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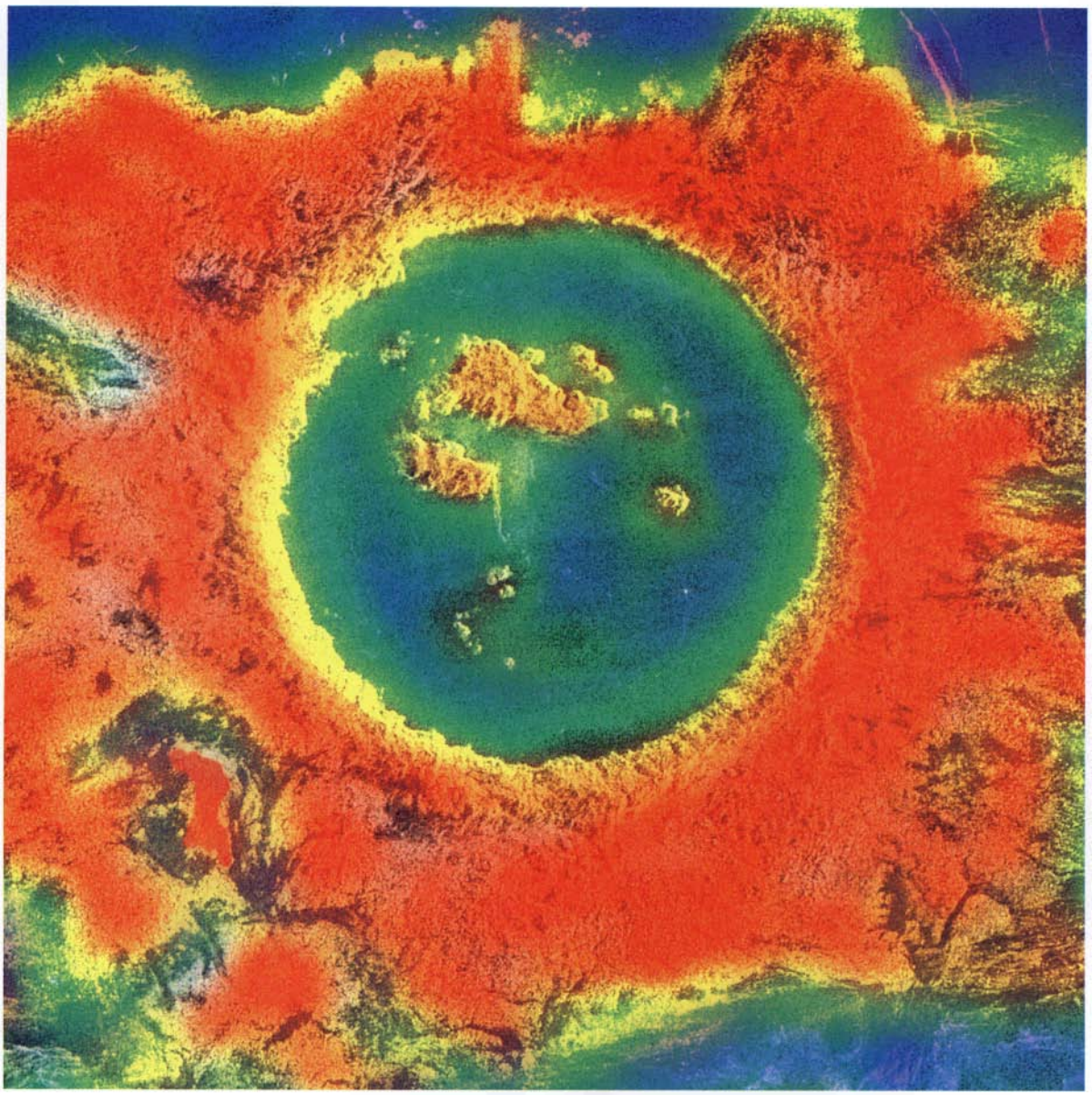
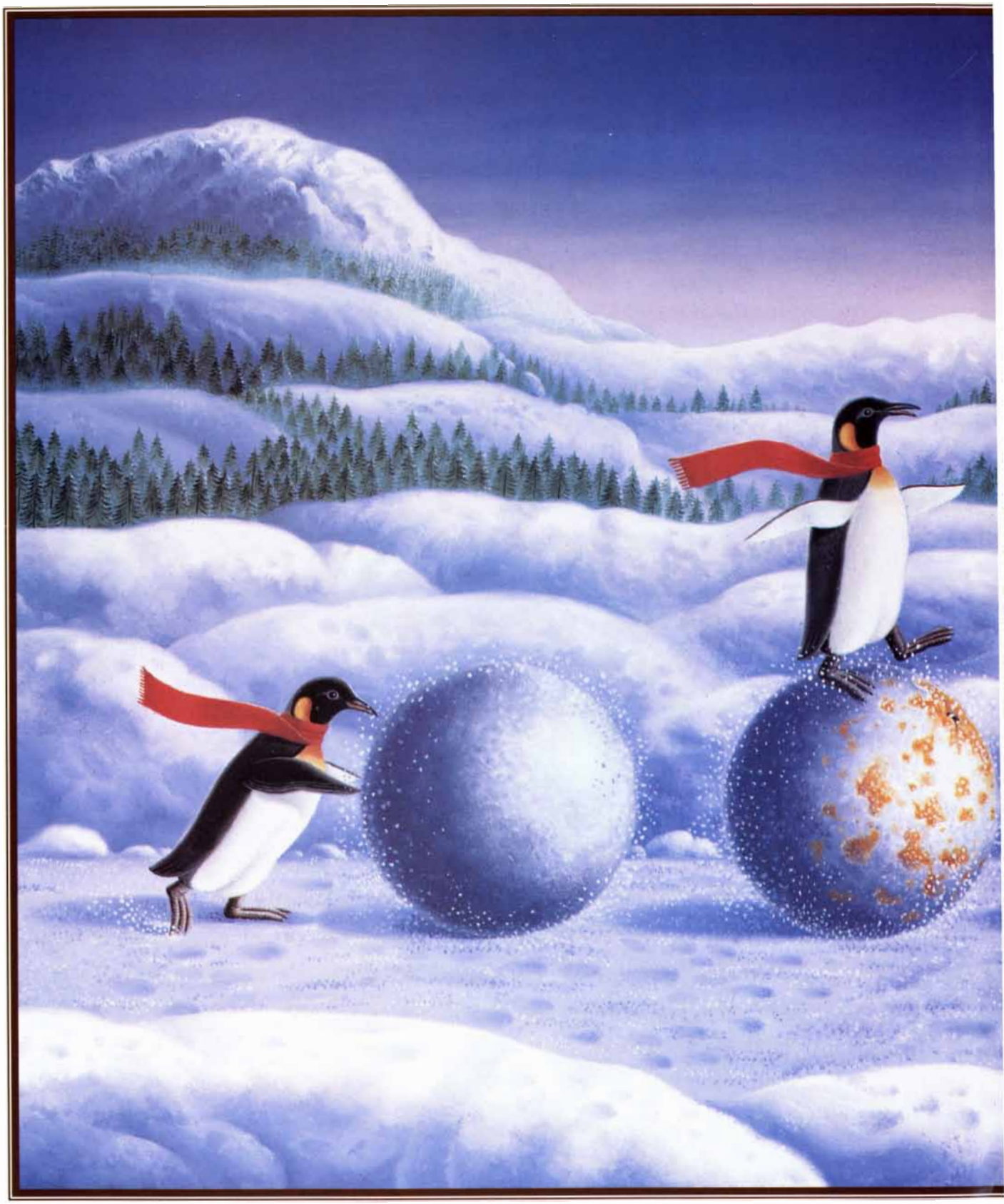
Photographing the birth of molecules with laser pulses.

Animals that survive winter by freezing solid.

The nuclear holocaust could still happen—by accident.



Venus close-up: *radar images from the* Magellan *spacecraft offer the clearest look yet at the forbidding terrain of the second planet.*



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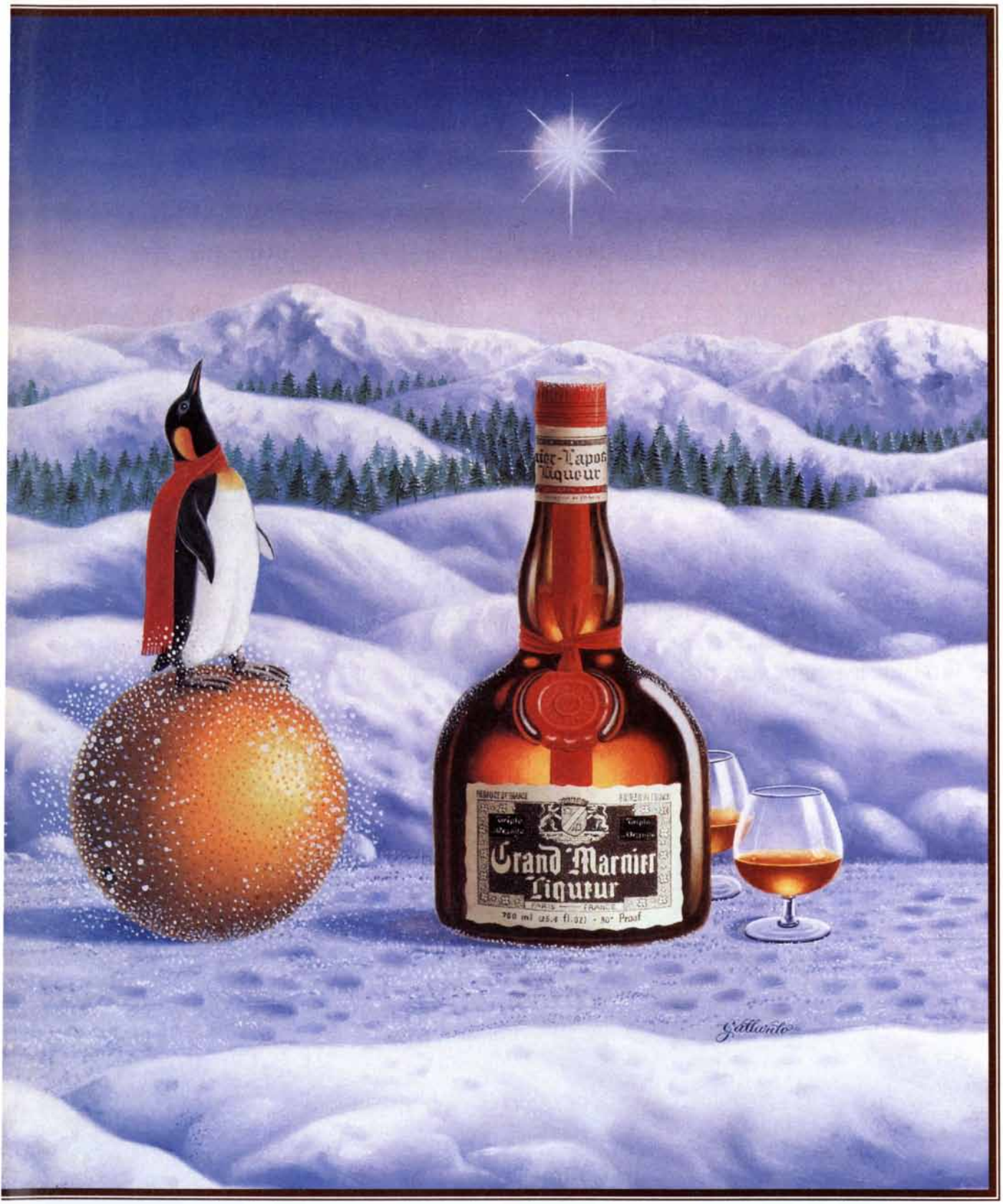

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They would

They try. But somehow Honda always seems to be a car ahead of everybody else. That's not hard to understand.

When you look at the fourth generation Honda Accord, it becomes easy. This latest Accord was designed and engineered to create a new standard of automobile. Our engineers always take that approach to building a new car. It's one that apparently works, too.

The Honda Accord is the best selling car in America. *Car and Driver* magazine considers it to be among the Ten Best Cars in the World. In fact, since they first began the Ten Best list eight years ago, the Accord is the only car to appear on it every time. For that, we thank you.

While our technology puts the Accord out in front of others, it's the workmanship that keeps it there. You will begin to notice it when you take a closer look at the car.

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Inside you will see smooth and soft surfaces. Controls and instruments are all logically placed. A bright, airy environment greets you. And when you close the door,

if they could.

you will be astonished at just how quiet everything has suddenly become.

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HONDA

The Accord

SCIENTIFIC AMERICAN

December 1990 Volume 263 Number 6

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DEPARTMENTS

We'd like to recycle the thinking

Before.

Contrary to public opinion, plastics are among the easiest materials to recycle.

In South Carolina, one company is recycling 100 million pounds of used plastic soft drink bottles a year into carpet yarn, flower pots, toys, and fiberfill for ski parkas.

In Chicago, another company is recycling 2 million plastic milk jugs a year into "plastic lumber" for decks.

In Tennessee, another company is recycling plastic beverage containers into bathtubs and shower stalls.

The recycling of plastics is rapidly catching on. Recycling is transforming used plastics into a "natural resource" that can be used to produce many new products. Recycling is a critical issue as America grapples with its growing solid waste problem.

Our landfills are filling up.

We dispose of 160 million tons of garbage a year. In the past 10 years, our landfills have decreased from about 18,500 to 6,000. Within 5 years 2,000 more will close.

In their haste to find solutions, some policymakers propose to ban plastics. The fact is, plastics make up less than 8% by weight of our solid waste, and although naturally light in weight, only about 20% by volume when compressed in a landfill.

If plastic packaging is banned, the need for packaging won't go away. The idea is to replace plastic with biodegradable materials. Studies show, however, that degra-

that plastics can't be recycled.

After.

dation is so slow in today's landfills so as to almost not exist.

How Amoco Chemical is helping. At Amoco Chemical, we believe all recyclable materials should be recycled—glass, metals, paper and plastics—in addition to source reduction, waste-to-energy incineration and landfilling when appropriate.

Amoco Chemical is sponsoring a recycling program in New York State demonstrating that used, polystyrene foam food service containers from schools and restaurants can be recycled into insulation board for commercial construction, cafeteria trays and home and office products.

We're participating in a consortium with other major plastics manufacturers which will support construction of regional polystyrene recycling plants.

We're encouraging the start-up of new recycling efforts, helping to find better ways to collect and sort recyclables, and helping to create markets for recycled plastics products.

At Amoco Chemical, we believe the more we recycle, the more we'll bring a huge problem down to size.

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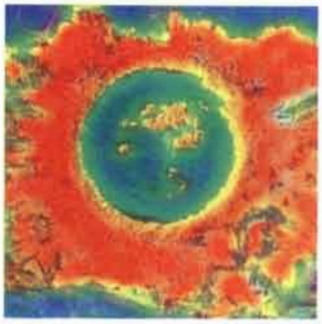

THE COVER radar image shows a 50-kilometer-diameter impact crater on Venus, one of the exquisitely detailed views returned by the *Magellan* spacecraft (see "The Surface of Venus," by R. Stephen Saunders, page 60). False color highlights detail: blue indicates the smoothest, least reflective areas, whereas red indicates the roughest, most radar-reflective ones. The crater appears sharp and fresh, indicating that little surface erosion occurs on Venus despite the planet's dense atmosphere.

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Cover photograph by the National Aeronautics and Space Administration / Jet Propulsion Laboratory

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LETTERS

A Deadly Deterrent

To the Editors:

John Horgan's article on capital punishment ["Science and the Citizen," SCIENTIFIC AMERICAN, July] refers to the usual left-wing sources and arrives at all the popular arguments for abolishing the death penalty. I would like to point out that there is still a case to be made in favor of it.

In his book *Memoirs of an Unregulated Economist,* George J. Stigler, the Nobel laureate in economics, pointed out work done in 1975 showing that "when states executed murderers, for every person executed there was a substantial reduction in the number of murders." He added that "we know that during a period when capital punishment in America was virtually abolished (1960–1970), the annual number of murder victims rose from 8,464 to 16,848, or almost seven times as fast as the population grew."

Furthermore, a committee of the National Academy of Sciences published *Deterrence and Incapacitation* in 1978 and, while apparently feeling that studies on the effects of capital punishment as a deterrent were inconclusive, did not deny the possibility of deterrence.

MICHAEL SCHREINER
Glendale, Wis.

To the Editors:

The reason so many Americans favor capital punishment is glossed over by Horgan but was expressed well by Gilbert and Sullivan: "To make the punishment fit the crime." We should have the death penalty because it's an appropriate punishment for heinous crimes.

PHILIP T. BRISKA
Gulf Breeze, Fla.

Animal Rights Wronged?

To the Editors:

Deborah Erickson's report on the animal-rights movement ["Science and the Citizen," SCIENTIFIC AMERICAN, June] reflects no awareness of the past abuses that have inspired the movement and assumes uncritically that current regulations prevent their recurrence. The great many who have taken up the banner of animal rights are depicted patronizingly as befuddled dupes of a highly organized, unscrupulous elite. With apparent approval, the report cites countermeasures that would deny funding to any researchers acceding to complaints by animal-rights groups, as if there were no possibility that they might be well founded. And nowhere is there recognition that a substantive moral question lies at the heart of the controversy: When may one sentient entity, for its own advantage, deprive, maim and murder another? This is not a matter to be settled by dueling public relations campaigns.

GERALD HULL
Binghamton, N.Y.

To the Editors:

I am a member of People for the Ethical Treatment of Animals as well as other groups dedicated to a more compassionate interpretation of our world. I see an animal, or a plant for that matter, as a living organism that is unique by the fact of its life force. Creatures have only one life to live (Shirley MacLaine notwithstanding) and should be allowed to do so with dignity and in their natural environments.

I am confused by the photograph of the researcher feeding the chimpanzee: he is spoon-feeding it as one might feed a baby, and he obviously cares about its health, yet the chimpanzee is peering through a small opening like one in a jail-cell door. Would that same researcher force his child to live under such conditions or subject himself to such deprivations?

PETER SIMMONS
Valley Center, Calif.

To the Editors:

Your article is an effective and accurate description of the argument between scientists and animal activists. Yet the caption for the accompanying photograph is potentially misleading. The photograph was taken in Africa, not at the New York University Medical Center. The veterinarian shown in the picture had diagnosed the chimpanzee as having life-threatening anemia brought on by a massive hookworm infection, and the animal was being housed in a small transport cage to restrict her movements while the veterinarian awaited blood to be sent from N.Y.U.'s primate colony in the U.S.

At the N.Y.U. Medical Center, the cages for our primates are significantly larger, and our researchers are garbed in the appropriate protective clothing. We adhere to all protocols for the care and treatment of our primates.

JOHN R. DEATS
Director, Office of Public Affairs
New York University Medical Center
New York City

Heaviside and Einstein

To the Editors:

In his otherwise excellent article, "Oliver Heaviside" [SCIENTIFIC AMERICAN, June], Paul J. Nahin states that Heaviside foresaw several aspects of Einstein's theory of relativity. In truth, the theories that Heaviside and Einstein developed were worlds apart.

Heaviside did publish a relativistic correction for the energy levels of a moving electron and an equation describing the electrodynamic fields of an electron, both 16 years before Einstein. Although his equation is identical to Einstein's, according to Heaviside, mass does not increase with velocity. Instead the field of the electron decreases. The two explanations are experimentally equivalent.

Heaviside's genius was not that he foresaw Einstein's theory but that he didn't need it to explain anything.

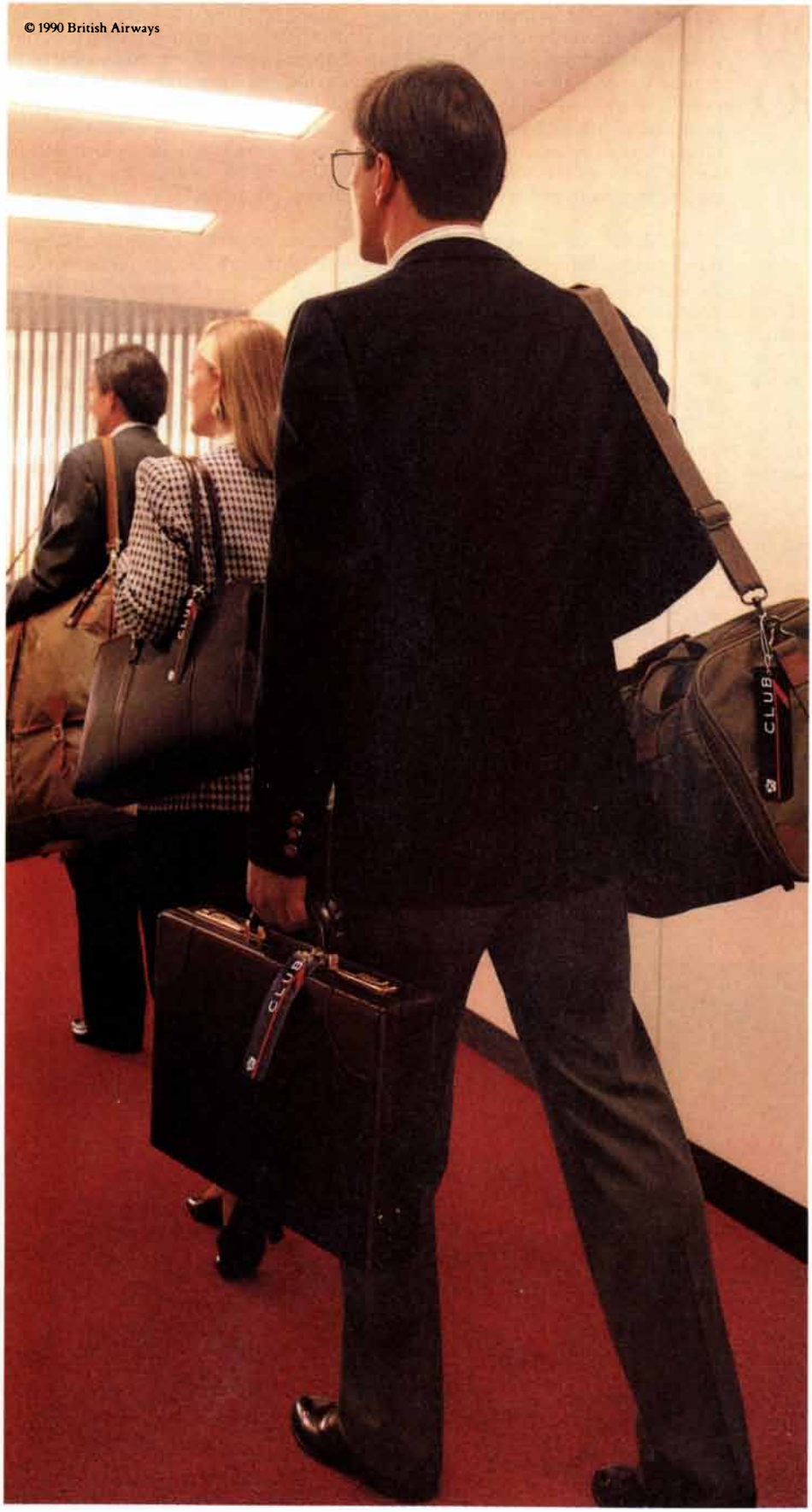
MARTIN J. KEELER
Needham Heights, Mass.

ERRATA

In "Energy from Fossil Fuels," by William Fulkerson, Roddie R. Judkins and Manoj K. Sanghvi [SCIENTIFIC AMERICAN, September], three lines were inadvertently lost between the end of page 131 and the beginning of page 132. The sentence should have read: "Because of their higher efficiency, advanced repowering technologies can help limit the more copious, and more troubling, emissions of CO_2, which is a major and long-lived greenhouse gas and accounts for about half of the volume of such gases in the atmosphere."

In "Universal Truths," by John Horgan [SCIENTIFIC AMERICAN, October], the affiliation of Geoffrey R. Burbidge was identified incorrectly. He is a professor of physics at the University of California at San Diego. Also, in the illustration on pages 108–109, the star map shows a region 650 million light-years long and wide and 450 million light-years deep.

We and our authors thank our readers for sharing their thoughts with us. Because of the volume of mail that we receive, we are unable to answer more than a fraction of it.



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"History records several cases in which entire nations have within a few years developed wide-spread alcoholism. In all such cases the cause has been the introduction into popular consumption of high proof spirits with low taxes, or none. This occurred in England in the reign of Queen Anne. England was at war with France, and allied with Holland. So French wines were so far as possible excluded, and 'Hollands,' or gin, was favored as a sign of patriotism. As a result, habitual drunkenness became appallingly general."

"Venus—the most conspicuous of the planets—is in many ways the most disappointing to the astronomer. The casual visitor to an observatory, enjoying a daytime telescopic view of the planet near the time of its greatest brightness, is likely to exclaim with delight at its brilliance, its whiteness, its crescent phase. The experienced planetary observer looks at the same featureless view with something very like despair."

