology and Tokyo University have demonstrated catalytic capabilities for these solid Keggin ion systems. In particular, they have been able to convert alkenes such as ethylene and propylene into alcohols such as ethyl alcohol and isopropanol, which are in great demand. Normally, corrosive liquids, including concentrated sulfuric acid, are used for this reaction.

Although Keggin ion acid catalysts lack the shape selectivity of zeolites, it has become possible to insert positively charged, aluminum-rich analogues of the Keggin ions into the interlamellar spaces of clays. The study of the resulting pillared clays, pioneered by Barrer, has been actively pursued by D.E.W. Vaughan of Exxon Research and Engineering Company in New Jersey.

Pillaring the clays for catalysis has two benefits. First, this process renders the interlamellar space of the parent clay two-dimensionally porous. Also, the process confers thermal stability on the clay by preventing the collapse of the layers during heat treatment. Pillared clays do not, however, seem to be sufficiently able to withstand the severe conditions required for the catalytic cracking of oil. But they do show great promise as clean and effective acid catalysts for the production of esters and ethers, which are in ever increasing demand as commodities in myriad manufacturing processes.

Clearly, great strides have been taken in designing viable solid acid catalysts that can serve as alternatives to the harmful liquids or inferior solids cur-

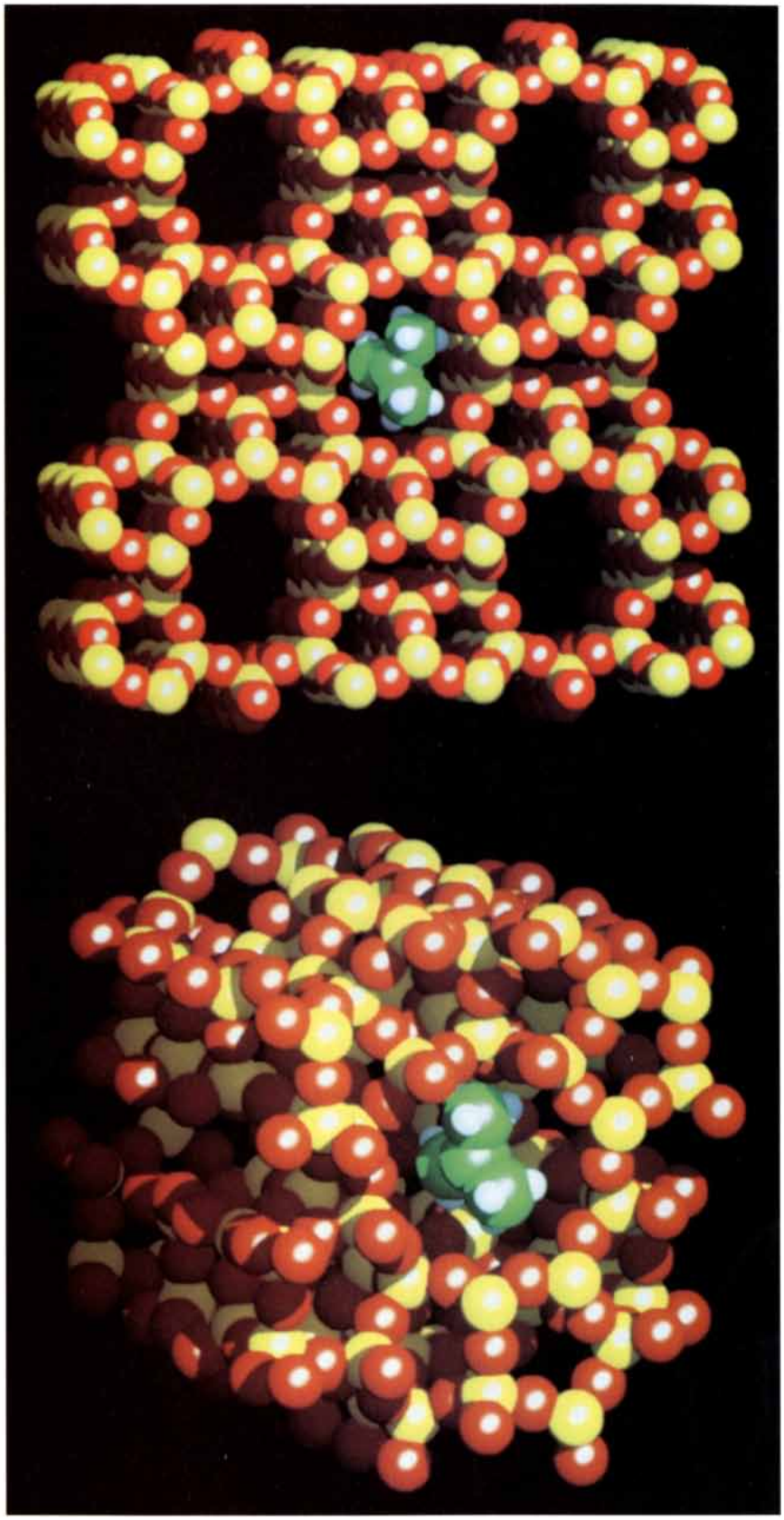
rently in use. But the demanding goal of producing ever cleaner fuels remains. As oil supplies dwindle, hydrocarbons from the bottom of the barrel will be used to make fuels. This heavier oil is richer in contaminants and must therefore be catalytically cracked in a way that suppresses the release of sulfur-rich or nitrogenous by-products. In addition, automobile gasoline must be devoid of benzene. Most demanding of all, solid acids must be found that are capable of catalyzing the production of isooctane from the alkylation of butane by 2-methylpropene, the key reaction in the production of high-octane gasoline.

Several strategies can be used to achieve these goals. One approach is to exploit the vast range of microporous structures composed of aluminophosphates. A decade ago Stephen Wilson and Edith Flanigen and their colleagues at Union Carbide reported finding a wide variety of aluminophosphate, or ALPO, molecular sieves. Some of the sieves had framework structures like those of zeolites; others were quite novel. The Union Carbide group and others—notably, Mark E. Davis of the California Institute of Technology, Joseph V. Smith and his group at the University of Chicago and Charis Theocharis and his colleagues at Brunel University in England—discovered that many metal ions, such as cobalt, zinc, magnesium and manganese, could replace aluminum ions. This substitution led to the creation of several solid acids.

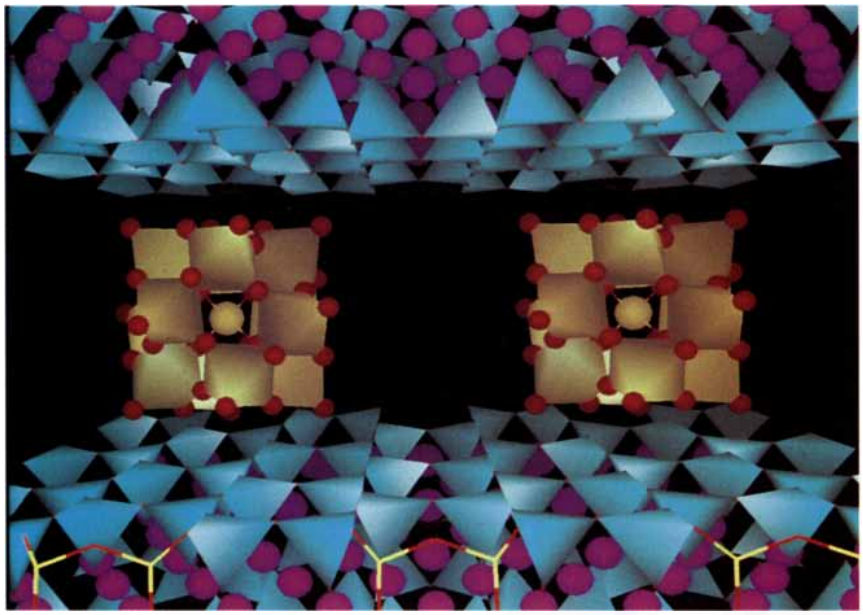
The precise acidity of the resulting solid depends in part on the structure of the molecular sieve and in part on the nature of the metal ion. In general, ALPOs in which the aluminum has been partly replaced with magnesium tend to be more acidic than their manganese or cobalt counterparts. Much more investigation is required before we can tell whether these three-dimensional inorganic templates can function as powerful catalysts.

My own work, carried out with Richard Jones in association with Ruren Xu and Jiesheng Chen of Jilin University in China, has led to the discovery of a structure with porous sheets of aluminophosphates. This structure is an intermediate between the three-dimensional zeolites or ALPOs and the two-dimensional clays. Although this constructed solid is not intrinsically acidic, it should be possible to manipulate this fascinating structure so as to confer on it the appropriate acidity.

Another approach to the creation of solid acids is to adapt the structure and properties of existing zeolites subtly, using computational chemistry as



TWO SOLID ACID CATALYSTS, Theta-1 (*top*) and ZSM-5 (*bottom*), have pores that are similar in size to the diameter of two isomers of butene: 2-methylpropene (*green and white*), which is commercially valuable, and 1-butene (*not shown*), which is less so. Because of the shape of the pores, both catalysts isomerize 1-butene into 2-methylpropene. Unneeded by-products can also form in ZSM-5, however, making it less effective than Theta-1 for this process.



PILLARED CLAY, depicted here as a polyhedral model, is a form of solid acid catalyst that combines acidic clays with Keggin-like ions. The clay layers are composed of silicon (*blue*) and magnesium (*purple*). The Keggin-like ions—composed of oxygen (*red*) and aluminum (*yellow*)—reside in the spaces between the layers.

a guiding principle. Indeed, synthesizing known zeolitic structures with enhanced silicon to aluminum ratios offers much promise. For instance, cracking catalysts can be endowed with considerably more acidity—even though the number of protons released falls—by increasing the silicon to aluminum ratio 20 to 30 percent. The reasons for this result are not understood. Ostensibly, there is an optimum ratio at which the intrinsic acidity is greatest.

Using zeolite catalysts with greater amounts of silicon, Ian E. Maxwell, Wim Stork and Arend Hoek of Shell Research Laboratory in Amsterdam achieved a 250-fold decrease in the sulfur content of some gasoline products. New Shell catalysts that incorporate minute particles of nickel and tungsten have also facilitated hydrocarbon cracking and the conversion of benzene and other aromatics to their noncarcinogenic forms. Similar strategies, using a zeolite called mordenite, which contains small amounts of platinum, have enabled Shell researchers to develop high-octane gasolines from the hydroisomerization of a pentane-hexane mixture.

The different forms of solid acid catalysts described above were discovered in the chemist's laboratory through a combination of patience, passion and serendipity. Of late, however, rational computational approaches have increasingly been involved in the search for new catalysts. This work is one of the most exciting developments in the realm of solid acid catalyst research today.

Catalysts of the uniform heterogeneous variety—in which the detachable protons are uniformly and accessibly distributed through the solid—are easier to analyze mathematically. Computers can readily deal with systems that repeat. Because of their regularity, such catalysts are amenable to molecular dynamics and quantum mechanical calculations. Not so readily amenable to computational analysis are nonuniform catalysts like silica gels or multiphasic ones consisting of finely divided metals supported on alumina that convert syngas (a mixture of carbon monoxide and hydrogen) into hydrocarbons [see "Chemical Fuels from the Sun," by Israel Dostrovsky; SCIENTIFIC AMERICAN, December 1991].

For example, my co-workers and I wanted to design a zeolite acid catalyst for the production of MTBE, the important gasoline component I described earlier. MTBE is made from 2-methylpropene, one of the four isomers of butene. Although one of the isomers, 1-butene, is reasonably abundant because it is released during the cracking of oil, 2-methylpropene is relatively scarce, as are the remaining two, unneeded isomers. We therefore set about finding a catalyst that could produce 2-methylpropene from 1-butene.

For our computational analyses, Clive M. Freeman, C. Richard A. Catlow and I selected two promising solid acid zeolites: ZSM-5 and Theta-1, the latter a zeolite discovered at British Petroleum Laboratories eight years ago. We chose them because their channels are almost exactly 5.5 angstroms wide—a distance, if it can be called that, roughly comparable to the diameter of the two isomers with which we are concerned. The difference between the two zeolites lies in the structure of the channels: in ZSM-5 the channels intersect, creating a regular set of bigger cavities; in Theta-1 the channels do not intersect, and there are no extra cavities.

Using a blend of Monte Carlo and molecular dynamics calculations, we compared the mobility and the binding energy of all four isomers inside the two microporous solids. We discovered it is much easier for 2-methylpropene than for any of the three other isomers to be released from both of the catalysts. Taking account of spatial calculations, we would expect undesirable by-products—that is, unneeded dimers (linked pairs of isomers)—to form in the larger cavities where channels intersect. We therefore predicted Theta-1 would be superior to ZSM-5 for the isomerization of 1-butene to 2-methylpropene. Our prediction proved true.

The design and development of catalysts are tasks that will challenge us for a long time. Better solid acid catalysts will secure a cleaner, more efficient future in which zero waste production in industrial processes is the ultimate goal.

FURTHER READING

UNIFORM HETEROGENEOUS CATALYSTS: THE ROLE OF SOLID-STATE CHEMISTRY IN THEIR DEVELOPMENT AND DESIGN. John M. Thomas in *Angewandte Chemie,* International Edition in English, Vol. 27, No. 12, pages 1673–1691; December 1988.

ZEOLITES AND OTHER MICROPOROUS MATERIALS. D.E.W. Vaughan in *Studies in Surface Science and Catalysis: Zeolites: Facts, Figures, Future,* Vol. 49A, pages 95–116; 1989.

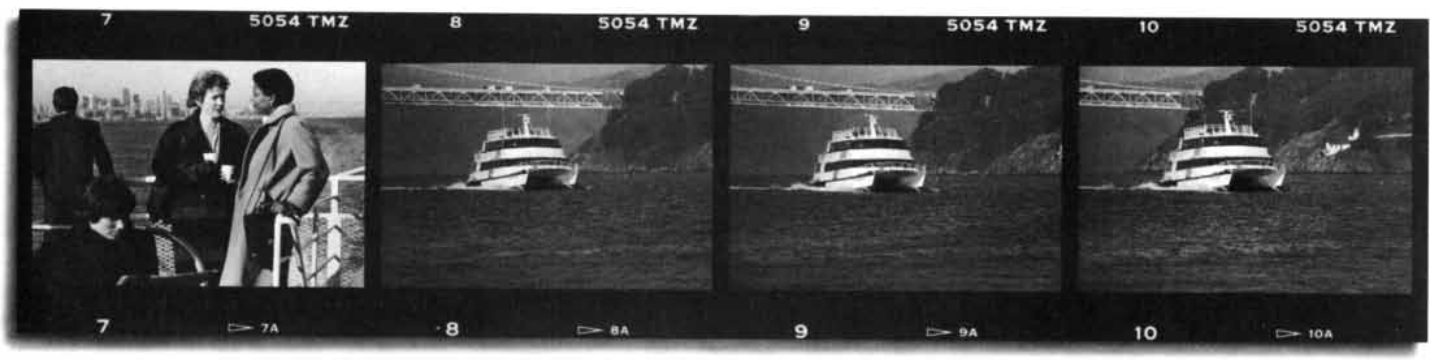
COMPUTING THE LOCATION AND ENERGETICS OF ORGANIC MOLECULES IN MICROPOROUS ADSORBENTS AND CATALYSTS: A HYBRID APPROACH APPLIED TO ISOMERIC BUTENES IN A MODEL ZEOLITE. Clive M. Freeman, C. Richard A. Catlow, John M. Thomas and Stefan Brode in *Chemical Physics Letters,* Vol. 186, Nos. 2–3, pages 137–142; November 8, 1991.

NEW AND IMPROVED CATALYTIC PROCESSES FOR CLEAN FUELS. I. E. Maxwell and J. E. Naber in *Catalysis Letters,* Vol. 12, pages 105–116; April 1992.

PERSPECTIVES IN CATALYSIS: A "CHEMISTRY FOR THE 21ST CENTURY" MONOGRAPH. Edited by John M. Thomas and Kirill I. Zamaraev. Blackwell Scientific Publications/International Union of Pure and Applied Chemistry, 1992.

"I hear you made a breakthrough in the lab."

"That's right. No one's published on it yet."



"Terrific! You'll be the first."

"Looks that way. I even checked patents."

"This is going to be really big."

"I think so."

"So where are you getting so much help?"

Phantom Limbs

People who have lost an arm or a leg often perceive the limb as though it is still there. They can also feel excruciating pain in specific parts of the phantom limb

by Ronald Melzack

In 1866 S. Weir Mitchell, the foremost American neurologist of his time, published his first account of phantom limbs, not in a scientific journal but in the *Atlantic Monthly,* as an anonymously written short story. In his tale, "The Case of George Dedlow," the protagonist loses an arm to amputation during the Civil War. Later, he awakens in the hospital after, unbeknownst to him, both his legs have also been amputated.

"[I was] suddenly aware of a sharp cramp in my left leg. I tried to get at it ... with my single arm, but, finding myself too weak, hailed an attendant. 'Just rub my left calf, ... if you please.'"

"'Calf? ... You ain't got none, pardner. It's took off.'"

Some historians have speculated that Mitchell chose to publish in the *Atlantic* as a way of testing the reaction of his peers to the concept of phantom limbs. He feared they would not believe amputated arms and legs could be felt after the limbs were gone.

In fact, the phenomenon of phantom limbs is common. So is the occurrence of terrible pain in these invisible appendages. Yet neither the cause of phantoms nor the associated suffering is well understood. My colleagues and I have recently proposed explanations that are leading to fresh research into treatments for the often intractable pain. The concepts also raise questions about basic assumptions of contemporary psychology and neuroscience.

RONALD MELZACK is E. P. Taylor Professor of Psychology at McGill University and research director of the Pain Clinic at Montreal General Hospital. His work on the neurophysiology of pain spans almost four decades. After obtaining his Ph.D. in psychology at McGill in 1954 and taking up fellowships in the U.S. and abroad, he joined the faculty of the Massachusetts Institute of Technology in 1959. There he and Patrick D. Wall began discussions that led to the publication in 1965 of their now famous "gate control" theory of pain. Melzack joined the McGill faculty in 1963. This is his fourth article for *Scientific American.*

The most extraordinary feature of phantoms is their reality to the amputee. Their vivid sensory qualities and precise location in space—especially at first—make the limbs seem so lifelike that a patient may try to step off a bed onto a phantom foot or lift a cup with a phantom hand. The phantom, in fact, may seem more substantial than an actual limb, particularly if it hurts.

In most cases, a phantom arm hangs straight down at the side when the person sits or stands, but it moves in perfect coordination with other limbs during walking; that is, it behaves like a normal limb. Similarly, a phantom leg bends as it should when its owner sits; it stretches out when the individual lies down; and it becomes upright during standing.

Sometimes, however, the amputee is sure the limb is stuck in some unusual position. One man felt that his phantom arm extended straight out from the shoulder, at a right angle to the body. He therefore turned sideways whenever he passed through doorways, to avoid hitting the wall. Another man, whose phantom arm was bent behind him, slept only on his abdomen or on his side because the phantom got in the way when he tried to rest on his back.

The eerie reality of phantoms is often reinforced by sensations that mimic feelings in the limb before amputation. For example, a person may feel a painful ulcer or bunion that had been on a foot or even a tight ring that had been on a finger. Such individuals are not merely recollecting sensations but are feeling them with the full intensity and detail of an ongoing experience. The reality of the phantom is also enhanced by wearing an artificial arm or leg; the phantom usually fills the prosthesis as a hand fits a glove.

The sense of reality is also strengthened by the wide range of sensations a phantom limb can have. Pressure, warmth, cold and many different kinds of pain are common. A phantom can feel wet (as when an artificial foot is seen stepping into a puddle). Or it can itch, which can be extremely distressing, although scratching the apparent site of discomfort can actually relieve the annoyance sometimes. The person may also feel as if the limb is being tickled or is sweaty or prickly.

Naturally, of all the sensations in phantom limbs, pain, which as many as 70 percent of amputees suffer, is the most frightening and disturbing. It is often described as burning, cramping or shooting and can vary from being occasional and mild to continuous and severe. It usually starts shortly after amputation but sometimes appears weeks, months or years later. A typical complaint is that a hand is clenched, fingers bent over the thumb and digging into the palm, so that the whole hand is tired and achy. In the leg the discomfort may be felt as a cramp in the calf. Many patients report that their toes feel as if they are being seared by a red-hot poker.

A final striking feature of phantoms, which reinforces the reality still further, is that they are experienced as a part of oneself. That is, patients perceive them as integral parts of the body. A phantom foot is described not only as real but as unquestionably belonging to the person. Even when the foot is felt to be dangling in the air several inches beneath the stump and unconnected to the leg, it is still experienced as part of one's body, and it moves appropriately with the other limbs and with the torso.