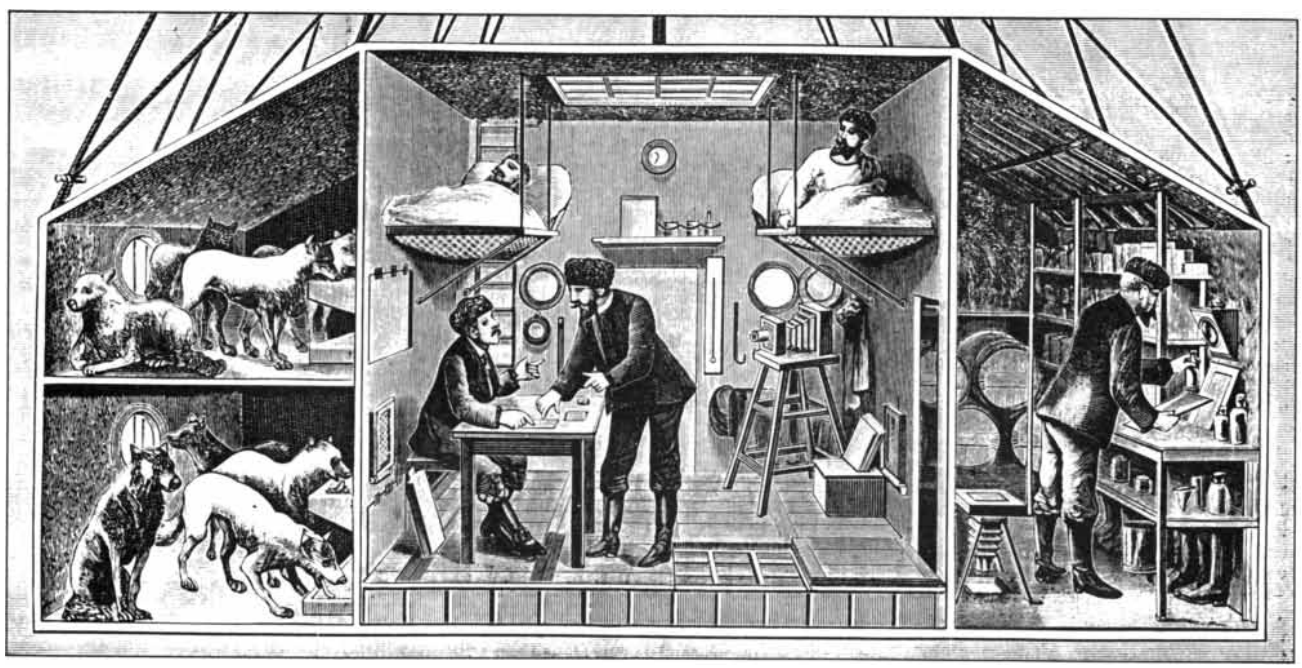
"With the announcement of the building of a new nylon plant to raise the aggregate production to 16,000,000 pounds, Du Pont declares that this total is five times what was contemplated when the first plant was authorized in 1938. It is a snowball rolling up to huge proportions and it is a safe guess that world conditions are giving some of the shove. The United States takes about 78 percent of Japan's silk output. If we take last year's consumption of 50,000,000 pounds, we see that nylon will be ready to fill one third of silk requirements by 1942."

SCIENTIFIC AMERICAN

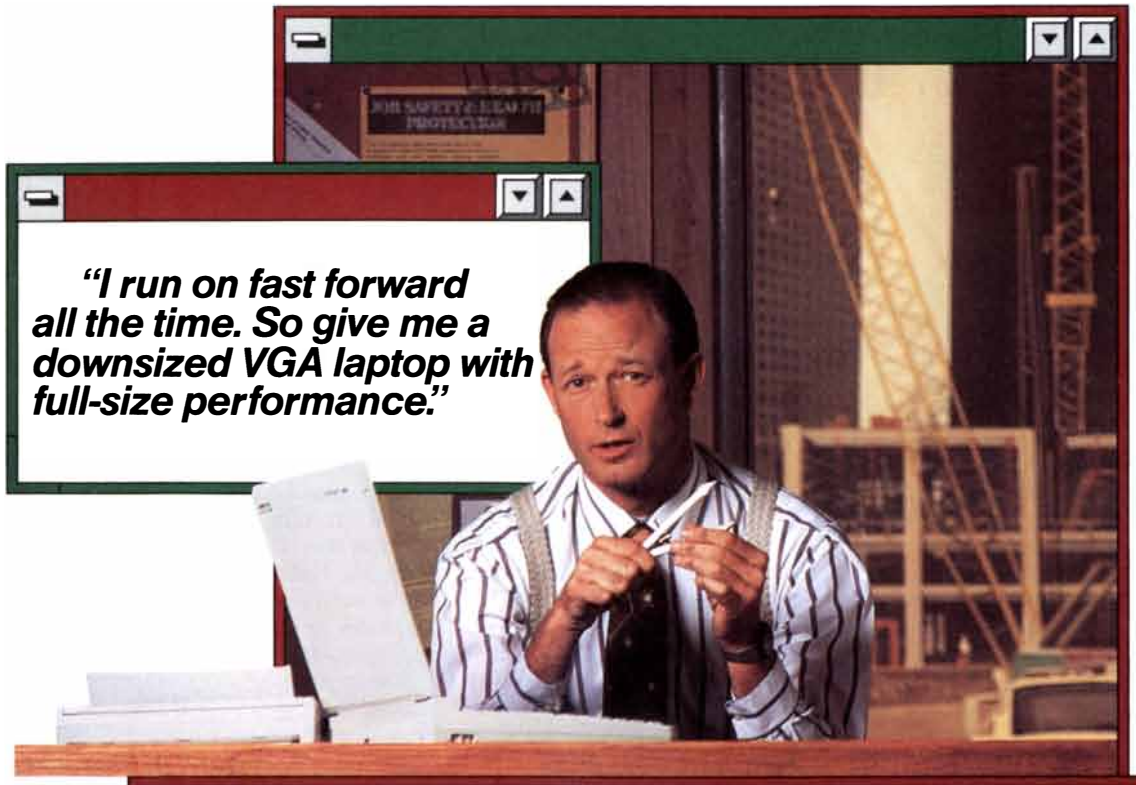
DECEMBER, 1890: "Any plain-spoken physician will say at once that there can be too much exercise and that unwise forms of exercise can be injurious. He will also say that there is very slight essential connection between muscle and that supreme physical quality—vitality. Cultivating muscle does more for beauty, probably, than for health, and since beauty is really one of the proper objects of effort, the forms of exercise which bestow most symmetry of outline and grace of movement are to be studied. Running is the great beautifier of figure and movement: the muscle comes where it ought to be, the shoulders go back, the loins hold the trunk well balanced, and the feet take their correct positions."

"Many treat the phenomenon of globular lightning as an optical illusion due to the excessively minute duration of the spark discharge, just as, when we have for an instant gazed upon the noonday sun and turned away, we see a reddish globe of fire float slowly straight before our eyes. This explanation would be irresistible were it not for the fact that these portentous spheres are alleged to terminate their alarming promenades by a deafening explosion. Will none of the votaries of the camera at least attempt to fix a globular discharge while it is perambulating across the landscape?"

"A Parisian aeronaut and a Parisian astronomer, Messrs. Besancon and Hermite, propose to reach the North Pole by a balloon, which, when inflated, will measure 16,250 yards, and have a diameter of 32 1/2 yards. The car is so strengthened by steel armatures as to be absolutely rigid. It is ten feet wide by sixteen long, and will contain, besides the two explorers, eight Esquimaux dogs, a sledge, an unsubmersible canoe, provisions and water rendered unfreezable by a chemical procedure."



A view of the interior of the car



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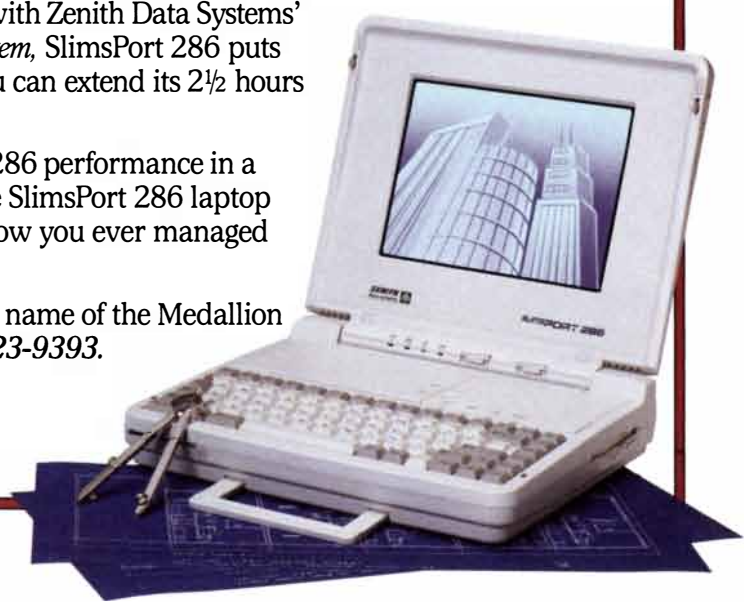


*Source: 1990 Dataquest estimate for U.S. battery-powered laptops. Graphics simulate Microsoft® *Windows™ version 3.0,* a product of Microsoft Corporation. *Intelligent Power Management* is a trademark of Zenith Data Systems Corporation.

Measuring Eternity

New observations favor a younger age for the cosmos

Voyagers *keep voyaging, cancer-killing protons, turbulent mussels, global warming guru*

Are astronomers finally coming to an agreement on the age of the universe? For years textbooks and scholarly articles have cited an unsatisfyingly broad range of official values: from 10 billion to 20 billion years. But recent observations have convinced many astronomers—although certainly not all—that the correct figure is probably 12 billion years or less.

If confirmed, these findings could necessitate a major overhaul of current theories about the nature of the universe. "A young age creates more problems than it solves," notes George H. Jacoby of the National Optical Astronomy Observatories, who has been involved in the new observations.

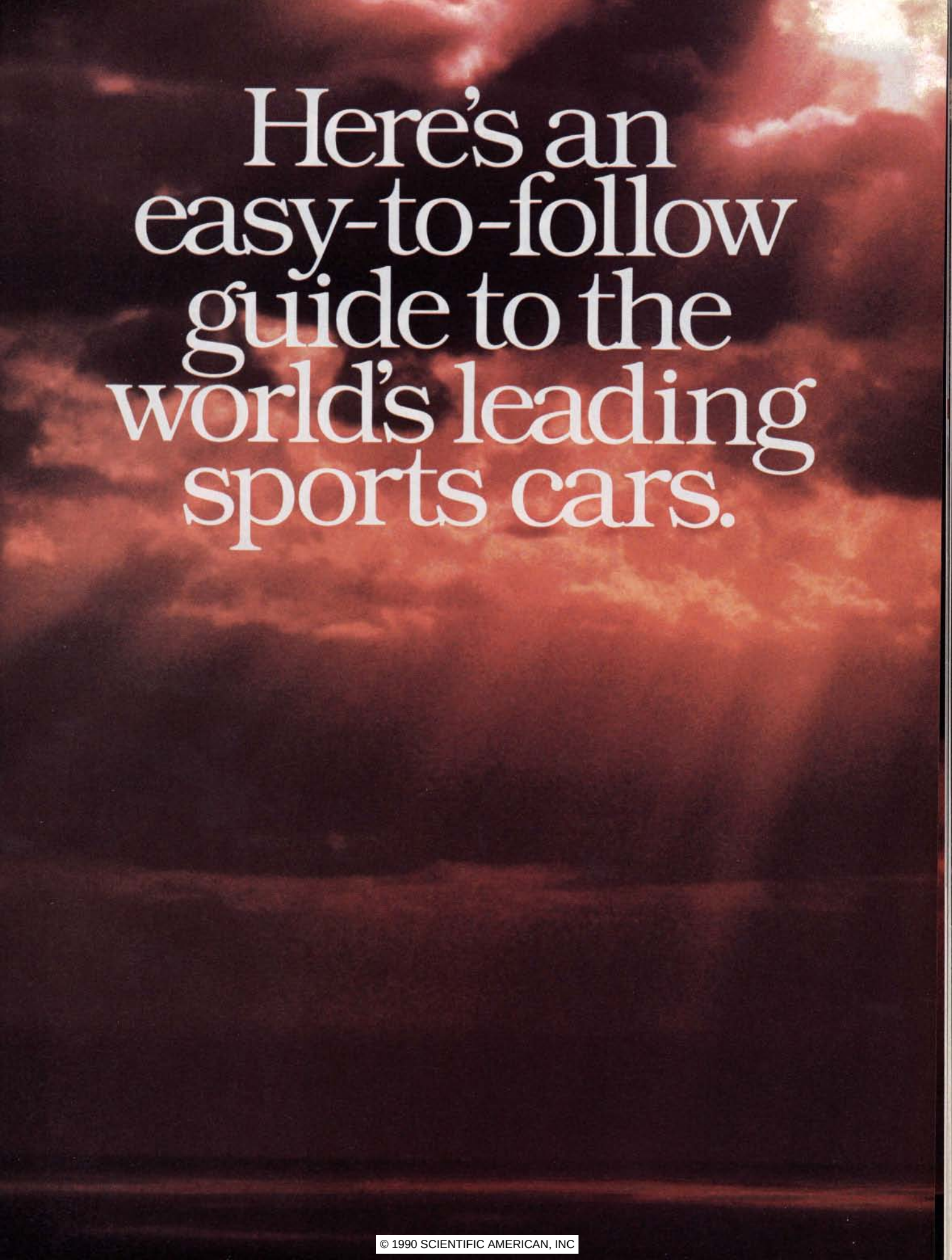
Edwin P. Hubble was the first modern astronomer to suggest that the universe, like its mortal inhabitants, has a finite age. Some 60 years ago he discovered that the light from galaxies tends to be reddened—a sign that they are receding—in proportion to their relative distance from the earth. A galaxy twice as far away as another, in other words, is receding from us twice as fast. This relation between distance and recessional velocity led Hubble to conclude that the universe is expanding.

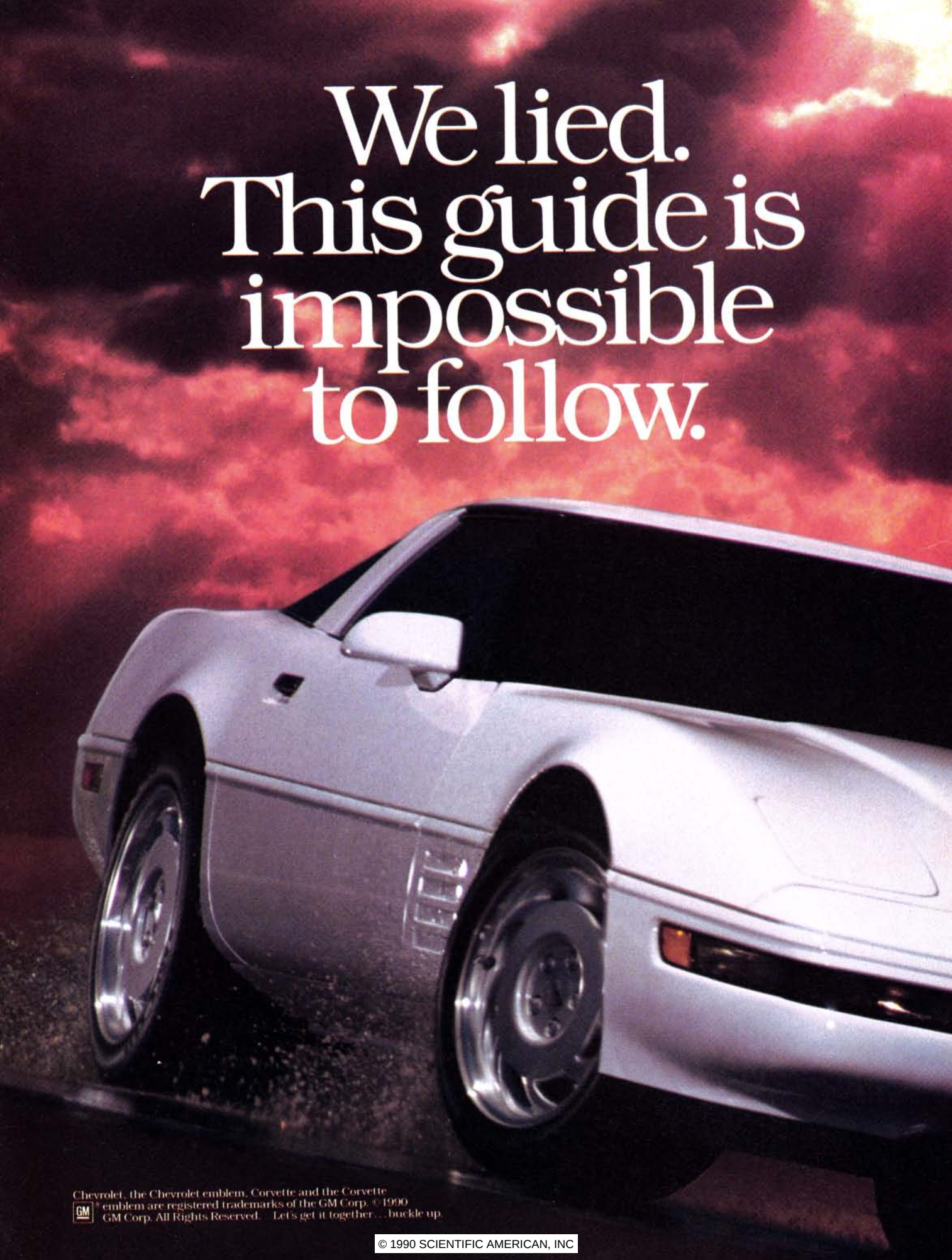
The rate of cosmic expansion is expressed in a ratio known as the Hubble constant, which is calculated by dividing the recessional velocity of a given galaxy by its distance from the earth. To compute the age of the universe, one merely inverts the Hubble constant, dividing distance by recessional velocity. (This method assumes that the universe has expanded at the same rate since its birth in the big bang.)

Recessional velocities are easily derived from the breadth of redshifts. But measuring the true distances of galaxies, the nearest of which are millions of light-years away, is extraordinarily difficult. Moreover, the redshift of any single galaxy—and nearby ones in particular—may be distorted by "peculiar motion" resulting from the gravitational attraction of other galaxies. To pin down the Hubble constant and the age of the universe, then, one must obtain distances to many galaxies, preferably remote ones.

The most common method of estimating distance involves scanning galaxies for so-called standard candles, objects whose intrinsic brightness is known; the apparent brightness of such objects then provides a measure of their distance. The standard candles thought to be the most reliable are Cepheid variables, stars whose light pulsates at a rate that is dependent on

***GALAXIES IN THE VIRGO CLUSTER** are only 48 million light-years away, according to astronomers at the National Optical Astronomy Observatories. The group arrived at this finding, which suggests that the universe is only 12 billion years old, after scanning the galaxies for planetary nebulas* (inset), *aging stars surrounded by spherical clouds of gas.*





Corvette ZR-1

The American landscape is littered with a rag-tag collection of pseudo "sports cars" that, over the years, have challenged Corvette's supremacy. We've seen it all. Turbo this. Supercharged that. All-wheel drive. Front-wheel drive. Even port holes. But in the end, after the hype is long gone, they all find out the hard way. You don't take on 38 years of experience in building America's only true sports car unless you can match our seriousness of purpose, our relentless dedication and our flat-out will to win.

Consider the Corvette ZR-1. This is the machine that obliterated a 50-year-old speed record for production cars, averaging over 175 MPH for 24 hours. Brandishing 5.7 liters of fuel-injected, 32-valve, double overhead cam V8 fury, the 1991 ZR-1 is one of the best sports cars in the world. But the ZR-1 is just one chapter of the Corvette story. Boasting a fierce V8 of its own, the 1991 Corvette thrives with new low-restriction mufflers and 245 horsepower. With either the 6-speed manual or 4-speed automatic gear box, there's enough stump-pulling torque to please even the most jaded enthusiast. All Corvettes get tasteful visual tweaks, including wraparound fog and parking lamps, new side "gills," and newly designed 17" alloy wheels. Corvette coupe and convertible also share the beautiful rounded tail of the ZR-1. And FX3 selective ride control is available on all models. We hope you enjoyed this handy guide. We know our competition did. After all, it's the only time they're allowed to get close enough.

Corvette Convertible

Corvette Coupe

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their size and so their intrinsic brightness. Unfortunately, Cepheids are so dim that they can be observed from ground-based observatories in fewer than a dozen galaxies.

Astronomers have therefore used other objects as standard candles, including variable stars called RR lyras and certain types of stellar explosions, or supernovas. Two other distance measuring techniques exploit correlations between the size (and so the brightness) of galaxies and the velocity of stars within them. These different methods have yielded a wide range of distance estimates.

A crucial assignment for the *Hubble Space Telescope* was to narrow the range of estimates by observing Cepheids in more distant galaxies. The flaw discovered in the telescope's primary lens after its launch last spring has deferred that mission. Nevertheless, new measurements may have resolved the issue, at least to a degree.

One set of measurements, by Jacoby and Robin Ciardullo of the National Optical Astronomy Observatories and Holland C. Ford of Johns Hopkins University, derives from observations of planetary nebulas, spherical clouds of gas ejected by aging stars. Planetary nebulas have a distinct spectrum that can be discerned in distant galaxies, and they also peak at a certain level of brightness. The brightest nebulas serve as standard candles.

Jacoby and his colleagues measured distances to six galaxies scattered within the Virgo cluster, a conglomeration of thousands of galaxies beyond the Virgo constellation. They concluded that the Virgo cluster is relatively near—about 48 million light-years away. This figure suggests that the universe is some 12 billion years old.

Another method has produced at least partial agreement with the conclusions of Jacoby's group. Developed by John Tonry of the Massachusetts Institute of Technology, the technique exploits the fact that detecting individual stars and even clumps of stars within galaxies becomes more difficult as their distances increase. The degree of texture detectable within a given galaxy thus indicates distance.

Tonry says that when he applies this technique to M32, a nearby galaxy whose distance is known, he obtains distances to Virgo only slightly larger than those from Jacoby's group. But he adds a caveat: when calibrated on a computer model of a galaxy, which may be more typical than M32, his technique produces much greater distances to Virgo. These distances imply a cosmic age nearer to 20 billion years.

The short distances to Virgo obtained by Tonry's and Jacoby's groups match those from R. Brent Tully of the University of Hawaii and Michael J. Pierce of the Dominion Astrophysical Observatory in British Columbia. Tully and Pierce estimated distances with the so-called Tully-Fisher technique, developed in the 1970s by Tully and J. Richard Fisher of the National Radio Astronomy Observatory. The method exploits the fact that the rate of rotation of a spiral galaxy, which can be determined from deviations in its redshift, increases with its size.

Analyzing images of five nearby galaxies obtained from extremely sensitive electronic detectors, Wendy L. Freedman of the Carnegie Institution recently obtained the same distances as Tully and Pierce did. Freedman says she would like to calculate distances for several more galaxies before she feels confident enough to support the values that Tully and Pierce espouse for the distance to the Virgo cluster—and for the age of the universe. "But I do think," she adds, "that the most reliable data to date" support the position that the universe is only some 12 billion years old. Tully is less cautious. The evidence for this value "has become overwhelming," he asserts.

Allan Sandage of the Mount Wilson Observatory, the most vehement advocate of high estimates for the age of the universe, rejects the short distances to galaxies obtained by Jacoby, Tully and others. "None of these young people understand statistical astronomy," Sandage says. He notes that observations of supernovas, which he insists are the most reliable long-range standard candles, yield distances consonant with a cosmic age of 20 billion years.

Yet another point of view is taken by John Huchra of Harvard University. After years of studying the issue, Huchra thinks the uncertainties involved in determining distances to galaxies have been underestimated and that the universe may be anywhere from eight billion to 22 billion years old. Only the *Hubble Space Telescope*, he says, when and if it is fixed, can narrow that range.

Nevertheless, many astronomers are beginning to take the evidence for the lower cosmic ages seriously and to face their theoretical consequences, according to Lennox L. Cowie of the University of Hawaii. The biggest problem associated with low cosmic ages, he explains, is that they conflict with the ages obtained for dense pockets of stars known as globular clusters. An analysis of the chemical composition of stars in the clusters suggests that they are at least 13 billion years old.

The conflict becomes even sharper for cosmic models incorporating two closely related and highly popular theories called inflation and dark matter. Inflation holds that the universe underwent an enormous growth spurt shortly after its genesis. It also predicts that the universe contains a vast amount of invisible, or dark, matter that has been steadily slowing down its expansion.

According to this view, galaxies were once receding from the earth faster than they are today, and so their average recessional velocities through time are greater than their current redshifts indicate. Dividing these higher recessional speeds into the short distances obtained by Jacoby and others yields ages of the universe as low as six or seven billion years, in total disagreement with the ages of globular clusters.

The discrepancy could be resolved by resorting to the cosmological constant, which refers to a hypothetical energy inhabiting empty space. This residue of energy, when folded into cosmological models, increases estimates of both the size and the age of the universe. Theorists have spurned the constant because it complicates their models and lacks empirical support. But it "is beginning to look like the most attractive solution to a lot of problems," Cowie says. —*John Horgan*

Far Out

Voyagers *prepare to probe interstellar space*

Where do you go after visiting four planets and 57 moons? Into a bleak, cramped basement office, apparently. "Isn't it awful?" asks J. Pieter de Vries, since 1985 manager of the Voyager Flight Science Office, viewing his new quarters. The high-profile, planetary encounter phase of the Voyager mission has ended, and de Vries and his co-workers have been moved out of their upstairs offices at the Jet Propulsion Laboratory in Pasadena, Calif., to make room for the upcoming Cassini mission to Saturn.

Voyagers 1 and *2* will not fly by any more planets, and so the imaging cameras and most of the other scanning instruments have been turned off. Nevertheless, as de Vries is quick to point out, the probes' mission is far from over. Particle, field and wave detectors are still collecting data. And the scan platforms continue swiveling to orient a single active experiment: a spectrometer that detects ultraviolet radiation.

The ultraviolet spectrometer is sensi-

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tive to wavelengths between 500 and 1,200 angstroms, which are absorbed by the earth's atmosphere and are not being observed by any other currently operating instrument. Although these wavelengths also tend to be absorbed by interstellar gas, the spectrometer has detected radiation from very hot white dwarf stars, like "light coming through the fog," says Jay B. Holberg of the University of Arizona.

The implication is that there are holes in the tenuous clouds of hydrogen that lie between the stars. Perhaps the biggest surprise has been the discovery of strong ultraviolet emissions from globular clusters, indicating that these ancient objects somehow maintain a population of young, hot stars.