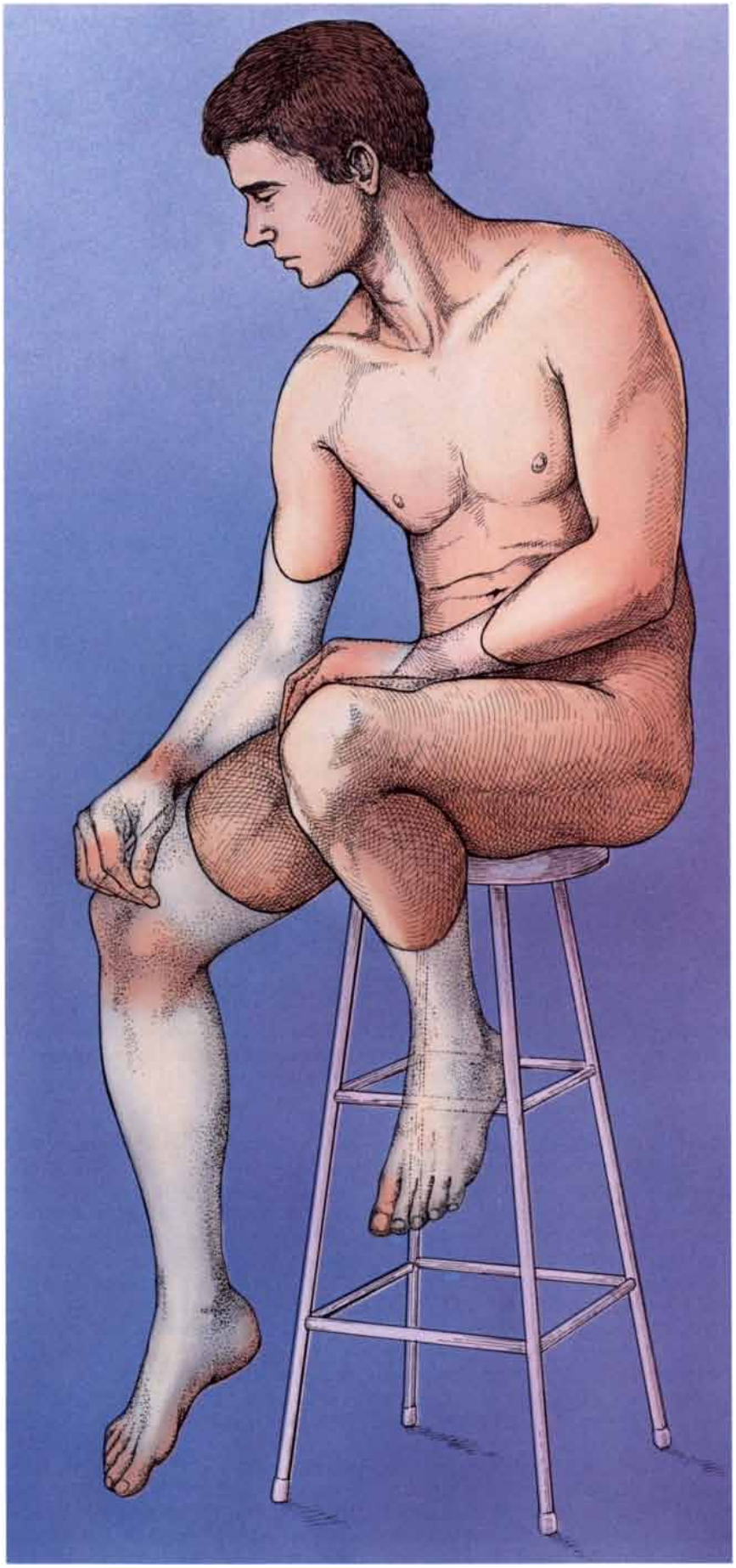
Amputation is not essential for the occurrence of a phantom. In some accidents, particularly when a rider is thrown off a motorcycle and hits the pavement, the shoulder is wrenched forward so that all the nerves from the arm are ripped from the spinal cord, a condition known as a brachial plexus avulsion. The resulting phantom oc-

cupies the now useless true arm and is usually coordinated with it. But if the victim's eyes are closed, the phantom will remain in its original position when the real arm is moved by someone else. Although the flesh-and-blood arm is incapable of responding to stimulation, the phantom version is usually extremely painful. Regrettably, surgical removal of the true arm has no effect on the phantom or the pain.

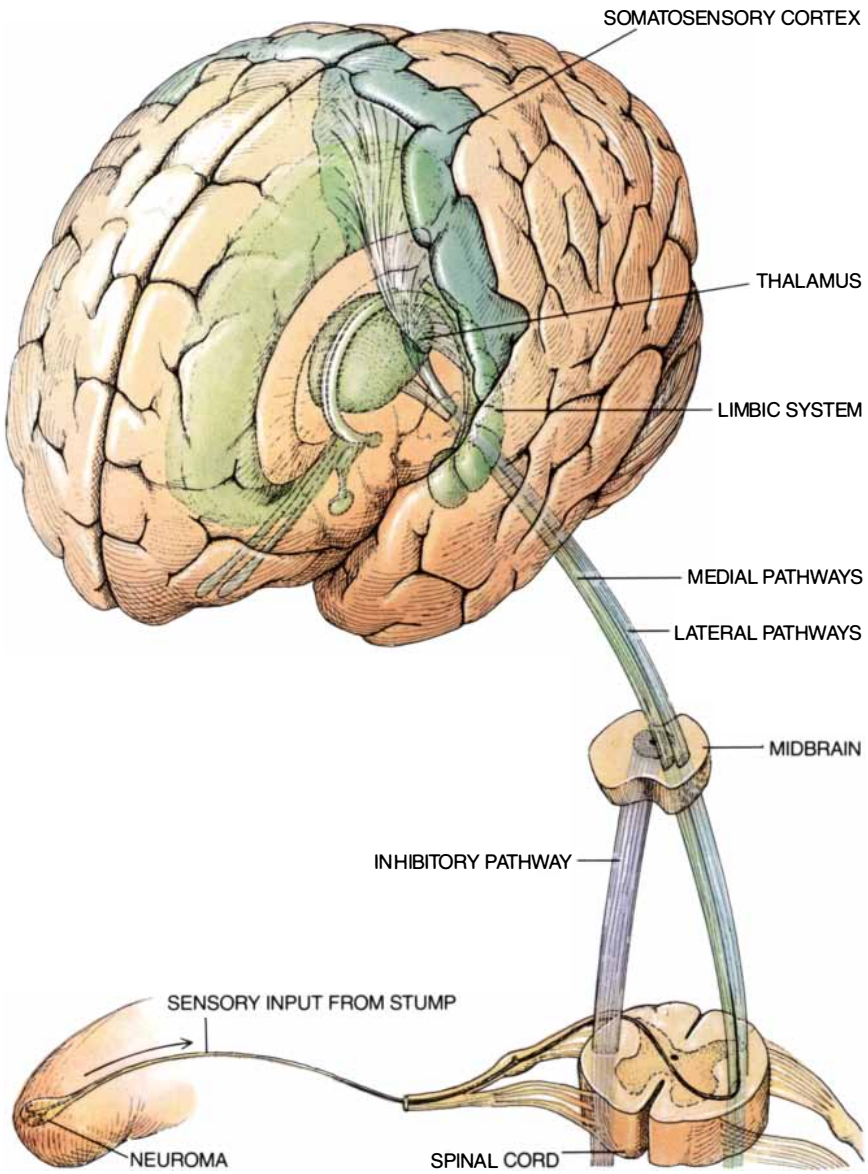
Similarly, paraplegics—persons who have had a complete break of the spinal cord and therefore have no feeling in, or control over, their body below the break—often have phantom legs and other body parts, including genitals. Immediately after an accident, the phantom may be dissociated from the real body. For instance, a person may feel as if the legs are raised over the chest or head even when he or she can see that they are stretched out on the road. Later, though, phantoms move in coordination with the body, at least when the person's eyes are open. Some paraplegics complain that their legs make continuous cycling movements, producing painful fatigue, even though a patient's actual legs are lying immobile on the bed. Phantoms are also reported by patients whose spinal cords are anesthetized, such as by a spinal block during labor.

The oldest explanation for phantom limbs and their associated pain is that the remaining nerves in the stump, which grow at the cut end into nodules called neuromas, continue to generate impulses. The impulses flow up through the spinal cord and parts of the thalamus (which is a central way station in the brain) to the somatosensory areas of the cortex. These cortical areas are the presumed centers for sensation in classical concepts of the nervous system.

On the basis of this explanation, treatments for pain have attempted to halt the transmission of impulses at every level of the somatosensory projection system. The nerves from the stump have been cut, usually just above the neuroma or at the roots—small bundles of fibers that arise when the sensory nerves divide into smaller



TYPICAL EXAMPLES of phantom limbs reported by patients are combined in this human figure. Some parts of the phantom are felt especially vividly (*highlighted areas in transparent limbs*). The phantom limb is perceived as perfectly real to the patient, who describes it as being in various positions and often reports feeling pain in it.



PATHWAYS OF SIGNALS from the body to the brain are shown. After the loss of a limb, nerve cells in the denervated areas of the spinal cord and brain fire spontaneously at high levels and with abnormal bursting patterns.

branches, just before they enter the spinal cord. Pathways within the spinal cord have been cut as well, and the areas of the thalamus and cortex that ultimately receive sensory information from the limb have been removed.

Although these approaches may provide relief for months or even years, the pain usually returns. Moreover, none of these procedures abolishes the phantom limb itself. Hence, neuroma activity cannot by itself account for either the phenomenon of the phantom limb or for the suffering.

A related hypothesis moves the source of phantom limbs from neuromas to the spinal cord, suggesting that phantoms arise from excessive, spontaneous firing of spinal cord neurons that have lost their normal sensory input from the body. The output of the cells is transmitted to the cortex, just as if the spinal neurons had received external stimulation. This proposal grew in part out of research done in the 1960s showing that after sensory nerves in the body are cut, neurons in the spinal cord spontaneously generate a high level of electrical impulses, often in an abnormal, bursting pattern.

Other observations indicate that this explanation is insufficient. Paraplegics who have suffered a complete break of the spinal cord high in the upper body sometimes feel severe pain in the legs and groin. Yet the spinal neurons that carry messages from those areas to the brain originate well below the level of the break, which means that any nerve impulses arising in those neurons would not traverse the break.

Some recent work has led to the proposal that phantom limbs can arise still higher in the central nervous system—in the brain itself. One hypothesis holds that phantoms are caused by changes in the flow of signals through the somatosensory circuit in the brain.

For example, Frederick A. Lenz, then at the University of Toronto, observed abnormally high levels of activity and a bursting pattern in cells of the thalamus in a paraplegic patient who had a full break of the spinal cord just below the neck but nonetheless suffered pain in the lower half of his body. The overactive cells, it turned out, also responded to touches of the head and neck, even though the cells were in the area of the thalamus that normally responds only to stimulation of the body below the level of the cut. This finding suggested that neural inhibition was lifted on the flow of signals across existing but previously unused synapses in sensory neurons projecting to the thalamus from the head and neck.

Such changes in the somatosensory thalamus or cortex could help explain why certain feelings arise in limbs that no longer exist or can no longer transmit signals to the brain. Nevertheless, alterations in this system cannot by themselves account for phantoms and their pain. If this explanation were sufficient, removal of the affected parts of the somatosensory cortex or thalamus would solve both problems.

Clearly, the source of phantom limbs is more complex than any of these theories would suggest. No other hypotheses have been proposed, however. As an outgrowth of my interest in the brain mechanisms that give rise to pain, I have pondered the causes of phantoms and phantom-limb pain and studied patients with these problems for many years.

My work and that of others have led me to conclude that, to a great extent, phantom limbs originate in the brain, as the work of Lenz would suggest. But much more of the cerebrum than the somatosensory system is involved.

Any explanation must account for the rich variety of sensations a person can feel, the intense reality of the phantom and the conviction that even free-floating phantoms belong to the self. I have proposed such a model. It has been well received, but it must, of course, be tested more fully before its value can be assessed completely. Meanwhile, though, it has already generated new ideas for research into stopping the

pain that arises from phantom limbs.

In essence, I postulate that the brain contains a neuromatrix, or network of neurons, that, in addition to responding to sensory stimulation, continuously generates a characteristic pattern of impulses indicating that the body is intact and unequivocally one's own. I call this pattern a neurosignature. If such a matrix operated in the absence of sensory inputs from the periphery of the body, it would create the impression of having a limb even when that limb has been removed.

To produce all the qualities I have described for phantoms, the matrix would have to be quite extensive, including at least three major neural circuits in the brain. One of them, of course, is the classical sensory pathway passing through the thalamus to the somatosensory cortex.

A second system must consist of the pathways leading through the reticular formation of the brain stem to the limbic system, which is critical for emotion and motivation. I include this circuit in part because I and others have noted that paraplegics who suffer a complete spinal break high in the upper body continue to experience themselves as still being in their old body, and they describe the feelings in the denervated areas with the same kinds of affective terms as they did before they were injured, such as "painful," "pleasurable" or "exhausting."

A final system consists of cortical regions important to recognition of the self and to the evaluation of sensory signals. A major part of this system is the parietal lobe, which in studies of brain-damaged patients has been shown to be essential to the sense of self.

Indeed, patients who have suffered a lesion of the parietal lobe in one hemisphere have been known to push one of their own legs out of a hospital bed because they were convinced it belonged to a stranger. Such behavior shows that the damaged area normally imparts a signal that says, "This is my body; it is a part of my self."

I believe that when sensory signals from the periphery or elsewhere reach the brain, they pass through each of these systems in parallel. As the signals are analyzed, information about them is shared among the three systems and converted into an integrated output, which is sent to other parts of the brain. Somewhere in the brain the output is transformed into a conscious perception, although no one knows exactly where the transformation that leads to awareness takes place.

As dynamic as this description may seem, the processing is probably still more dynamic than that. I further propose that as the matrix analyzes sensory information, it imprints its characteristic neurosignature on the output. Thus, the output carries information about sensory input as well as the assurance that the sensation is occurring in one's own body. The neurosignature may be likened to the basic theme of an orchestral piece. The collective sound changes when different instru-

Phantom Seeing and Hearing

Phantom seeing and hearing, like phantom limbs, are also generated by the brain in the absence of sensory input. People whose vision has been impaired by cataracts or by the loss of a portion of the visual processing system in the brain sometimes report highly detailed visual experiences. This syndrome was first described in 1769, when the philosopher Charles Bonnet wrote an article on the remarkable visual experiences of his grandfather, Charles Lullin, who had lost most of his vision because of cataracts but was otherwise in good physical and psychological health. Since then, many mentally sound individuals have reported similarly vivid phantom visual experiences.

Phantom seeing often coexists with a limited amount of normal vision. The person experiencing the phantom has no difficulty in differentiating between the two kinds of vision. Phantom visual episodes appear suddenly and unexpectedly when the eyes are open. People usually describe the visual phantoms as seeming real despite the obvious impossibility of their existence. Common phantom images include people and large buildings. Rarer perceptions include miniature people and small animals. Phantom sights are not mere memories of earlier experiences; they often contain events, places or people that have never before been encountered.

First appearances of phantom images can be quite startling. A woman in one of our studies who had lost much of her vision because of retinal degeneration reported being shocked when she looked out a window and saw a tall building in what she knew to be a wooded field. Even though she realized that the building was a phantom, it seemed so real that she could count its steps and describe its other details. The building soon disappeared, only to return several hours later. The phantom vision continues to come and go unexpectedly, she told my student Geoffrey Schultz.

Phantom seeing occurs most among the elderly, presumably because vision tends to deteriorate with age. Some 15 percent of the people who lose all or part of their vision report phantom visual experiences. The proportion may be higher because some people avoid discussing phantom vision for fear of being labeled as psychologically disturbed.

Phantom sounds are also extremely common, although few people recognize them for what they are. People who lose their hearing commonly report noises in their heads. These noises, called tinnitus, are said to sound like whistling, clanging, screeching or the roaring of a train. They can be so loud and unpleasant that the victim needs help to cope with the distress they cause.

Some people with tinnitus report hearing "formed sounds," such as music or voices. A woman who had been a musician before losing her hearing says she "hears" piano concertos and sonatas. The impression is so real that at first she thought the sounds were coming from a neighbor's radio. The woman reports that she cannot turn off the music and that it often gets louder at night when she wants to go to sleep. Another woman, who had lost much of her sight and hearing, experienced both phantom sight and sound. In one instance, she delightedly described seeing a circus and hearing the music that accompanied the acts.

Phantom sights and sounds, like phantom limbs, occur when the brain loses its normal input from a sensory system. In the absence of input, cells in the central nervous system become more active. The brain's intrinsic mechanisms transform that neuronal activity into meaningful experiences.

ments play their parts (the input), but the product is continually shaped by the underlying theme (the neurosignature), which provides the continuity for the work, even as the details of its rendition change.

The specific neurosignature of an individual would be determined by the pattern of connectivity among neurons in the matrix—that is, by such factors as which neurons are connected to one another and by the number, types and strengths of the synapses. Readers familiar with neuroscience will note that my conception of the neuromatrix has similarities to the notion of the cell assembly proposed long ago by Donald O. Hebb of McGill University. Hebb argued that when sensory input activates two brain cells simultaneously, synapses between the cells form stronger connections. Eventually the process gives rise to whole assemblies of linked neurons, so that a signal going into one part of an assembly spreads through the rest, even if the assembly extends across broad areas of the brain.

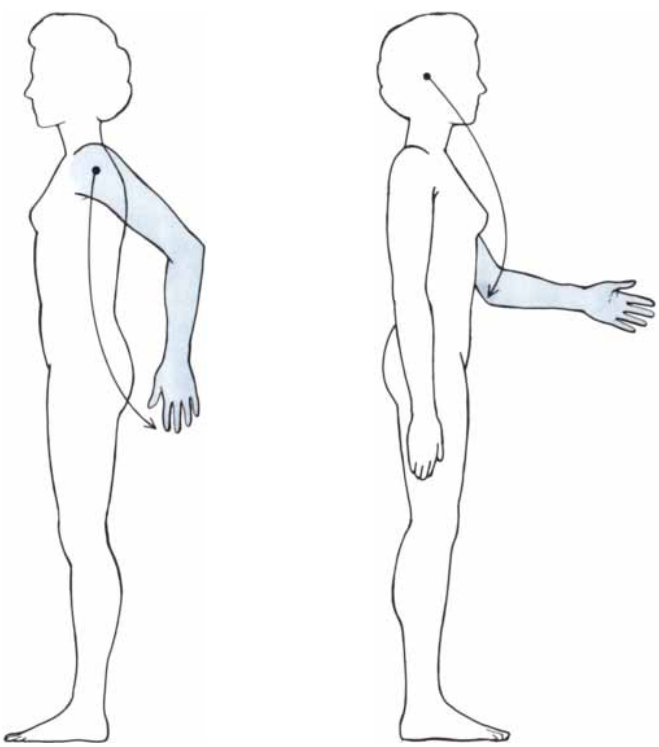
I depart from Hebb, however, in that I visualize the neuromatrix as an assembly whose connections are primarily determined not by experience but by the genes. The matrix, though, could later be sculpted by experience, which would add or delete, strengthen or weaken, existing synapses. For instance, experience would enable the matrix to store the memory of a pain from a gangrenous ulcer and might thus account for the frequent reappearance of the same pain in phantom limbs.

I think the matrix is largely prewired, for the simple reason that my colleagues and I have encountered many people who were born without an arm or a leg and yet experience a vivid phantom. For example, an intelligent and serious eight-year-old boy, who was born with paralyzed legs and a right arm that ends at the elbow, tells us that when he fits his elbow into a small cup so as to manipulate a lever that allows him to move his wheelchair, phantom fingers, "like everyone else's fingers," emerge from his elbow and grasp the edges of the cup. Phantoms such as these may persist into adulthood: a 32-year-old engineer who was born without a leg below the knee reports that his phantom leg and foot remain vivid but vanish for several hours once or twice a week. He is always astonished and delighted when they return.

Parenthetically, I should note that the long-held belief that phantoms are experienced only when an amputation has occurred after the age of six or seven is not true. My postdoctoral student Renée Lacroix and I have confirmed earlier reports that children who lose a limb when they are as young as one or two years old can have phantom limbs. We have also encountered children who have painful phantoms of legs lost before age two.

Under normal circumstances, then, the myriad qualities of sensation people experience emerge from variations in sensory input. This input is both analyzed and shaped into complex experiences of sensation and self by the largely prewired neuromatrix. Yet even in the absence of external stimuli, much the same range of experiences can be generated by other signals passing through the neuromatrix—such as those produced by the spontaneous firing of neurons in the matrix itself or the spinal cord or produced by neuromas. Regardless of the source of the input to the matrix, the result would be the same: rapid spread of the signals throughout the matrix and perception of a limb located within a unitary self, even when the actual limb is gone.

The fading of phantom limbs and their pain, which sometimes occurs over time, would be explained if cerebral neurons that once responded to lost or paralyzed limbs develop increasingly strong connections with still sensate parts of the body and then begin to serve those regions. In the process the neurosignature pattern would change, resulting in changes in the phantom and the pain. But phantoms do not usually disappear forever. In fact, they may return decades after they seem to have gone, which indicates that the neuromatrix, even when modified, retains many of its features permanently.



REFERRED SENSATIONS in a painful phantom arm were reported by a woman receiving electrical stimuli at two different places (*dots*). Stimulation at the stump gave the sensation of electric shocks that jumped from finger to finger. Stimulation on the right ear made the phantom elbow feel warm and caused a pulsing sensation that traveled down the phantom wrist and thumb. The observations were made by Joel Katz, now at the University of Toronto, and the author.

My students Anthony L. Vaccarino, John E. McKenna and Terence J. Coderre and I have already gathered some direct evidence supporting my suggestion that the brain—and by implication, the neuromatrix—can generate sensation on its own. Our studies relied on what is called the formalin pain test.

We injected a dilute solution of formalin (formaldehyde dissolved in water) under the skin of a rat's paw, which produces pain that rapidly rises and falls in intensity during the first five minutes after the injection. (The degree and duration of discomfort are assessed by such behaviors as licking the paw.) This "early" response is followed by "late" pain, which begins about 15 minutes after the injection and persists for about an hour.

By means of this test, we found that an anesthetic block of the paw completely obliterates the late pain, but only if the anesthetic is delivered in time to prevent the early response. Once the early pain occurs, the drug only partly reduces the later response. This observation of pain continuing even after the nerves carrying pain signals are blocked implies that long-lasting pain (such as that in phantoms) is determined not only by sensory stimulation during the discomfort but also by brain processes that persist without continual priming.

But what exactly causes the pain in phantom limbs? The most common complaint is a burning sensation. This feeling could stem from the loss of sensory signaling from the limb to the neuromatrix. Without its usual sensory stimulation, the neuromatrix would probably produce high levels of activity in a bursting pattern, such as Lenz observed in the thalamus. This kind of signal may very well be transformed into an awareness of burning.

Other pain may result from the effort of the neuromatrix to make the limbs move as they normally would. When the limbs do not respond in amputees and paraplegics, the neuromatrix (which would be prewired to "assume" the limbs can indeed move) may issue more frequent and stronger messages urging the muscles to move the limb. These outputs may be perceived as cramping. Similar output messages might also be felt as shooting pain.

Research to test some of these ideas and explore new ways of eliminating pain is still in its infancy, but some intriguing results are beginning to emerge. The need for such treatments is urgent, both because the suffering can be severe and persistent and because, sadly, few existing methods are permanently effective.

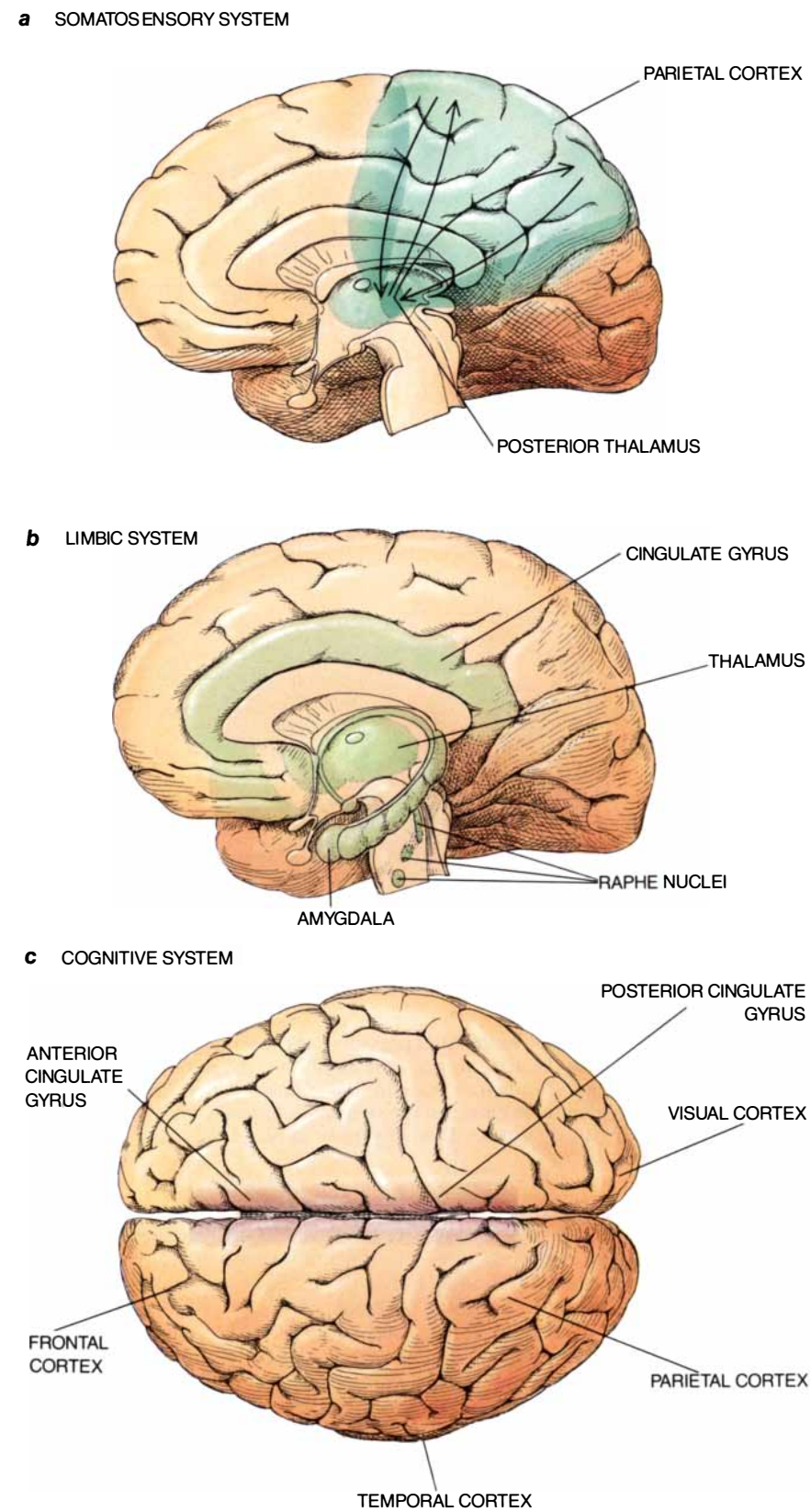
At the moment, a number of different therapies are used. Stimulation of the stump with electric currents, a vibrator or acupuncture helps some amputees. Relaxation and hypnosis aid others. Some individuals obtain considerable relief from drugs that are usually given to counteract epilepsy or depression, and other patients find their pain is eased by a combination of an antidepressant and a narcotic (such as methadone). But about half of those with persistent, long-term phantom pain fail to respond to any approach.

On a more promising note, an experimental treatment called the DREZ (dorsal root entry zone) procedure selectively abolishes phantom-limb pain, but not the phantoms themselves, in about 60 percent of the patients treated. In this method, developed by Blaine S. Nashold of Duke University, neurosurgeons destroy the spinal cells that receive input directly from the sensory nerves of the stump, specifically eliminating the cells at the site where the sensory roots enter the spinal cord. (Past efforts at dampening the somatosensory projection system generally cut the sensory roots or the transmission pathways in the spinal cord.) The DREZ procedure is so new that no one yet knows how long the relief persists.

REAL ARM made insensate by an inflated pressure cuff resembles a phantom arm. The subject could not see the arm, because the table was covered by a black cloth. The positions of the hand felt before the cuff was inflated and at intervals thereafter, as the hand seemed to be closer to the body, are shown. This study was carried out with Yigal Gross, now at Bar-Ilan University in Israel.

Because my model of brain functioning posits that the neuromatrix as a whole may contribute to pain, the model also suggests that altering the activity of pathways outside the somatosensory system might be important, either alone or in combination with other treatments. One place to begin work is the limbic system. Until now, limbic structures have been relegated to a secondary role in efforts to treat pain, because injurious stimuli do not activate them directly. Nevertheless, if the limbic system contributes to output by the neuromatrix, as I have proposed, it might well contribute to the pain felt in phantom limbs.

Vaccarino, McKenna, Coderre and I have begun to test the value of manipulating the limbic system as a way of easing pain. We have shown that localized injection of lidocaine (a relative of cocaine that prevents neurons from transmitting signals) into diverse areas of the limbic system produces striking decreases in several types of experimen-



SOURCE OF PHANTOM LIMBS is thought by the author to involve activity in three of the brain's neural circuits. One of them (*a*) is the somatosensory receiving areas and the adjacent parietal cortex, which process information related to the body. The second area (*b*) is the limbic system, which is concerned with emotion and motivation. The third (*c*) encompasses the widespread cortical networks involved in cognitive activities, among them the memory of past experience and the evaluation of sensory inputs in relation to the self.

tally produced pain in rats, including a model of phantom-limb pain. A similar approach could be feasible in humans but needs more study.

The phenomenon of phantom limbs is more than a challenge to medical management. It raises doubts about some fundamental assumptions in psychology. One such assumption is that sensations are produced only by stimuli and that perceptions in the absence of stimuli are psychologically abnormal. Yet phantom limbs, as well as phantom seeing and hearing, indicate this notion is wrong. The brain does more than detect and analyze inputs; it generates perceptual experience even when no external inputs occur. We do not need a body to feel a body.

Another entrenched assumption is that perception of one's body results from sensory inputs that leave a memory in the brain; the total of these signals becomes the body image. But the existence of phantoms in people born without a limb or who have lost a limb at an early age suggests that the neural networks for perceiving the body and its parts are built into the brain. The absence of inputs does not stop the networks from generating messages about missing body parts; they continue to produce such messages throughout life.

In short, phantom limbs are a mystery only if we assume the body sends sensory messages to a passively receiving brain. Phantoms become comprehensible once we recognize that the brain generates the experience of the body. Sensory inputs merely modulate that experience; they do not directly cause it.

FURTHER READING

BODY IMAGE: DISSOCIATION OF REAL AND PERCEIVED LIMBS BY PRESSURE-CUFF ISCHEMIA. Y. Gross and R. Melzack in *Experimental Neurology,* Vol. 61, No. 3, pages 680–688; September 15, 1978.

PHANTOM LIMBS, THE SELF AND THE BRAIN: THE D. O. HEBB MEMORIAL LECTURE. R. Melzack in *Canadian Psychology,* Vol. 30, No. 1, pages 1–16; January 1989.

CENTRAL NERVOUS SYSTEM PLASTICITY IN THE TONIC PAIN RESPONSE TO SUBCUTANEOUS FORMALIN INJECTION. T. J. Coderre, A. L. Vaccarino and R. Melzack in *Brain Research,* Vol. 535, No. 1, pages 155–158; December 3, 1990.

PAIN "MEMORIES" IN PHANTOM LIMBS: REVIEW AND CLINICAL OBSERVATIONS. J. Katz and R. Melzack in *Pain,* Vol. 43, No. 3, pages 319–336; December 1990.

THE ROLE OF THE CINGULUM BUNDLE IN SELF-MUTILATION FOLLOWING PERIPHERAL NEURECTOMY IN THE RAT. A. L. Vaccarino and R. Melzack in *Experimental Neurology,* Vol. 111, No. 1, pages 131–134; January 1991.

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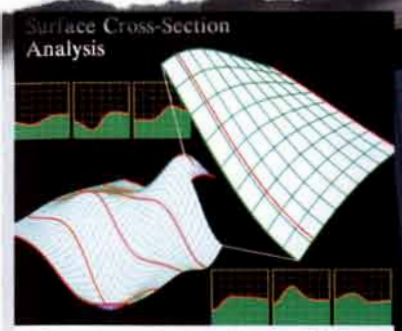

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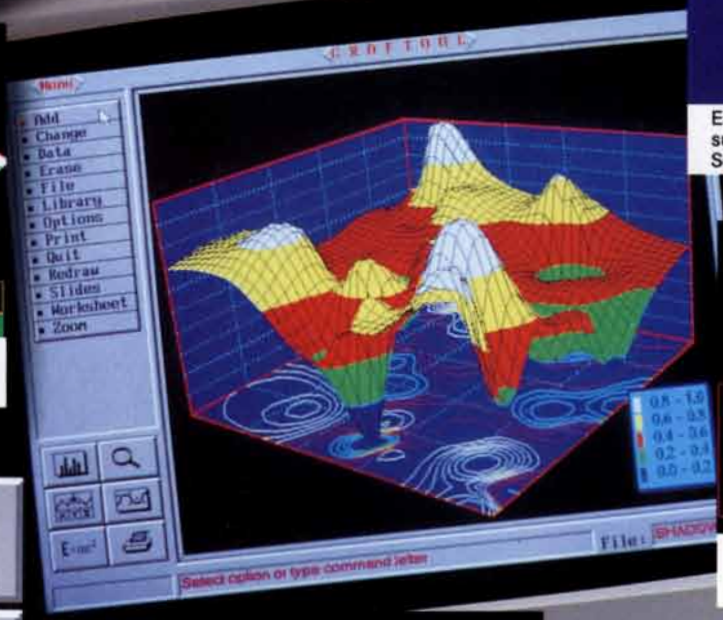

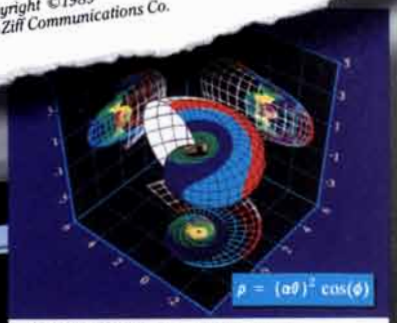

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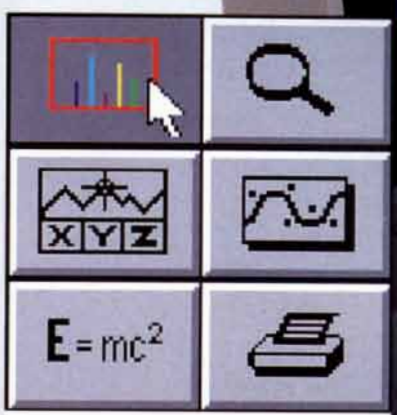

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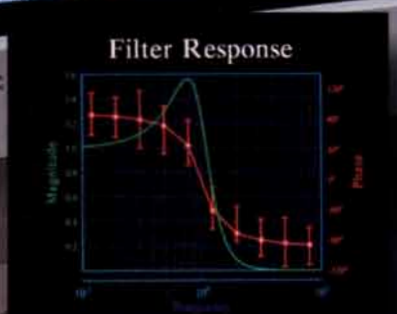

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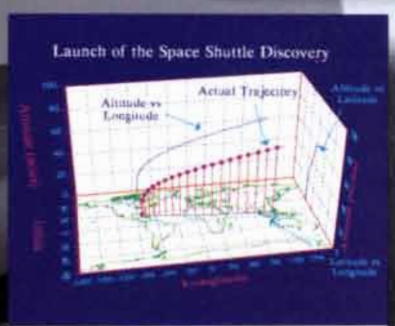

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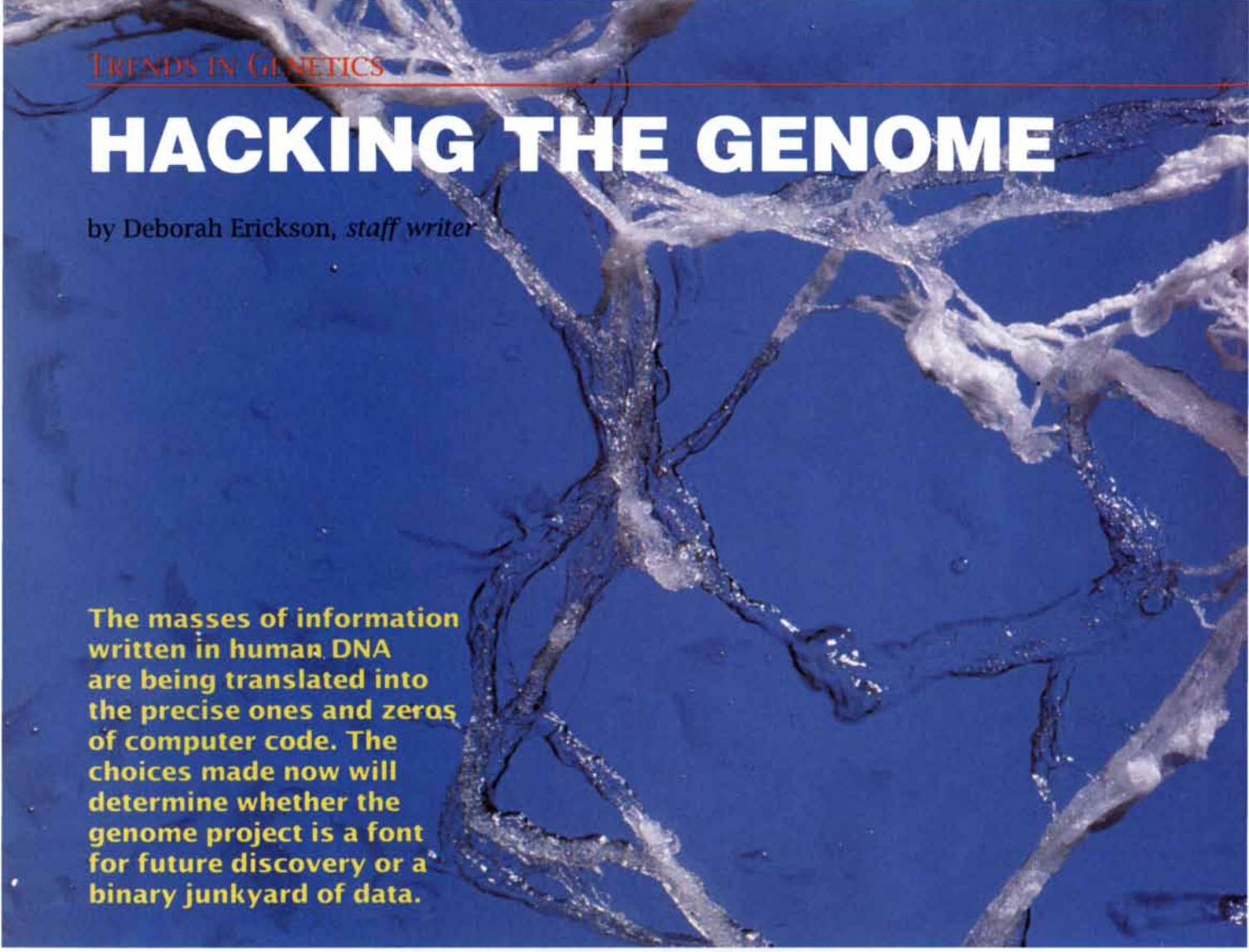
HACKING THE GENOME

by Deborah Erickson, *staff writer*



The masses of information written in human DNA are being translated into the precise ones and zeros of computer code. The choices made now will determine whether the genome project is a font for future discovery or a binary junkyard of data.

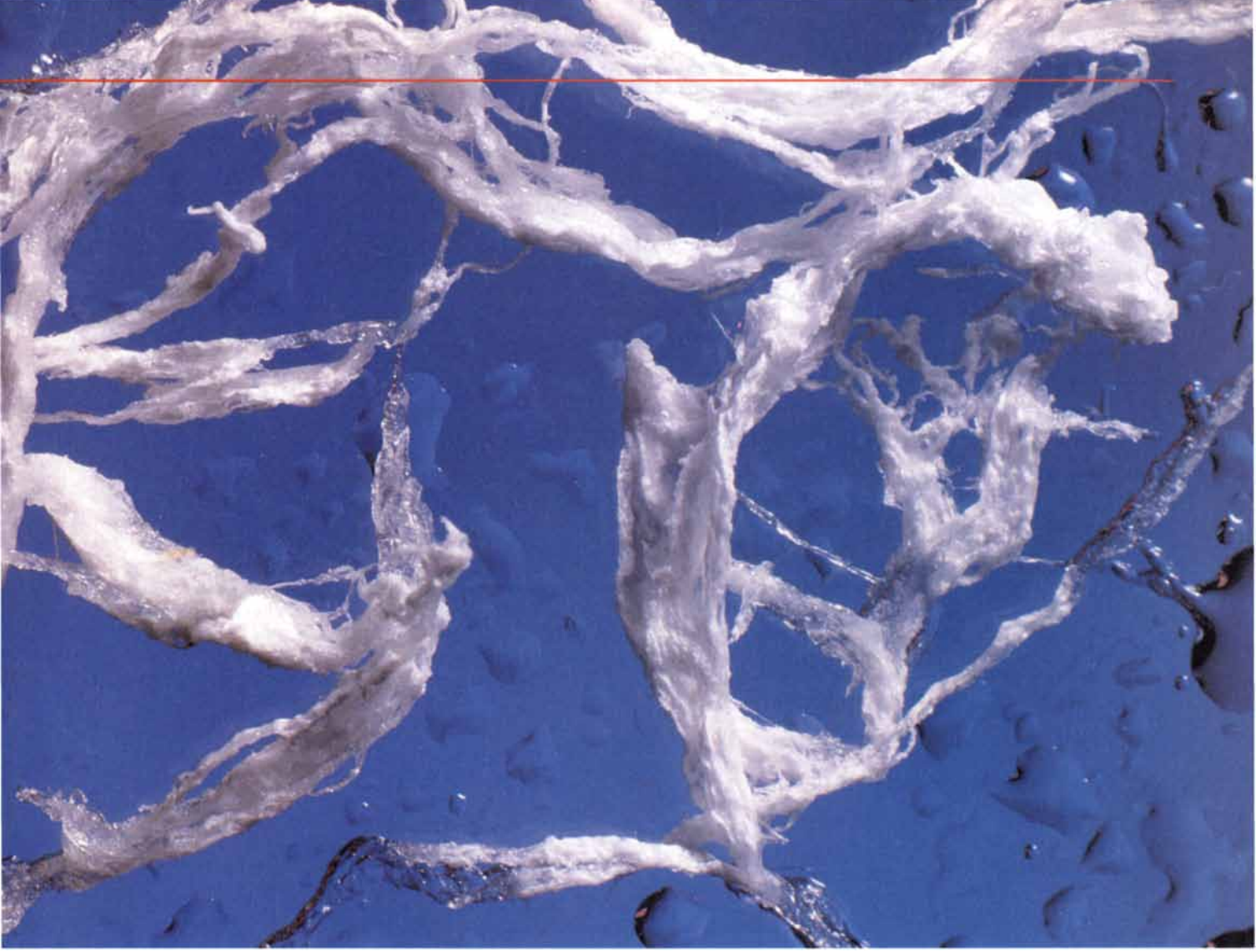
The human genome, the totality of genetic information encoded in the coiled DNA of the chromosomes, is an immense document. Written in a language with only four letters—G, C, A, T—for the nucleic acid bases guanine, cytosine, adenine and thymine, the genome fits comfortably into the nucleus of all living cells. But were the genome published in book form, it would take a third of a lifetime to read through the estimated three billion nucleotides.

Such a tome's description of a human being would contain between 50,000 to 100,000 genes. Perhaps 5,000 of these have been partially deciphered so far. By 2005 the researchers participating in the ambitious endeavor known as the Human Genome Project hope to have parsed the rest. Genes will be but some 2 percent of the entire document they plan to transcribe. This year the lead agencies in the effort, the National Institutes of Health and the Department of Energy, will spend approximately $160 million on the genome. The research groups that they and other agencies, such as the National Science Foundation, support have generated over 70 million nucleotides to date. The quantities of accumulated sequences are doubling every two years.

Yet that vast amount of information could turn out to be as mute as the Sphinx, unless it can be accessed, integrated, queried, interpreted, visualized, tested and studied. The task of making the data useful falls to a group of researchers whose job is described as providing the "informatics" of the project. Their function, which may turn out to be the linchpin of the entire $3-billion effort, is to join the clean, precise realm of computer science to the fluid, changing world of biology. It is these workers who will decide how the output of the genome project will be made available to other researchers and what methods should be followed in building the software to store and manage the data.

As in querying an oracle, the clarity of the answers will depend on asking the right questions. Decisions made now will determine the kinds of questions researchers can ask in five or 10 years. "Informatics will be a lot more than frosting on the genome project—it will be most of the cake," says Charles Cantor, principal scientist for the Department of Energy's genome project.

The luxury of time is not affordable. Already the flood of data pouring out of laboratories promises to become a torrent. The effort to decode the human chromosomes is well under way by teams and individual scientists at many laboratories. At the moment, most of the Energy Department's funding is channeled to genome centers at three national laboratories: Lawrence Livermore, Lawrence Berkeley and Los Alamos. Meanwhile the NIH supports seven academic centers at universities, such as Washington University and the Whitehead Institute at the Massachusetts Institute of Technology.



Each center has the primary responsibility for a major piece of the overall project, for example, mapping a single chromosome or group of chromosomes. The NIH also administers some 150 other grants to individual researchers who are mapping or sequencing on a smaller scale, looking for new kinds of genetic markers for specific genes or building hardware for automated sequencing.