The ultraviolet spectrometer is hanging by a slender thread of funding, however; its fate is uncertain as the National Aeronautics and Space Administration prepares the probes for their second incarnation as the Voyager interstellar mission, or VIM, which will emphasize the capabilities of the spacecrafts' bevy of other detectors.

VIM picks up where the Voyager planetary mission left off, as the probes now venture into the unexplored realm between planetary and interstellar space. A continuous stream of charged particles, the solar wind, creates a huge, bubblelike structure known as the heliosphere. The solar wind carries the sun's magnetic field with it, keeping the solar system relatively free of interstellar matter and hindering the entry of cosmic rays.

At some point, the solar wind bumps into denser but slower-moving currents of material in interstellar space, forming a boundary called the heliopause. Current best guesses place the heliopause at 80 to 100 times the earth's distance from the sun (12 billion to 15 billion kilometers), roughly two to three times the distance the *Voyagers* have traveled so far. Variations in the solar wind probably cause the heliopause to undulate back and forth, so it may be detectable at "only" 50 earth orbital radii, a distance the *Voyagers* will attain around the year 2000.

In the meantime the probes' instruments are returning a wealth of information on conditions in the outer solar system. Perhaps the most intriguing findings have come from the cosmic ray instrument, which senses the high-speed charged particles that come from the sun, the Milky Way and intergalactic space. The *Voyagers* have also detected an unanticipated fourth component of medium-energy particles. Edward C. Stone of the California Institute of Technology explains that these probably are atoms from interstellar space energized by turbulent processes occurring near the heliopause. These atoms constitute the first direct samples of the interstellar medium.

So far the abundances of the elements neon, argon and helium determined from the cosmic ray measurements fit the composition expected of the matter between stars. On the other hand, the abundance of carbon relative to oxygen in solar flares seems quite a bit lower than expected. The cosmic ray instrument may provide further surprises as the sun progresses through its 11-year cycle of activity. At the same time, instruments sensitive to less energetic particles will monitor density and latitude variations in the flow of the solar wind.

Complementary observations will be performed by *Voyagers'* magnetic field instruments. The solar cycle and the rotation of the sun combine to create a complex spiral of magnetic fields that fill the heliosphere and guide the passage of cosmic rays and the solar wind through the solar system. This structure is many billions of times the volume of the visible sun. Deflected flows of particles, in turn, generate their own magnetic signatures. The *Voyagers* will work with NASA's other interstellar probes, *Pioneers 10* and *11,* to map the

magnetic topology of the heliosphere and search for the heliopause.

Researchers have produced a five-year science plan for VIM, and NASA promises that VIM will continue for 25 years. But getting the information back to the earth may pose some difficulty. During the 1980s, in part because of the dearth of space science missions, "*Voyager* enjoyed a very high level of priority," notes Norman F. Ness, president of Bartol Research, located at the University of Delaware. Now Voyager is the old kid on the block; Ness worries that scientists will lose valuable information about the small-scale features of the heliopause because the probes will be competing with newer spacecrafts for time on NASA's Deep Space Network of radio receivers when they transmit back their data.

The slow pace of the *Voyagers'* second life may not be glamorous, but it does evoke a certain grandeur. Eventually the *Voyagers* will sail beyond the solar system and look back to examine the heliopause flapping in the interstellar wind. James W. Warwick of the University of Colorado at Boulder admits that this majestic perspective lies years, maybe decades, in the future, but he remains philosophical. "Science," he says without a trace of regret, "is slow business." —*Corey S. Powell*

Going to Pot

A grassroots movement touts hemp's environmental virtues

Worried about global warming? The depletion of forests? U.S. dependence on foreign oil? World hunger? How about the cost of bailing out savings and loan banks? A small but vocal group of Americans is promoting a simple solution to these problems: hemp, also known as *Cannabis sativa,* or marijuana.

Pot enthusiasts have lobbied for the drug's legalization for decades—in vain. But recently they have put an environmental spin on their pitch. They claim that the fast-growing, hardy weed can yield more cellulose per acre than trees; it can be woven into textiles while doing less damage to the environment than synthetic fibers or even cotton; its seeds, which are not psychoactive, are second in protein content only to soybeans; and its seed oil and raw biomass make a renewable source of fuel.

The guru of this grassroots movement is Jack Herer, a large, hirsute Californian and admitted marijuana partaker. "I'm smoking right now," he growled in a recent telephone interview. Herer says he has a "pipe dream" in which people live in homes made of hemp particleboard, read hemp newspapers, wear hemp clothes, drive cars powered by hemp-based methanol and even dine on hemp-seed tofu.

Five years ago Herer wrote and published a history of hemp called *The Emperor Wears No Clothes.* The book, which Herer says has sold more than 100,000 copies so far, is chock-full of marijuana Americana. It notes that Thomas Jefferson, among other forefathers, grew hemp on his farm and that the sails and shrouds of the USS *Constitution* were made of the stuff, as were the original Old Glory sewn by Betsy Ross and the first Levi jeans.

Indeed, hemp was once a major crop in the U.S., used to make textiles, rope, paper and other products. Herer contends it was banned in the 1930s not because of its health risks but because it posed an economic threat to industrialists—notably newspaper magnate William Randolph Hearst—committed to wood and petroleum-based products. If hemp is allowed to return, Herer says, "it could save the planet."

Other experts say Herer's claims are a bit exaggerated. David F. Musto, a Yale University historian of illegal drugs, notes that Hearst campaigned in his newspapers against all drugs, not just marijuana. Quentin Jones of the

U.S. Agricultural Research Service adds that while hemp is certainly versatile, other plants can fulfill its various roles more economically.

Herer retorts that he has a standing offer of $10,000 to anyone who can prove him wrong. He has formed two groups—the Business Alliance for Commerce in Hemp and Help End Marijuana Prohibition (HEMP)—to promote the cause. He also lectures and organizes rallies across the country. In late September he spoke at a pro-marijuana "festival" in Madison, Wis., attended by 14,000 people.

Herer has had difficulty enlisting mainstream types in his movement. Yet he did inspire a Kentucky attorney named Gatewood Galbraith to enter his state's 1991 gubernatorial race on the hemp-legalization platform. Galbraith, who has made campaign appearances in a car powered by diesel fuel and hemp oil, insists his candidacy is for real. He points out that in 1983 he won more than 40,000 votes in a losing bid to become commissioner of agriculture and that country and western star Willie Nelson has endorsed his current bid. "Politically," proclaims Galbraith, who shares Herer's passion for smoking pot, "I'm right on the cutting edge."

Now about the S&L crisis. A plan devised by the Business Alliance for Commerce in Hemp calls for legalizing marijuana, now conservatively estimated to be a $50-billion-a-year business, and then allowing ailing banks to recoup their losses by investing in the trade. Call it a joint venture. —*John Horgan*

***MARIJUANA** can grow 10 feet or more in less than three months. Photo: U.S. Agricultural Research Service.*

Beam of Hope

A proton accelerator is the most costly medicine yet

Loma Linda University Medical Center in southern California does not shy away from ambitious projects. In 1984 it gained worldwide attention with the attempt to transplant a baboon's heart into an infant known to the press as "Baby Fae." Although that operation failed, the hospital has since achieved an international reputation for infant-heart transplants, expanding beyond its early identity as a training school for Seventh-Day Adventist missionaries.

Now Loma Linda is making another big leap. This time it is what may be the world's single most costly medical machine—a $30-million proton-beam accelerator for cancer therapy dubbed the "Beam of Hope." Having treated a patient for ocular melanoma in October, the Loma Linda machine adds a new page to the record books. Including the cost of imaging machines and the 110,000-square-foot building in which the accelerator complex is housed, the bill reaches $60 million—about $20 million of which was funded by the U.S. Department of Energy. The hospital has launched a campaign to raise $40 million to pay the rest of the costs.

Hospital officials and specialists in using high-energy particle beams for cancer treatment say the accelerator's design holds promise of treating more patients with more precise and, in some cases, more penetrating beam delivery than existing proton-therapy machines. Those devices were built for physics research—medical experiments came later. Since 1961 the Harvard Cyclotron Laboratory has treated 5,000 patients with protons for various diseases, including cancer. Since 1954 an experimental particle accelerator at Lawrence Berkeley Laboratory at the University of California at Berkeley has used helium ions to achieve similar therapeutic results on 2,000 patients. "This is an effort to bring into the hospital gains already established at research facilities," says Michael Goitein, professor of radiation therapy at Harvard Medical School.

Many of the relatively rare, superficial cancers treated have responded well to proton-beam therapy. The five-year survival rate for patients with cancers at the base of the skull—chordoma and chondrosarcoma—is 70 percent, double that for X-ray treatment, says Herman D. Suit, chief of radiation therapy at Massachusetts General Hospital, which uses the Harvard accelerator and wants to build its own clinical machine.

The Loma Linda accelerator technology is a direct hand-me-down from the world of quarks and muons. Designed and fabricated by the Fermi National Accelerator Laboratory in Batavia, Ill., the 50-ton synchotron strips electrons from hydrogen atoms before injecting the remaining protons into the accelerator. There the protons are speeded around a 20-foot-diameter ring until they reach energies of between 70 million and 250 million electron volts before being channeled into one of four treatment rooms.

Three of the four rooms contain three-story-high, 90-ton gantries that resemble Ferris wheels. Partly encased in a tubelike cavity (with piped-in music and communications systems), the patient will be reminded to hold still while inside an encircling plastic foam and fiberglass body mold. The gantry will rotate around the patient to the desired angle, and then its four magnets will twist the incoming beam to focus on its target for a minute or so. (The patient with melanoma was treated with a less complex, fixed beam in the fourth treatment room.)

By varying the energy and number of protons accelerated, the Loma Linda beam will be able to scan line by line, like a television cathode-ray gun on a thin slice of tumor. The radiation can be distributed in successive layers within the tumor. Like X rays, protons can destroy tissue by splitting apart DNA molecules or forming reactive oxygen free radicals from water molecules. But X rays, on entering the body, deposit most of their ionizing radiation in the first few centimeters—and do not stop once they reach the tumor site. Protons, in contrast, give up most of their energy only when they slow to a stop, allowing higher-radiation doses while leaving nearby tissue intact.

With equipment specifically designed for the hospital, Loma Linda hopes it will be able to treat tumors more effectively than do the experimental devices. But hospital officials' belief that their therapy may have some use for treating localized tumors of the lung, pancreas and other highly malignant sites has raised a few eyebrows. "Radiotherapists don't like to admit that even though they gain local control of the tumor, they may not help overall survival because of micrometastases," says Eli Glatstein, chief of radiation oncology at the National Cancer Institute in Bethesda, Md.

Loma Linda's proton-beam therapy

will not come cheaply, although hospital officials say it is still less costly than many surgical procedures. There is going to be a full-time staff of at least eight physicians, 12 engineers, eight physicists and 12 technicians—and an electric bill of more than $80,000 a year. The cost for treating each of as many as 2,000 patients every year will range from $10,000 to more than $20,000.

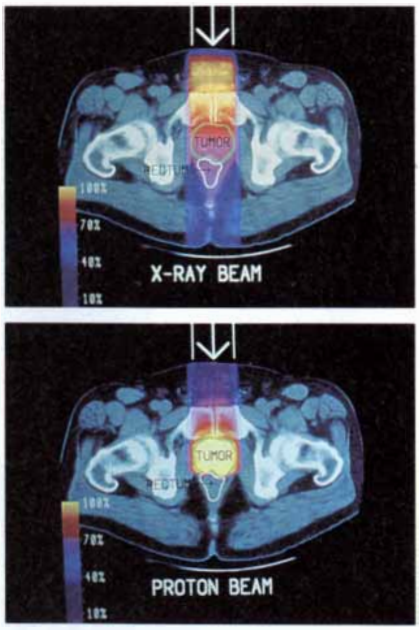
Moreover, Loma Linda is in negotiations with increasingly cost-conscious Medicare and private insurers to decide whether the procedure is reimbursable. In October a neutron-beam therapy center at the University of California at Los Angeles—three quarters of whose patients are older than 65 years—shut its doors because the insurer who administers Medicare for southern California refused to pay. (A neutron facility costs from $5 million to $10 million.)

Indeed, radiation oncologists wonder whether virtually the same therapeutic benefits of proton therapy can be obtained for a fraction of the cost. Some specialists hold out hope that new X-ray therapies, using linear accelerators priced between $450,000 and $1.2 million, can deliver multiple beams to a tumor site, nearly matching the effectiveness of a proton machine. "In general, you spend considerably less money, and you get a dose distribution nearly as good," says Robert L. Goodman, chief of radiation oncology at the Hospital of the University of Pennsylvania.

While it may bear the price tag of a small hospital, the Loma Linda machine will retain its distinction as the most costly medical device for a relatively short time. The National Institute of Radiological Sciences of Japan has begun building a $235-million-plus synchotron in Chiba—the Heavy Ion Medical Accelerator—that will treat cancer by accelerating helium, carbon, argon and other nuclei at energies up to 800 million electron volts.

Loma Linda, however, is not necessarily a one-of-a-kind facility. If clinical proton therapy proves a success, a marketing plan already exists to sell similar machines to other hospitals. Science Applications International Corporation (SAIC), a billion-dollar, high-technology contractor that has done work on directed-energy technologies for the Star Wars program, has licensed the technology from Loma Linda. It believes it may be able to sell as many as 20 of the machines to teaching hospitals. Without development costs borne by Loma Linda, the machines might sell for $20 million.

Finding buyers outside of a small group of elite hospitals will probably prove tough, however. The average equipment budget last year for hospitals with more than 500 beds was $6.5 million, according to the Hospital Equipment Report, a data base of capital purchasing for acute-care hospitals. This means that synchotrons may remain largely the province of the physicist and not the physician. —*Gary Stix*



***PROTON BEAMS** deposit most of their energy directly into a prostate tumor, whereas X rays lose most of their energy, as shown in these computer simulations. A rotating gantry at Loma Linda* (right) *will aim the beam at the area being treated.*

Double Trouble

When identical twins are not identical

John and James Brick are both physicians living in West Virginia. They are also identical twins; a blood test has confirmed that fact. Yet John has always had a bigger appetite and waistline than James. The brothers recently reported on their case in the *New England Journal of Medicine*. The journal has published numerous articles claiming that body weight, like many other human traits, is determined largely by genes. If that is true, John and James asked, why is one Brick brother thicker than the other?

Why indeed? Identical twins are a staple of nature-nuture studies because, supposedly, they are born equal. Researchers assume that physiological or behavioral divergence between them stems from environmental influences.

Yet so-called identical twins may emerge from the womb with significant physiological and even genetic differences. This phenomenon, which probably accounts for the case of the Bricks, is "widely unappreciated" even among twin researchers, according to E. Fuller Torrey, a psychiatrist who has done twin studies for the National Institute of Mental Health and has raised the issue of biological divergence at recent conferences.

Identical twins, who account for about half of 1 percent of the population, are known as monozygotic: they occur when a zygote, or fertilized egg, for reasons that are unclear, splits into two distinct zygotes immediately after conception. (Fraternal twins derive from two eggs fertilized by two sperm.)

From 10 to 20 percent of monozygotic twins, Torrey notes, are subject to a condition called fetal transfusion, in which one twin receives more oxygen and nutrients than the other one does. The twins may differ in weight by a factor of two at birth. Moreover, only one twin may be affected in utero by viruses, bacteria or drugs consumed by the mother. The effects may be permanent. "There are cases where only one twin has fetal alcohol syndrome or is affected by thalidomide," Torrey says.

Genetic divergence between monozygotic twins can occur in several ways, according to Torrey. In the most extreme cases, one twin somehow loses an entire chromosome or obtains extra chromosomes during or soon after the initial egg splitting. Chromosomal mutation may cause Down's syndrome or other types of physical and mental re-

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tardation in the twin; it may even alter the twin's sex.

Cases involving chromosomal divergence are rare and easy to spot. But twins that are apparently identical may have subtle genetic differences that affect behavior or physiology, Torrey says. Such genetic divergence may be difficult to detect with the blood tests used to confirm monozygosity.

Torrey's message has a disturbing implication. Studies of identical twins separated at birth already give postnatal environmental factors such as diet and education a relatively minor role in shaping human traits such as body weight and intelligence. Could the role played by nurture be even *smaller* than the studies suggest? "That is certainly a possibility," Torrey says.—*John Horgan*

Acacia trees kill antelope in the Transvaal

Some ranges are just not safe places for the antelope to play. At many game ranches in South Africa, hundreds of kudu, a kind of antelope, died during each dry season. The cause was neither virus nor bullet. The killers, according to Wouter van Hoven, a zoologist at the University of Pretoria, were acacia leaves.

The acacia is ordinarily a prime source of food for the kudu. Like many other plants, it too produces tannin as a defense against herbivores. Under most conditions, the tannin levels do not harm the kudu. But under extreme environmental stress, such as extensive foraging or drought, the leaves step up their production of the astringent toxin. They then develop an unpleasant taste.

Free-ranging kudu search for leaves that have low levels of tannin, but fenced-in antelope have no choice but to eat ones that have a great deal of the poison. Van Hoven found that during drought acacia trees on some ranches produced enough tannin to inactivate the liver enzymes of kudu, killing many of the animals in about two weeks.

Apparently the acacia trees do not wait for an attack before they mobilize defenses. In fact, they seem capable of conspiring against foragers by communicating with one another. In 1983 Jack C. Shultz and Ian Balwin, two biologists then at Dartmouth College, offered the first evidence of plant communication. They found that healthy sugar maple plants tend to produce greater amounts of tannin and other defense compounds in the presence of plants whose leaves are damaged.

Preliminary work by van Hoven indicates that when an antelope forages on an acacia tree, the leaves emit ethylene. This compound appears to signal other trees up to 50 meters downwind that a herbivore is nearby. The intact trees then step up their own production of tannin before any damage has occurred to the foliage. Under laboratory conditions, van Hoven found that damaged leaves release 20 times more ethylene than uninjured ones do. "When an intact plant is exposed to the [high levels] of ethylene," the tannin levels increased "within 30 minutes," van Hoven observes.

The short-term increase in tannin production acts "as a natural population regulatory mechanism," van Hoven adds. The more frequently a tree is browsed on, the more tannin it produces. To solve the problem, the ranchers reduced the number of kudu on the range and fed them alfalfa during extreme drought. —*Philip Yam*

***KUDU** browse in a grove of acacia trees. Photo: Animals Animals.*

Clearing the Airways

Cystic fibrosis may be treated with gene therapy

Recent laboratory successes have raised the prospect that gene therapy for cystic fibrosis (CF) might be possible in the foreseeable future. Within the past few months, work aimed at correcting the genetic defect that clogs the lungs of CF victims with thick mucus has moved into high gear.

CF is the most common genetic disease of white people, affecting one in every 2,000 live births. As many as one in 20 are carriers of the defective gene. Few CF victims survive beyond the age of 30, often succumbing to infections that ravage their congested lungs.

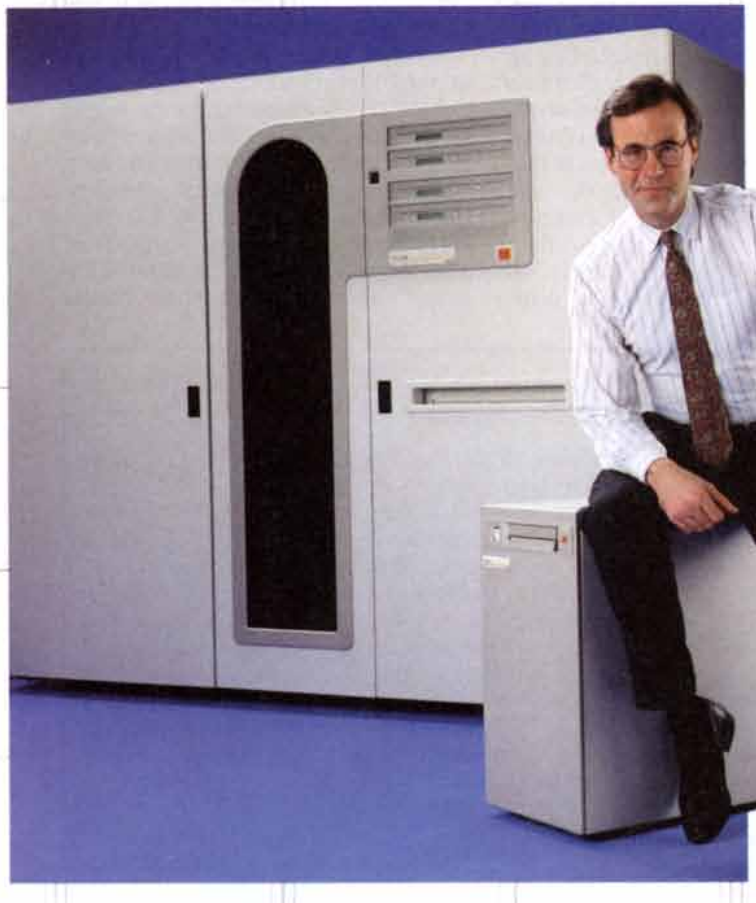
Investigators pinpointed the gene that causes CF last year and earlier this year identified the protein that the gene produces. That protein, called CFTR, for cystic fibrosis transmembrane regulator, resides in the membranes of cells that line the airways of the lungs. Just exactly what it does there is still not clear, but many different mutations in the CFTR gene that alter the protein cause CF.

Researchers are now concentrating on finding out how much CFTR needs to be delivered and to what type of cells. The most ambitious approach is gene therapy: adding a healthy gene to supplement the defective gene in some cells. "I think gene transfer will be done," predicts Ronald G. Crystal, a CF researcher at the National Institutes of Health in Bethesda, Md.

The possibility of gene therapy took a step closer to reality with the September publication of two papers. Both showed that if the normal CFTR gene is introduced into diseased cells growing in culture, the cells regain an ability that healthy lung cells have: regulation of chloride ions. Michael J. Welsh of the University of Iowa College of Medicine and his colleagues published their findings in *Nature,* and related work was described in *Cell* by James M. Wilson of the University of Michigan Medical School and his co-workers.

The inability of CF patients to regulate chloride ions is suspected of being related to their tenacious lung mucus, although the link is not proved. Other types of cell regulation, such as sodium ion regulation, are also affected in CF patients. In addition, they suffer from pancreatic disease, although it is usually manageable.

"I don't think chloride regulation is the sole defect, and I'm not sure it's the primary pathology," cautions Rich-



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ard C. Boucher, a CF researcher at the University of North Carolina at Chapel Hill. Boucher points out that CF patients fall prey to characteristic infections not found in patients with other lung diseases. To him, that suggests there may be more to CF than a failure to clear lung mucus.

Nevertheless, the race is now on to put the CFTR gene into CF victims' lungs. The consensus is that CFTR is somehow involved in transporting substances across cell membranes but probably as a regulator of other channels. "We think maybe it snuggles up between sodium and chloride channels and coordinates them," Boucher says.

Crystal has found that the CFTR gene is normally expressed at a low and fairly constant level in airway cells—encouraging news, because if complex regulation were necessary, gene therapy would be far more difficult. "If you're going to introduce a gene, you've got to know if you'll have to regulate it," Crystal says.

Another issue still to be fully addressed is whether CFTR might cause disease if it is expressed in the wrong kind of cells, which could happen in attempted gene therapy. Jeffrey Whitsett, a researcher at the Children's Hospital Medical Center in Cincinnati, has, however, found a promising regulator of gene expression. He identified "promoter" DNA sequences that cause

Mussels may clump together to improve their food supply

Often stuck on top of one another in dense clumps or hummocks, mussels seem to prefer close quarters to more open marine real estate. But this apparent chaos may be purposeful. Scientists who study the interaction of physics and biology are finding that living in such proximity may actually help the mussels feed more efficiently. "The mussels enhance their own food supply by causing turbulence," says Cheryl Ann Butman, a biologist at the Woods Hole Oceanographic Institution.

Stacks of these mollusks cause turbulence as water flows over them. The resulting eddies draw phytoplankton from near the surface of the water down to the bottom dwellers.

In the late 1970s scientists proposed that turbulence played an important role in controlling the food supply of benthic suspension feeders—creatures such as mussels that live on the seafloor and feed on particles and phytoplankton. But only recently have researchers determined that the size and roughness of the beds of these organisms may also be factors.

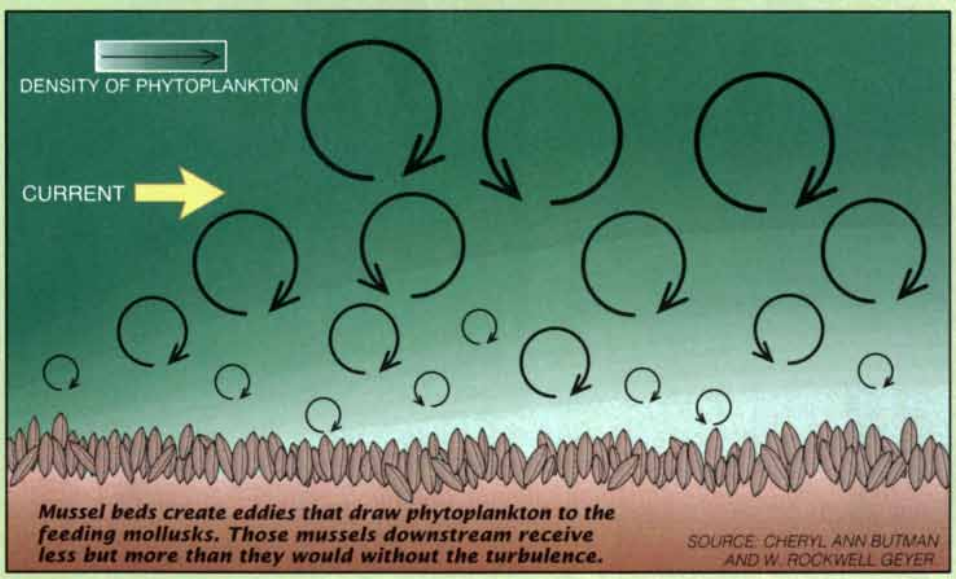
By measuring concentrations of phytoplankton in the water column above mussel patches, Butman and her colleagues—including Marcel Fréchette of the Canadian Department of Fisheries and Oceans and W. Rockwell Geyer of Woods Hole—found that the mussels' consumption rate increased with the velocity of the current. In addition, the more irregular the arrangement of the mussels in a patch, the greater the turbulence—and the more phytoplankton shuttled down to the waiting mollusks.

Using a laser to measure the turbulence over a bed of mussels in a flume—an experimental tank where flow can be controlled—the researchers found that eddies created by the protruding mussels were great enough to cause food to descend. Butman also suggests that hummocks—often considered a response to competition for space—may be advantageous to mussels in the interior of a bed. Mussels in the middle of a bed do not get the benefit of fresh current. Because of the turbulence, however, their chances for food are increased.

Understanding these effects has economic as well as scientific ramifications. "If we can maximize roughness, we can get a better yield," explains Carter R. Newell, a marine biologist at Great Eastern Mussel Farms in Tenants Harbor, Me. Newell, who has collaborated with Woods Hole researchers, studies mussel feeding, patch size and population density.

Although optimal conditions vary with the speed and direction of the current as well as with the water depth and circulation, Newell discovered that the smaller the patch, the better the mussels grow. If the patch is too broad, some mussels get less food because of a "shadow effect" that deprives those downstream of food.

Mussels are not the only benthic suspension feeders whose physical form may affect their local food supply through hydrodynamics: the siphons of clams also cause turbulence. Stephen G. Monismith, a civil engineer at Stanford University, has built model siphon pairs—one siphon inhales, the other exhales—and tested them in a flume. He found that the height, orientation and size of the siphons all affect the vertical movement and mixing of the current.



Mussel beds create eddies that draw phytoplankton to the feeding mollusks. Those mussels downstream receive less but more than they would without the turbulence.

SOURCE: CHERYL ANN BUTMAN AND W. ROCKWELL GEYER

In the end, however, the clever strategies that clams and mussels have for finding food may give way to the harsh reality of demographics. Charles H. Peterson, a marine biologist at the University of North Carolina at Chapel Hill, has found that "the overriding pattern is that there is reduced growth associated with higher density of the organism."

—Marguerite Holloway

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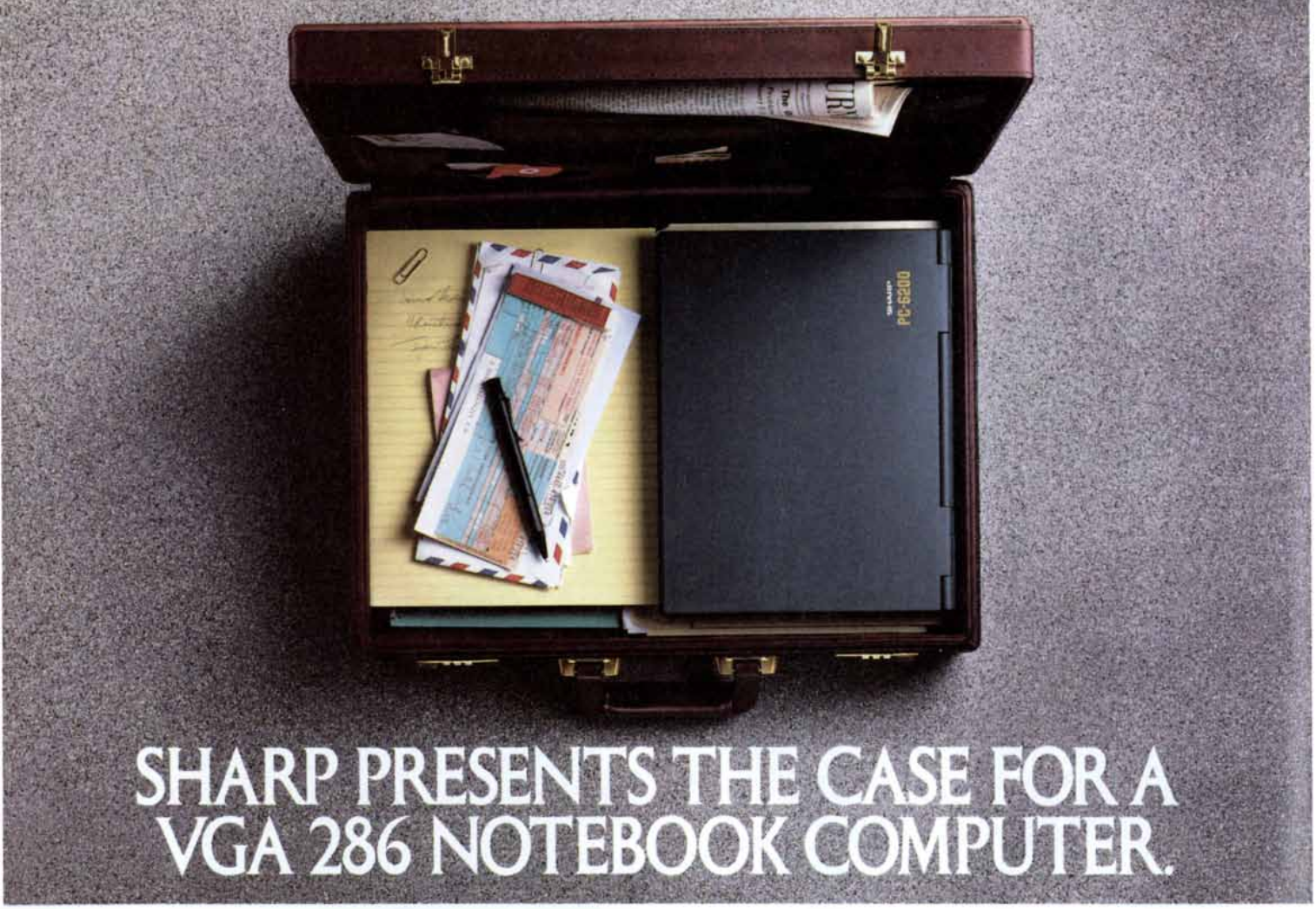

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genes to be expressed only in the small branches of the lungs. Such promoters, linked to the CFTR gene, might be crucial if it turns out to matter where the CFTR gene is expressed.

Many research groups are now experimenting with ways to deliver the CFTR gene to the lung cells of CF patients. So far animal research indicates that engineered viruses carrying the human gene may be a viable approach. Crystal is working with an adenovirus—a type that normally causes colds and is attracted to lung cells.

Crystal introduces the virus into lungs of animals in a liquid but says the virus could be aerosolized. He has shown that rodents will take up a foreign marker gene—one that codes for the bioluminescence enzyme luciferase—when it is introduced into their lungs by an adenovirus. The gene is expressed on their airway cells.

In addition, Crystal has shown that the adenovirus can be used to transport the human $alpha_1$-antitrypsin gene into rodents' lung cells, which then make the human protein. $Alpha_1$-antitrypsin destroys damaging enzymes and might be a separate therapeutic approach to CF.

Crystal's, Wilson's and Boucher's groups, among others, are all experimenting with retroviruses as possible vehicles. Retroviruses have the disadvantage of requiring actively replicating target cells, which most lung cells are not. But their advantage is that very safe delivery systems have been developed for them. Wilson says preliminary experiments have been promising: expression of the CFTR gene in cultured airway cells that do not normally express it does not appear to create problems.

Another approach to delivering CFTR into lung cells would be to use liposomes—microscopic, hollow lipid spheres that can be put in aerosols and filled with some therapeutic agent. Whitsett has made liposomes to carry receptors that bind to surfactant proteins found in the lungs. Such liposomes deliver their cargoes directly to the cells that need them. Whitsett hopes to test liposomes containing the CFTR gene and his lung-specific promoters in animals. Alternatively, liposomes could be used to carry the CFTR protein itself into lung cells, if it lasts long enough to be useful.

"It is very exciting," Whitsett says. "Delivering genes to epithelial cells is now possible." Nobody is yet taking bets on when gene therapy for CF will start. "There's a lot of work to be done," Crystal cautions. "But having said all that, it's feasible." —*Tim Beardsley*

PROFILE: DR. GREENHOUSE

Roger Revelle started the world thinking about global warming

French philosopher François de La Rochefoucauld once wrote that "there are those who would never have been in love if they had not heard about it." Likewise, there are many who would never have believed in global warming if Roger R. Revelle had not written about it in 1957.

That year, the director of the Scripps Institution of Oceanography in La Jolla, Calif., and his colleague Hans E. Suess threw some cold water on a myth. The two oceanographers wrote a paper arguing that the oceans would not soak up most of the carbon dioxide humans dump into the atmosphere. Instead they estimated that about half of the CO_2 belched into the air would stay there. Calling the burning of fossil fuels "a large-scale geophysical experiment," they predicted that a total increase in atmospheric carbon dioxide of 20 to 40 percent was likely "in coming decades."

Although his ideas were not then widely accepted, Revelle successfully lobbied to establish regular CO_2 measurements on Mauna Loa as part of the 1957 International Geophysical Year. With a record that now extends back 33 years, those measurements are one of the best-known curves in science. Each year has added another wiggle at the end of an increasingly upward slope—and the atmospheric CO_2 concentration has reached a little more than 350 parts per million, an 11 percent increase from 1957.

The Mauna Loa data have thrust Revelle's once heterodox opinions on greenhouse warming into the mainstream. But Revelle has also been the driving force in the establishment of the University of California at San Diego, as well as an educational innovator, a population expert and a scientific emissary to developing countries. He remains a forceful advocate of social responsibility in science. In November, Revelle was scheduled to receive the National Medal of Science from President George Bush.

Revelle has for decades been one of the most physically imposing presences in oceanography (he is 6'4" tall). An inspiring teacher sparked his interest in geology when he was still an undergraduate at Pomona College. Then in 1931, while pursuing a graduate geology course at the University of California at Berkeley, he was recruited to study deep-sea mud at Scripps, which at that time was a remote field station.

Revelle had just married Ellen V. Clark, a grandniece of Ellen Browning Scripps and Edward Willis Scripps, who were major benefactors of the institution. The appointment at Scripps was the start of a life-long association. Now 81 and recovering from heart surgery, Revelle walks carefully. These days he monitors the scientific and political tempest that he caused from an office with a commanding view of the atmosphere/ocean interface.

That setting is fitting for a director emeritus and professor of science and public policy at the school he brought into being. But whether bemoaning the "god-awful public education too many of our students get in public schools" or the excessive number of administrators at Scripps, Revelle doesn't pull his verbal punches. It is easy to see why he has trodden on a few toes during a career of more than five decades.

Even today Revelle acknowledges that uncertainties over the effect of clouds and the ability of the biosphere to absorb CO_2 mean "there is no way of deciding" exactly how much global warming will occur. But he remains characteristically blunt about deficiencies he sees in the scientific program. "The study of global change has got to be done on a worldwide basis," he declares. "The problem is the Third World—the scientific effort is very uneven." Moreover, collaboration with the Soviet Union in oceanography has been "less satisfactory than in other areas of science" because of "relatively crude" Soviet instruments.

Closer to home, Revelle is skeptical about the National Aeronautics and Space Administration's plans to monitor global change from the proposed space station and other large orbiting platforms carrying multiple instruments. "What they need is small, dedicated satellites," he insists. As for political leadership, Revelle says President Bush's science adviser, Yale physicist D. Allan Bromley, is "a good counterirritant to [White House Chief of Staff John H.] Sununu." But Revelle can't resist a sly remark that physicists are "not very apt on environmental phenomena."

Revelle has never been one to back down on moral issues. In 1950 he earned notoriety by lobbying in support of academic colleagues who refused to sign a loyalty oath disavowing membership in the Communist party. The University of California regents had set an ultimatum for dismissing

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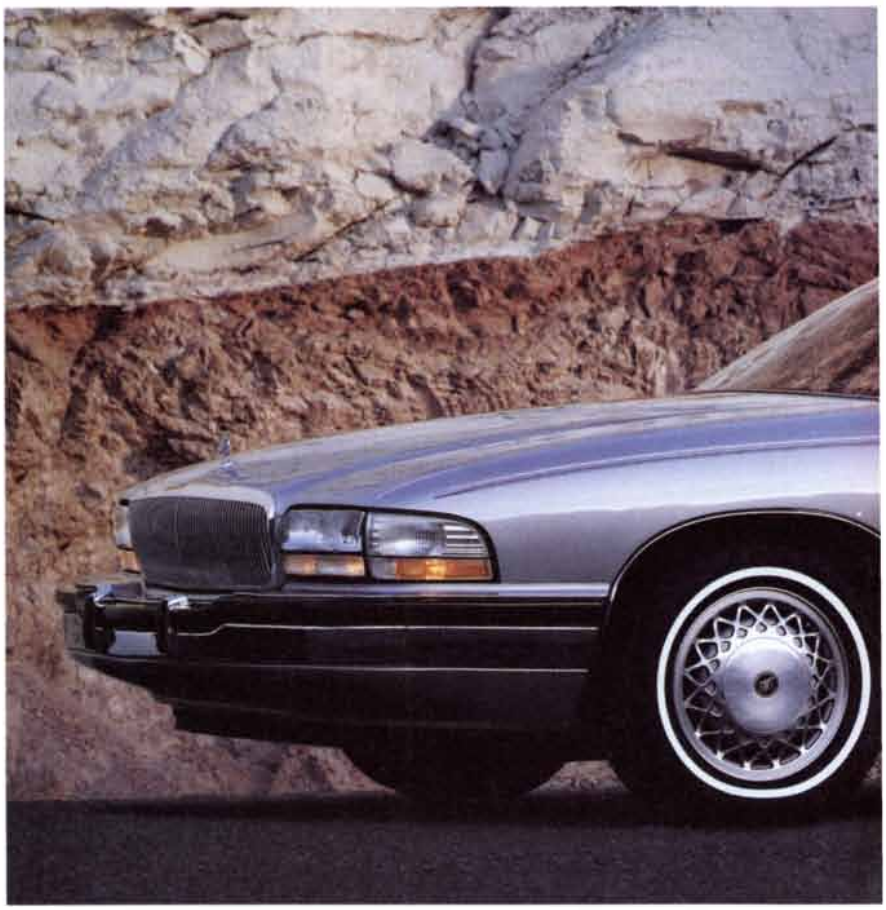

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any faculty members who refused to sign. After a tense public confrontation, the regents and faculty settled on a compromise that Revelle played a large part in negotiating: a Communist disclaimer in contracts, with a hearing provision for those who objected. "I really risked my career," he says.

He was asked to testify on behalf of the faculty "because of my lily-white reputation as a naval officer." In the Navy in 1946 and 1947 he organized scientific surveys at Bikini Atoll, the site of the atom-bomb test known as Operation Crossroads. (Drilling there, incidentally, proved the theories of Charles Darwin and James Dwight Dana that atolls have sunken volcanic cores.) During his tour of naval duty, Revelle had already signed similar disavowals, but a principle was at stake. "Academic tenure is a fundamental pillar of the modern American university, and I took a very dim view of those attempting to abolish it," he says. The fight earned Revelle enemies as well as friends, but he was appointed director of Scripps the next year.

Under his leadership during the 1950s, Scripps organized expeditions that laid the foundations of much of modern oceanography, discovering evidence for seafloor spreading, for magnetic reversals and for mantle convection. But Revelle became concerned that Scripps graduate students were performing poorly on basic science in doctoral examinations, and in 1956 he took on the regents again, proposing a new campus at San Diego. He had local support but faced stiff opposition from university officials at Los Angeles, who feared a drain on their funds. Revelle later wrote of his antagonists that "they were experts at seeing clouds no bigger than a man's hand."

The San Diego campus was founded in 1959, but Revelle failed in his ambition to be appointed as chancellor. "I antagonized some regents, and one regent in particular," he recalls with no indication of regret. He was, however, appointed dean of the school of science and engineering—while retaining his post at Scripps, which became an affiliated institution.

As dean, he attracted impressive scientific talent to San Diego. "We built from the roof first," he explains, appointing senior professors before establishing an undergraduate curriculum. As a result, U.C.S.D. has become "a great research university" in only 30 years. "It is by far the most important thing I've ever been involved with," Revelle says.

Revelle was a champion of the plan to divide the U.C.S.D. campus into separate colleges, believing that collaborations between faculty would flower in small communities. It didn't work. "The faculty didn't give a damn," he says. "Professors are journeyman-scholars with very little loyalty to their institutions. What you have now is dozens of little empires."

Although Revelle insists he is an optimist about humankind's ability to survive global changes, he has long been concerned about air, soil and water in developing countries. His transformation from oceanographer to development expert began in 1962 when, as science adviser to the secretary of the interior, he led a team of 20 researchers to Pakistan to advise on soil salinity. As Revelle remembers it, President John F. Kennedy felt diplomatically obliged to offer technical assistance to Pakistan. Jerome Wiesner, then Kennedy's science adviser, suggested Revelle—"Roger knows about salt," he told Kennedy. As a result of the team's visit, Pakistani agricultural productivity in affected regions doubled over the next 10 years, Revelle says.

ROGER REVELLE relaxes in his office at Scripps, which overlooks the Pacific Ocean. Photo: Tim Beardsley.

In 1964 Revelle left U.C.S.D. to found the Harvard University Center for Population Studies. At the time, he says, most similar institutions were studying birthrates. Revelle's experience in Pakistan had taught him the importance of environmental resources. He therefore concentrated, "much to everyone's disapproval," on making resources "a real university subject." It turns out "we were right," he adds.

Revelle has since consulted extensively on development in the Indian subcontinent, Asia and Africa. "The developed countries have so much technology at their fingertips," he observes. "I don't think their resource problems are serious—we can always fix them." But he is pessimistic about Africa and in particular those countries that are hamstrung by weak governments and zero economic growth.

Revelle returned to his present post at U.C.S.D. in 1975. As recently as 1988, he led a scientific party to Africa to study hunger. "Agriculture is going backward rather than forward," he says. "It's very, very discouraging." Reversing that situation will require "a whole new green revolution," Revelle insists, to apply modern genetics and tissue culture techniques to African crops, principally maize. But in many countries, he says, scientists are not paid well enough to make research an attractive career.

"Drought is a very serious problem," he says, believing water management will be an urgent challenge in the greenhouse world—even in the U.S. He points out that dams and reservoirs are built to last for decades and designed on the assumption that average rainfall does not change. Revelle is dismayed by recent domestic trends: "During the whole decade of the 1980s, we behaved in a disgraceful fashion on many fronts."

Revelle is also disappointed that scientists are not setting a better example in matters of social conscience. A former president of the American Association for the Advancement of Science, he points to poor attendance at the association's meetings and says it is "not achieving what I'd hoped" in increasing participation of the handicapped and minorities. "All these are things the AAAS is trying to do," he says, "but most scientists just don't give a damn."

As for himself, Revelle shows little sign of reducing his efforts. He and Ellen still live in La Jolla, in the house they moved into 50 years ago, where the couple are well-known local patrons of the arts. Revelle still conducts undergraduate seminars on technology and poor countries and on marine policy. How does one manage to do so many things in a career? "Do them in sequence," he advises. —*Tim Beardsley*

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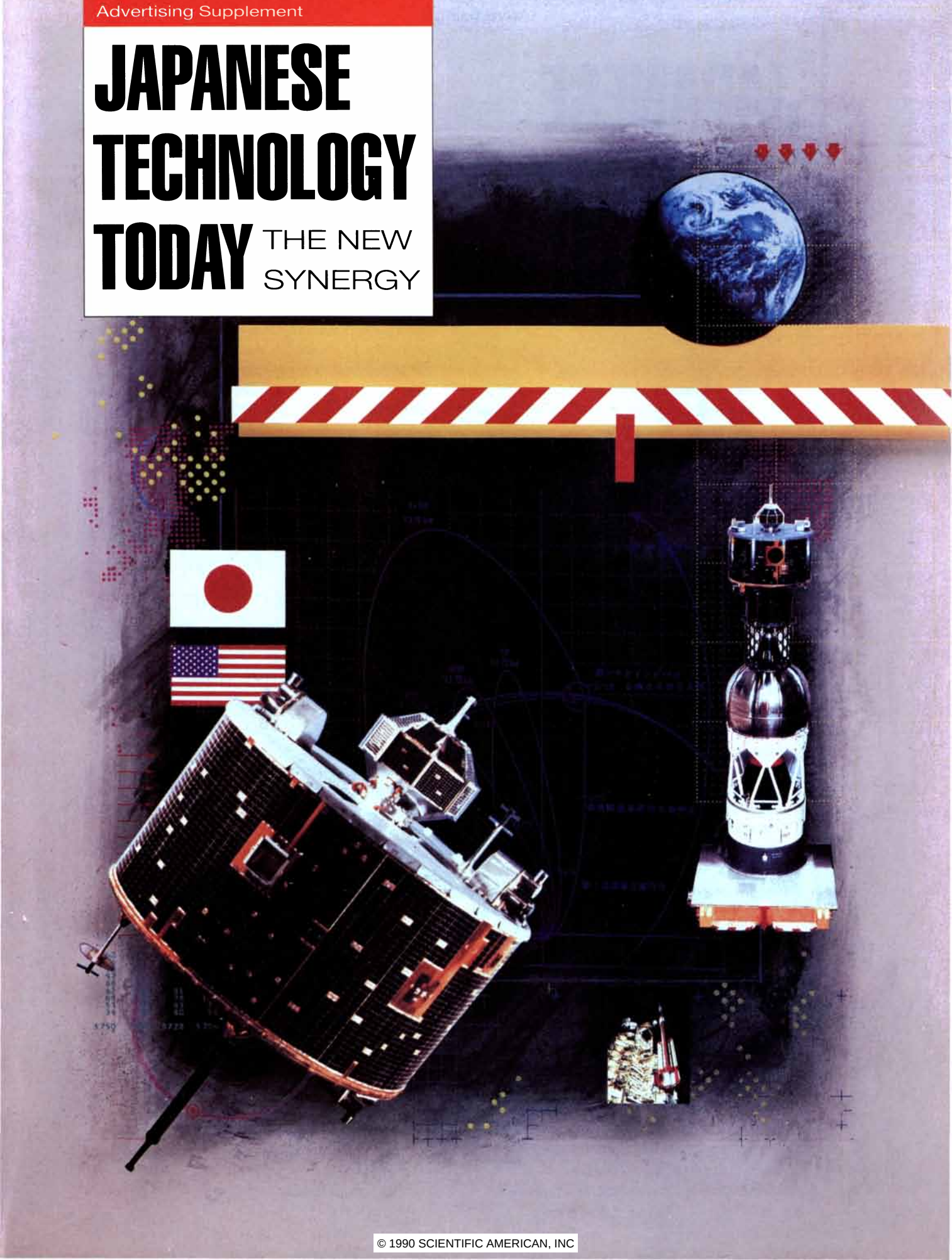

JAPANESE R&D GOES GLOBAL

The internationalization of corporate Japan is entering a new phase: International research and development. After progressing from exporters of goods to overseas producers, Japanese businesses now are establishing R&D bases around the world and cooperating with local researchers and joint venture partners to create truly international creative organizations.

Indeed, this push for global R&D comes as Japanese companies step up their research efforts on the home-front as well. Reflecting an emphasis on long-term, basic research, this trend may well result in a dramatic impact on the future of specific companies. Japan's total scientific and technological research expenditures reached ¥10.6 trillion in fiscal 1988 (about $75 billion in current US dollars), up 8% over the preceding year and surpassing the ¥10 trillion mark for the first time. R&D spending as a share of the gross national product rose to 2.85%, an all-time high. Reflecting the business boom, corporate research expenditures recorded a healthy 11.2% growth rate.

Fully two-thirds of the 870 corporations with capital of ¥1 billion and over responding to a Science and Technology Agency survey indicated "strengthening research and development activities" as one of their management policies. This figure is 10.2% greater than responses to a similar survey conducted three years ago. Manufacturing companies typically say they would like to allot 10% of their total sales to research and development. By 1989, 25 companies had already attained this goal.

THE DRIVING FORCES

More than half of the respondents also said that their research emphasizes long-range pursuits and basic themes, in spite of any drag on short-term profits. Thus, many Japanese companies are taking a medium- and long-range view in their efforts to upgrade their technological abilities.

Several macro factors motivate this commitment to reinforced R&D. Throughout Japanese corporations, executives indicate that the unique technologies they expect will result from basic research will drive future corporate development. As companies strive to deal with structural changes in industry in this era of technological innovation, many are tackling new areas often unrelated to their original business lines. And when entering new fields, managements recognize that their technological level must surpass that of competitors.

Another factor propelling Japanese R&D is keener competition with overseas manufacturers. Partly because of rising trade frictions, the United States and European nations are strengthening their protection of intellectual property rights. Meanwhile, other Pacific Rim companies are accelerating their efforts to catch up with Japanese firms. For these reasons, Japanese corporations are increasingly pressed to develop their own, unique technologies.

> The international R&D push parallels Japanese companies' efforts to step up research on the home-front as well.

To strengthen their research efforts, companies are forming international research and development networks. In addition to beefing up their own efforts with R&D facilities overseas, a number of local Japanese subsidiaries are exploring common projects with their new neighbors. Joint research with foreign corporations and educational institutions is increasing rapidly on the theory that an international division of R&D labor will best emphasize the fortes of individual countries.

Meanwhile, foreign companies with a market presence in Japan are building international research networks by establishing laboratories in Japan and employing Japanese researchers. In this way, internationalization is progressing in all fields. In the future, competition in the area of research and development will also be waged among the companies' networks.

It is in this context that we want to introduce specific research and development strategies of major Japanese corporations, with the emphasis on the internationalization of their efforts.