These investigators are working toward the project's near-term goal of creating so-called genetic and physical maps of each chromosome. Genetic maps will reveal the approximate positions of genes coding for various phenotypic traits. These maps will also be punctuated with "markers" spaced at convenient distances, perhaps every 100,000 bases on average. These reference points help scientists follow genes through family trees, enabling them to see how often genes such as those involved in disease appear near which markers.

Physical maps, on the other hand, are something like patchwork quilts, ordered collections of small DNA fragments from a chromosome, each of which can be cloned, or made to reproduce itself indefinitely. The fragments are then stitched together to cover the original chromosome. In time, the pieces and their overlaps will be used to construct a third type of map—a complete sequence map of the bases G, C, A, T. This ultimate resolution view of the chromosomes is a long-term goal of the project but will not be feasible until technology improves dramatically, perhaps after 10 years.

As if collecting the human data were not daunting enough, the project also includes sequencing the genomes of experimental organisms such as the bacterium *Escherichia coli,* yeast, fruit flies, mice and worms. Data about the genetic makeup of these species will provide close-up information for researchers in those particular fields, but more important, they will open avenues of investigation into the often striking similarity, or homology, between species.

The *ubx,* or ultrabithorax locus, for instance, contains a cluster of genes involved in defining how the body plan of the fruit fly *Drosophila* develops. A closely related group of genes controls the organization of the human and mouse nervous systems during embryonic development. Experimental organisms offer the added benefit of allowing hypotheses about gene function to be tested by inducing genetic deletions and mutations that would be unethical and impossible to do in humans. Cross-species "aha!"s promise to become much more common as the genome project advances, but only if the groups generating the information can render it meaningful and accessible to distant researchers using disparate computers.

The task of entering all that information into computers and assuring its accessibility falls to workers on the informatics side of the genome project, who sometimes describe

themselves as "split-brains" and "oddballs." Not necessarily trained formally either as biologists or as computer scientists, their backgrounds are as diverse as theoretical physics and zoology. "We don't fit in anywhere," says Chris Rawlings, chief of informatics at the Imperial Cancer Research Fund in Great Britain. Timothy Hunkapillar, director of computation at the NSF's Center for Molecular Biology at the California Institute of Technology, adds: "You don't talk about this stuff at a general biology meeting; they'd think you were crazy."

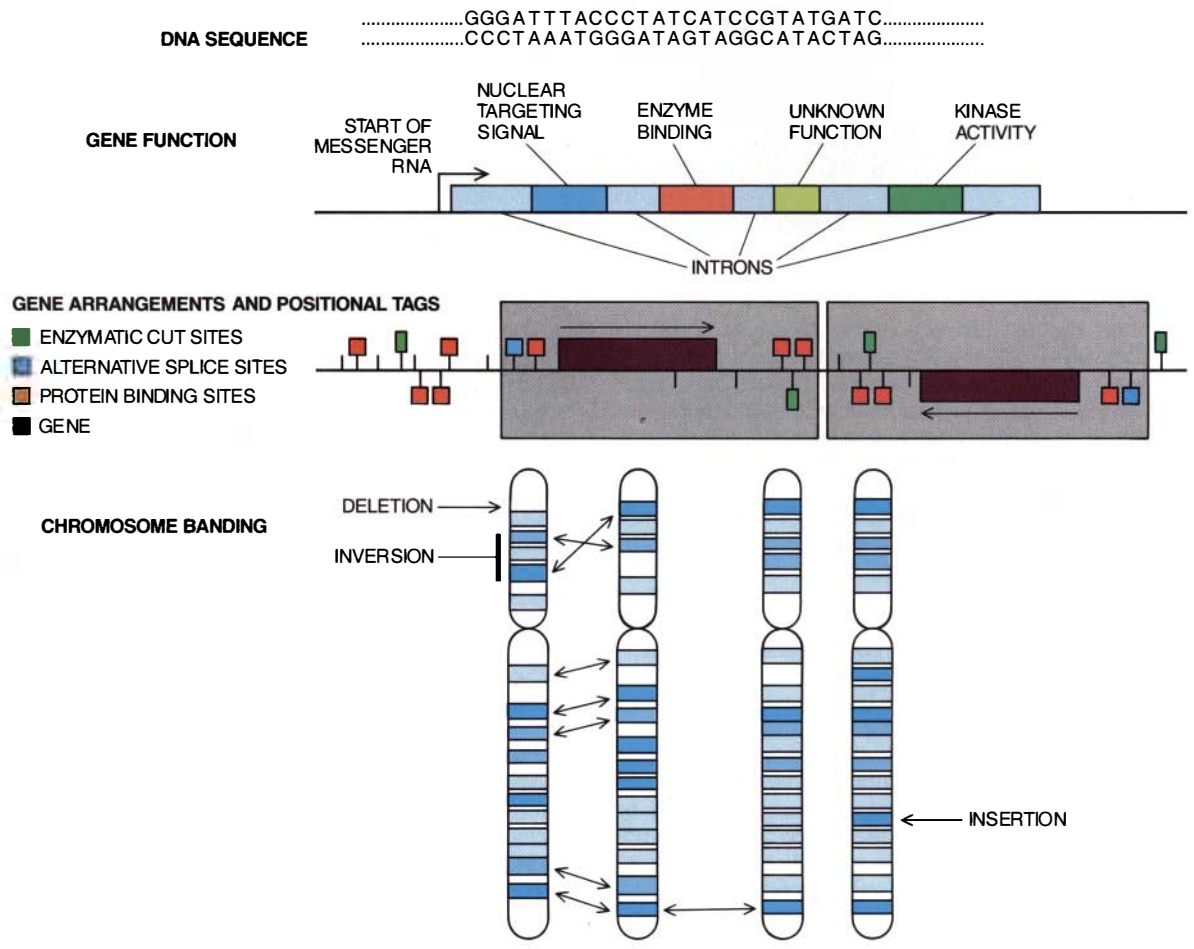
The term "informatics" is meant to describe every kind of support activity that might come from a computer to help the genome project, from data management and processing to DNA sequence analysis and the construction of different kinds of genetic maps. Laboratories may need to spend as much as 30 percent of their total budgets on informatics, some experts predict.

For now, the most important challenge to the informatics groups is designing and managing the diverse computer data bases in which the human genome will be stored. What data models should be used? Should access be through preordained query paths or through more time-consuming but flexible inquiry protocols? Should direct access across electronic networks be provided? "Everyone would like a data base that works like an excellent graduate student," says Chris Fields, a computational biologist at the National Institute of Neurological Disorders and Stroke. "You tell it, 'I have a hunch, can you go find out if I'm right?' But no one knows how to ask for that from a computer."

Looking for Motifs in Chromosomes

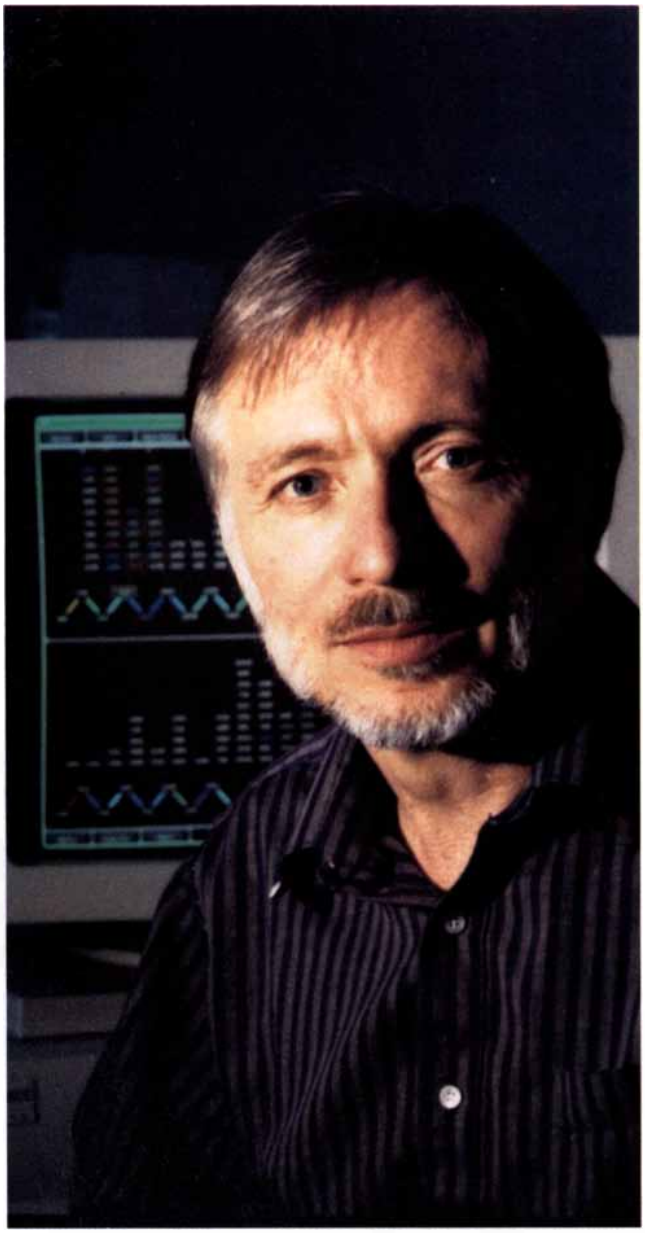
Why don't you try looking at it from a different perspective?" This bit of wisdom is often easier said than done—especially when one is looking at chromosomes. The vast strings of nucleotides that spell out DNA quickly boggle human eyes. So scientists are teaching computers to see through the complexities. Software programs like the one designed by collaborators from the Department of Energy and the National Institutes of Health recognize detailed sequences of DNA and translate them into symbols more readily perceived by the human brain.

Patterns emerge when genes are displayed with positional tags, such as protein or enzyme binding sites, that bracket them on the chromosome. The gene arrangements in the gray shaded boxes below, for instance, may be ancestrally related. The mirror images could be the result of an evolutionary flip of a DNA fragment or of a retroviral invasion of the chromosome. Similarly, chromosome banding—a way of painting chromosomes with characteristic patterns—can reveal how segments of the genetic material are arranged. Comparing chromosomes prepared this way yields clues to disease by exposing inversions, deletions, insertions and massive rearrangements.



Even deciding what to put in the computer is difficult. Biologists are accustomed to storing relatively small amounts of data in notebooks with cryptic scribbles in margins; a coffee stain may be a tag for a really important page. Computers, on the other hand, are linear, rigid and therefore intolerant of quirks and foibles in notation. Data-base builders find themselves further challenged with the assembly of many types of rapidly changing data from sources that are themselves changing—often without really understanding what they are gathering or what scientists will eventually want to do with the material.

Because different scientists want different kinds of information, various data bases are being spawned. A molecular biologist studying lung cancer, for instance, might want to examine a small region of a chromosome to look for genes that possess certain cancer-related structures. Others might be more interested in the experimental methods used to locate and sequence those genes. "To assume that we can anticipate now what people will want to see is just wrong," says Elbert Branscomb, the informatics leader at Lawrence Livermore National Laboratory. "Individual efforts are moving far too fast."



ELBERT BRANSCOMB, the informatics leader at Lawrence Livermore National Laboratory, thinks data bases should be fully and directly accessible across electronic networks. "The old ways are dying, and the sooner the better," he says.

For this reason, Branscomb's laboratory favors keeping as many data as possible, even if they are preliminary. Livermore's data base, currently dedicated to chromosome 19, is detailed, constantly updated—and known to contain errors. This fast and loose approach, Branscomb says, is acceptable because the entire contents of the data base are intended for active research "as is," within the laboratory itself and by groups of research collaborators who understand its uncertainties. Livermore has structured the data base so that anyone anywhere can peruse its contents, if they can live with the collection's fluid character.

Other systems are intended to function as central archives that present very clean, high-confidence data in a standardized, easy-to-follow format. One example is the human gene mapping data base, called simply GDB, at Johns Hopkins University. It will also cross-reference the contents of other data bases, including Genbank, the U.S. repository of author-submitted DNA and amino acid sequences from 3,000 species. Robert J. Robbins, one of the leaders of the Johns Hopkins effort, sees GDB primarily as a vehicle for rushing new information to waiting researchers. As an example of its prowess, he cites a conference attended last August by 600 or 700 researchers: the meeting concluded on a Friday, and by Tuesday the presentations were all up on GDB.

Some data bases are very specialized, recording, for instance, each occurrence of a particular genetic feature, such as the so-called zinc finger genes. The metal-containing proteins that these genes code for play an important role in controlling the expression of other genes. Still other systems, such as the interactive data base shared by a close-knit group of researchers studying the genetics of the nematode *Caenorhabditis elegans,* are designed for browsing. Users will not only ask specific questions but can also graphically wander around, looking at their colleagues' doings as they seek flashes of inspiration.

To the scientists at Livermore and many other research groups, the key to widespread use is flexibility. Therefore, they have chosen to store their findings in relational data bases originally designed for financial and business applications. The approach allows a logical unification of physically separate and conceptually independent data sets, which can then be shared in full detail across electronic networks, without repackaging.

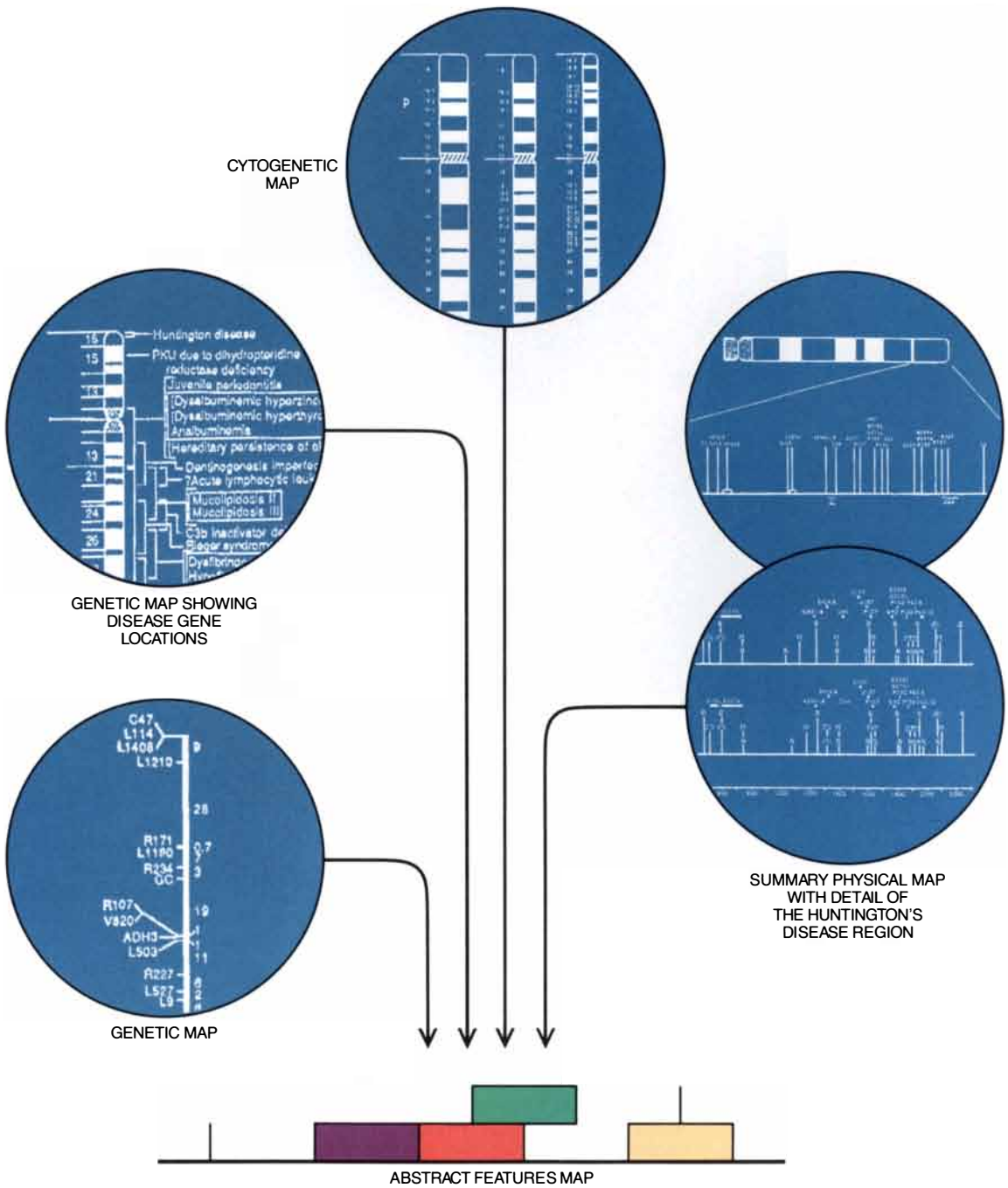
Relational models store data in tables of rows and columns that function like drawers; as the data are stored, their relation to data in other drawers is noted. For example, a DNA sequence can be connected to any number of different items, such as methods used to achieve the experimental results, sources of material, or the location of a sequence on a chromosome and whether it contains a gene. The Principle of Sufficient Ignorance shaped Livermore's data base, recalls computer scientist Tom Slezak with a laugh: "I have no idea what they'll want to do with this stuff in five years—nobody does—so I made it as flexible as possible. To me, parts is parts."

But as relational data bases accumulate more data, each bit of which must be stored in a separate drawer, the rows and the connections between drawers multiply. So other groups are exploring newer approaches that may be simpler to construct and more pow-

Visualizing the Genome as a Collection of Objects

By design and intent, scientific experiments are always asking questions in new ways. Sometimes the answers that return do not fit a researcher's mental constructs. Consequently, the data fit no better into computer data bases hard-wired to store only certain kinds of results in predetermined formats. Computer scientists such as Nathan Goodman of the Whitehead Institute at M.I.T. believe new styles of data bases may simplify the inevitable retooling process and so help data storage systems keep pace with changing views of biology.

The key is classifying data as "objects" that share explicit abstractions, such as size, order and position. The many kinds of maps being generated by the Human Genome Project can all be seen as the same kind of object, Goodman points out, no matter what they actually portray. All maps consist of abstract features that have size (big or small) and position within that context. It is possible to compute the distance between a pair of features, in order to determine their relative order (which may be above, below, contained and so on) and the next neighbor of a feature in a given direction. In a cytogenetic map, such as the portion of chromosome 4 shown here, positions are bands along the chromosome. In the physical map, positions are expressed in kilobases.



erful to use, such as object-oriented data bases. These systems fit data into classes of objects defined by their common abstractions, which include the connections to other objects and the things that can be done to objects of this type. New data can be described as a variation on a theme already accounted for. Objects might make it easier to reflect changing views of scientific information.

Still other informatics investigators contend that standardizing the way data are stored will prove the most useful and economical method. David J. Lipman, director of the National Center for Biotechnology Information (NCBI), is one of the main proponents of this approach. It has worked well since NCBI was founded as part of the National Library of Medicine in 1988. Lipman's group has linked DNA sequences, protein sequences and literature citations from many scientific publications and written a series of questions that enables users to obtain data joined by those links. Researchers can, for example, ask for listings of all the papers published about a specific sequence. Or they can ask for data about the protein encoded by a particular gene.

Eventually, Lipman hopes, NCBI's current offerings will be just the beginning of a far more extensive "GenInfo" data base he would like to see distributed on CD-ROM disks every two months. Researchers who have very limited computer facilities or do not want the bother of being connected to wide-area networks could use the data. "We want to store genetic maps, physical maps, three-dimensional structures of proteins—as much as we can get," he declares.

DAVID LIPMAN, head of the National Center for Biotechnology Information, is integrating genetic data and predetermined menus of questions into powerful retrieval systems distributed on CD-ROM disks.

Much more information is already on the way. In October, NCBI will begin assuming responsibility for Genbank, which is compiled at Los Alamos National Laboratory. The Protein Information Resource (PIR), built by the National Biological Research Foundation in Washington, D.C., has agreed to share its files within a year, as have the two overseas public data bases: the European Molecular Biology Laboratory and the DNA Data Bank of Japan.

The key to NCBI's scheme is a data description language called Abstract Syntax Notation 1 (ASN-1). Nothing will be stored in the data base unless it is first translated into this language, which determines the way the data are exchanged between "agents," such as users, computer programs and so on. It is as though pieces of data are put together into suitcases that the computer can recognize and move to the appropriate place—green suitcases going here, blue ones there—without the contents being known. "We're deliberately making the data standardized to encourage commercial involvement," Lipman asserts.

To that end, NCBI recently put out a call for proposals to create value-added overlays to the main data base that might be of particular use to, say, immunologists or other types of clinicians. "Hitachi was all over this idea" at a recent conference on computational biology, Lipman says. "They wanted to send a team of their computer guys over right away to see what we're doing. If U.S. companies don't get involved, this could be another opportunity lost."

But the idea of requiring a fixed description language for all important data rankles some researchers and other data-base builders who argue that it compromises needed flexibility in manipulating raw data in new ways, and is impractical for most data being produced in the genome project. "The genome business is too fluid, too protean, to agree on description languages now," insists Branscomb of Lawrence Livermore. "It's Stalinistic to force everyone to see the data the same way."

Instead Livermore and others rely on the standard query language (SQL) for addressing relational data bases. The SQL lets scientists design whatever questions they like, so they can venture far beyond predetermined lines of inquiry—even into Livermore's raw data if they desire. Branscomb asserts they most certainly will. "Any serious researcher of any question needs to get quickly at data not yet in centralized data bases," he says. "They need to get into the nitty-gritty, to the numbers that estimate reliability; they need every last hair and follicle for the same reason that it's worth getting."

At a conference last fall, Branscomb and Slezak demonstrated how SQL enables on-line, real-time data retrieval through computer networks such as Internet, administered by the NSF. From a hotel auditorium in San Diego, they used computer workstations to connect three independent data bases across the country and simultaneously fetch information from each.

The researchers instantly had a multilevel snapshot of everything known about a chromosome region associated with muscular dystrophy. Not only could they examine the markers and their sequences, they could see detailed physical mapping information for the region. In early February of this year, Livermore researchers and four teams of international collaborators announced they had found the genetic defect for myotonic dystrophy, the most common form of the disease: an unusual gene mutates progressively as it is passed through generations.

"There is a substantial alternative to

Happily, there is nothing at all

Up with the dawn on what appears at first as a flight of fancy. And our spirits soar.