THE PHILOSOPHY OF C,C & C

Sei-ichi Takayanagi
Senior Vice President,
Corporate Technology
Toshiba Corporation

Toshiba's management philosophy emphasizes the concepts of "C, C & C," or Competition, Cooperation and Complementary relationships.

Any corporation naturally attempts to win in business competition. But aggressive competition can lead to head-on encounters with problems such as trade friction. If a company is to develop alongside other businesses in and out of Japan, cooperation is necessary also. And cooperation implies appropriate, complementary relationships with partners.

Based on "C,C & C," Toshiba has launched joint research and development projects with many foreign corporations and organizations designed to make the best use of the technologies of the two participants. Overall, the projects range from microelectronics to medical treatment and energy.

One example is a joint venture with IBM to manufacture color liquid crystal displays using thin film transistors (TFTs). This undertaking represents the culmination of joint research efforts between Toshiba's Tokyo research institute and IBM's counterpart in Watson, New York, over the past several years.

Similarly, in the semiconductor field we are working with Motorola Inc., of Roselle, Illinois. While we are good at dynamic random access memory (DRAM) engineering, Motorola has excellent microprocessor unit technology. Thus, two companies' abilities function in complementary ways.

In our attempts to develop phosphate fuel cells, a new high-efficiency energy source, we tied-in with another American firm, United Technologies, headquartered in Hartford, Connecticut. United Technologies has accumulated a great deal of technical expertise concerning fuel cell materials and the structural design of these cells, while Toshiba's technology is strong in fuel tracking and system control.

Other multinational R&D projects include joint research with the Medical Department of Arizona State University for digital image diagnosis systems, and a boiling water reactor project being undertaken by five companies from Japan, the United States and Europe. In order to effectively utilize limited technological resources and disperse risks in developing massive endeavors, intercompany collaboration efforts will assume increasing importance in future management strategies.

BUILDING MUTUAL UNDERSTANDING

In Japan, Toshiba employs 30 foreign researchers and engineers, 18 of them engaged in fundamental research at our general research institute. In addition, we have accepted seven scientists through the "Toshiba Fellowship," instituted in the United Kingdom in 1988. Mutual understanding among people of different cultures and the consequent mutual stimulation bring great benefits to all participants.

Overseas, especially in the United States, we are enhancing our research and development

Toshiba emphasizes joint R&D with foreign corporations and organizations to best use the technologies of the two participants.

sector. In May 1990, we opened the Advanced TV Technology Center in Wayne, New Jersey. This is our fourth R&D base in the US, following establishment of centers studying such fields as industrial electronic equipment, nuclear magnetic resonance image diagnosis instruments (MRI), computer-aided design (CAD) and semi-custom integrated circuits.

Apart from these business activities, Toshiba considers R&D efforts to protect the global environment as increasingly urgent. In November 1989, we opened our Environmental Engineering Laboratory to develop chlorofluorocarbon (CFC) alternatives and new organic solvents, and to research recycling technology for industrial wastes. Through such efforts, Toshiba plans to cut its consumption of CFCs in half by 1995.

Environmental preservation is a common issue for all mankind, and Toshiba is determined to cooperate with the efforts of other companies and countries in its pursuit.

INFORMATION, ELECTRONICS, AND SYSTEMS

Dr. Yasutsugu Takeda
Executive Managing Director
Hitachi Ltd.

Hitachi's research and development parallels three trends that, in our view, will characterize future customer needs: information technology advancement, greater use of electronics and systemization.

Our interest in the information technology sector ranges from computers to communications equipment, communication media, network devices, and software. Products and R&D in the enhanced use of electronics include semiconductors, display devices, optical devices and superconductive systems. Systems-related products are in fields as varied as energy, urban systems, health and medical equipment, traffic systems and computer-integrated manufacturing (CIM).

Since Hitachi is a diversified electronic equipment manufacturer, our products are many and varied. But many share common development themes. Hitachi attaches importance to the balanced development of both hardware and software in these endeavors, and also to meeting customer needs through systems rather than discrete products.

HITACHI OVERSEAS

In pursuing those aims, Hitachi has actively established development bases in a number of overseas locations. The basic idea is that conducting both hardware and software research at places with strong traditions of scientific activity will produce synergies. The combination of one and one—the blending of local research results with our previous technology—will yield more than two.

Hitachi is backing up our local production with R&D. In the US, we are conducting exploratory research in the semiconductor field in San Francisco, automotive parts in Detroit and communications in Atlanta. In Europe, our Cambridge University laboratory is engaged in electronic device research, while our Dublin University lab conducts in-depth research on super-high level computer languages, such as those for the neurocomputer.

In tandem with our international research efforts, Hitachi holds that it is important to contribute to global society. Following the opening of a research institute in Europe two years ago, we committed to contributing to the European culture that we greatly respect while also learning a great deal from our European operations. We believe it will be wonderful if we can trigger new innovation abroad and create new industries in other parts of the world based on Hitachi-sponsored innovation.

The combination of one and one—the blending of local research efforts with our technology—will yield more than two.

To mention one step toward internationalization, Hitachi has graduated more than 100 people to date from our "HIVIPS" program. Believing in the value of sharing each other's cultures, HIVIPS invites 30 trainees from abroad to our research division every year. These trainees study at our research establishments, getting to know our way of thinking.

International cooperation between companies takes the form of joint ventures in most cases. Compared with most companies, Hitachi's level of R&D funding is rather high. But we feel that we still lack both potential and results, especially in fundamental research areas. As we tackle major projects, we should humbly admit our weaknesses and turn to international cooperation.

Now, many years after the industrial revolutions of the 18th and 19th centuries, a third industrial revolution is taking place in Japan, the United States and Europe. In the next revolutionary period, the most drastic technological change is likely in the Pacific Region, particularly Asia. Thus we would like to promote cooperation with this region in coming years. We believe that overseas investment without technology transfer will fail to spur progress and may cause friction. In this spirit, Hitachi considers technology transfers to local areas essential for amicable cooperative relations.

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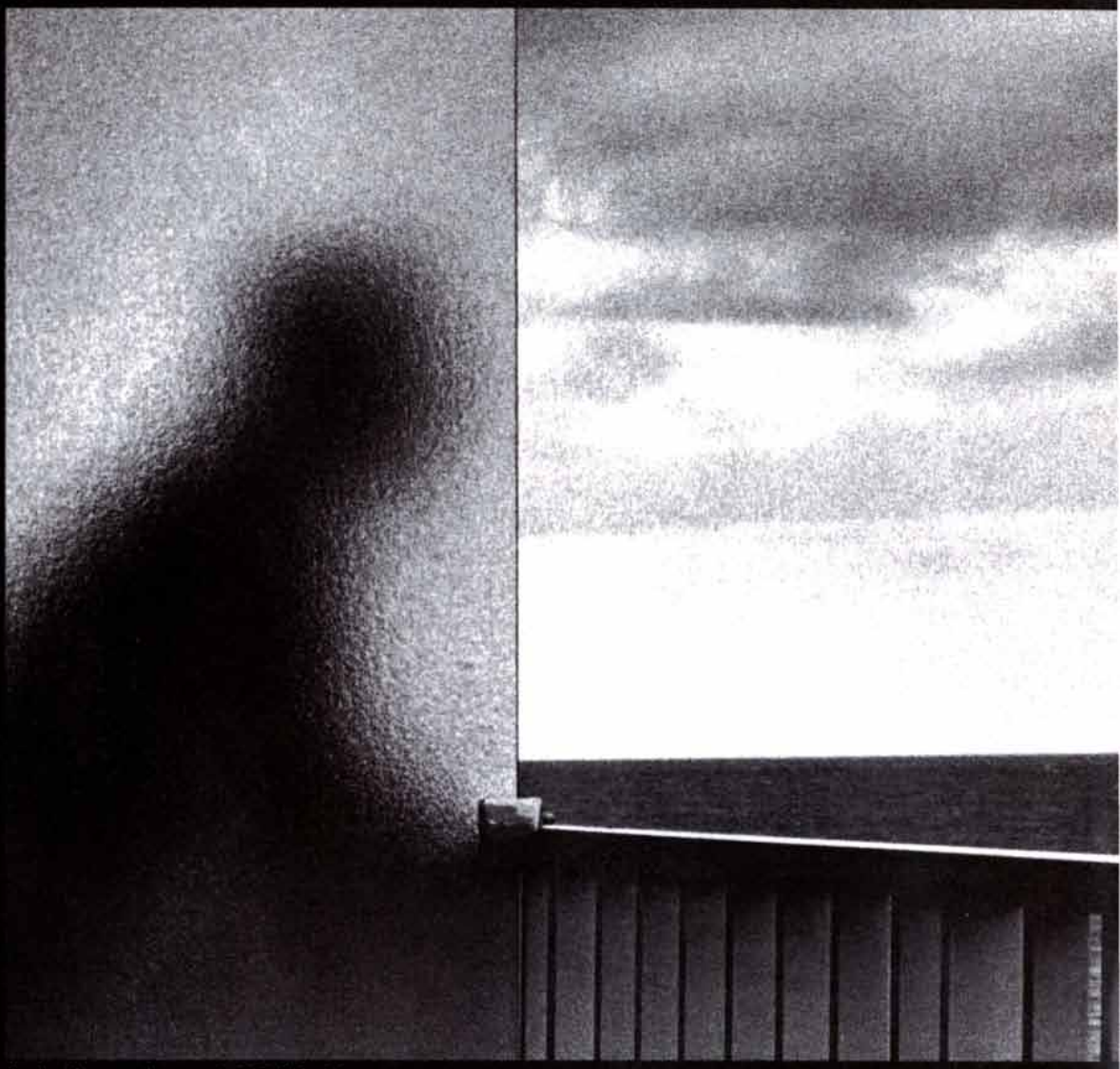
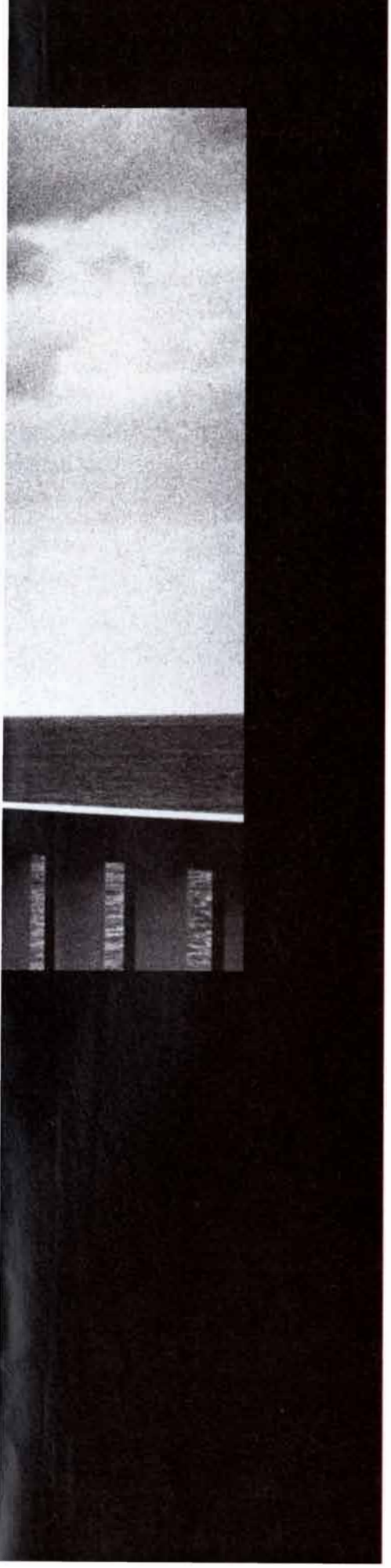


Andre Kertesz, *January 1, 1972, Martinique*



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OPTO Electronic Devices

Picture Tubes

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Professional Video Systems

Room Air Conditioners

Semiconductors

Telecommunication Systems

Turbines & Generators

Ultrasound

Uninterruptible Power Supply

Variable Speed Drives

X-Ray Systems

THE SPECIALIST APPROACH TO SYSTEMS

Dr. Norio Tashima
Executive Director,
Systems Equipment Operations
Minolta Camera Co. Ltd.

Our research and development objective is simple—Minolta Camera wishes to pursue areas in which we excel. One reason for limiting our activity to these fields is that, because of the shortage of development staff, the assignment of engineers to scattered endeavors is difficult. But mainly we believe that specialization provides more opportunities for future business expansion.

Minolta has identified three principal R&D areas of the future:

- Laser optical systems, based on printing technology,
- Electronic microfilm and
- Facsimile technology

Our philosophy of specialization seemingly flies in the face of how we view the future—which increasingly will involve sales of systems made up of various elements rather than single products. For example, the computer environment requires a variety of practically unrelated parts that mesh together, including telecommunications equipment, terminals, image systems, storage equipment and printers.

However, believing that no company can do everything equally well, Minolta's goal in the computer arena is to provide superior optical systems for printer technology. Only by building confidence that Minolta is without peer in our areas of specialty will we be able to survive systems-related sales competition.

CROSS-BORDER SPECIALTY PARTNERS

Minolta also bases its internationalization efforts on this specialization strategy. For example, five years ago 3M Company of St. Paul, Minnesota, proposed that we jointly produce medical system products. At that time, 3M was involved in the development of silver-salt films that allow high-precision image reproduction. However, 3M lacked the laser technology to print its images, which we possessed. Minolta now provides the world market with digital laser printers for computerized tomography (CT) scanners under the 3M brand.

Another specialization example is our approach to the Minolta Integrated Information and Image Management System (MI^{3}MS), a document filing system that employs microfilm, which we began marketing in May 1989. While there is limited strength from US industry in terms of hardware manufacturing technology, the Americans excel in software development. Recognizing our own shortcomings in this area, we enlisted cooperation from a US software developer.

The MI^{3}MS consists of a personal computer, a microfilm reader printer, an optical disk unit and a laser printer. The software developer's technology accurately controls these units and operates them as a system that American users can easily handle. Minolta plans more of this type of tie-in with foreign companies in the future.

We intend to promote the full-fledged international exchange of engineers and to build personal connections with researchers in US universities.

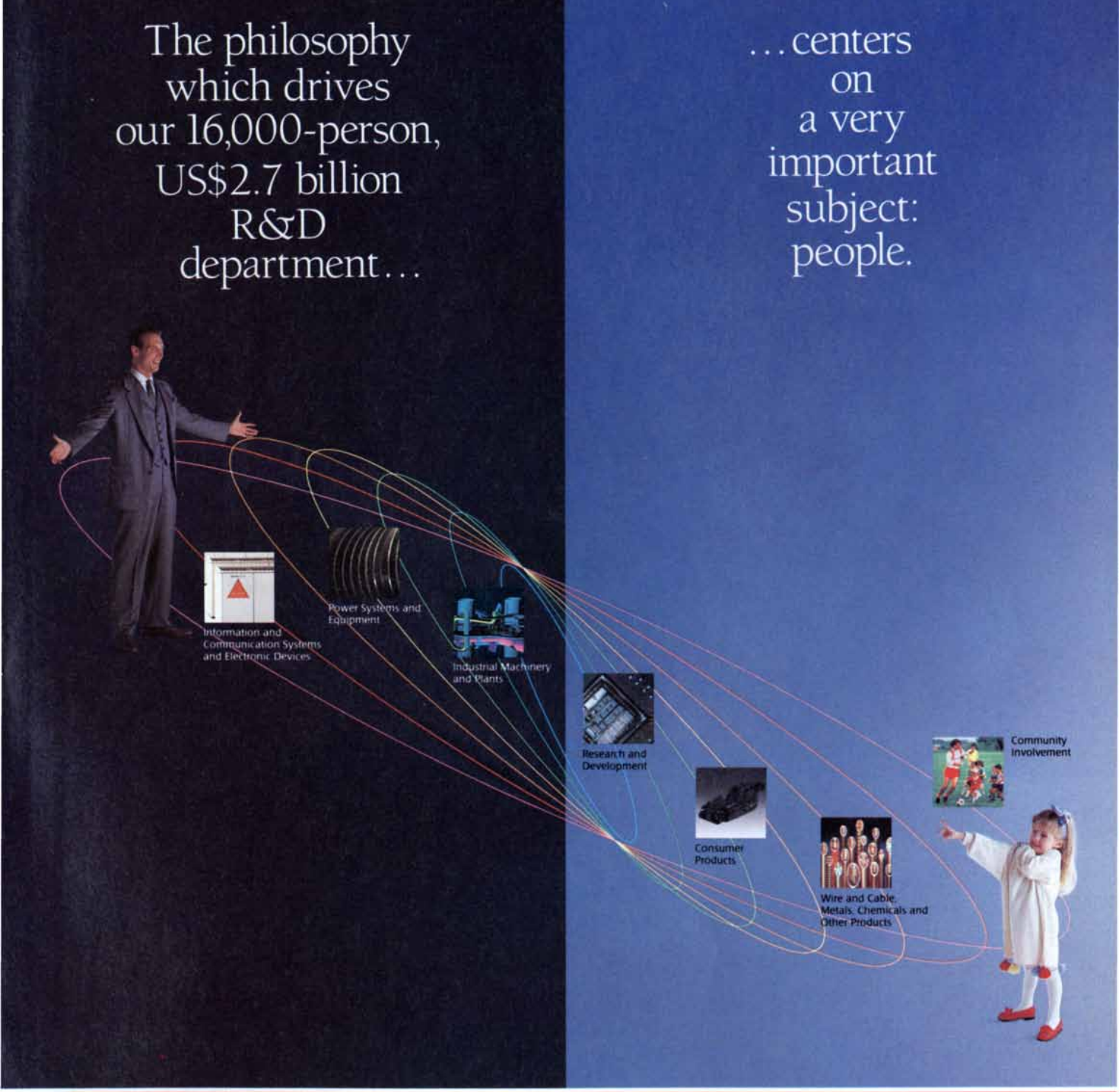
PERSONNEL EXCHANGE

We also intend to promote the full-fledged international exchange of engineers. Already, we have enlisted two Irish engineers to develop programs for printers. In another instance, we have invited personnel from our US toner-producing subsidiary, which began operations in September 1989, to visit Japan for training in manufacturing technology.

Additionally, we have inaugurated an overseas study program for Minolta engineers. Under this system, we will send optical technology researchers to the Massachusetts Institute of Technology this year. Our long-range goal, beyond further raising the technological level of Minolta Camera, is to build personal connections with researchers in US universities.

The philosophy which drives our 16,000-person, US$2.7 billion R&D department...

...centers on a very important subject: people.



To Hitachi, the true measure of a company's worth is its commitment to enhance the quality of life. Few corporations can compare with Hitachi in this regard.

Our R&D department creates technologies that directly affect the lives of people everywhere. We're involved in the development of a vast range of medical diagnostic equipment. Hydroelectric and thermal power plants. As well as consumer electronics, new materials and telecommunication systems.

With 33 research laboratories located in Japan, Europe and the United States, R&D is *the* lifeblood of Hitachi.

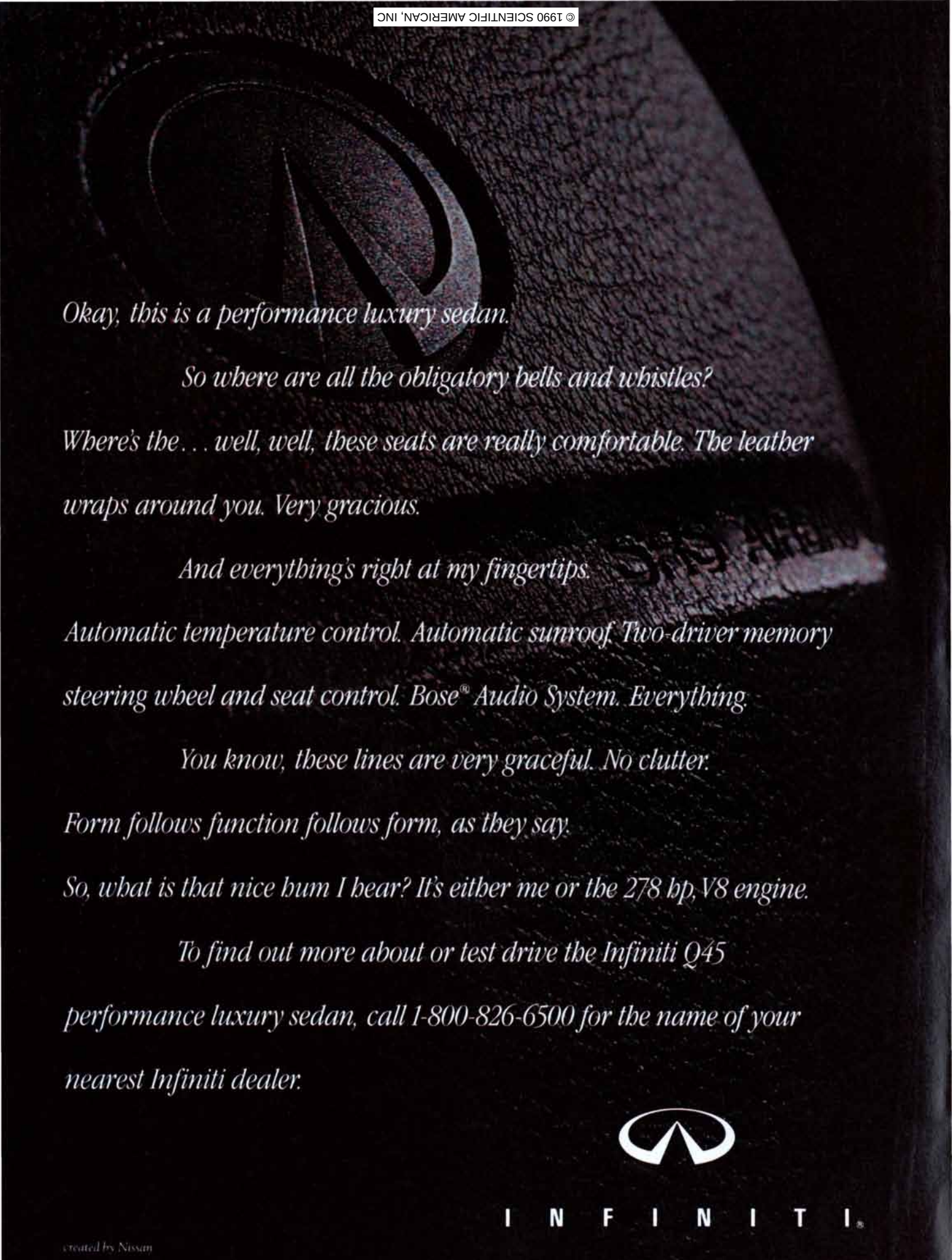
We're a people company in other ways, too. Our recently established GREEN Center (Global Resources, Environment & Energy System Center) will soon join the battle to solve such problems as acid rain, the greenhouse effect and ozone depletion.

The breadth and scope of Hitachi is deep, indeed. Our products are found in offices, stores, factories, hospitals and homes around the world.

And with a people-oriented philosophy, Hitachi will continue to grow and secure a place as a citizen of the world.

*$2,718 million; net R&D expenditures for the year ended March 31, 1990. US$1=¥158

HITACHI



Okay, this is a performance luxury sedan.

So where are all the obligatory bells and whistles?

Where's the . . . well, well, these seats are really comfortable. The leather wraps around you. Very gracious.

And everything's right at my fingertips.

Automatic temperature control. Automatic sunroof. Two-driver memory steering wheel and seat control. Bose® Audio System. Everything.

You know, these lines are very graceful. No clutter.

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To find out more about or test drive the Infiniti Q45 performance luxury sedan, call 1-800-826-6500 for the name of your nearest Infiniti dealer.

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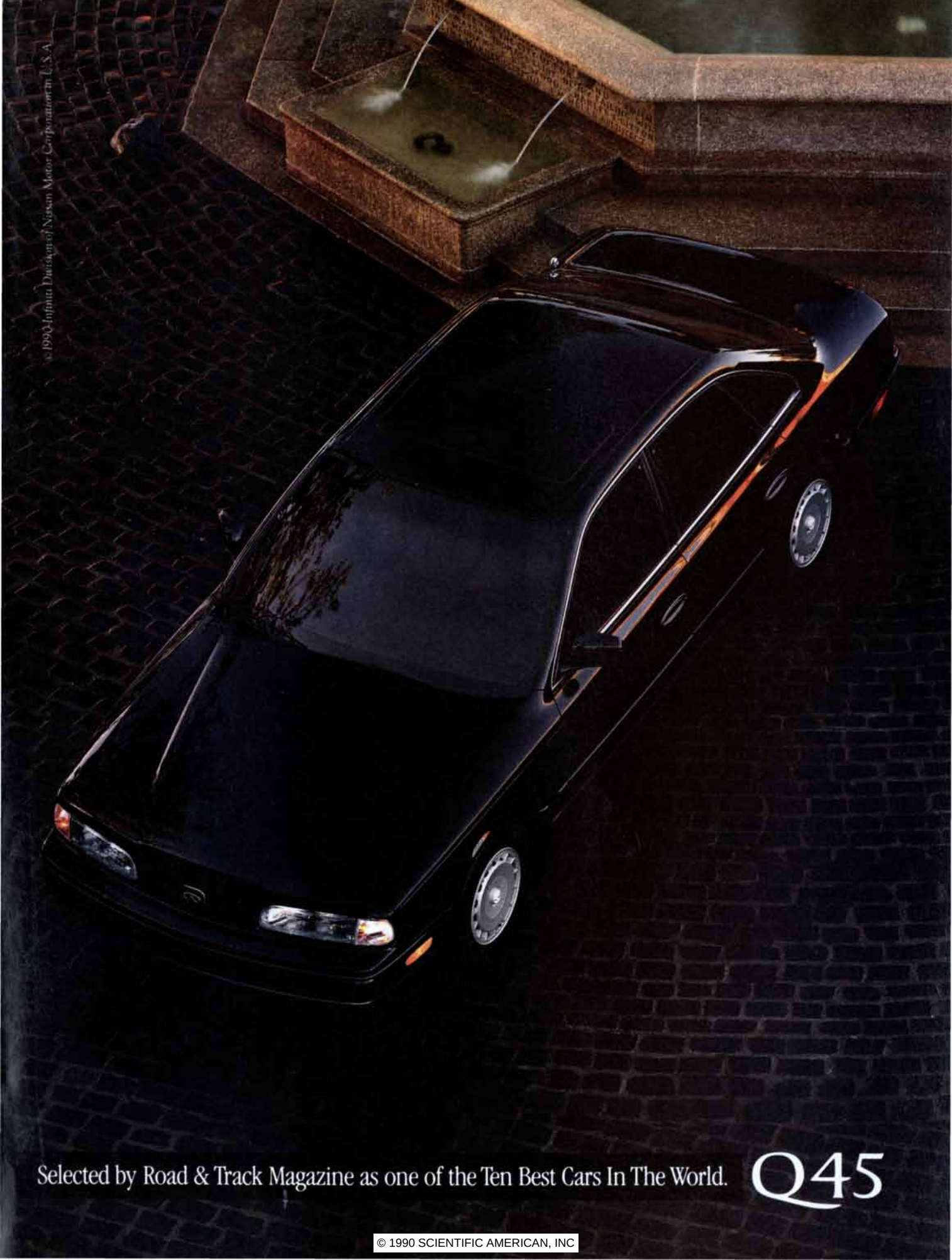


BUILDING UPON THE CORE

Hideharu Takemoto
President
Canon U.S.A. Inc.

Canon has always been a technology-driven company. As far back as 1937 when our first 35mm camera was introduced in Japan, we planted the seed for future products employing precision optics technology. Fifty-three years later, Canon has diversified in industries ranging from semiconductors to business machines, from medical to photographic equipment. Our technology has changed the shape of existing markets as well as led the advance of new markets.

The key to our strength lies in our ability to build upon our core technologies—optics, electronics, chemicals and precision mechanics—to create innovative, state-of-the-art products. Canon has been instrumental in developing maintenance-free toner cartridge, plain-paper copying, laser beam printing, digital color laser copying, bubble-jet printing and i-line stepper technologies.

Considering our reliance on internal resources for future growth, it is not surprising that Canon continually ranks among the top R&D spenders. In 1989, our $525 million R&D outlay (11% of our parent company's revenues) helped Canon earn 949 patents in the United States, ahead of such respected global giants as IBM and Eastman Kodak.

Manufacturing is one key to Canon U.S.A.'s emergence as an independent enterprise. In 1990, we expanded our Virginia copier, laser beam printer and toner cartridge plant; expanded California electronic typewriter and facsimile production; and opened new parts facilities to localize parts supplies. By 1992, we hope to achieve $4.4 billion in sales, with $1 billion from US production and $100 million from exported products. More than 60% of parts will be procured locally in North America.

EARNING LEADERSHIP THROUGH R&D

R&D is the other key to independence. We have transferred our entire electronic typewriter operation to Canon Business Machines, making our Costa Mesa, California, plant the world headquarters for Canon typewriters. This year, we also established two R&D centers in the United States. Canon Research Center America in Palo Alto, California, will focus on future computer technologies in the areas of optical recognition, image- and data-compression algorithms, multitasking real-time operating systems, image database management and network management and architecture. Our other new R&D facility, Canon Information Systems in Costa Mesa, will develop systems and applications software for computers and peripherals as well as for some existing product lines.

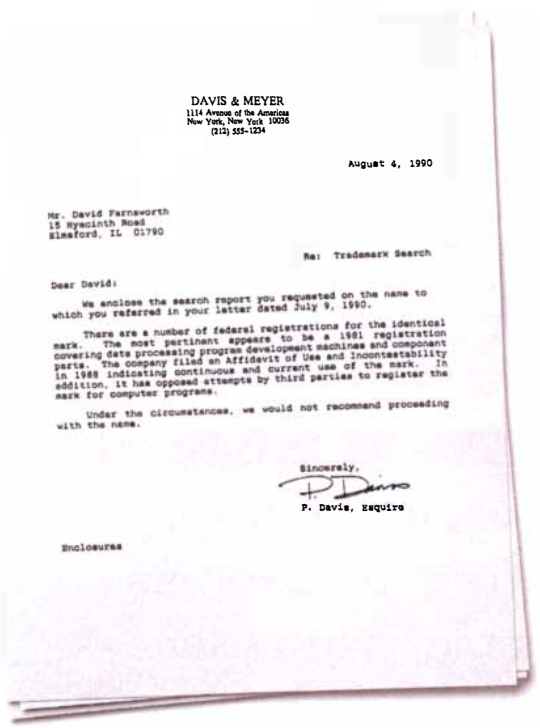
We should emphasize that R&D is not an insular activity at Canon. For years we have paired with such large, high-tech companies as Eastman Kodak, Motorola and Hewlett-Packard. Such joint efforts have led to significant breakthroughs in laser imaging technology in the medical field, special CPU for advanced camera applications and laser beam printers for desktop publishing applications. More recently, we have invested in the NeXT computer that utilizes the Canon magneto-optical disk system.

From semiconductors to business machines, to medical and photographic equipment, Canon taps internal resources for growth.

Joint ventures with highly specialized American firms include United Solar Systems Co., established to produce photovoltaic cells for solar energy panels; Zygo Corp., to develop high-precision measurement devices; and Lepton, to develop sophisticated semiconductor equipment. Also, we have enhanced the computer connectivity of our Color Laser Copier 500.

Canon, ranking 118 in the world according to the 1990 Fortune 500 list, is unique as a formidable R&D contender. We are presently working on intelligent business equipment that will change the way we process information and communicate. We are also looking at new businesses that will benefit society, especially in the areas of the environment and ecology. We believe that a massive commitment to R&D has earned Canon a leadership position in our markets. This continued commitment can only strengthen Canon in the global community of the 1990s and beyond.

The Canon personal copier. What you use it for at home is your business.



DAVIS & MEYER
1114 Avenue of the Americas
New York, New York 10036
(212) 555-1234

August 4, 1990

Mr. David Farnsworth
15 Hyacinth Road
Elmsford, IL 01790

Re: Trademark Search

Dear David:

We enclose the search report you requested on the name to which you referred in your letter dated July 9, 1990.

There are a number of federal registrations for the identical mark. The most pertinent appears to be a 1981 registration covering data processing program development machines and component parts. The company filed an Affidavit of Use and Incontestability in 1988 indicating continuous and current use of the mark. In addition, it has opposed attempts by third parties to register the mark for computer programs.

Under the circumstances, we would not recommend proceeding with the name.

Sincerely,

P. Davis, Esquire

Enclosures

Mr. Davis, age 43

Mr. Davis, age 7

If you're one of the many people who now work at home, the Canon PC-1 is made for you.

It's portable. Needs no warm-up time. And is virtually service-free thanks to our own single-cartridge system.

Best of all, it creates originals of recipes, school projects, greeting cards, invitations, and business documents in seconds.

Which leaves you more time to play.

Canon
PERSONAL COPIERS
Nothing but originals.

MULTIMEDIA R&D

Hitoshi Aoike
Senior Managing Director
of Information Products
General Manager of R&D
Victor Company of Japan

As a corporate target for the 21st century, Victor Company of Japan is aiming to achieve technology leadership in the multimedia era. The "multimedia era" can be described as an expanding world of new images and sound, created by the merger of Hollywood and Silicon Valley.

The ultimate multimedia system seems to be a television with a built-in computer, or a computer linked to a TV. Able to supply motion pictures, still pictures, text and audio information (including voice responses), such a system is expected to satisfy nearly all information needs. The impact of combining information processing technology and image technology will immeasurably change both social and business aspects of our lives. Victor Company (better known in the United States as JVC), a pioneer in the new audio-visual world centered on video, expects to achieve the next jump forward by riding this new wave. International technological exchanges will support our efforts.

MARRYING TECHNOLOGIES WITH LOCAL SOFTWARE

Various factors spur companies to globalize their technological development, including the intensification of international friction surrounding advanced technologies. But for Victor Company, globalization represents an aggressive management strategy, with an eye on the 21st century.

Individual technologies for building a multimedia system have already reached a high level of development. Recent advances have been scored in image-compression technology, high-density record reproduction and high-speed processing devices. When it comes to creating a practical, cost-effective system, however, many technical problems remain. And even when hardware problems are solved, what kind of software will enjoy smooth market acceptance? Such solutions vary with the history and culture of each market concerned, and therefore country-specific research achieves the best results. With this in mind, Victor Company is now energetically working to create a worldwide research base.

JVC Laboratory of America, founded two years ago in Santa Clara, California, is our first attempt at local research. Currently, some 20 American staff researchers collaborate with the main research group at Kurihama Technological Center in Yokosuka, Kanagawa Prefecture. In addition, we are working to promote technology exchanges with Alabama State University, which is increasingly emphasizing high-technology research.

The most important gauge of success in the multimedia field is attaining the integrative function—assembling all the individual technologies into a closely knit system. Since the United States possesses a strong multimedia "infrastructure," measured in both human and technological resource terms, we have concentrated our R&D efforts so far in that country. However, it is high time to establish research bases in Europe as well. We would like to organize, as soon as possible, a tri-polar development setup, based in Japan, the US and Europe.

We would like to organize, as soon as possible, a tri-polar development setup, based in Japan, the US and Europe.

SETTING THE STANDARDS

Paralleling our research activities, Victor Company is participating in the establishment of international standards for the basic technologies that underlie multimedia operations. The image and voice compression standardization project, now underway at the International Standardization Organization, exemplifies these efforts.

By drawing on technologies we have cultivated in our video-related research and development, our company is playing a central role in compiling the standards of the multimedia era. We are sure that, through such involvement, Victor Company of Japan will come a step closer to the goal of achieving a global research and development network.

Access Japan

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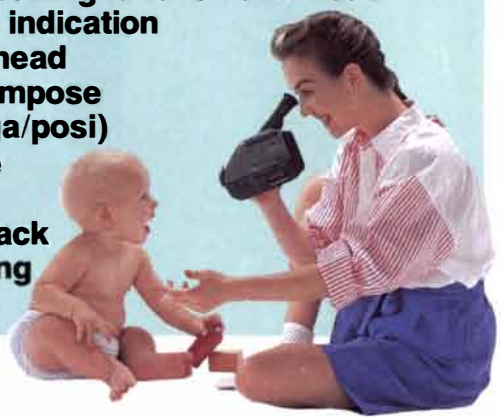
Fits Like A Glove!

GR-AX7 BKU/GYU Miniature Compact VHS Camcorder

JVC's new palm-sized GR-AX7 camcorder weighs a mere 1.7 pounds yet is still packed with the kind of sophisticated features you would expect from a much larger unit. The secret behind this compact miracle is a newly developed tape transport and head mechanism 40% smaller than the mechanisms used in conventional VHS-C camcorders. As a result, this ultra-small camcorder is able to offer a host of user-friendly features such as a Full Range AF system, 6:1 power zoom, 3-lux low-light sensitivity, and Auto Head Cleaning, which virtually guarantee great shooting results and ensure worry-free operation. Small enough to fit in a coat pocket and light enough to carry anywhere, the amazing GR-AX7 represents the most advanced concepts in camcorder design, yet is so easy to use that anyone can use it.

Major Features

- **Ultra-compact, ultra-lightweight: a mere 1.7 lbs**
- **Full Range AF system with Auto Macro**
- **F1.4, 6x power zoom lens**
- **3-Lux low-light sensitivity**
- **Multiple-speed shutter with 1/4000-sec. setting**
- **Auto Head Cleaning function and Head Clog Warning indication**
- **Flying erase head**
- **Digital Superimpose (8 colors, nega/posi)**
- **Cinema mode facility**
- **Encore playback**
- **Digital Tracking**
- **Age insertion**



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Fits your hand

The GR-AX7 is an ultra-compact, ultra-lightweight, ergonomically styled camcorder that fits right in the palm of your hand for true one-handed shooting. Recording all those great memories has never been simpler.

Fits your VCR

The GR-AX7 uses Compact VHS cassettes that fit into any VHS video deck.* So you can view what you've shot right on your own VHS deck at home, and you can share your memories with friends, family — anyone else who also owns a VHS deck.

*Via provided "VHS Playpak" cassette adapter on most decks; directly on JVC's HR-FC100 and HR-SC1000.

Available in black (GR-AX7BKU) or gray (GR-AX7GYU)

VHS: The Universal Video Language

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SCIENTIFIC AMERICAN December 1990 Volume 263 Number 6

Accidental Nuclear War

Modifications to superpower arsenals and to procedures for handling them could substantially reduce the risk of unintended Armageddon

by Bruce G. Blair and Henry W. Kendall

If nuclear war breaks out in the coming decade or two, it will probably be by accident. The threat of a cold-blooded, calculated first strike is vanishing, but beneath the calm surface of constructive diplomacy among the traditional nuclear rivals lurks the danger of unpremeditated use of nuclear weapons. The accidental, unauthorized or inadvertent use of these weapons has become the most plausible path to nuclear war.

Both superpowers, as well as France, Great Britain and China—long-standing members of the nuclear club—are potential sources of accidental missile launch. The emergence of fledgling nuclear powers such as India, Pakistan and Israel—some armed with ballistic missiles—pushes nuclear safeguards even closer to the top of the international security agenda.

The political stability of some nuclear newcomers is questionable, and so any physical and procedural safeguards they place on their weapons might readily be overriden. It is unlikely, however, that a nuclear attack by one of these nations—either on one of the superpowers or a client state—could trigger a massive nuclear response. U.S. and Soviet arsenals still pose the greatest controllable threat of unintended war, and so changes to those arsenals offer the greatest hope of alleviating that risk.

The chances of unwanted nuclear war would be reduced significantly if tamperproof, coded locks were installed on all nuclear weapons and if methods were put in place to disarm nuclear forces even after launch. In addition, the U.S. and the Soviet Union should reduce their reliance on the dangerous policy of launch on warning and reduce the launch readiness of their nuclear forces.

The social and political upheavals in the Soviet Union underscore fears of unintended nuclear war. Civil turmoil raises the possibility that rebellious ethnic groups or splinter organizations could capture nuclear weapons. Other, deeper fault lines run through the whole of Soviet society and may be capable of cracking the foundations of its nuclear command system. Although the U.S. faces no such civil unrest, the country's system of nuclear command carries some risk that nuclear weapons might be used contrary to the intentions of legitimate authorities.

The organization of missile forces in the U.S. and the Soviet Union makes it just as likely that many missiles could be launched without authorization as easily as a single one. A breakdown of control at the apex of the command chain or at lower levels (perhaps resulting from a violent rupture of Soviet political institutions) could lead to an attack causing vast destruction—and possibly trigger a larger nuclear exchange.

Were an unauthorized attack to occur from the Soviet Union, the minimum launch could involve a battalion (six to 10 missiles) or even a regiment (18 to 30 missiles). Each missile carries up to 10 warheads; the salvo could result in as many as 300 nuclear explosions. In the U.S. a minimum launch could involve either a flight of 10 missiles or a squadron of 50, carrying as many as 500 warheads, each more than 25 times as powerful as the bomb that destroyed Hiroshima. Even if no retaliation ensued, the resulting destruction and loss of life would dwarf any previous calamity in human experience.

Both U.S. and Soviet nuclear commanders face an unavoidable dilemma: they must exert negative control over nuclear weapons to prevent unwanted use, but they must exert positive control to ensure that weapons are used when duly authorized. Measures that reduce the chance of unwanted launch may increase the chance that legitimate launch orders will not be carried out. Military commanders have thus resisted improved safeguards on the grounds that those safeguards would weaken nuclear deterrence. Deficiencies in negative control have been tolerated, and although some remedial measures have gradually been implemented, a completely satisfactory trade-off has yet to be found.

BRUCE G. BLAIR and HENRY W. KENDALL are, respectively, senior fellow in foreign policy studies at the Brookings Institution in Washington, D.C., and professor of physics at the Massachusetts Institute of Technology. Blair studies U.S. and Soviet nuclear operations, targeting, command and control, and safeguards. He received a Ph.D. in operations research from Yale University and has served as a Minuteman missile launch officer in the Strategic Air Command. Kendall is a founding member and current chairman of the Union of Concerned Scientists. His primary physics interest is the electromagnetic and weak interactions of elementary particles. He shared the 1990 Nobel Prize in Physics for the discovery of quarks.

An alarmist position is unwarranted; the dominant peacetime requirement of both the U.S. and the Soviet nuclear command systems is to prevent reliably the illicit or accidental release of even a single nuclear weapon. The nuclear hierarchy is well aware that it would probably not survive the political repercussions of any major failure to perform this function. Both sides have developed sophisticated weapon-design principles and operational procedures to preserve effective negative control over tens of thousands of widely dispersed warheads; their record has been perfect to date.

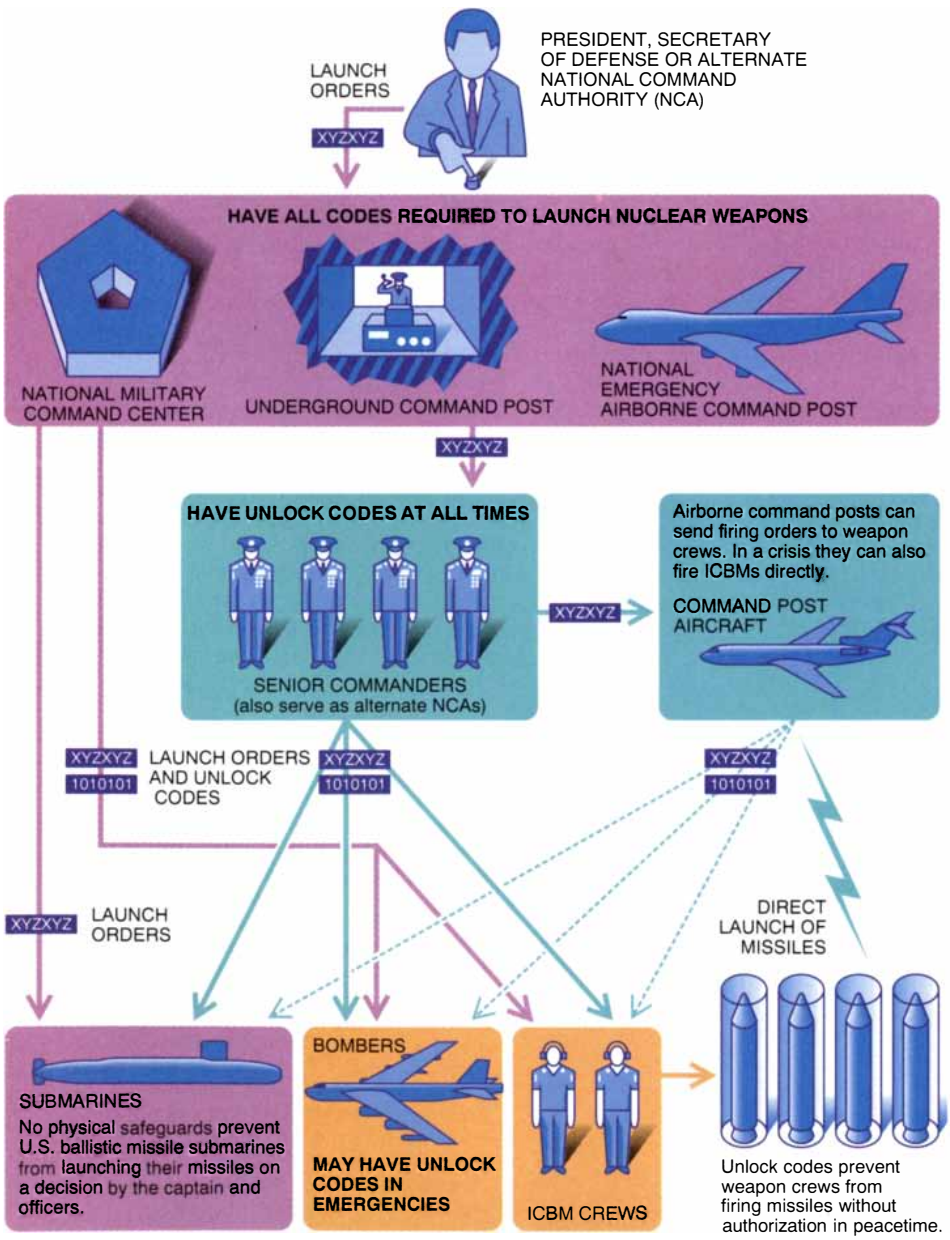
Complete confidence, however, is equally unwarranted. Even the most thorough study of ways that a disaster might occur cannot exhaust the perverse possibilities, as the explosion of the *Challenger* space shuttle and the nuclear accident at Three Mile Island attest. Furthermore, weaknesses in current safeguards are most likely to surface in a crisis—circumstances under which neither superpower has much experience in preserving negative control.

Crises shift the priority of nuclear command systems toward positive control at the expense of safeguards. When the Soviets invaded Czechoslovakia in 1968, they placed at least one army of their strategic rocket forces one notch below maximum alert. Nuclear warheads were removed from storage depots and affixed to missiles at the launch pads. These actions compromised a strong safeguard against unintended launch: separation of warheads from their means of delivery.

The U.S. engaged in comparable actions during the 1973 Arab-Israel war. Additional long-range bombers were placed on ground alert, ballistic missile submarines left port and nearly all land-based strategic missiles were readied for launch. Individual weapon commanders removed launch keys and presidential launch codes from their dual-lock safes—increasing the possibility of unauthorized release of weapons.

Current procedures since added to this alert level include the activation of special radio communications links that enable a military command aircraft to fire all 1,000 land-based American intercontinental ballistic missiles (ICBMs) by remote control. This decreases the power of ground crews to veto an illicit launch command.

U.S. NUCLEAR WEAPON COMMAND



The actions taken in such alerts cannot be completely governed by political leaders. The vulnerability of nuclear forces and the command system itself to nuclear attack generates pressure to delegate authority for nuclear alerts and weapon release down the chain of command.

The U.S. and the Soviet Union, however, appear to differ substantially on the extent to which positive control is delegated in a crisis. The U.S. command system is decentralized and allows individual weapon commands to take virtually all alert steps short of firing weapons. Military commanders can send bombers to their holding stations near Soviet territory. They also launch the airborne command posts, which issue launch orders in case of an attack that destroys ground-based centers.

Orders affecting the disposition of nuclear forces flow through strictly military channels, with marginal civilian oversight. Furthermore, historical documents leave little doubt that past presidents have delegated to key military commanders the authority to execute nuclear war plans in the event of a communications failure and verification of a nuclear strike against the U.S. There is strong evidence that such arrangements are still in effect. Numerous military installations possess all the codes needed to authorize launch. The portion of the U.S. arsenal that is restrained by hardware locks can be readied for use by many sources within the military chain of command.

In contrast, no Soviet military commander has significant authority to alert or maneuver nuclear forces, much less order an attack. Changes in alert status require the explicit approval of

the highest political leaders. Furthermore, nuclear orders are apparently processed in parallel by several separate control channels to ensure strict conformity to political plans. Units of the KGB—the Soviet political secret police—have custody of tactical nuclear weapons and, it is believed, disseminate weapon unlock codes to tactical and most strategic forces, ensuring central political control. The scope for unauthorized release would expand, however, if codes were distributed as part of the preparation for war.

A further weakness in protection against unwanted war stems from launch-on-warning strategies, which call for commanders to fire retaliatory missiles after an attack is confirmed but before incoming warheads detonate. Both the U.S. and Soviet Union rely heavily on this strategy. It requires flawless performance from satellite and ground-based sensors and from human beings.

Launch on warning compels authorities to decide whether to fire—and against which targets—in a short time and without a clear picture of the attack supposedly under way. They must respond with no definitive warhead count, no clear idea of the intended targets, no prediction of expected damage and casualties, no knowledge of the objectives of the attack and possibly no way to tell whether the attack is deliberate, accidental or unauthorized. Even if this information were available, commanders could not easily comprehend it and react in measured ways in the time allowed by launch on warning.