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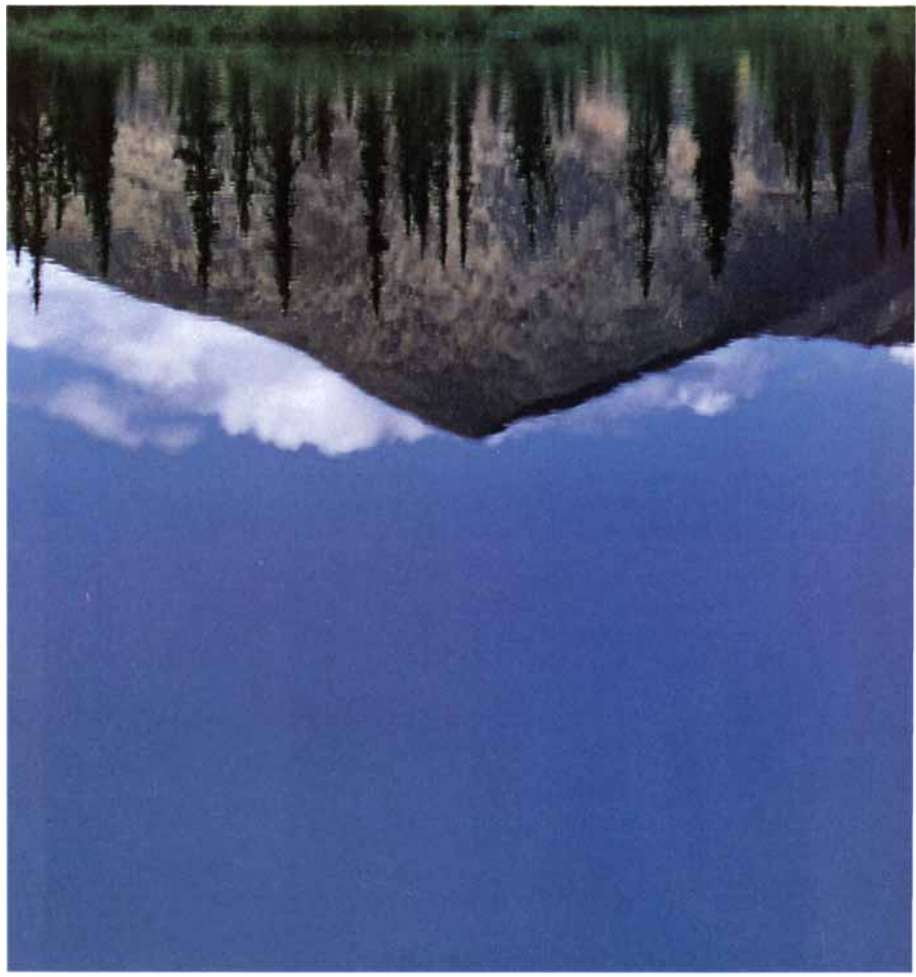

It's one of those ineffable feelings you get when you happen upon a herd of reindeer as interested in you as you are in them. (You'll be pleased to note that great stretches of this land are protected by parks that also put the lifelong residents at ease.)

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enforcing a rigid degree of data definition conformity," Branscomb observes. "There is a uniformity that is significantly softer"—and perfectly doable with off-the-shelf technology. For the on-line retrieval to work, the data bases need only be connected to a network, willing to agree to allow access in the first place and willing to share with the user their "dictionaries" of information. All that was necessary for the Livermore team's three-way query was for the clients and servers to use the same basic names for markers and the same sequence access numbers, so that queries could link on those keys. "The old ways are dying, and the sooner the better," Branscomb declares.

The new ways will invite problems of their own, points out GDB's Robbins. The myriad data bases may make so much information available that researchers simply will not be able to cope. As a result, Robbins thinks the users of data bases are more likely to be computers than people. "Right now, if I say 'Give me all the genes on chromosome 21,' I'd get some 220 hits," he says. That is but a fraction of what will become available. GDB is already being rigged to notify users when the answer to a request is too big to transmit in one piece electronically.

If genome data bases are to be accessed by multiple users, they will need to be much more complex internally than any single user will see, Robbins says, adding that he thinks it is worth paying for. Genome data bases should be open to "anybody with any interest for any reason," he declares. Overly simplified systems may constitute a false economy. "I have a hard time justifying spending significant taxpayer dollars for a select community's benefit when there might be a whole lot more benefit available with a little more access."

Other informatics workers are less concerned with the issues of data accessibility and more concerned with the engineering of data management tools. Some researchers, such as those at Livermore, favor the use of conventional, commercially available software. Others, such as computer scientist Nathan Goodman of the Whitehead Institute, believe this is a significant mistake. Biological data fit awkwardly into the tables of relational data bases, he says: "You have to spend a lot of time programming to fit the structure. If that's the only technology we have, the genome project will go bust before it produces what we've promised. We need to find a cheaper, more efficient way."

Biological data would be better represented as objects embodying generic concepts, Goodman believes. For instance, there are many kinds of landmarks to reveal position along the chromosome. All may be considered markers, whether they are short sequence stretches known to exist near genes or restriction fragment length polymorphisms, sections of DNA snipped to

Is It Nice to Share?

Being first has always been important in science. Competition is particularly fierce in the field of genetics. Multiple laboratories pursue the same goal—a gene associated with disease or with proteins, such as insulin—knowing that only one team will be credited with the discovery. Traditionally, findings are rushed into print in peer-reviewed journals.

But the vast amounts of information being generated by the Human Genome Project have begun changing the way scientists receive recognition for their work. And as groups maneuver to maintain their scientific edge, some are not rushing to disseminate their new data. "We don't have a firm rule for sharing data from the genome project," acknowledges Elke Jordan, deputy director of the National Center for Human Genome Research.

An advisory committee of the National Institutes of Health is developing general guidelines for releasing data, and the consensus, Jordan says, seems to be that six months is enough private time to study data produced with public money. Still, it will be difficult to censure those who sit on their research: the NIH will promulgate only statements of understanding, not actual rules. "How do you define when someone actually develops a piece of information? Is it the first day they come across it, or the day they feel sure, or the day they finally put it into their own data base?" Jordan asks.

Some scientists crave a form of credit more substantive than the respect of their peers: they want their contributions formally noted by the U.S. Patent and Trademark Office. Sharing is not then out of the question, but it will come at a price. The spearhead of this approach is J. Craig Venter, chief of receptor biochemistry at the National Institute of Neurological Disorders and Stroke. He has filed patent applications for thousands of short coding DNA sequences, called cDNAs, that pinpoint genes.

No one knows for sure how Venter is describing the "inventions" that machines in his laboratory crank out by the hundreds weekly. But many scientists fear that if the patent office protects these cDNAs, then anyone who later wants to do something with the genes containing these sequences will be indebted to Venter. "The greatest danger," observes Robert P. Merges, a professor of law at Boston University, "is not so much that someone will own a DNA sequence—that's quite common these days—but that someone will have claimed an invention without having developed any real applications."

Merges likens Venter's move to someone claiming huge plots of land on the theory that there might be gold underneath. Mining law in the U.S. protects against this kind of action, he notes. "There are limits to what you can claim, and you actually have to work the land for the rights to mature. That's what we need here."

Yet Venter may be doing exactly what Congress asked when it passed the Federal Technology Transfer Act of 1986. Reid Adler, director of the NIH's Office of Technology Transfer, explains that the law directs government agencies to develop technology that can be transferred to industry for a fee, to encourage commercialization of science. Protecting DNA sequences will ensure that private companies have incentive to develop drugs and other products based on them, he says.

But patents given at too early a stage could disrupt the international flow of information vital to the progress of science, warns Richard A. Gibbs, head of sequencing technology for the genome center at Baylor College of Medicine. "Issues of economic materialism are stepping in and restricting how scientists communicate," he observes. If everyone's primary concern becomes chipping off profitable pieces of the genome, researchers could soon be diverted from the project's ultimate goal. The idea is to decode information valuable not just to a few individuals but to the entire human species.

variable sizes by specific enzymes, or any of many targeting tools. "Only parts of the program have to know what kind of a marker it is; the bulk of the data base thinks, 'Ah, a marker is a marker,'" Goodman says.

Details about the markers, such as the strain of mouse or laboratory they came from, can be grafted to the object like branches to a tree, finer ones added like twigs. Changing an object once it has been initially described is not simple, but "it's easier than altering relational data bases," Goodman claims. In the M.I.T. laboratory where Goodman works with Eric Lander to map the mouse genome, they expect to introduce a radically different computer system every six months.

For now, though, object-oriented data bases have a serious drawback—the lack of a query language. "We can get very good information out by writing programs, but that's just about the only way we can get it out," Goodman admits. Writing a new language might be part of the solution, but then again "queries probably aren't going to be enough to give answers to most things people want to ask: getting numbers printed out on a screen won't be enough." What is really needed is not just language, Goodman says, but visualization tools that have not been invented yet.

ROBERT ROBBINS predicts that computers, not people, will increasingly be the users of genome data bases like GDB at Johns Hopkins University.

Almost any kind of redesign is doomed to be clumsy or wasteful, contends Suzanna Lewis, an informatics researcher at Lawrence Berkeley National Laboratory (LBL). "The genome community needs software to reflect changes in the lab, and there are many independent efforts to do that, but right now everything is being built custom," she explains. LBL alone has three different mapping groups and one major sequencing effort, and they all have different requirements. At present, sharing software in-house is difficult, let alone with other laboratories.

There could be a solution. "Most of what happens in a laboratory, if not everything, is a process flow," Lewis says. She and her collaborators at the California Institute of Technology think it will be possible to build a computer-aided design system in which a scientist simply lists the inputs and the outputs expected from a protocol and thereby instructs the computer system to build a data base to match.

Still other researchers are concerned that both conventional data bases, and those that must be programmed for individual needs, suffer limited power. They would rather put more responsibility on the computer. Data bases that do this are already changing the way biologists do their work. "People wouldn't dream of starting experiments before consulting them," declares George Michaels, a computational biologist who holds a joint appointment with the National Institute of Child Health and Human Development and the Division of Computer Research and Technology. He cites the data base built around the genome of *E. coli,* the ubiquitous bacterium popular for its ability to "express," or manufacture, products of inserted genes.

Although more data have been generated around the world about *E. coli* than about any other free-living organism, until recently "there was no way of bringing these flat files together," Michaels recalls. The view is much different now that another NIH researcher, Kenn Rudd, has completed the laborious process of stringing end to end all the DNA sequences ever reported for *E. coli.* These contiguous sequences, called "melds" or "contigs," enable scientists to describe the positions of genes in a way that is not possible when DNA sequences are viewed as separate entities. Placing the contigs on maps of a chromosome "lets us do the genetic equivalent of saying 'Washington is between New York and Miami,'" Michaels says. "This is the way biologists are thinking now—where does a gene exist on a chromosome in relation to known markers?"

The ability to view DNA positionally is also encouraging scientists to examine the function of particular sequences that are not genes but that also seem important in their own right. So-called short, functional units appear to influence the structure and the times at which gene products are produced. More of these are being recognized as scientists gather longer sequences of DNA.

Representing emerging biological concepts in the physical world is a demanding intellectual challenge—one ably met by physicist Ray T. Hagstrom and computer scientist Ross Overbeek, both of Argonne National Laboratory, with Michaels of the NIH and Karou Yoshida of LBL. Together they have built computer software to spot characteristic bits in *E. coli* or other large assembled sequences and display them on a computer screen. The visualizations are as yet crude—just shaded triangles and boxes—but they show researchers a selection of elements (classed as introns, exons, promoters, terminators and such) and how they are arranged upstream and downstream of known genes.

Informatics workers are already making it possible for biologists to gain new insights and connections. These early successes may help resolve what remains one of the most difficult aspects of the genome project—the culture gap between biologists and computer programmers. "The education of a biologist involves pulling buckets of mud out of swamps and looking at nice fuzzy animals," Overbeek observes. "Biologists are experimentalists. They're taught to change what they're doing if they're not getting the results they want. Computer scientists are trained to follow problems through in every possible linear, logical way. We just plain think differently. It's a major problem." The truth is that both ways of thinking are necessary to unravel the mysteries of the genome.

Charlotte's Patent

Spider webs and other proteins inspire engineers

In the late 1960s U.S. Army scientists realized that spider silk is both so strong and elastic that it would make a superb shield against jarring impacts. But even the military could not stomach the cost of equipping its troops with bulletproof vests woven from spider webs.

There may soon be an alternative. Instead of simply using natural materials such as silk, scientists are studying their physical structure, design and manufacturing for hints on how to create classes of synthetic materials that have unusual properties. The nascent discipline, called biomolecular materials, or biomimetics, has yet to turn a profit. But new polymers based on protein structures are fueling enthusiasm.

"The potential is magnificent," declares Stephen J. Brewer, who manages bioproducts chemistry at Monsanto in St. Louis. "Products are still a long way off," he adds, but in the process, "we're going to learn a lot of protein chemistry that will feed back into other products."

The novel materials are a triumphant example of the rewards that attend crossbreeding scientific disciplines. For decades, polymer chemists have engineered compounds by combining various monomers, or single-unit chemical building blocks. But even the most closely controlled manufacturing process results in a mixture of polymer chains of various lengths and so affects the properties of the final product.

Genetic engineers, on the other hand, have specialized in copying existing proteins precisely. By inserting genes into microorganisms, workers have been able to express, or produce, essentially identical molecules.

That kind of precision manufacturing has been the envy of polymer chemists. "Historically, polymer science has advanced whenever we have increased the control we can exercise over the polymer chains," points out David A. Tirrell, director of the materials science laboratory at the University of Massachusetts at Amherst. So the "absolute" processing control of genetic engineering promises to lead to unexplored realms of materials, he adds.

GOLDEN ORB-WEAVER, or* Nephila clavipes, *provides silk that army researcher David L. Kaplan uses to study protein structure and processing. Photo: Stanley Rowin.

At the same time, genetic engineers have been impressed by the unit-by-unit design approach of the polymer chemists. Proteins, like polymers, are made up of regular subsequences—in this case, combinations of the 20 naturally occurring amino acids. "So we thought, if we can synthesize artificial proteins, shaping their properties, then we'd have a new class of materials," explains Joseph Cappello, research director of protein engineering at Protein Polymer Technologies in San Diego.

Acting on this strategy, Protein Polymer introduced ProNectin F in March 1991. The company, which made its stock-market debut in January, is now busily designing a series of follow-up products. ProNectin F can be formulated into a thin, transparent coating or membrane on which cells can grow. Based on eight amino acids arranged in a precise sequence, the polymer incorporates receptors that enable it to bind to plastics (such as petri dishes), withstand very high temperatures and remain active for months. Next on the company's list is likely to be a fabric coating, which may find an early use in high-performance running shoes. The protein coating should give artificial fabrics a silklike texture and improve their ability to breathe, Cappello says.

Such ventures may seem a modest start. As interesting as protein-based polymers may be, most experts reckon the first materials will cost hundreds of dollars per pound to produce, a high price for all but niche applications.

Yet within a few years, researchers predict, their specialty materials may make inroads in the heady—and lucrative—market for biologically compatible products. The goal is to design proteins that would not trigger an immunologic reaction. And if scientists can engineer in specific functions, uses for such polymers could balloon.

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Future products from Protein Polymer will be designed by plugging various combinations of the 20 naturally occurring amino acids into four generic frames sketched by company researchers to resemble natural protein structures. The targets are silk, elastin (found in skin and other elastic organs), collagen (the fibrous component of skin and connective tissue) and keratin (which makes up nails and hair). The structures built by the company may or may not completely reflect their natural role models. "No one understands protein folding," Cappello says, "but you don't have to be able to completely understand something to make use of it."

Others are painstakingly characterizing the natural proteins first, then improving variation on those themes. For instance, Dan W. Urry, director of the laboratory of molecular biophysics at the University of Alabama at Birmingham, has spent the past 20 years studying the flexible but resilient elastin protein. Now he has designed a collection of elastinlike polypeptides based on five amino acids. The chains naturally fold (or contract) in response to increases in temperature; Urry has also tailored them to react to concentrations of chemicals and changes in pressure.

Potential applications for such materials abound, particularly if they can be programmed to disintegrate on cue. For instance, abdominal surgery requires a physician to cut through and later stitch separately five layers of tissue. To prevent the layers from knitting together as they heal, a doctor might separate them with sheets of polymers, which would then gradually dissolve.

Because Urry's polymers convert one form of energy into another (such as chemical into mechanical energy), they could also be considered a type of micromachine. A visiting navy official recently suggested Urry consider using his polymers as miniscule spheres for delivering drugs to disease sites in the body. "Within a few hours, I put together the basis for another patent application," Urry chuckles.

Teams at both the army's Natick Research, Development and Engineering Center in Massachusetts and the University of Wyoming are exploring the protein structures that have made spider silk famous. "Silk is the gold standard by which everyone works," says Brewer of Monsanto, who is collaborating with the army scientists. The chemists who invented nylon, for instance, deliberately tried to make use of the same chemical bonds they knew existed in silk proteins, he points out. "We have putative evidence we've cloned one type of spider silk," says David L. Kaplan, a researcher at Natick.

Understanding how a spider spins its fibers should also prove valuable, Kaplan adds. A spider synthesizes a water-soluble protein and spins it into a tough fiber, insoluble in water. Synthetic fibers, in contrast, are often spun from strong acids and require special processing techniques, such as high temperatures.

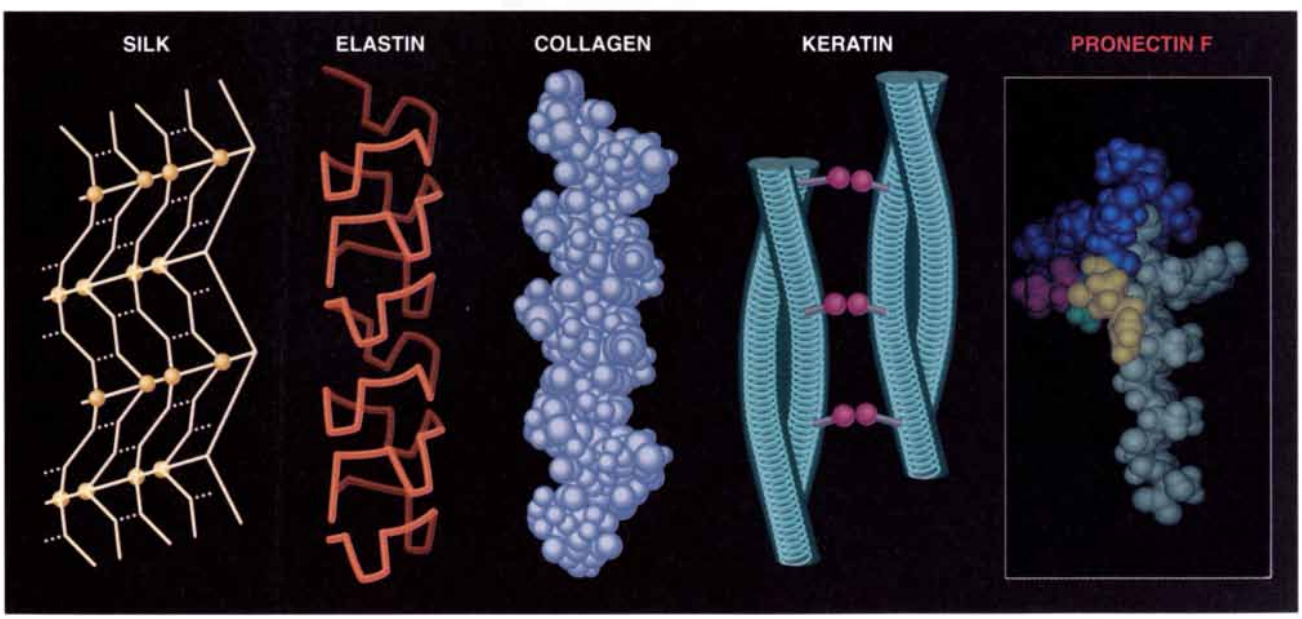
Collagen and keratin also have their fans. These workers are probing everything from sea urchin spines and abalone shells to rat teeth for clues about the design of the proteins as well as the way the materials crystallize. Companies, such as Du Pont and Allied-Signal, have projects under way, although they are reluctant to discuss details.

At another corner of the field, Tirrell, working with Maurille J. Fournier and Thomas L. Mason of the University of Massachusetts, has adopted an even more radical approach. Rather than stick to the array of natural amino acids, they are devising their own. They are trying, for instance, to make a novel photoconductive polymer in this way.

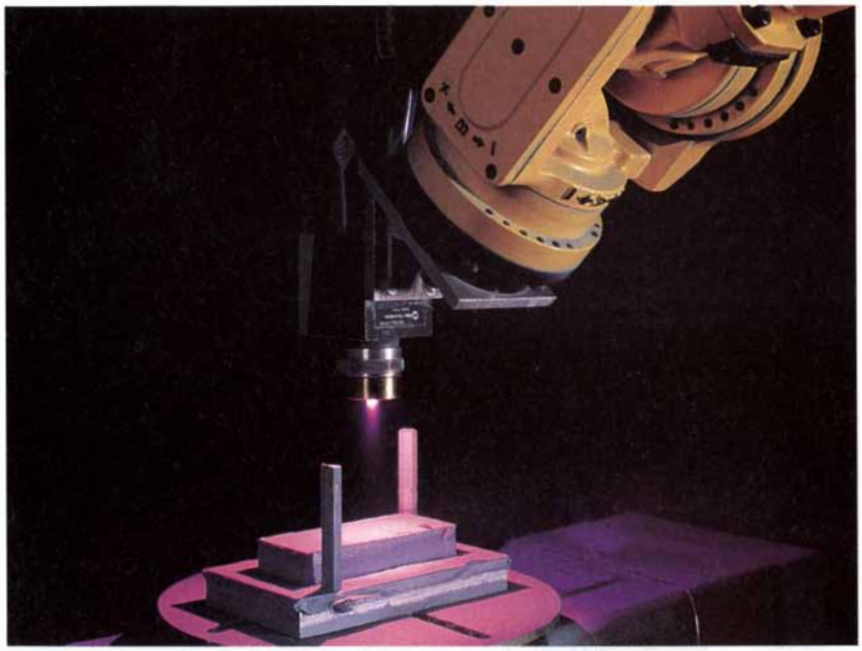
Tirrell is also exploring how to use the malleable proteins to control the structures of inorganic polymers and crystals. By growing inorganic crystals (such as magnetite) around the polymer chains and then washing away the polymers, Tirrell aims to create slender spikes of material. "Those kinds of elongated shapes, in magnetite, may prove useful in magnetic recording applications," he proposes.

In spite of his optimism, Tirrell sounds a cautionary note. "There has been some uncritical enthusiasm for this approach," he concedes. In some cases, the novel materials may not offer a clear advantage over existing ones. Biologically inspired materials will not, moreover, offer a single, dominant advantage over competing products. Instead the attractiveness of the new polymers lies in the diverse portfolio of characteristics they promise.

Still, the field is gaining momentum. "And obviously," Brewer teases, "I'm not going to tell you the most exciting possibilities." —*Elizabeth Corcoran*



FOUR MODELS OF ENGINEERED PROTEINS, developed by workers at Protein Polymer Technologies, serve as the building blocks for novel synthetic protein polymers, such as the company's first product **(far right).**



LAYER BY LAYER, a metal spray gun at Carnegie Mellon University builds up a model of a zinc turbine blade. Photo: Jim Schafer.

Desktop Artisans

Personal manufacturing weds design with part fabrication

It used to be that people designed parts, and then they went over to the forge and started hammering them out," says Emanuel Sachs, a professor of mechanical engineering at the Massachusetts Institute of Technology. "There was an intrinsic coupling of design and manufacturing because the designer really understood how the thing was made."

A new technology, sometimes called desktop manufacturing, promises to make the engineer into an artisan yet again. The increasing power of personal computers may soon enable engineers to "print out" completed parts with the ease of printing an engineering diagram. These systems can pare weeks or months from the laborious process of making prototypes. And they may enable engineers to fabricate real parts for short production runs directly from their computer screens.

The most visible examples of desktop manufacturing so far are plastic prototypes that allow engineers to evaluate a part for fit and looks. A Valencia, Calif., company, 3D Systems, which is 37 percent owned by pharmaceutical and chemical maker Ciba-Geigy, is the largest seller of desktop manufacturing equipment. It has sold hundreds of machines to produce prototypes from a technique known as stereolithography.

Like a computer printer, the system takes a set of coordinates from a computer to control the positioning of an ultraviolet laser. The laser builds up layers of plastic a few thousandths of an inch at a time by tracing successive cross sections of the part onto the surface of a bath of liquid polymer, causing it to solidify. The process can produce everything from a prototype of an engine block to a model of a diseased hip bone patterned from data from a medical scanner.

These plastic prototypes are still just a few steps removed from the world of the hobbyist. True, plastics can be cured by a laser to precise accuracies, and sometimes they may even be used as real parts. Many parts, though, are made from metal—and so behave differently than plastics do when they are exposed to heat or vibration. A plastic air manifold for a jet engine cannot be subjected to a temperature test.

With this in mind, the National Science Foundation and a group of industrial companies are supporting research to make parts and prototypes from a full range of industrial materials, from steel to ceramics. Sachs and his colleagues at M.I.T., with funds from the NSF, General Motors, United Technologies and other major companies, are developing a technique called three-dimensional printing. It takes a three-dimensional, computer-aided design (CAD) and chops it up into minute slices. A nozzle, similar to the ones used for some types of computer printers, squirts a binder chemical onto a bed of

powdered ceramic, stainless steel or another metal. After this process is repeated for hundreds of layers, the semisolidified part is then fired in a furnace.

The M.I.T. technology has already been licensed by Soligen, a new Los Angeles company that plans to sell machines to fabricate ceramic molds. After the ceramic powder has been solidified, metal will be cast in the resulting mold. Known as CAD-Casting, it bypasses the task of manufacturing metal dies for producing wax patterns that are then dipped in a ceramic slurry to create such a mold.

Lee E. Weiss and Fritz B. Prinz of Carnegie Mellon University's Robotics Institute and Engineering Design Research Center believe they can make metal or other parts with nearly the same material density as those produced through conventional casting and milling. They plan to adapt a technique used in the aerospace industry to spray ceramic coatings onto metal parts. The process uses a low-powered carbon dioxide laser to cut a series of masks. Then a robot-controlled thermal spray gun deposits a layer no more than 0.005 inch in thickness through openings in the stencil-like masks. Each of the 162 layers that make up a zinc turbine-blade model took six minutes to build.

Researchers at the University of Texas at Austin are exploring the possibility of employing a high-powered, 1,100-watt carbon dioxide laser to fuse metal or ceramic powders in a system similar to one the university has used with thermoplastics. But, says Joseph J. Beaman, a professor of mechanical engineering, the Austin investigators immediately found that "you can't just turn on the laser and take a polymer part and plan to make it in metal."

If technical obstacles can be overcome, desktop manufacturing will hasten the making of the metal-casting molds and tool dies to mass-produce an engine housing or another part. And researchers believe it could enable manufacturers to forgo casting altogether in building small lots of customized parts. The possibilities range from vanes and blades for gas turbine engines to dental fittings, packaging for semiconductor chips, spare equipment parts and so on.

It may be as simple as printing a document from a computer. "When someone wants a part," Beaman says, "a technician will just grab a bag with powder, walk over and turn on the machine." Then the desktop artisan may be constrained not by present limits of the manufacturing process but only by what can be visualized within the three dimensions of a CAD drawing.—*Gary Stix*

Waste Not...

New pollution laws will be considered this spring

Every year as it makes and consumes its gross domestic product, the U.S. churns out 13 billion tons of "nonhazardous" waste, including 180 million tons of municipal refuse. The growing torrent is overloading landfills and incinerators and has occasionally had coastal residents literally swimming in garbage.

Congress made an attempt to address the burgeoning waste calamity in 1976, when it passed the Resource Conservation and Recovery Act, known as RCRA. The act has put strict controls on hazardous effluents, but it has not stemmed the rising tide of nonhazardous waste. This year RCRA is up for renewal, and industry associations, environmental groups, members of Congress and administration officials have begun to square off. The 80-odd bills that have been introduced to revise RCRA are symptomatic of the issue's high political profile.

Comprehensive bills introduced by Senator Max S. Baucus of Montana and Congressman Al Swift of Washington State are likely to become the vehicles for RCRA reauthorization. They echo the mantra of orthodox environmental management: minimize, recycle, landfill, compost and store. Specifically, the bills would force industry to reduce waste and meet national recycling goals. They would also strengthen the Environmental Protection Agency's oversight of landfills and incinerators and possibly regulate industrial effluents that are now exempt. The reauthorized RCRA could even break new ground by requiring for the first time that industries reduce their use of toxic chemicals.

Avoiding the Potholes on Optical Highways

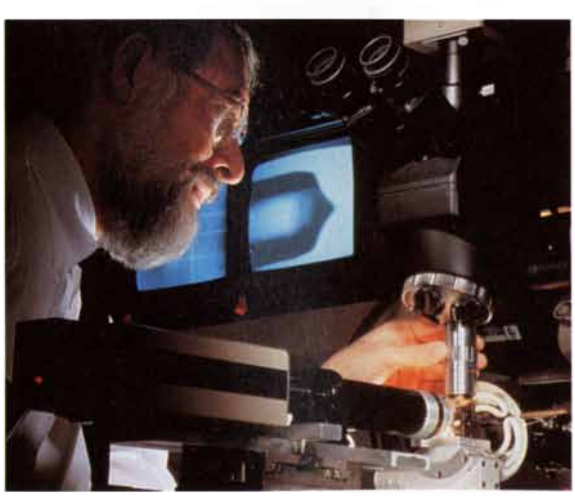
Just as potholes plague any highway, trouble spots that waste energy and weaken passing signals afflict long-distance optical-fiber networks, which serve as expressways for voice and data communications. Several recent research achievements offer ways to smooth over those rough spots and so boost communications.

For instance, much energy is dissipated at the beginning of an optical link, where the lasers generating signals are coupled to fibers. Typically more than half the laser light is lost. "It seemed like an awful waste, like throwing away half a tank of gas," says Herman M. Presby, a researcher at AT&T Bell Laboratories. By turning the tips of the fibers into carefully sculpted microlenses, Presby was able to direct 90 percent of the light into an optical cable.

The tips of optical fibers are generally tapered to channel as much light as possible from the laser to the fiber. But after some experimentation, Presby found that some tips, or lenses, captured dramatically more light than others. Eventually he realized that the hemispheric shape of conventional tips introduced aberrations that prevented the lenses from properly focusing incoming light. According to classic optics theory, Presby knew he could skirt the problem by designing an aspheric, hyperbolic shape.

More problematic, Presby says, was developing a technique for churning out identical aspheric tips automatically. Last spring he won a patent for his method of mechanically carving an aspheric tip in 30 seconds by rotating silicon fibers in and around a carbon dioxide laser beam. "It's like machining a rod in a lathe," he says, but with a precision measured in tenths of a micron.

Unveiled at the Conference on Optical Fiber Communication, held in San Jose in February, the microlenses are unusually mature for a Bell Labs announcement. "We've been working on these lenses for about two years," Presby concedes. Research is still about "sharing information," he adds, but these days AT&T "wants to make use of items from research before giving it to the world."



ASPHERIC TIP* (projected on screen), *at the end of a silicon fiber, was invented at AT&T by Herman M. Presby.

Another sure problem for optical communications typically occurs in midtransmission, as signals lose energy and become distorted. Existing long-distance systems employ costly electronic repeaters to regenerate the signal; AT&T's next generation of transoceanic cables, however, will use optical amplifiers. These segments of fiber incorporate rare-earth atoms and boost the energy of passing light signals.

As well as promising to make obsolete costly and inefficient electronic repeaters, optical amplifiers may make possible the ideal long-distance signal, namely, solitons, or pulses of light that do not disperse or dissipate but maintain their size and shape indefinitely. Solitons have promised to be a tantalizingly elegant technique for transoceanic communications ever since the early 1970s, when a researcher hypothesized that these long waves could exist in optical fibers. But even Bell Labs managers argued that the work was too speculative to support.

Last fall Linn F. Mollenauer, a Bell Labs physicist who has been a devoted champion of solitons, triumphed in his efforts to show that soliton pulses could bridge the distances between continents. In a laboratory demonstration that relies on loops, or racetracks, of optical fibers, Mollenauer transmitted 2.5-gigabit soliton pulses essentially without errors for more than 14,000 kilometers. In December he sent 10 gigabits of data more than 11,000 kilometers by using various techniques for interleaving, or multiplexing, four 2.5-gigabit signals. "We really do expect to be able to double the bit rate once again to 20 gigabits" by multiplexing the existing 10-gigabit channel with another similar stream, he says.

The new record buttresses Mollenauer's view that solitons will be practical. Now, "I'm very confident of AT&T's backing," he declares, "and can safely say we're more than meeting our research goals." —*Elizabeth Corcoran*

Each bill contains unique provisions. The Swift measure would grant states the right—already claimed by some—to impose higher fees on extraterritorial wastes. In exchange, those states would have to prepare waste disposal plans and have them approved by the EPA (only 25 states now have such plans). The bill would also set a minimum content of recyclable material for packaging, require states to divert set amounts of recyclable materials from the waste stream and expand federal procurement of recycled products.

Baucus's staff wants to establish as law the concept of "responsible corporate entities." Such a provision would shift responsibility for recycling to owners of trademarks. A manufacturer of a brand of soft drink would, for example, have to ensure that some percentage of its cans were recycled, although not necessarily to make more cans. The plan is designed to answer industry's objection to an earlier proposal that would have required entire manufacturing sectors to incorporate specified percentages of recycled material.

Even though nonhazardous waste is dominating the agenda, some proposals also cover other kinds of waste. Baucus, for example, seeks tighter controls over what are called "special" wastes—those produced by mining and milling operations and by oil and gas drilling. Such wastes are now controlled inconsistently by the states, but an environmental coalition led by the Sierra Club argues that many of the wastes are toxic enough to warrant federal control. Congressman Gerry Sikorski of Minnesota has written a bill that proposes a "right to know more" provision for toxic chemicals: it would expand the list of chemicals that must be reported to the EPA if they are released.

Like the Baucus bill, the Sikorski bill would also require industries to draw up plans to reduce use of toxic chemicals and have them approved by the EPA. A staff aide to Sikorski points out that several states already have toxic-chemical reduction programs in place and asserts that they, together with the EPA's existing toxic-emissions register, have prompted several companies to reduce their use of toxic chemicals. Some have declared that they have saved money by doing so.

Whatever the outcome of the congressional deliberations, the reauthorized RCRA promises to clamp more regulations and costs on industry. And that, from the point of view of industry, is the rub. The American Paper Council and the American Petroleum Institute, for example, insist that their voluntary recycling initiatives and reductions in waste are bringing environmental benefits without the need for regulation.

They and other industry groups are now lobbying to ensure their wastes do not fall under stricter controls. "Our biggest concern is that a regulatory program like that for hazardous wastes might be extended to nonhazardous materials," says Margaret Rogers of Dow Chemical. The National Association of Manufacturers deplores the proposed measures to reduce use of toxic chemicals because they specify the actions that industry must take, rather than allowing economics to decide the most efficient way to reach targets.

For William K. Reilly, the administrator of the EPA, the proposals are apparently too much of a good thing. Reilly indicated in congressional testimony last year that the administration opposes revising RCRA, which he pointed out already costs about $32 billion per year. Reilly reminded Congress that the EPA already has a voluntary toxic-waste reduction scheme, which more than 250 companies have joined. Further controls, especially on nonhazardous materials, "would be unlikely to result in substantial benefits except in a limited number of cases."

All sides in the debate face some hard realities. One is the NIMBY (not in my back yard) syndrome. Local opposition to landfill sites and incinerators is one of the principal reasons for the drastic increases in disposal costs of recent years. Then there is the soft market for recycled commodities: the administration has adopted the voluntary goal of 25 percent recycling of municipal waste by 1995, but many local programs have succeeded only in filling warehouses with old newspapers and glass that nobody will buy. Although the political pressure to decrease the waste stream is intense, only 13 percent of household refuse is now recycled.

Undaunted, the environmental contingent in the RCRA debate believes some of the proposals now being considered will jump start the market. Reilly has pointed out that judicious stimulation of the pocketbook can get results. In Seattle, where households that produce more garbage are charged more for disposal, the amount of waste recycled is much higher than it is in more tolerant jurisdictions.

While they wait for the forces that are reshaping RCRA to find the least-energy state, known in politics as a consensus, veterans of the environmental movement can celebrate important progress. The argument is no longer focused on whether waste recycling and reduction will become the norm, but on how. —*Tim Beardsley*

Ballpark Physics

Automating the scribbles on engineers' envelopes

The engineers at Xerox who design photocopiers usually spend little time contemplating the kinetics of a machine's moving parts and the principles of static electricity that lie behind xerography. Eschewing detailed equations, they might reduce the physical connections between a copier motor, clutch or drive belt to a series of boxes with connecting lines that represent torque. "The way engineers and technicians work in the field, they may not even use $f=ma$," says Johan de Kleer, who heads an artificial-intelligence research group at Xerox's Palo Alto Research Center (PARC).

De Kleer and other AI researchers have been trying to elevate back-of-the-envelope methods into a new generation of computer expert system that can help engineers gain a better intuitive understanding of how a complex system works from its earliest conceptual design. Their models, embodying what they refer to as qualitative physics, improve on the well-used envelope by making a rough estimate of how an electrical or mechanical failure can spread throughout a larger system.

The idea behind qualitative physics is to take physical phenomena that are usually calculated with differential equations—oscillations and feedback, for example—and represent them with a qualitative notation that expresses engineers' informal descriptions. Variables may be reduced to values such as plus, minus or zero to show whether a physical force such as the torque from a copier motor is increasing, decreasing or static. Or values might be compared by order of magnitude, a staple in making ballpark estimates.

Unlike conventional expert systems, which rely on a set of "if..., then" rules, those based on qualitative physics often resemble a model of a circuit diagram in which a relatively large number of components behave in a limited number of ways, such as the on or off state of a transistor. The ebb and flow of forces represented by qualitative approximations can be used to trace a path through a schematic showing how the failure of a part may propagate to other components. In conventional expert systems, a separate rule would have to be stated for each affected component.

Qualitative physics got its start about 15 years ago, when de Kleer, then working at the Massachusetts Institute of Technology's Artificial Intelligence Lab-

oratory, devised a qualitative program to solve simple mechanics problems for roller coasters. Today de Kleer supervises a group of eight that specializes in qualitative reasoning and modeling techniques at PARC.

There, a year-old project called Rapper—*rap* in Rapper stands for repair and adjustments procedure—uses qualitative concepts to explain why a copier has broken down. So far Rapper exists as a model of roughly 170 of the components in a copier's document-handling system, each component connected by lines in a schematic that can represent forces such as voltage or torque. The PARC researchers are now using the model to produce a series of flow diagrams that can help a service technician locate a point of failure.

Building a workable model required making the world a more simple place: time was ignored almost completely. Each component recognizes only the moment when a piece of paper passes by. Disregarding time makes it easier to do things such as reason backward to determine what previous event could have caused a motor to fail. Eventually the PARC team must come up with a model that accounts for time's linear march, says Brian Falkenhainer, a PARC researcher.

Outside of Xerox, qualitative modeling is being contemplated for everything from creating self-teaching electronic books to telling pilots the status of their engine. Fault finder, an expert system developed at the National Aeronautics and Space Administration Langley Research Center, picks out abnormal sensor readings from a jet engine, then runs them through a qualitative model that displays a diagnosis. "Pilots don't necessarily need numbers; they need to be told what's wrong and to be given advice about what to do about it," says Kathy H. Abbott, a NASA researcher. The Boeing Company is now evaluating this software for use in its aircraft.

Despite its promise, qualitative physics has some critics. In a paper scheduled to be published in May in an AI journal, *Computational Intelligence,* Elisha P. Sacks, a professor of computer science at Princeton University, and Jon Doyle, a researcher at M.I.T., argue that qualitative physics simplifies physical dynamics to the point that real-world problems become unsolvable. They maintain that AI researchers can best help engineers by finding ways to automate hard-core numerical models.

In fact, some researchers are trying to merge qualitative physics with more formal numerical modeling. A qualitative assessment might choose the best numerical model to execute a problem. In modeling the transition from smooth to turbulent flow, for example, "qualitative physics will help you to decide when the equations for turbulence should be used," says Kenneth D. Forbus, a professor of computer science at Northwestern University.

The few applications in qualitative physics so far have been primarily for use in diagnostic systems. By integrating multiple models, Forbus and other researchers, such as Daniel S. Weld, a professor of computer science and engineering at the University of Washington, hope to produce more precise answers about physical behavior that are better suited for design and instructional tools. If this vision does materialize, qualitative physics could conceivably move from the back of the envelope to the forefront of design, diagnostics and computerized instruction. *—Gary Stix*

Helping the Little Guy Buy a Computer

When a small Japanese manufacturing firm wants to learn about new production technology, it can turn to one of 170 regional centers dotted across that island nation. In contrast, the 350,000 industrial firms in the U.S. with fewer than 500 employees have recourse to only a few dozen state-run programs. At about $50 million a year, funding in the U.S. for these efforts is about a tenth of what the Japanese spend.

Getting new technology into small machine shops is a critical step in setting up networks of suppliers that can reliably furnish the nuts and bolts that make big automobiles and other products. The absence of such a system is one reason cited for the U.S. lag in manufacturing. "A lot of time these companies are operating with technology from the '50s and '60s," says Maryellen R. Kelley, a professor of management and public policy at Carnegie Mellon University.

A nascent attempt by the federal government to expand small companies' access to more advanced manufacturing technology started in 1989, when the National Institute of Standards and Technology (NIST) established its first three Manufacturing Technology Centers (MTCs). The centers—in Ohio, New York and South Carolina—have tried to supplement the efforts of technical colleges and state and private industrial extension programs. Two more centers have been set up more recently in Michigan and Kansas—and contracts for yet two others are to be let by April.

During their first 30 months, the initial three centers dealt with about 6,000 companies. The MTC program's annual budget has ranged between $5 and $15 million, but the companies it aided generated new revenues or achieved cost savings that totaled $140 million, estimates Philip Nanzetta, director of the MTC program for NIST. Much of the centers' time has been devoted to helping companies with simple projects, such as reorganizing plant layouts or buying personal computers for keeping track of inventory. "The return to the small company is much, much larger than what it costs to provide the service," Nanzetta says.

In its first congressionally mandated review of the program to determine whether funding should continue, a nine-member review committee appointed by the secretary of commerce gave two of the original centers a passing grade, while criticizing the management of the South Carolina center.

The oldest centers now face a series of funding challenges. The law that established the program specified that federal contributions must be matched by the states and that each center should be self-sustaining after six years. The Reagan administration initially opposed the program; the Bush administration has given it lukewarm backing, although congressional supporters have continued to stand behind the effort at levels exceeding the amount requested by the current administration.

Senator Ernest Hollings of South Carolina, one of the original sponsors of the legislation, and other lawmakers have proposed helping MTCs establish satellite programs in other states. But the Bush administration objects. "There's no strong evidence that we can afford to address this problem through present methods," says an official with the Office of Management and Budget. "We can't afford to create a center in every county." It may be a long time before a demonstration of just-in-time production or statistical quality control is only a local telephone call away. *—Gary Stix*

Compensation beyond the Call of Duty

In these days of generally depressing economic numbers, one statistic continues to move ahead briskly: the compensation of U.S. chief executive officers. Even as the real pay (that is, dollars discounted by inflation) of the average American worker has slipped by almost 13 percent during the past 20 years, the pay of CEOs has grown almost fourfold, reports Graef S. Crystal, a professor at the University of California at Berkeley, in his recent book, *In Search of Excess: The Overcompensation of American Executives.*

Such reports have fueled public outrage and prompted calls for government action. Yet most economists argue that such caps attack the symptoms rather than the underlying problem.

From an economist's vantage, the dramatic increases in CEO compensation are indicative either of a chronic shortage of CEOs or, more likely, of a market that has ceased to function properly. Data assembled by Kevin J. Murphy and Michael C. Jensen of Harvard University show just how small a vestige of efficient market behavior is left in executive compensation. A typical large company that gains $400 million in market value pays its CEO $1.04 million; one that loses the same amount pays its CEO $800,000.