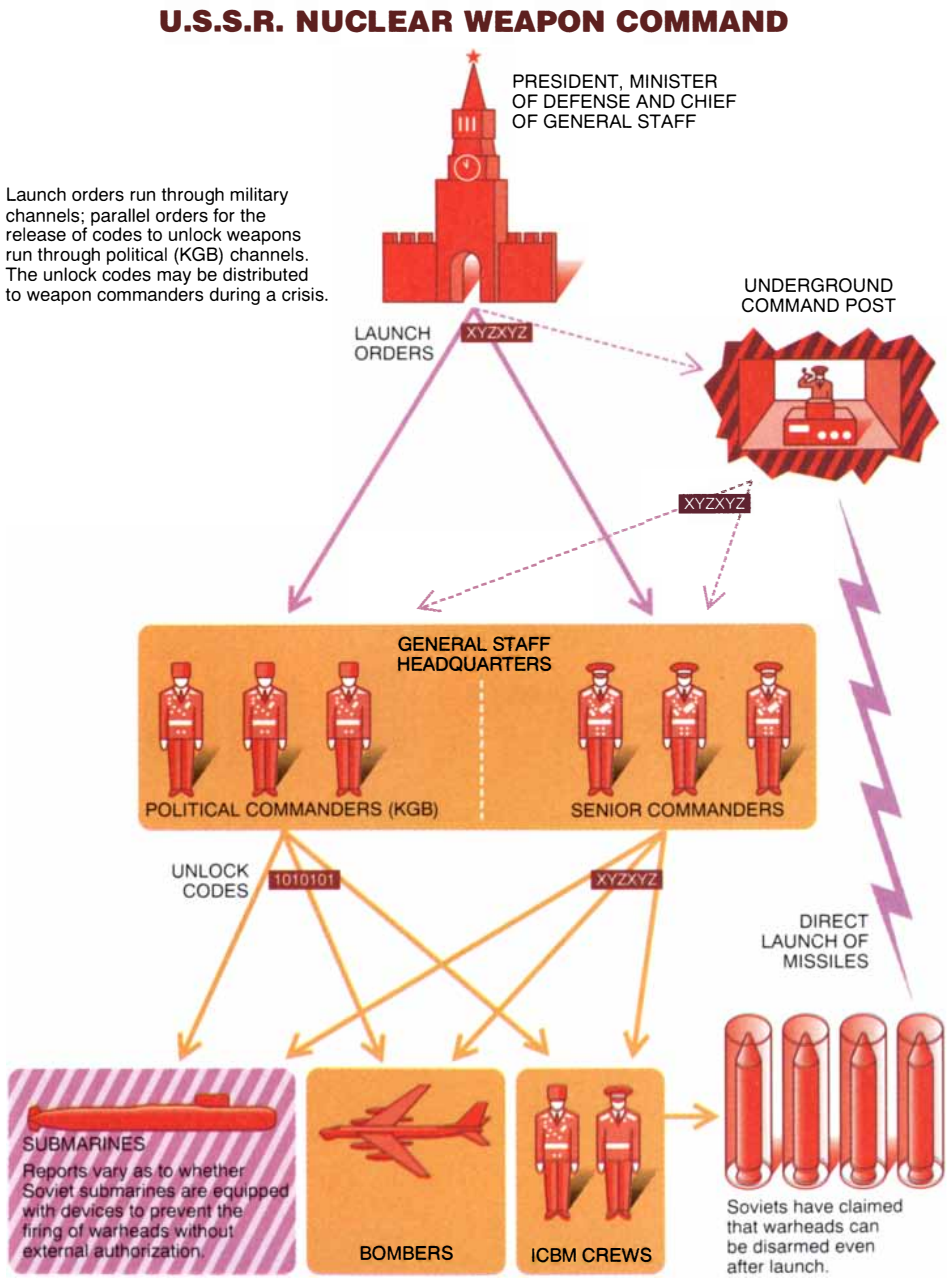
The commander of the North American Air Defense Command (NORAD), for example, would have only three minutes from the time of an initial attack indication to pass judgment on whether the continent is under fire or not. Clearly, this decision—and the subsequent ones that must be made during the 10-minute flight time of submarine-launched missiles or the 30-minute flight of ICBMs—entails major risks of premature release of weapons based on false alarms, miscalculations or confusion.

In the U.S. a so-called missile event—indication of a potential attack—typically occurs several times a day. When each event occurs, the command director at NORAD must establish a special conference with the Strategic Air Command and the Pentagon and declare his assessment of the threat to North America. In addition, thousands of anomalous sensor signals annually require urgent attention and evaluation. Each year between 1979 and 1984, the only period for which official information is available, NORAD assessed about 2,600 unusual warning indications. One in 20 required further evaluation because it appeared to pose a threat.

Most false alarms, whether generated by incorrect data, defective computer chips or other malfunctions, are quickly recognized, but perhaps once or twice a year an alarm persists long enough to trigger a nuclear alert. The last such incident to be publicly disclosed occurred in 1980, when a faulty computer chip generated indications of a massive Soviet attack.

In the ensuing confusion, a nuclear alert was declared, and the command director failed to issue a proper evaluation on time. (He was dismissed the next day.) The nuclear alert lasted longer and reached a higher level than the situation warranted. In the midst of a superpower crisis, such confusion could have been far more likely to lead commanders to act as if an attack were actually under way.

Similar Soviet procedures for evaluating indications of attack and initiating retaliation are apparently equally vulnerable to false alarms. A retired Soviet general recently told how he once witnessed signals from space-based sensors warning of the launch of U.S. Minuteman missiles against the U.S.S.R. A "competent operator," the general recalled, determined that the supposed missile exhaust plumes were

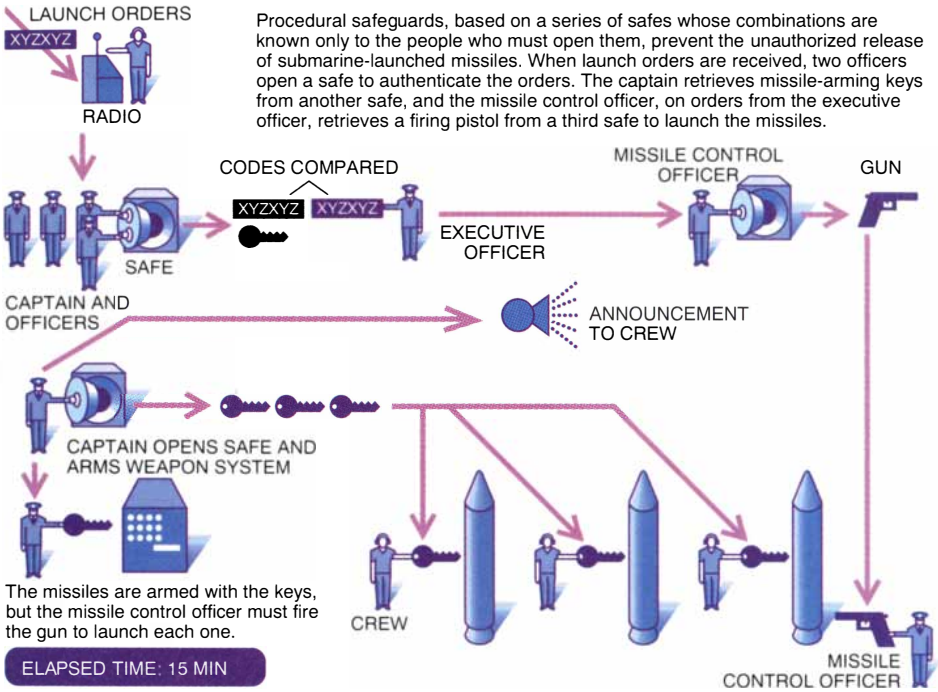


in fact merely "patches of sunlight."

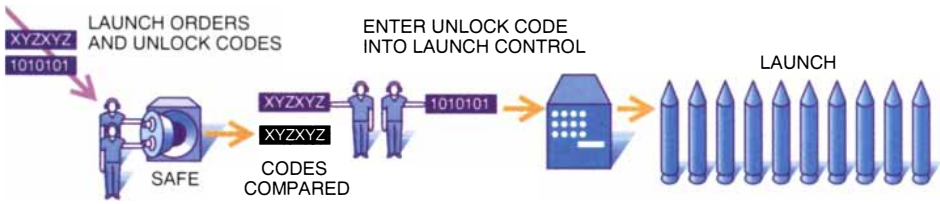
Thus far, humans have recognized hardware failures that produced false warnings of attack in time to avoid war. The corrective mechanisms have repeatedly passed muster—albeit during peacetime when alert and anxiety levels were low.

Still, in each case, certain safeguards against unwanted launch were discarded. In the U.S., Minuteman launch crews, for example, removed authorization codes and launch keys from safes. Bomber crews were scrambled, and command aircraft were launched without the knowledge of political authorities. Such actions run some indeterminate risk of provoking precautionary Soviet responses, which could in turn have reinforced the U.S. perception of an immediate threat. The question of whether such interactions based on a false alarm could trigger a nuclear attack is an open one.

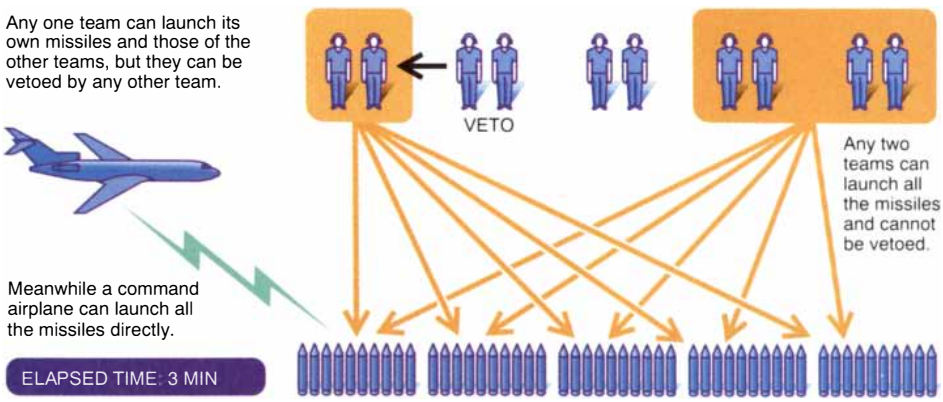
U.S. SUBMARINE LAUNCH



U.S. ICBM LAUNCH



Physical safeguards prevent unauthorized release of land-based ICBMs. Missile launch officers receive launch orders and missile-enabling codes. They match the orders against those in a dual-lock safe and must then enter the enabling codes into a control panel to launch the missiles.



A number of technical and procedural changes would reduce the chance of unintended war. Heading the list is the comprehensive use of so-called permissive action links (PALs). These electromechanical locks prevent warheads from detonating unless an essentially unbreakable code is inserted. Codes are disseminated to individual weapon commanders by higher authorities only when launch has been properly authorized. PALs prevent unauthorized release by a weapon's own crew or by enemy soldiers or terrorists who might seize a warhead. Similar devices, called coded switch systems, can be employed to prevent bomb bays from opening and missiles from firing.

Such devices were first installed by the U.S. in the early 1960s on tactical warheads assigned to allied forces stationed overseas; today all land-based U.S. tactical weapons are protected by PALs. By the end of the 1970s all Strategic Air Command nuclear warheads were equipped either with PALs or coded switch systems. We believe that Soviet land-based missiles and bombers are similarly equipped.

Naval nuclear forces on both sides, however, are generally not equipped with PALs. The resulting danger of accidental launch is particularly significant in the case of sea-launched cruise missiles. These weapons have a long range, and they are carried by surface vessels and attack submarines that would be in combat during the earliest phases of a conflict. Some British and French warheads are in similarly exposed forward positions.

Another way to reduce the risk of unintended nuclear war is to lower the levels of nuclear readiness. We estimate that 50 to 80 percent of the Soviet ICBM force is routinely maintained in a launch-ready configuration. In peacetime 15 percent of their submarine-launched ballistic missile force is deployed at sea, and none of the long-range bombers are on alert or even loaded with nuclear weapons.

The U.S., meanwhile, maintains about 90 percent of its ICBMs in launch-ready status, capable of firing within three minutes. Half of the ballistic missile submarine force is at sea at any time, and half of those vessels can fire their missiles within 15 minutes. A quarter of the strategic bomber force is on a five-minute ground alert.

This high state of launch readiness is an anachronism in the new era of U.S.-Soviet relations and poses an unnecessary danger. The percentage of both ar-

senals that is on alert should be cut down to a fraction of current levels. A threefold reduction could be carried out unilaterally without eroding deterrence, and deeper cuts could be made in stages under a verifiable agreement.

Furthermore, the warheads for units no longer on ready alert should be placed in the custody of civilian agencies, as they were during the 1950s when the Atomic Energy Commission held custody of nuclear weapons during peacetime. The civilian role in managing warhead stockpiles should be strengthened to maintain tight political control over the arming of nuclear-capable units in a crisis. Although some analysts argue that the risk of misperception in a crisis is lower if nuclear forces maintain high readiness at all times, such a posture runs contrary to current trends in superpower relations.

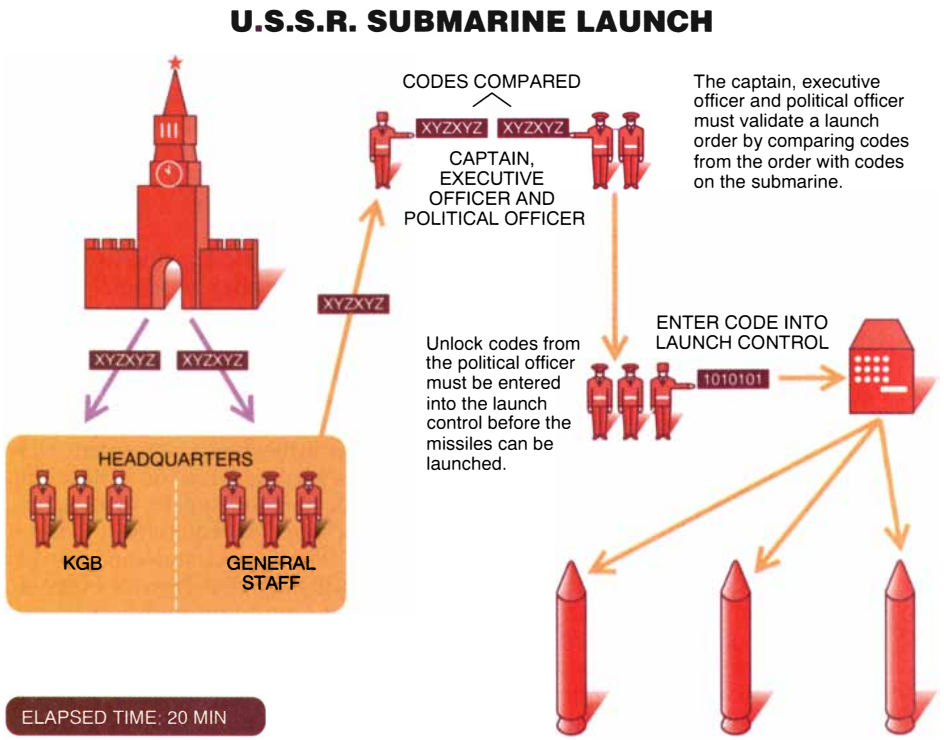
The adoption of lower alert levels would permit removing warheads or some other necessary component from some portion of the strategic arsenal, thus absolutely preventing an unwanted launch from causing a nuclear detonation. This danger is quite real. The Soviets recently disclosed that a nuclear-tipped ballistic missile had been launched by accident during routine maintenance. Fortunately, it fell a short distance from the launch pad.

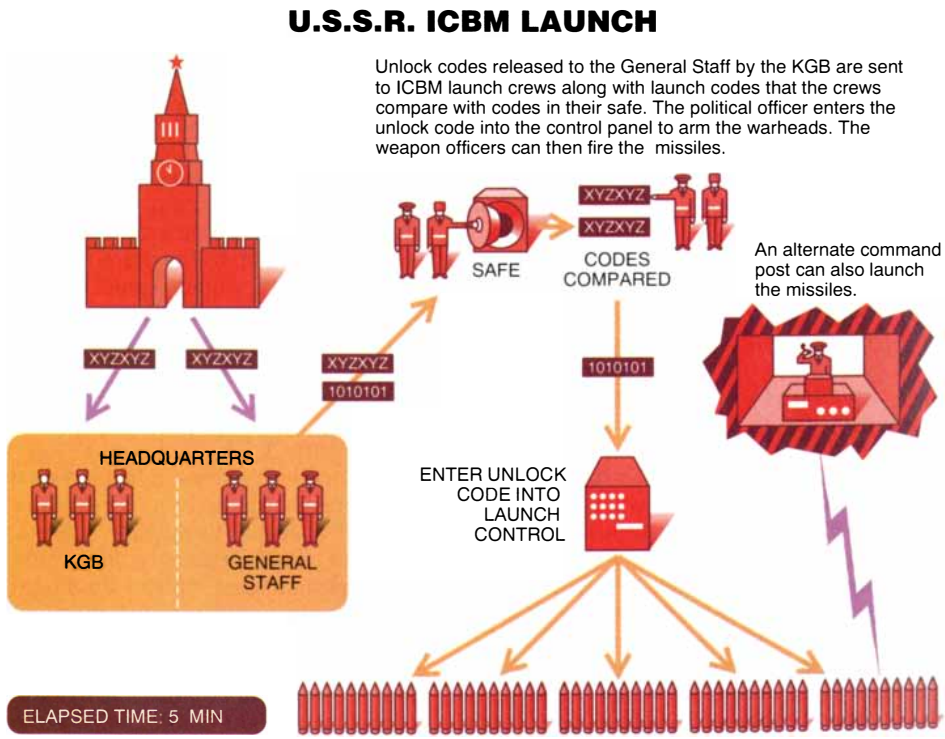
Most missiles (including virtually all active strategic missiles belonging to the major nuclear powers) now have warheads attached to them. Launch-on-warning strategies and current alert levels preclude any other configuration. A verifiable agreement to move toward separable warheads and missiles—a common Soviet practice during the 1960s—would reduce the scope for unintended launch. Furthermore, converting weapons to this configuration would be a less drastic, and therefore more palatable, form of arms control.

Restoring the missing parts in time of crisis could be construed as a preparation for attack, thus increasing the possibility of unintended war. On balance, however, the reduced chance of unwanted launch and the easing of tensions resulting from fewer missiles poised for immediate strikes outweigh the possible danger of misperception in a crisis. Furthermore, that risk could be mitigated by agreements that define the conditions for reassembling weapons and by nuclear alert procedures that ensure firm civilian control.

Whatever the alert level, human factors play a key role in the risk of unwanted launch. All those involved in the nuclear weapon chain, from top decision makers to launch officers, are subject to human frailties and instabilities. These frailties are aggravated by work conditions that are boring and isolated. (Duty on missile submarines adds the further stress of trying to adapt to an unnatural 18-hour "day" for the two months of a typical patrol.) Such conditions can sometimes lead to severe behavioral problems, including drug or alcohol use and psychological or emotional instability.

In 1989, for example, of the roughly 75,000 members of the U.S. military with access to nuclear weapons and related components, nearly 2,400 had to be removed from duty. Seven hundred and thirty abused alcohol or drugs, and the rest had psychological or emotional problems, were insubordinate or engaged in criminal behavior. Herbert Abrams of Stanford University has recommended that drug and alcohol use among soldiers with nuclear responsi-





bilities be monitored more closely and that physicians who examine the soldiers be aware of the peculiar nature of their duties. In addition, much more can be done to alleviate stressful working conditions. (All these problems and remedies apply in at least equal measure to the Soviet nuclear apparatus.)

World leaders, meanwhile, are no less subject to stress. They may come to a crisis dependent on alcohol or drugs—whether self-administered or prescribed. Such problems afflicted Winston Churchill and Anthony Eden. Richard M. Nixon was too distraught over Watergate to participate in crucial discussions that resulted in a global U.S. nuclear alert in 1973; senior government officials later took precautions against the possibility that he might act irrationally in his capacity as commander in chief. Even a leader as ruthless as Stalin experienced severe stress during periods of crisis. Such infirmities can lead to behavioral changes, impaired judgment and even irrational actions. Some psychologists have suggested leaders be monitored.

If all these measures fail to prevent an unwanted launch, steps can still be taken to mitigate the consequences. One obvious step is to reduce the number of warheads each missile carries; another is to develop methods for destroying missiles after launch. A third step is to implement launch-detection systems to provide warnings of unintended launches to both sides. Some combination of acoustic and optical sensors would serve for ICBMs; sea-launched ballistic missiles and cruise missiles would require small transmitters that would send signals to relay satellites. Such a detection system might contain provisions for disabling it at the onset of a crisis.

Improvements in the "hot line" (first put in place in 1963) would reduce risks of misperception related to unintended launches, reassembly of missiles and warheads, and other apparently hostile acts. Currently the link between the U.S. and the Soviet Union runs through a Soviet and an American satellite primarily used for civilian communications, with alternate routes provided by cable and radio links. This configuration, however, cannot ensure reliable communication under the adverse conditions in which it is most needed. All parts of the system are vulnerable to nuclear attack. Moreover, the cable routes have been cut inadvertently a handful of times already. Dedicated, radiation-resistant satellites operating in the extremely high frequency band would prevent nuclear static from interrupting signals and would make it possible to continue hot-line conversations through mobile terminals that could accompany relocated command centers.

The critical action, however, is to implement mechanisms for disarming missiles once they have been launched. Costly attempts to develop antiballistic missile systems have led to a dead end. Continuing compliance with the Antiballistic Missile Treaty would limit deployment to 100 interceptors based at Grand Forks, N.D. Such a system (at a cost of about $10 billion) could destroy only about 50 reentry vehicles and would be ineffective against cruise missiles or submarine-launched ballistic missiles. A more capable system, exceeding treaty restrictions, would cost far more. Furthermore, there is currently no realistic prospect of pursuing such a project.

The only practical method for stopping a missile after accidental launch is for the country of origin to destroy it or to allow the target country to destroy the warheads prior to impact—a "command destruct system." Indeed, in 1971, the Soviet Union and the U.S. signed a little-known agreement that specifies what each is to do in the event of an unwanted launch. That agreement includes the requirement that the nation "whose nuclear weapon is involved will immediately make every effort to take *necessary* measures to *render harmless or destroy* such weapon without its causing damage."

A typical U.S. system might be based on a coded key automatically generated at launch time to prevent its theft. After the unwanted launch had been verified, the key would be transmitted to the warheads by dedicated relay satellites from a special command and control system located in the National Military Command Center. It would also be sent by hot line to the target country, along with data on warhead trajectories, so that destruct attempts could be made up to the point of reentry. A destruct system could be disabled—by special command units not involved in the launch process—just prior to an authorized launch, to preclude the remote possibility that an adversary would be able to disarm an intentional attack.

Destruct devices should be placed on the warheads themselves to maximize the time available to decision makers. The best place for destruction would be in the midcourse part of the flight, where it would do the least damage.

It would be particularly important, especially during a crisis, that destruction or disarming be verifiable by both sides. ICBMs might emit a coded radio signal or emit a burst of chaff visible to radar. Alternatively, warheads could be fired with minimum yield by draining their tritium before detonation. Cruise missiles might disarm their warheads, then climb to high altitude, transmit a coded signal and then fly into the ocean or the Arctic ice cap, where they could crash or be destroyed by an explosive charge.

Although such a system would add weight and complexity to nuclear reentry vehicles, this penalty is more than balanced by the reduction in the danger of unwanted launch. Nevertheless, the U.S. military and the Defense Department have shown no interest in implementing command destruct systems. This is particularly puzzling in view of attitudes in the Soviet Union: Deputy Foreign Minister Viktor Karpov has told us that Soviet ICBMs already carry command destruct systems.

The risk of accidental nuclear explosions and the worse risk of nuclear war, however low they may be, should be lowered further. The U.S. and the Soviet Union should move promptly to bring about acceptable compromises. There is ample latitude for each country to act independently in this area—most improvements in safeguards can be accomplished unilaterally. The Soviets, for example, have recently moved nuclear weapons from areas of ethnic unrest to storage depots in the Russian Republic. They plan to dismantle ICBM forces in Kazakhstan, the only ethnic region that "hosts" Soviet strategic forces.

It would also be worthwhile for the two governments to exchange views on particular risks of unwanted launch and measures to reduce those risks. Those discussions should be broadened to include other nuclear states. Relations have never been more conducive to fruitful talks on the issue.

FURTHER READING

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The Surface of Venus

Razor-sharp images of the earth's near twin reveal a mix of familiar and perplexing geologic features

by R. Stephen Saunders

Venus is the earth's near twin in size, mass and distance from the sun. Yet the nature of its surface long remained a mystery. The silvery clouds that make it such a lovely sight in terrestrial skies also completely obscure the planet itself.

Fortunately, radio waves a few centimeters long can easily pierce the clouds, permitting earthbound radiotelescopes and U.S. and Soviet space probes to reconstruct a crude picture of the Venusian landscape. And when the National Aeronautics and Space Administration's *Magellan* spacecraft started mapping Venus on September 15, the planet at last began to reveal its true nature. The overall impression is that Venus is a dynamic world that has been shaped by processes fundamentally similar to those that have taken place on the earth, but often with dramatically different results.

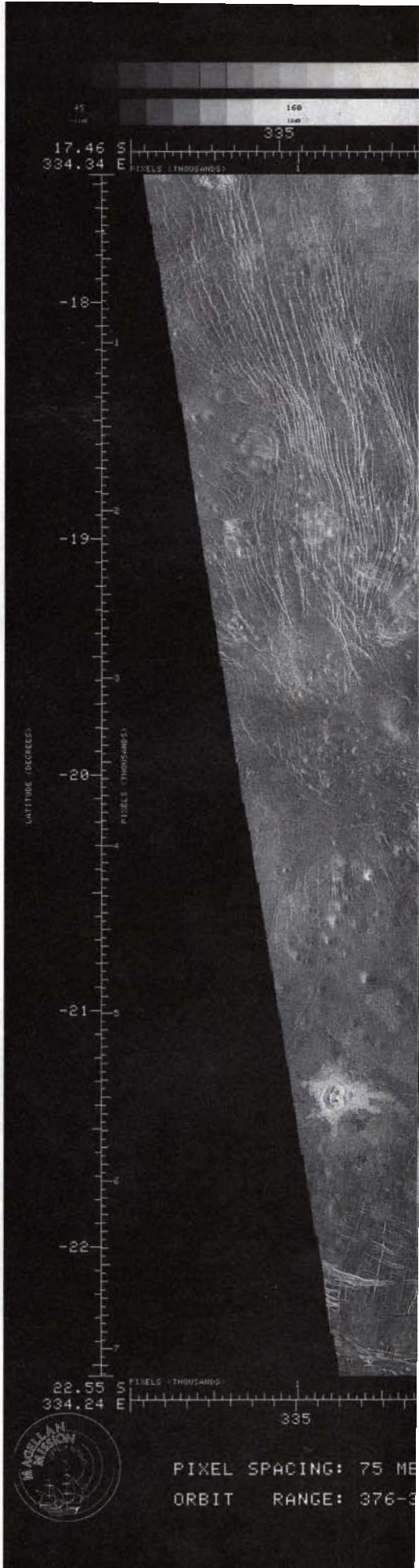
Magellan's sophisticated synthetic aperture radar reveals details as small as 120 meters across, one tenth the size of those previously detectable. In the images shown here, rough regions appear bright and smooth areas dark because of the way different surface textures reflect radar.