To see why the CEO marketplace does not work, consider the elements of a well-functioning one, say, the market for new automobiles. In this case, the forces of supply and demand regularly lift and depress vehicle prices. Well-informed manufacturers, who can gauge the attitude of consumers, provide the supply of cars. At the same time, well-informed consumers, armed with copies of *Consumer Reports* and advice from family and friends, determine the demand. Because buying a car is considered an expensive, long-term investment, consumers have an enormous incentive to get the best deal. They eventually wind up in tough negotiations with car dealers, who, in turn, fight for the highest price because their own take-home pay is on the line.

In contrast, the market for chief executive officers lacks such efficiency-producing factors, Murphy says. First, the supply of CEOs is not very fluid. Companies usually pick a CEO from among their existing managers. According to studies by Murphy and Jensen, roughly 90 percent of CEOs have been with their company for 10 years or more at the time they are promoted. Second, good measures of CEO performance are scarce. Boards of directors—the nominal buyers in the CEO market—hire a new chief or hang onto an old one based on much less information than the average car buyer brings to bear.

Once a CEO is running a company, Crystal says, most of the information a board receives on his performance comes from the CEO himself. The CEO's position is bolstered by compensation consultants he has hired, who either point to other executives who make more money or create measures of performance that showcase the executive's track record.

Not only are those who buy the services of a CEO ill informed, they lack incentive to push for the best deal. Because board members seldom own significant amounts of stock, their personal finances do not wax and wane with corporate performance. "There's no external mechanism, short of bankruptcy, that penalizes a board for foolish compensation decisions or for lax oversight," charges Joseph A. Grundfest, a former commissioner of the Securities and Exchange Commission, now a professor at Stanford Law School.

Short of bankruptcy, nothing punishes a board of directors for foolish compensation decisions.

Instead board members often have good reason to help the CEO win a better compensation package: they are likely to be either company insiders whom the CEO can fire or outsiders whom the CEO has picked as nominal representatives of shareholder interests. These outsiders, in turn, are likely to be CEOs of other large public companies or "professional" directors who sit on many boards. Rocking the boat could put their directors' fees at risk, says Benjamin Hermalin, also a professor at Berkeley.

Compensating CEOs was not always so incestuous. In the years shortly after World War II, most U.S. executives received stock options as an incentive for good management. When the company's stock rose, so did their wealth. But when stock-market growth stalled in the 1970s, executives argued that the market had gone awry and was undervaluing their companies—and their services. Compensation consulting came into vogue, Crystal recalls, and consultants devised ever more elaborate ways of ensuring that executives would be well rewarded, regardless of the company's financial performance.

The government can help unlock some of the mechanisms of the market for CEOs by demanding more forthright corporate disclosures, both about overall financial performance and about executive compensation. But really putting the market mechanisms back into working order requires that board members become smarter consumers, economists say. And boards must have strong incentives to strike a good deal for the shareholders whose interests they ostensibly represent.

One of those incentives is money. Economic necessity, Hermalin points out, is putting an end to the peculiarly American practice of having boards of directors governed almost entirely by people who have little to gain or lose from a company's market performance. Large shareholders such as pension funds are beginning to take a more active role in corporate governance.

If such corrections do not show their effects soon, however, public opinion may lead the government to make more radical changes to the corporate landscape. Congressman Martin O. Sabo of Minnesota has proposed increasing the taxes of companies that pay executives more than 25 times the rate of the lowest-paid worker (they now average about 160 times). Japanese executives, by comparison, make barely 20 times more than their workers.

Meanwhile both the Securities and Exchange Commission and Senator Carl Levin of Michigan have proposed a solution that combines the free market with poetic justice: give shareholders a direct voice on executive compensation. Although drastic, the proposal would apply the most rigorous of classic economic mechanisms to the question of what bosses are actually worth.

—Paul Wallich and Elizabeth Corcoran

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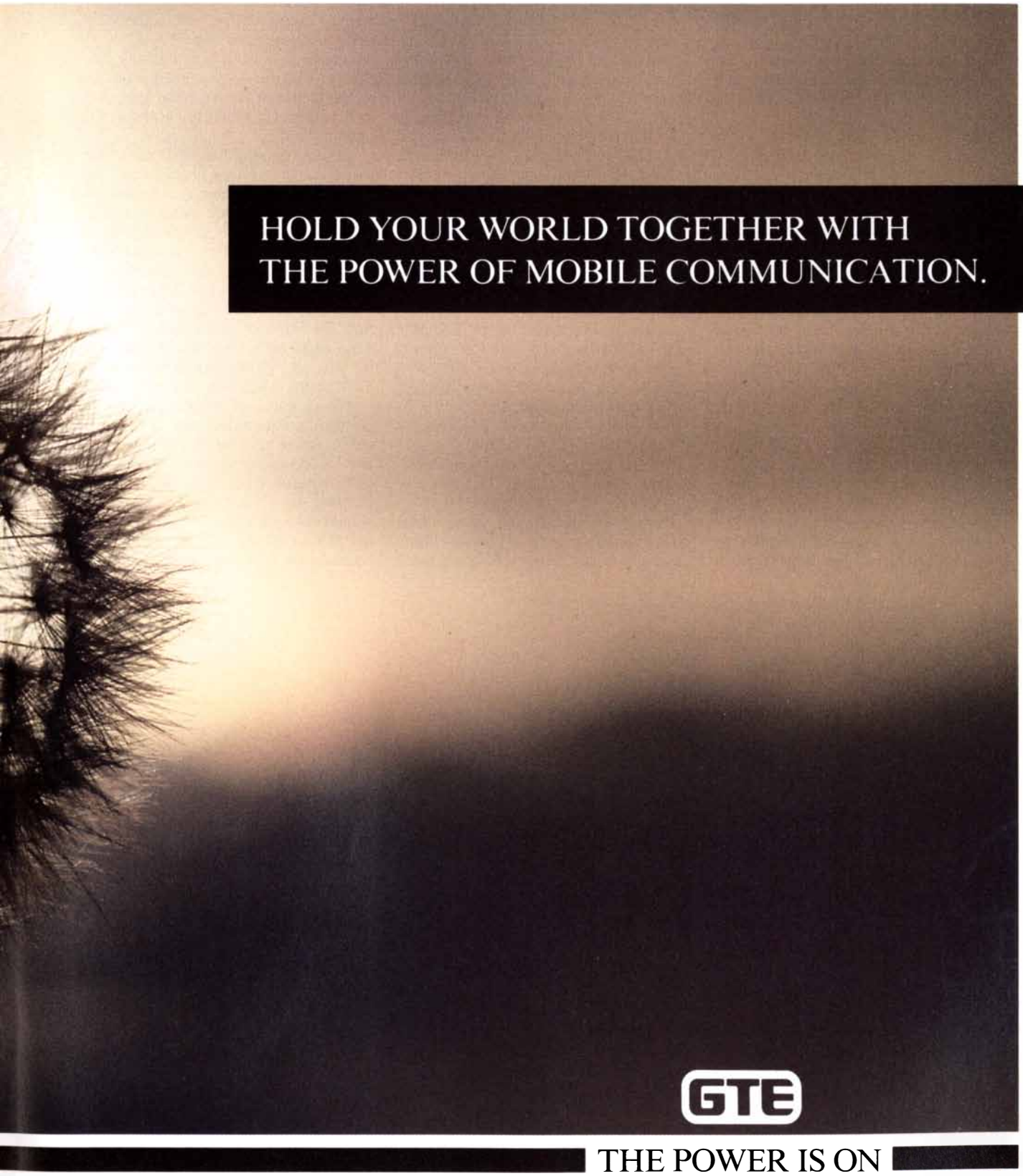


All Paths Lead Away from Rome

Never have Romans seen such a spectacle," Fastidius Finiki boasted to his inebriated friends as they relaxed in the Octagon Pub.

"Please, I can't bear to hear the story again," Barnumus Bailus pleaded, guzzling a shot of Roman whiskey.

Fastidius ignored him. "Barnumus convinced some crazy Gaul warrior to fight a lion. I believe he goes by the name of Egocentrix. Anyway, the barbarian enters the arena, the lion is released from his cage, and the crowd goes wild, anticipating a bloody frenzy. The beast crawls to the center of the arena and freezes. Egocentrix approaches the animal, his sword held high. But the cat doesn't budge. So Egocentrix gets the bright idea to poke the beast in the haunch. The lion roars and lunges at him. The warrior drops his weapon and runs for his life. What a dolt."

"He's no coward," Barnumus interrupted. "He was brave enough to face the lion armed only with a sword."

"Why in Zeus' name did you arm the lion with a sword?" Fastidius taunted. "Never mind, let me finish the story. Egocentrix ran around the arena like a barefoot eunuch on hot coals. To his credit, the warrior moved much faster than the lion. Whenever the lion got too close, he sprinted away. The lion soon grew tired of the chase, curled up in a ball and went to sleep. Egocentrix was left panting in the middle of the arena. The crowd became restless, jeering, 'Hurray for Egocentrix, the great lion hypnotist.'" All of Fastidius' friends laughed except Noblina, the emperor's geometry tutor.

Fastidius took a swallow of Gladiator Lite Ale. "After the event I overheard Emperor Scandalus say the fight was more boring than a meeting of the Society for Aqueduct Engineers."

Barnumus looked pale. "I'll be lucky if I avoid being fed to the lions."

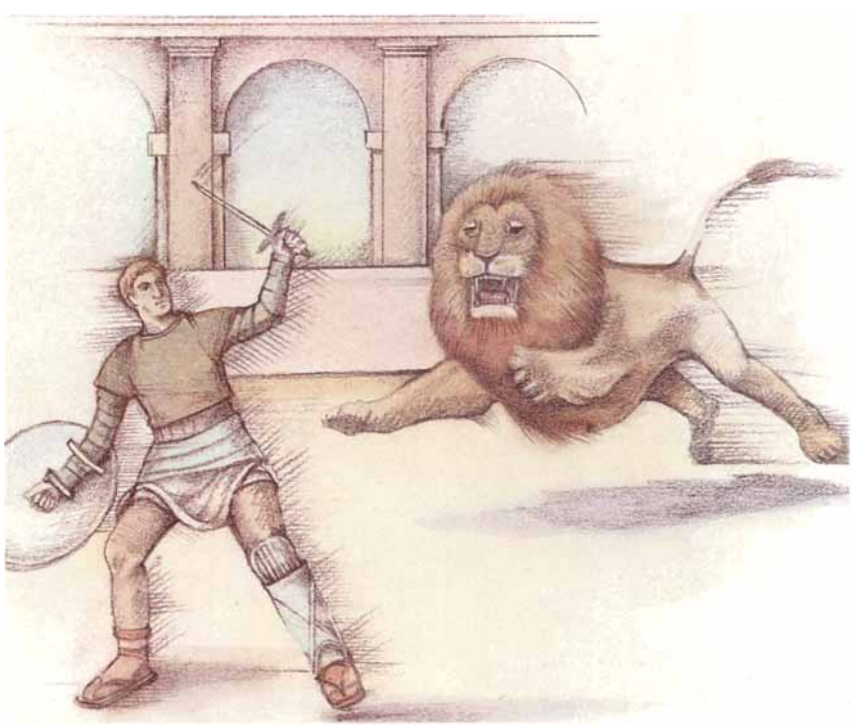
"Barnumus, it's not really your fault," Noblina said. "And I think I know a way to make the fights more interesting."

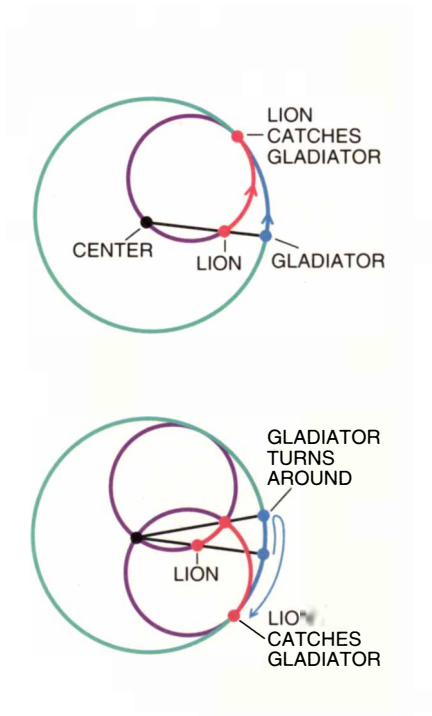
Barnumus spat on the sandy floor. "What could a geometer possibly know about fighting? Push off, protractor face." He turned back to address Fastidius. "I am working with a friend of mine to get a dozen lions for—"

Noblina persisted. "The mistake, Barnumus, was not so much in the lion as in the gladiator. There is no spectacle in a contest in which the warrior can outrun the lion."

"Noblina means," Fastidius said, "that if the man's speed is greater than the lion's, then the fighter can always escape from the—ha, ha—paws of death."

"Indeed, there is a simple geometric proof for that theorem," Noblina said. "Except, of course, if one subscribes to the paradoxical views of Zeno of Elea, a philosopher who lived 400 years before the reign of Gaius Julius Caesar. Zeno came up with a clever argument for why all motion should be impossible. If space is infinitely divisible, a finite length contains an infinite number of points. If so, no movement can be initiated because to move from any point to any other, one must always traverse an infinite number of intermediate points. In other words, Zeno proposed that it should take an infinite amount of time to cover an infinite number of points or, equivalently, to move a finite distance."





LION can always catch a gladiator running in a circle if both move at the same speed **(diagram at top right).** ***If the gladiator reverses his direction, the lion should modify its tactics*** **(diagram at bottom right).**

"Seems like Barnumus' lion is familiar with Zeno's work," Fastidius said.

"Enough nonsense," Barnumus exclaimed. "Next week I have scheduled Geriatrix to fight against the lion. He can scarcely stumble a dozen paces."

"There won't be much action if the lion can outrun the gladiator," Noblina remarked.

"You keep your nose out of this," Barnumus threatened.

"No, she's right. Just a few quick bites, and it will be all over," Fastidius said glumly. "Barnumus, you must find a lion and a warrior who are perfectly matched, each able to run at the same speed, so that neither has any obvious advantage. Then we will have a real contest."

"I would not be so sure of that," Noblina said.

"By Hera, there she goes again," Barnumus bellowed.

"I am wondering what happens if the fighter emulates what Egocentrix did today and runs as fast as he can away from the lion."

"Then the lion just runs after him," Fastidius said.

"Indeed," Noblina acknowledged, scratching her head. "And at the same speed, so that while the gap between them does not increase, neither does it diminish. Not, to my mind, an especially enthralling tactical battle."

"It would be a little boring," Fastidius conceded. "But the gladiator cannot run away indefinitely, or he will encounter the wall of the arena."

"An excellent point," Noblina said. "It is an interesting question. If a lion should pursue a warrior in a circular arena, and if each runs at the same, constant speed, can the lion always catch the warrior? Or can the gladiator, by cunning changes of direction, keep the lion at bay indefinitely?"

"It seems to me," Fastidius mused, "that whenever the fighter turns through an angle, the lion can take a shortcut and close the gap between them a little."

"True," Noblina affirmed, "but if the gladiator follows a smoothly turning path, then the change in direction at any given instant is vanishingly small."

"Well," Fastidius said in some irritation, "it just seems to me that if the lion stays between the warrior and the center of the arena—"

"On the radius joining the fighter to the center of the circle?" Noblina asked.

"Precisely. If the lion does that, then it can—in a manner of speaking—push the gladiator out toward the wall and trap him there. It has a smaller distance to move when it goes around the circle, and that leaves some spare movement along the radius. Because the lion is on the inside of the warrior."

"And soon the warrior is on the inside of the lion," Barnumus chuckled.

Noblina was not amused. "An excellent suggestion, Fastidius. But I do wonder whether—as Zeno hypothesized—the lion may approach indefinitely close to the gladiator without ever actually reaching him. The advantage of extra radial speed diminishes as the lion approaches the warrior. Hmm.... Suppose for simplicity that the fighter runs in a circle. Then the lion can run along a smaller circle that is tangent to it."

Noblina carved a simple diagram in the dirt floor [*see illustration on opposite page*]. "Elementary geometry proves that corresponding arcs of the two circles possess identical lengths, so such a track is possible. In which case the lion does indeed catch the gladiator after a finite period."

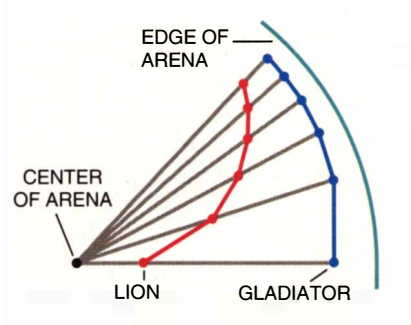
"Elementary geometry," Barnumus muttered. "No warrior is dumb enough to keep running in the same direction when he sees a roaring lion closing in on him. He'll spin around and run the other way!"

"But the lion can change its direction, too. It can simply reflect its circular path in that radial line and continue exactly as before," Noblina cried in triumph. "Barnumus, you must procure a lion whose speed precisely matches that of your most skillful fighter and train it to stay on the same radius as the gladiator while it chases him. That way, the crowds will be treated to an exciting spectacle as the warrior rushes to and fro trying to elude the ravenous beast. Eventually the two must fight."

"Noblina doesn't want much, does she?" Barnumus sighed. He stumbled out of the pub, wondering whether Noblina's plan would work.

With only seven days left before the next fight, Barnumus began to conduct speed trials on his lions. He discovered one that could run just as fast as Egocentrix. He rushed to train the beast, feeding it fresh gazelle as a reward for radially synchronized prowling. By the seventh day the lion was better trained than most gladiators.

Barnumus took pride in his accomplishment and hired three extra messengers to announce the fight. A huge crowd gathered in the amphitheater. Egocentrix entered the arena and bowed in the direction of the emperor's box. The lion's cage was conveyed to the center of the arena on a kind of crane and opened. The lion headed straight toward Egocentrix, who let out a screech and rushed off at right angles to the lion's path. As it had been trained to do, the lion quickly turned in order to stay on the same radius. Noticing this, Egocentrix once more turned at right angles to the radial line. The lion steadily closed the gap, but at a slower and slower rate.



SQUIRAL is the basis for a strategy that helps the gladiator avoid the lion. To move in a squiral, the gladiator imagines a line that passes through him and the center of the arena. He runs perpendicular to the line for a short distance. For each subsequent move, he continues to envision lines that pass through the center, and then he travels perpendicular to the line for a distance equal to the original times a factor of* n *to the -0.75 power.

"Whatever is the fool doing?" Fastidius asked.

"I have no idea," Barnumus said. "But the lion is pursuing his Gaul with single-minded attention."

Noblina slapped herself on the jaw. "Of course. Egocentrix is following a squiral—a spiral made up of successive line segments, each at right angles to the radius. Simple geometric arguments now demonstrate that if the lion stays on the radius joining Egocentrix to the center of the arena, the lion cannot catch him while he is running along any particular segment. And therefore it cannot catch him at all—even though it may approach indefinitely close."

"But if he—er—squirals ever outward, he must run into the wall eventually," Fastidius objected.

"Not necessarily," Noblina asserted. "If the radial component of the motion covers shorter and shorter distances, then the wall may never be reached. I have in mind a series such as

$$1 + {}^1/_2 + {}^1/_4 + {}^1/_8 + \ldots$$

which never exceeds 2, no matter how many terms are added."

"But surely," Fastidius said, "in that case his motion around the circumference of the arena will also remain under some limit, so the lion would soon catch up with him."

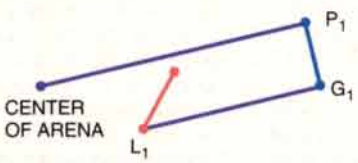
"I fear not," Noblina said. "If the length of the *n*th segment of his path is proportional to, say, the fourth root of the cube of the reciprocal of *n*, then

An Escape Strategy

A gladiator can always avoid being captured by a lion if he runs just as fast as the animal and if he applies the following strategy. Assume the gladiator starts at position G_1 in an arena, and the lion begins at position L_1.

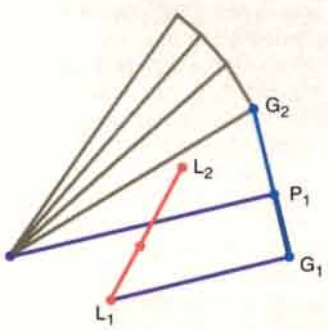
FIRST STEP

The gladiator runs perpendicular to the line G_1L_1 until he reaches P_1—the intersection of his path and the radius parallel to the line G_1L_1.



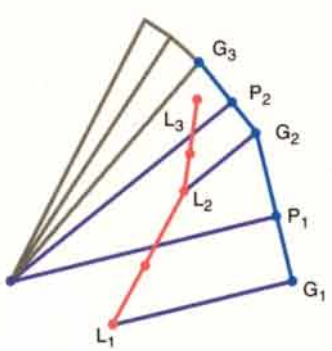
SECOND STEP

The gladiator continues past P_1 for a distance equal to the first segment of the squiral [*see illustration on preceding page*]. Meanwhile the lion moves to position L_2.



SUBSEQUENT MOVES

The gladiator runs perpendicular to the line joining G_n and L_n, and then he continues past P_n for a distance equal to the nth side of the squiral. By doing so, the warrior will never fall into the jaws of the lion.



a short calculation shows that the radial distance remains bounded, whereas the angular distance can be made to exceed any given quantity. I regret that Egocentrix can continue his squiral indefinitely without ever reaching the wall or being caught by the lion."

A messenger tapped Barnumus on the shoulder. "The emperor wishes to speak to you."

Barnumus left with the messenger and returned a few minutes later, looking very pale. "Noblina, you've got to help me! Now I've got to untrain the lion so that it's free to follow its own inclinations. And what's worse, the emperor wants *me* to fight next week!"

"It's a pity you run at exactly the same speed as the lion," Noblina said.

"Will of the gods. I knew I ought to have made a larger offering to the vestal virgins.... Please, Noblina."

"Well, you can't follow a squiral any more, because the lion can cut across the corners. But maybe we can do something about that—"

A week later Romans packed the amphitheater to watch the great fight between Barnumus and the lion. Noblina and Fastidius were invited to sit in the royal box. "I think I'm going to enjoy this," Emperor Scandalus said.

"Barnumus Bailus will certainly provide the lion's share of our entertainment," Fastidius replied with a grin. The beast was released. Barnumus set off at right angles to the line joining him to the lion. The lion cut across toward him, abandoning its failed radial strategy and heading roughly toward where it thought Barnumus was going. Barnumus ignored the lion's moves and suddenly changed direction, again at right angles to the line between himself and the lion.

"He won't keep this up much longer," Scandalus said. "Barnumus will stop and fight when he realizes it is inevitable that the lion will catch him."

Noblina nodded in apparent agreement, but her thoughts belied her expression. She had taught Barnumus a new strategy to keep the lion at bay. She watched him execute the strategy perfectly [*see box at left*]. First, he assumed the lion would always stay on the same radius as he did, and by doing so he was able to use Egocentrix's method to map out a squiral in his mind. But because the lion no longer used the radial strategy, he had to modify his movements according to the lion's actual position.

He began by moving at right angles to the line joining himself and the lion. He ran in that direction until his path intersected the radius parallel to that line. From there he continued in the same direction for a distance equal to the first segment of the squiral. At the end, he assessed the position of the lion and once again moved at right angles to the line between himself and the lion. He then ran across the parallel radius and beyond it by a distance equal to the second segment of the squiral. He calculated all further moves in a similar fashion.

Before the fight Noblina had proved that the strategy would work. Barnumus could not be caught by the lion along each segment of his path. Furthermore, his path always remained within the walls of the arena, and its total length exceeded any finite bound.

Afterward Barnumus walked over to Noblina and shook her hand. "Your strategy worked like a charm."

Fastidius appeared. "Ah, the star of our show. In fact, your performance was so wonderful that the emperor has decided to let you repeat it next week."

"I'd really prefer to retire while my career is at its peak—"

"Against two lions, this time." Fastidius turned on his heels. Barnumus looked imploringly at Noblina.

"Against two lions you're a dead duck, I'm afraid," Noblina said. "Unless the emperor rebuilds the arena, expanding it into the third dimension, thereby making it a sphere. It can be proved that n lions all running at the same speed as a gladiator can always catch him in an n-dimensional ball, but n-1 lions cannot if the warrior adopts the right tactics. Perhaps I can persuade the emperor to place some obstacles in the arena for you to hide behind."

"Will that help?" Barnumus asked.

"The point is arguable. One lion cannot catch you if there is an obstacle: you merely maneuver until the obstacle is between yourself and the beast and keep it there. But it is an unsolved question whether a warrior can always avoid two lions when there are several obstacles. You must exert every effort to find the solution, Barnumus. If Hera permits, you may yet survive."

"But I don't know any geometry!" Barnumus wailed.

"You should have realized it would be useful someday," Noblina countered.

"Why should I have come to that ridiculous conclusion?"

"Because, Barnumus, geometry reveals everything you ever wanted to know about ruling lots of lions."

FURTHER READING

LITTLEWOOD'S MISCELLANY. Revised edition. Edited by Béla Bollobás. Cambridge University Press, 1986.

Color and Shape

BASIC COLOR TERMS: THEIR UNIVERSALITY AND EVOLUTION, by Brent Berlin and Paul Kay. Paperback edition, with bound color chart. University of California Press, 1991 ($12.95). **THE CYCLADIC SPIRIT: MASTERPIECES FROM THE NICHOLAS P. GOULANDRIS COLLECTION**, by Colin Renfrew. Photographs by John Bigelow Taylor. Harry N. Abrams, 1991 ($49.50).

MONUMENTAL CYCLADIC FIGURE was sculpted from marble sometime around 2500 B.C. (Height: 55 1/8 inches.)

Together the two books under review display surprising invariances in the expression of human visual perception.

It was in 1969 that anthropologist Berlin and linguist Kay of Berkeley first published their ironclad experimental results. Join the study for yourself: the experimenters first elicit verbally your list of all the basic color terms you can recall. Basic terms are elementary, inclusive color names in common use, words such as black, white, green and red, whose meaning cannot be gained merely from the meaning of their parts, as for blue-green. *Lemon-colored* has a deducible meaning, unlike yellow; *crimson* is surely included under red; *like my aunt's car* is private. Recent foreign loan words (chartreuse) and all terms that name objects are suspect. (*Orange* makes it only because it satisfies all the other criteria well.)

Now match the terms against an array of colored samples. These 300 test colors are more than the rainbow; they are real surface colors, the full range from black to white, along with brown, gray, purple... arranged in a kind of flat Mercator map of the implied color solid. That abstract solid can be thought of as having two poles, white and black. Sample brightnesses shade smoothly down the meridians from one pole to the other; distinct hues circle the latitudes from red through yellow to green, blue, purple, then back to red. It is easy to mark out on the flat map all the color areas you would ever include for each name you list and to choose as well the best color location for each term, a focus for that color name.

Native speakers resident in the San Francisco Bay Area took part, a few or sometimes only one for 20 languages, from Arabic and Bulgarian on to Urdu and Vietnamese. The foci clustered into discrete neighborhoods; most of the map was blank of any focal location. A category focus was rarely displaced more than two chips on repetition. The differences among maps for individuals who spoke the same language was as great or a little greater than those found between languages.

Color perception is not random, nor are its linguistic categories. None of the lexicons tested held more than 11 basic terms, the number demanded by English and eight other of the test languages. Of course, not all languages use those same basic color categories. Among the tongues tested, the smallest number of basic terms required was in one language of the Native Americans of California; Pomo needs names only for white, black and red.

The authors extended their results to 98 languages by use of the linguistic literature. A couple of New Guinea Highlands languages use only two basic terms, white along with all light hues and black with all the dark ones. Of course, Jalé viewers, say, perceive many hues; it is their linguistic needs that are specialized. If they "have frequent oc-

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casion to contrast fine shades of leaf color" but have no "dyed fabrics, color-coded ... wires, and so forth, it may not be worthwhile to rote-learn labels for gross perceptual discriminations such as green/blue, despite the psychophysical salience of such contrasts."

A striking conjecture follows. Languages can be ranked in stages, more color terms entering in highly constrained order. After languages that name only the polar pair, called Stage I, come tongues that name red as well, then those that add first one and then the other of the pair green or yellow, then to blue, then brown, and in no fixed order, purple, pink, orange and gray, to plateau at 11. Among the 2,000 possible combinations of 11 terms, only 22 combinations actually occur among the almost 100 languages tested. The more people in the language community, the more it tends to the later stages.

There are few anomalies. Cantonese lacks brown, and pink is a Cantonese word only in this century; Russian may use two terms for blues; this reviewer, for one, would include pink among the reds (maybe only ten and a half terms in English?). All are minor quantitative exceptions. The authors have newly proposed a larger study, to test on the spot many speakers from each of 100 unwritten languages, avoiding all perturbations from bilingual experience. One hopes the grantors will soon agree; here is an insight into perceptual and linguistic unity we should deepen. This small jewel of the sciences of human behavior has been reprinted after 20 years without revision save for a new bibliography and a less ample color chart.

The first of these two books offers a stunning demonstration of universality across 100 languages. The second book, set on the boundary between art history and archaeology, attends instead to an invariance over time, a full recurrence in aesthetic judgment across several millennia.

Consider two descriptions of one sculptured piece, a nearly life-size marble head found in 1891 on the island of Amorgos. Its discoverer described it as a "repulsively ugly head." In 1991 our present author, distinguished senior archaeologist at the University of Cambridge, speaks of the head as "a masterpiece, commanding the respect and admiration of artists and of the general public." "What once seemed uncouth is now recognized as profound in its simplicity." (The reader may judge from several good photographs.)

One chapter of the attractive volume reconstructs the antique context; it is by Christos Doumas, the archaeologist who helped form and first catalogued the great Athens collection portrayed here. The Cyclades are a couple of dozen rocky islands and many islets in the Aegean Sea, found just offshore of the Attic mainland and then southeast, halfway to Crete. A few, among them Melos, Delos and Thera, are widely known. Not one is much larger than Martha's Vineyard. The austerely beautiful seagirt hilltops, mainly of marble and limestone, are the peaks of a long-drowned landscape. Small bands of farmers and fisherfolk first came from the mainland around 5000 B.C., bringing to the islands barley and wheat, olive and vine, sheep and goat, fishline and spear, to dwell frugally there ever since.

Most ancient island graveyards were searched out and robbed of their grave goods during the 19th century. Few of the museum artifacts shown here have, therefore, an archaeological context; what we know of the earliest settlement rests primarily on a single post-war excavation of a Neolithic site.

These islanders were not wholly isolated; the work of their hands is found also in Minoan tombs and on the mainland. The many-oared longships they used, without sails, are shown here in three touching hull models of lead and in one engraving on pottery. In time they worked silver and bronze. Their most characteristic art, in marble, is datable to a prosperous era in the Early Bronze Age, say, about 2700 to 2300 B.C. At length, those scattered family farmsteads clustered into larger, well-fortified island centers, each home to 1,000 or 2,000 people. The unique "Cycladic spirit" wrought in marble became only a memory by 2000 B.C. It was the careful burial of early island dead in cists, boxes made of flat slabs of rock, that preserved the fragile artifacts over four millennia.

The celebrated "canonical" Cycladic forms are elegantly narrow, flattened, nude sculptured figures, most of them female, arms folded, toes pointed. Nearly all are smaller figurines, but a few are monumental, almost life-size. It is hard now to be sure whether they represent deity or worshipper, whether they were used during life or only in the grave, whether the many breaks and repairs seen were made mainly during fabrication or after long use, and—most tantalizing—just how much the white marble was originally painted. For traces unmistakably demonstrate that even the purest figures once bore painted eyes, hair and possibly some features of dress. The author invokes analogies in later Greek work to argue that the original decoration was not dominant but restrained and secondary, though we cannot be sure. Those who made the figures were seeking some likeness of the flesh. Painted eyes were essential parts of their half-magical work of creation, even though when the sculptor first carved and smoothed that head of stone, it surely had "no eyes, just as there are none now." (A reader looks forward to intense, even microscopic, physical study of these objects.)

This century has opened our own eyes, to find delight anew in "simplicity arrived at through the abstraction of form." Did the old artists of those spare shores intend the final simplicity we so admire?

Power and Control

VISIONS OF A FLYING MACHINE: THE WRIGHT BROTHERS AND THE PROCESS OF INVENTION, by Peter L. Jakab. Smithsonian Institution Press, 1990 ($22.50).

At the height of its boom a few years before 1900, the American bicycle industry produced well over a million cycles a year. Its up-to-date products were fabricated with an eye to lightness and strength, using frames of steel tubing, chain and sprocket power drives and tensioned wire wheels. In the small, lively city of Dayton, Ohio, a dozen shops were making bicycles in those years; one of these belonged to two brothers of around 30 years old, avid cyclists with a local reputation as skillful mechanics. Their bicycles were their own artisanal metalwork, done in their own small shop, where they worked as close-knit partners within a supportive, middle-class family. Well-read, computationally adept, they were designers of ingenuity and flair, indifferent to credentials (both were formally high school dropouts, though excellent students).

In the late spring of 1899 Wilbur Wright (he was the older by four years) wrote to the Smithsonian Institution for publications on human flight that would aid "a systematic study of the subject in preparation for practical work." Assistant Secretary Richard Rathbun replied promptly (reflecting enduring credit on himself and his organization), listing five volumes, all of the 1890s, and sending four pamphlets as well. That exchange marked the recorded opening of the Wrights' brilliant campaign of engineering development, although their interest in flight probably came a couple of years earlier.

Their energy would lead them in five and a half years straight to "the world's first truly practical flying machine." It was Wilbur who took off in the third

of their powered planes on October 5, 1905, to fly around and around a wide pasture near Dayton, 30 laps under full control, making 25 miles at an average speed of 38 miles per hour, to land when his fuel ran low. Human flight had overtaken the birds.

This short, clear, nontechnical book by a young historian at the National Air and Space Museum of the Smithsonian focuses on the nature of the Wrights' inventive work over those five fruitful years. It is not a life of the brothers; an authoritative biography, *The Bishop's Boys: A Life of Wilbur and Orville Wright,* was published by Tom D. Crouch in 1989. Jakab's study is constructed from the lengthy documentary record, letters, diaries, papers and photographs (of course, the brothers had a darkroom), from reconstructions of their aerodynamic instruments and experiments, and from flights at Kitty Hawk, using full-size reproductions of Wright gliders. Dr. Jakab recalls: "Sailing down Big Hill on board the ... 1902 glider ... engendered a feeling of satisfaction beyond words.... There is a distinct feeling of power and control over the glider, yet at the same time there is a clear demand of respect by the machine for the forces it is harnessing.... Poring over the ... records ... sensory and emotional aspects of uncovering the secrets of flight can become lost." What the Wrights could express only sparingly they knew in their bones.

Intuition is always part of creative work; the Wrights were no exception. But their story is a narrative of rational growth in understanding the abstractions of aerodynamics, expressed in graphic, even visual terms. They pondered the latest technical literature, found a senior engineering correspondent (he was a maladroit glider designer but a valuable friend), and used the first gliders they made as tethered kites to measure the forces of the air.

Their photographs testify to growing understanding. They made a small wind tunnel for themselves, its fan powered by belting from their one-cylinder shop motor when the windstream generated by cycling proved unreliable. Reproductions of their devices verify their own excellent data. They designed a propeller from the highly original insight that it could be analyzed as a rotating wing. (A few pages on lift and drag seen at a more technical level might better have explained the nature of the long-standing errors the Wrights had to overcome.)

Their cycling experience was certainly significant. Their gliders have clever tensioned wire trussing; their power drive was scaled up from the best bicy-

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cle practice. They knew about air drag on the cyclist and piloted their gliders lying prone, at some risk of injury. Most important, they knew that a moving bicycle is not in stable motion but depends on its rider for constant corrections. Maneuverable but unstable Flyers did not confound them; by trial and analyzed error, building a grasp of the forces of flight with each new design, they reached the goal of controlled flight.

The Wrights understood from the first that their goal was an entire flight system: structure, control and propulsion. That system they developed—their engine was state of the art, but not beyond—in a five-year paradigm of engineering creativity. Wilbur's death from typhoid fever in 1912 ended the brothers' influence on flight. It is no criticism to recall that large-scale international engineering and analytic progress would soon outstrip the pioneers by an order of magnitude for structure, control and propulsion, all three.

Hazards and Disasters

NATURAL HAZARDS, by Edward Bryant. Cambridge University Press, 1991 ($79.50; paperbound, $29.50).

The 1990s have been declared by the United Nations as the International Decade for Natural Disaster Reduction, as proposed years back by Frank Press, president of the U.S. National Academy of Sciences. Hazards are grand natural events, rare and unstoppable, but disasters are their grim consequences. Preparation, education and warning—even remedy, if not prevention—lie increasingly within the reach of science and of governments if they will act. This book of rather grim wonders is a readable survey that treats the widest range of natural hazards and their disasters. Physical process and societal impact alike are surveyed at an unspecialized but serious level, with maps, diagrams, tables and graphs in plenty, along with a few formulas. It is a fine introduction for students and a ready reference for all readers.

A dozen rich chapters sketch just how we think these events occur and render the models quite real with case-histories, remarkable concrete examples that challenge and often extend common sense. Several other chapters assess the human responses, again at all levels, from touchingly beset individuals the world around to the international organizations of relief—not to forget rock musician Bob Geldof and his successful worldwide campaigns against

famine caused by drought. The greenhouse effect and other slowly emerging changes are not treated here; the author quite credibly argues that many of the events discussed are too hastily read as signs of long-range trends when they are instead built-in variability.

Climatic hazards have the widest impact, droughts most devastating for us, who are dependents of the green plants. Floods and tropical storms show the other implacable face of the Cloud Powers and bring the largest death tolls. The not quite solid earth takes second rank in human toll, earthquake temblor followed by the more localized violence of volcanoes. Then 30 other hazards march somberly past, wildfire and ice, hail and lightning, rockfalls and mudflows.

No survey of a survey is much use; let us rather sample element by element. *Earth:* An earthquake shock in 1970 loosed the ice cap of a Peruvian mountain, to cascade down a steep valley under trapped-air lubrication. It entrained enough water and gravel to end as a curly breaking wave of mud 80 meters high that engulfed and buried two entire towns within four minutes. *Air:* In 1869 a hurricane moved with just the right speed, so that its lowered barometric pressure raised a mass of water tuned to resonate with the tides as the storm went up the Bay of Fundy. The flood tide was doubled, in a surge of seawater 30 meters high. *Fire:* Semiarid and desert rural Australia was covered with an unusual "blanket of grasses and dense shrub." The next year was dry; widespread wildfires burned a sixth of the continent, an area of a million square kilometers with little loss of life. (No larger area of burn is known since the worldwide cometary fires at the Cretaceous-Tertiary boundary.) *Water:* During the past 20 centuries, the Yellow River, now suspended 20 meters above the dike-lined floodplain on a bed of its own silt, has found no fewer than 10 paths to the sea. Its shifting mouths are mapped out along more than 500 miles of coast, nearly all the way from present Shanghai to Beijing. The map of past Mississippi deltaic lobes over 6,000 years leaves little doubt that our great silty river slowly follows the same trends; one day it will leave New Orleans dry and seek the salt sea via a much older and larger subdelta about 100 miles to the west.

Professor Bryant's heroic compilation is an excellent guide. Few frank errors are to be found in this volume of high interest and general good sense, although critical readers will want here and there to consult the less casual of his many sources.

ESSAY: A CASE OF DÉJÀ VU by Richard Elliot Benedick

Memories are short. A scant five years ago there was no evidence of global depletion of the ozone layer. Skeptics maintained that the dangers were unproved, that better technologies were nonexistent and that the cost of developing such technologies would disrupt the economy.

The current debate about greenhouse warming conveys a distinct sense of déjà vu. The world again confronts a classic situation: weighing the risks of action and inaction in the face of uncertainties. Short-term costs loom large; long-term dangers seem remote.

Nature, however, is not in the habit of providing convenient early-warning signals. So astounded were scientists in the early 1980s to detect a dramatic seasonal drop in ozone levels over Antarctica that they spent two years rechecking their data. They soon discovered that satellites had dutifully been recording the ozone collapse for several years but had not raised any alert because the computers were programmed to reject such extreme data as anomalies.

The Antarctic ozone hole is an example of what scientists call a nonlinear response; that is, the ozone layer kept absorbing ever more chlorine from man-made sources without revealing any problem, until the concentrations reached a breaking point, and collapse ensued. With respect to greenhouse warming, scientists warn that the billions of tons of carbon dioxide and other gases being emitted by modern industrial economies constitute an unpredictable experiment on the atmosphere. Are we approaching other unknown thresholds?

If we heed those who counsel deferring policy action on global warming, we are betting high stakes that clouds or oceans will offset for a while the intrusions into the atmosphere. If they are wrong, the consequences will be grave. Even the most dire predictions are now shown to have *underestimated* ozone loss caused by chlorofluorocarbons (CFCs). Had CFCs been permitted to continue growing, they would have wrought irreparable damage on the ozone layer. And yet at the time, powerful voices in government and industry strongly opposed regulations, on the grounds of incomplete scientific evidence.

Under these circumstances, the lesson for the policymaker seems clear: if we are to err, let us err on the side of caution. The very existence of scientific uncertainty about global warming should lead us to action rather than delay, especially when most of the international scientific community persistently warns of the risks.

Against this background, at least one country, Japan, has unveiled an aggressive program for improving energy efficiency and developing technology to combat the dangers threatening the environment. The program, called Earth 21, clearly considers protecting the planet to be a commercial opportunity. Contrary to views in some influential circles in the U.S., environmental concern is not a pretext for central planning. Free-market forces can be harnessed to work for sustainable growth. For the market is essentially neutral with respect to the environment; relying solely on Adam Smith will not, as we have painfully learned, invariably lead to the right outcome.

It is our inadequate tools of economic analysis and accounting that often lead planners and investors to precisely the wrong decisions. Outmoded concepts of national accounting generally ignore the "externalities" of environmental damage and discount potential harm. A country's economy, for example, receives a double "boost" from production of toxic products and from their subsequent costly cleanup. Similarly, the more countries such as Malaysia and Indonesia destroy their tropical forests and export their patrimony, the more "growth" they register in their GNP. On a corporate level, the technique of discounting future values intrinsically minimizes the harm to future generations while predisposing managers toward investment decisions that maximize short-run profits.

Something is clearly wrong here. The outmoded system by which we measure income needs to be overhauled so that it reflects the future costs of environmental damage. Only then will financial markets reward environmental protection rather than regarding it as an irksome charge against current profits. Far-ranging benefits could flow from such a reform as markets begin receiving more balanced financial signals and their responses permeate the economy.

Here again, the experience with the ozone layer offers some lessons. Consumers showed that with the right information from the media, they were capable of changing purchasing habits, abandoning or even boycotting CFC-propelled aerosol sprays. And the ozone treaty signed in Montreal in 1987 demonstrated that, with the proper stimulus, industry can change old habits.

Significantly, the Montreal Protocol on Substances that Deplete the Ozone Layer departed from the customary accommodation of environmental regulation to commercial convenience. It did not merely prescribe "best available technology" to replace CFCs. Rather the designers of the treaty mandated a timetable for deep cuts in consumption of these useful chemicals with full knowledge that the technology did not yet exist to achieve those cuts.

The treaty furnished an unmistakable market signal that made it worthwhile for companies to invest in research into new chemicals and processes they had previously eschewed. The rules of the market were modified, creating conditions that mobilized the vast financial and intellectual resources of the private sector to find solutions formerly claimed to be impossible.

Given the most recent scientific revelations on the ozone layer, we are fortunate that the Montreal Protocol stimulated entrepreneurship on behalf of an environmental objective that had previously been ridiculed. Was this a "radical" treaty, as some antiregulatory politicians argued? Far from it: the protocol was an expression of genuine faith in the market system, in its ability to respond to incentives. As it turned out, economists had vastly overestimated the costs of CFC alternatives and new technologies; some industries even lowered expenses by redesigning processes to do without CFC substitutes.

Market signals imposed by an innovative international treaty achieved results for protecting the ozone layer. I suspect we would find the same forces at work if we would focus on reducing dependence on fossil fuels in the current international negotiations on a climate treaty. The moment of truth will be a historic United Nations conference in Rio de Janeiro in June.

RICHARD ELLIOT BENEDICK, formerly deputy assistant secretary of state for environmental matters and chief U.S. negotiator for the Montreal Protocol, is a senior fellow at the World Wildlife Fund.

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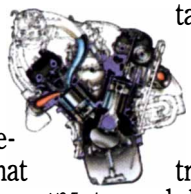

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