Early communications problems with *Magellan*—one of which caused loss of contact for an agonizing 17.5 hours—have largely been overcome. Roughly 98 percent of the signals now arrive trouble free. The crisp images shown here only hint at the remarkable volume of information that the spacecraft will collect. *Magellan* will map the whole surface of Venus, much as *Mariner 9* mapped Mars in 1971 and 1972. But in just its first three days of mapping, *Magellan* returned more data than did the entire *Mariner 9* mission.

Those three days' worth of images, covering only 1.5 percent of Venus's surface, have now been processed. The wealth of detail has already reshaped ideas about the earth's nearest planetary neighbor. The Venusian surface appears to be 100 million to one billion years old, quite ancient by terrestrial standards. Nevertheless, this age implies that the planet's outer layers have been significantly reworked and erased relatively recently in the solar system's 4.5-billion-year history.

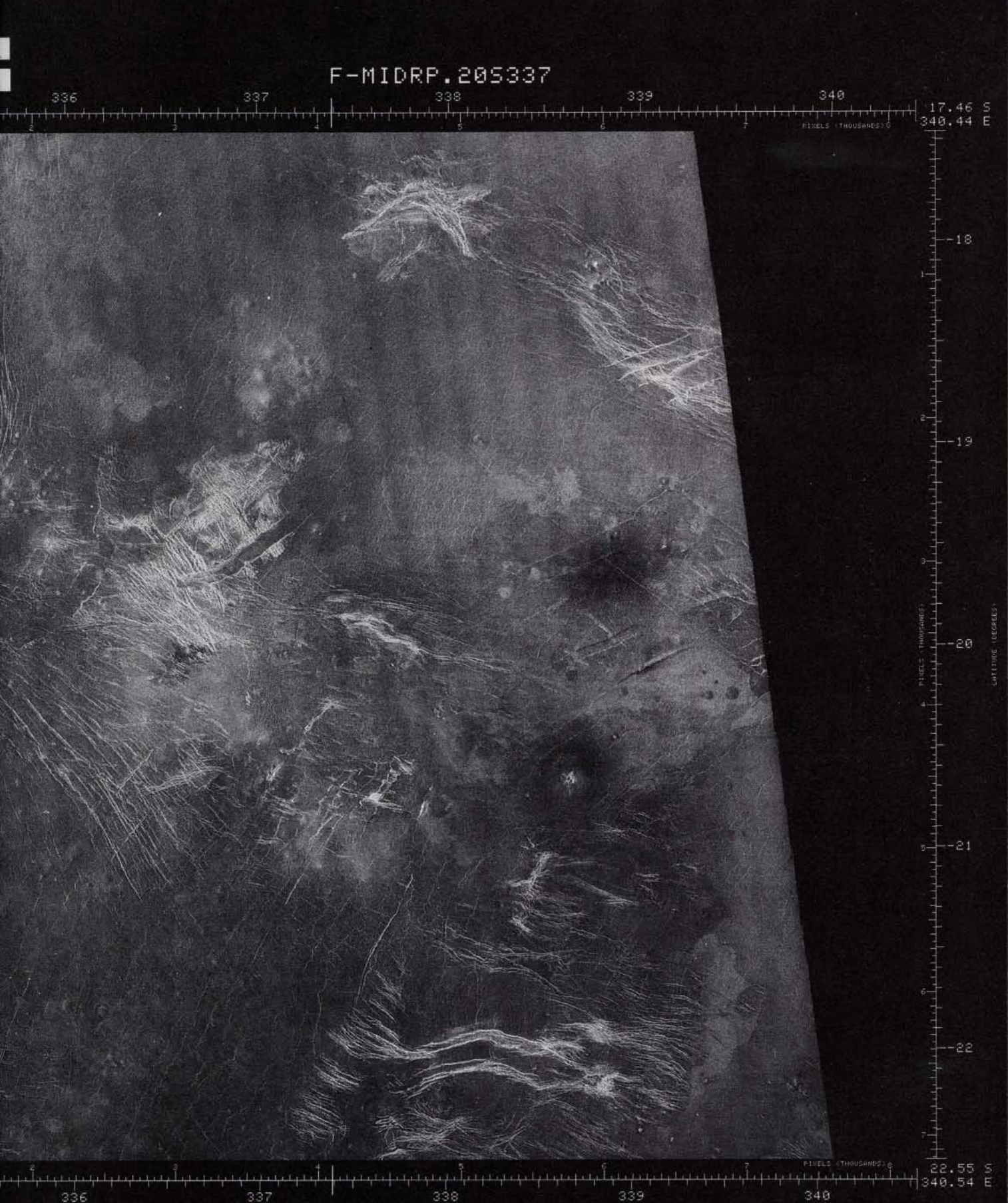
Terraced volcanic calderas, extensive lava flows, folded mountain ranges, and intricate, tortured networks of

R. STEPHEN SAUNDERS is project scientist for NASA's *Magellan* mission at the Jet Propulsion Laboratory in Pasadena, Calif. *Scientific American* staff editor Corey S. Powell assisted in the preparation of this article.



DIVERSE TOPOGRAPHY of Venus can be seen in this mosaic radar map. The imaged area covers a region 475 kilometers wide and 545 kilometers long between the Navka and Lavinia plains.

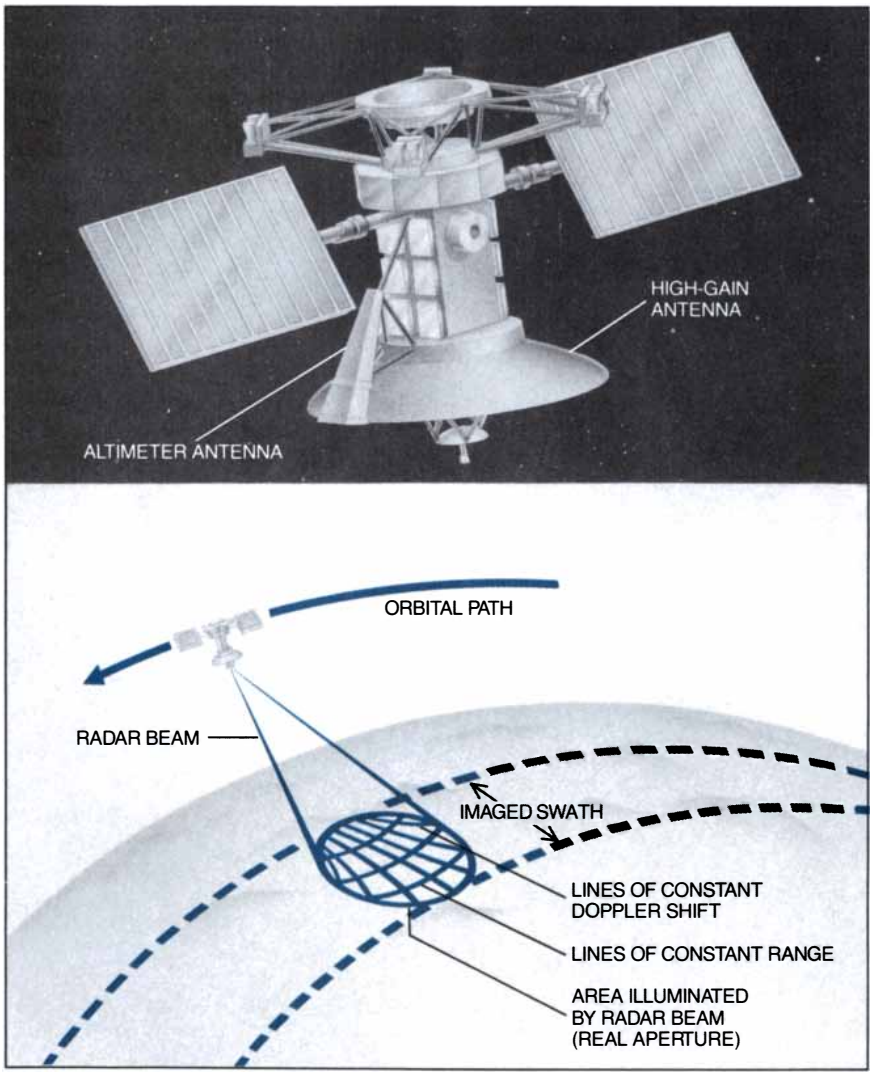
A cluster of volcanic domes ranging from 1.5 to 7.5 kilometers in diameter lies along the western central edge of the image. The domes and their lava deposits are located at the convergence of radar-bright linear markings, which appear to be faults and troughs. In some places the domes overlie the faults. The faults and troughs extend southward until they terminate against dark, smooth plains and are crosscut by additional, perpendicular faults. This configuration indicates that episodes of faulting and volcanism have occurred many times. An extremely radar-dark circular region near the eastern central edge of the image is thought to be a region of sedimentary deposits, perhaps related to a meteoric impact.

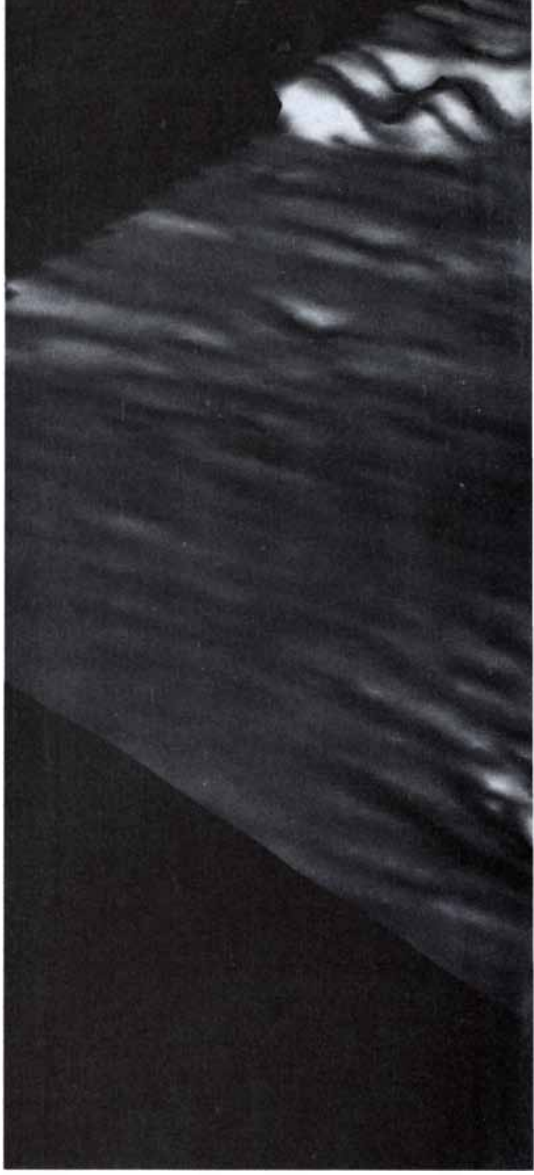


faults testify to Venus's internal activity. Evidence of earthlike, mobile crustal plates remains inconclusive, however. Many impact craters seem to be flooded with lava, perhaps from hot layers just below Venus's thin crust. Despite very low surface wind speeds, signs of wind erosion and windblown sedimentation appear in a number of locations.

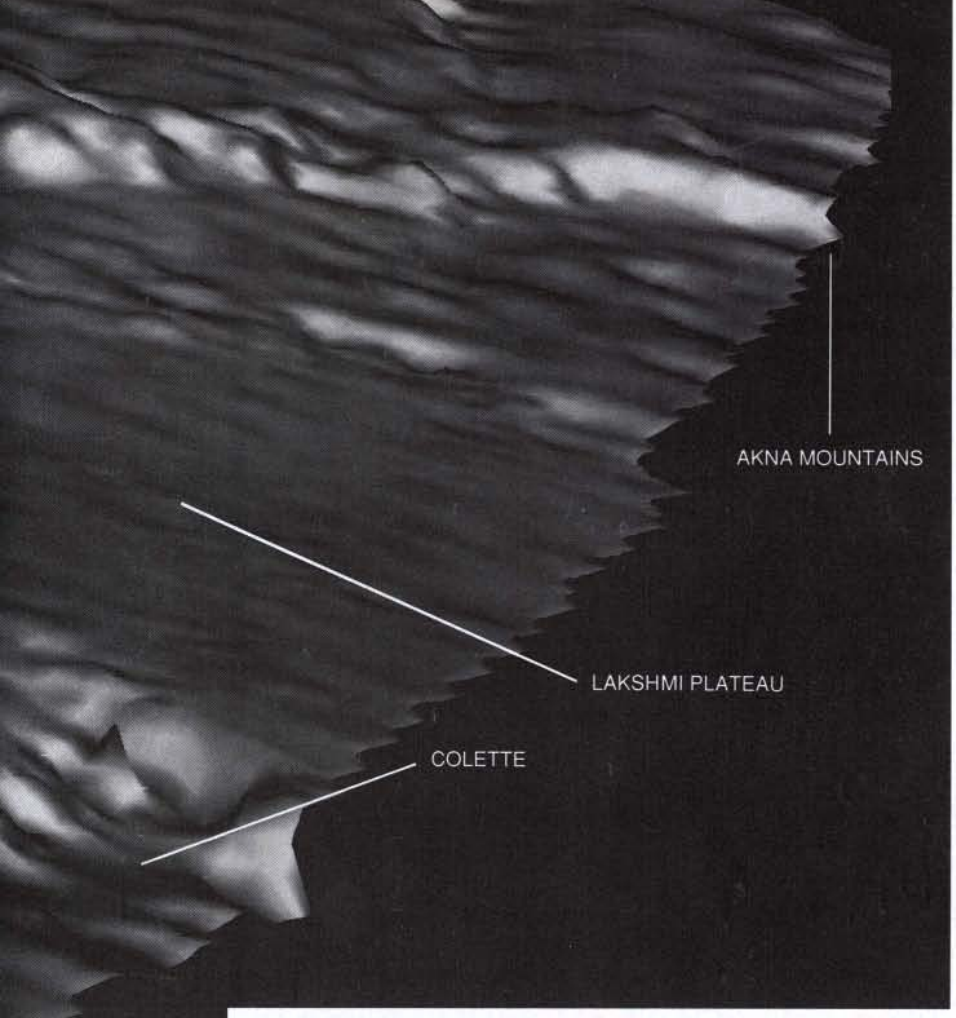
In addition to familiar-looking features, Venus also harbors some strange formations that have us planetary scientists scratching our heads. An unexpectedly large number of asymmetric impact craters hint that Venus's thick atmosphere affects the way that large meteors reach the surface or the manner in which ejecta are distributed. Eroded features resemble riverbeds except that water cannot remain liquid at Venus's surface temperature of 450 degrees Celsius. Perhaps extremely fluid lava or hot gas and dust from an impact produced the erosion. Smooth, dark areas, possibly caused by the blast associated with an impact, surround a number of craters. Some circular smooth areas, however, mysteriously lack a visible central crater.

So far *Magellan* has looked only at the low-lying plains of Venus. Starting this month, the probe is scheduled to begin mapping the equatorial highlands, and entirely new features may well appear. As wider swaths are examined, scientists will be able to make better sense of the planet's system of rifts and faults. Over the next five years *Magellan* should map the planet eight times, which will improve the resolution and fill in missing areas. It will also permit researchers to search for any short-term changes in the surface—changes that could show that Venus's geologic restlessness is very much a phenomenon of the present.





MAGELLAN'*s high-gain antenna maps one strip of Venus during each orbit and relays the data back to the earth. Multiple radar sweeps are combined to produce mosaic panoramas. The altimeter antenna measures the time it takes radar pulses to return to the spacecraft; from this, one can deduce the surface topography.*



a

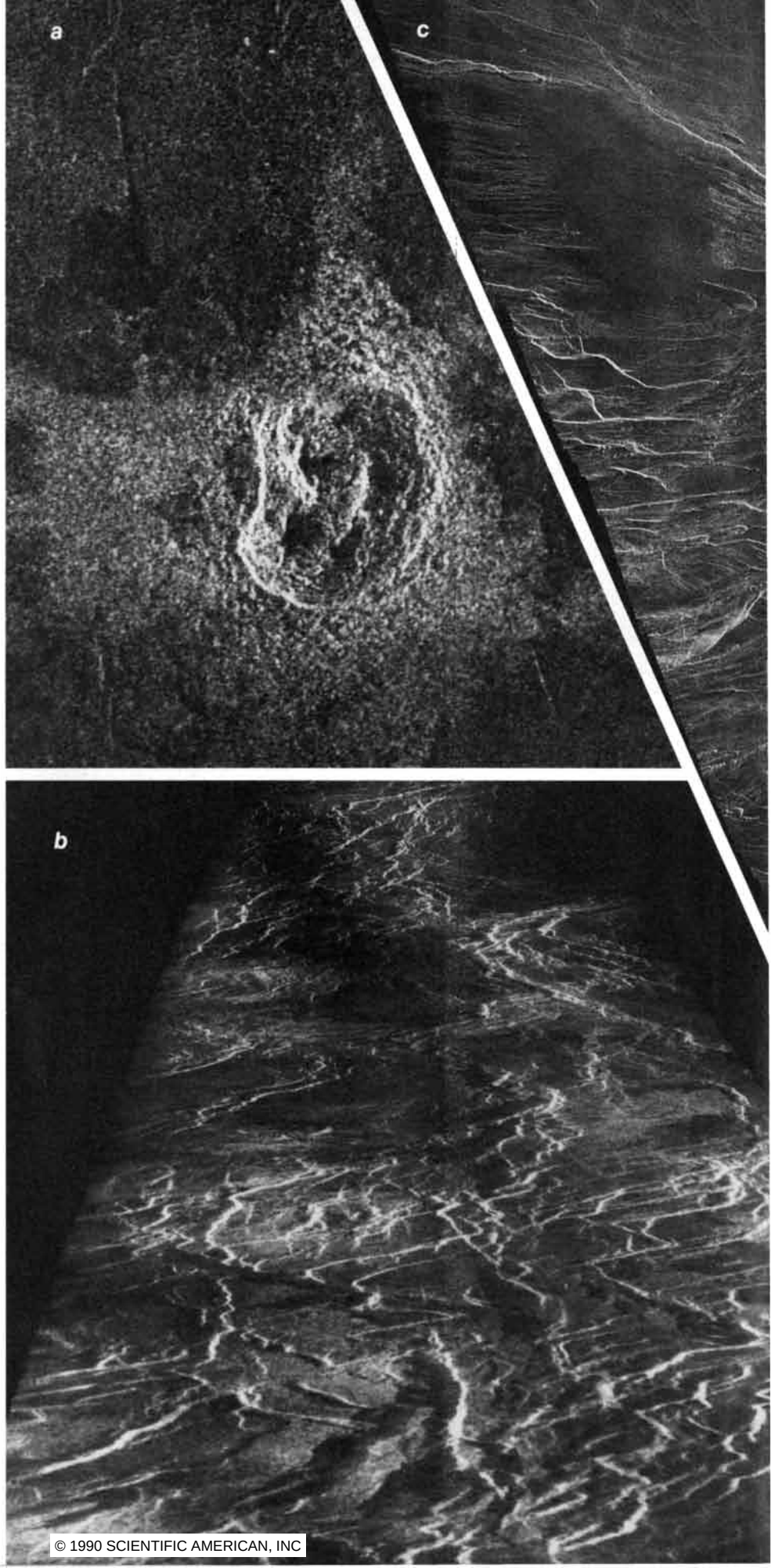
ALTIMETRY IMAGE reveals an abrupt rise at the Akna Mountains, which formed by the compressed folding of the planet's surface. The smooth plain of Lakshmi probably represents lava that flowed from the volcanic caldera Colette. As the lava drained out, Colette collapsed; it now lies three kilometers below the surrounding surface—far deeper than most terrestrial calderas.

b

MOSAIC IMAGE shows three impact craters having diameters from 37 to 50 kilometers that lie in a region of fractured plains. Impact craters are about as common on Venus as they are on the earth. On the earth, weathering, especially the action of water, quickly distorts and disguises these craters. On dry Venus, in contrast, craters appear sharp and fresh. Riverlike erosion features running from the largest crater in the image are as yet unexplained.

c

THREE-DIMENSIONAL representation of Magellan *radar reflections emphasizes the structure of the 34-kilometer diameter Golubkina crater. The terraced inner walls and central peak resemble those of impact craters on the earth, the moon and Mars. The crater's flat, smooth floor hints that it has been flooded with lava.*



a

KIDNEY-SHAPED CRATER appears unlike any other in the solar system. Perhaps an incoming meteor broke up as it passed through the dense Venusian atmosphere, causing several large chunks of material to strike almost simultaneously in an irregular pattern.

The crater measures nine by 12 kilometers; craters less than six kilometers across are not seen on Venus, presumably because small meteors disintegrate in the atmosphere.

b

GEOLOGICALLY YOUNG LOWLAND PLAIN abounds with complex canyon systems that were produced as Venus's crust extended and pulled apart. Some of the canyons were then filled by lava flows. The canyons average five to 10 kilometers wide and 50 to 100 kilometers long; they have rims about 100 meters high. The perspective simulates a northward view with a slant angle of about 10 degrees.

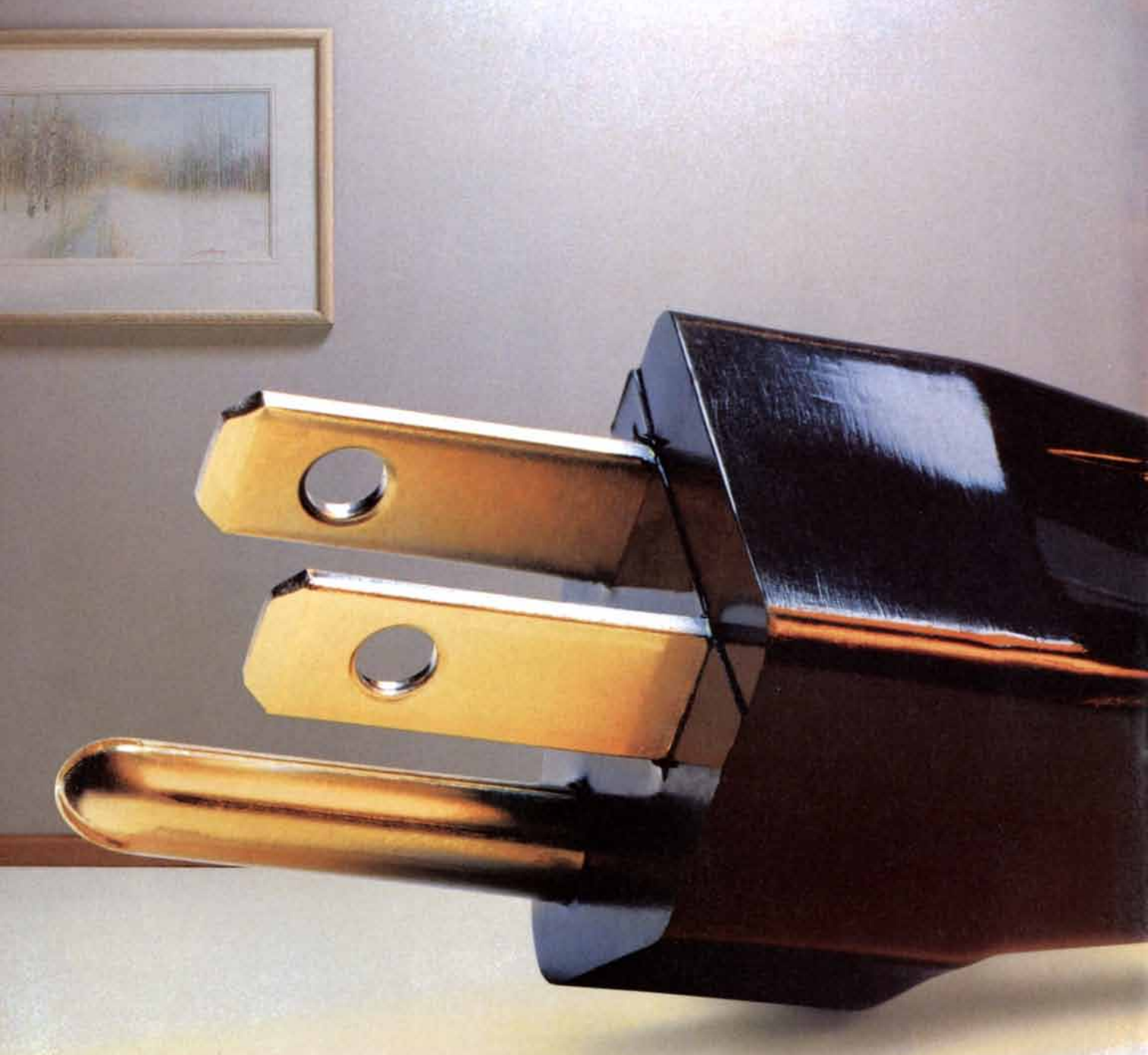
c

FAULTS AND FAULTED DEPRESSIONS extend along the lower half of this image of the Lavinia region of Venus. The structures range from 70 meters to seven kilometers in width. Their northern ends often widen into elongated pits whimsically called gumboids because of their resemblance to the animated character Gumby. These features may have formed as subsurface magma hit rocky barriers and escaped, causing the overlying crust to collapse.

The large circular feature appears to be a corona, the site of the large-scale upwelling of hot magma from the interior of Venus. Fault lines radiating from the corona resulted from stresses created when the magma reached the surface. Coronas are analogous to volcanic hot spots on the earth, such as the one that created the Hawaiian Islands. This image covers an area 165 kilometers wide and 575 kilometers long. The missing strip is being reprocessed to remove instrument artifacts.

d

EXPLOSIVE VOLCANISM may be responsible for the radar-bright deposit that extends roughly 10 kilometers from the kilometer-wide volcanic crater at the center of this image. The etched pattern of the surrounding plains becomes more obscured closer to the crater, which indicates that the deposit is thickest near the crater. The shape of the deposit suggests that local winds either carried the plume southward or else gradually eroded away the plume material except for that part located in the volcano's wind shadow.



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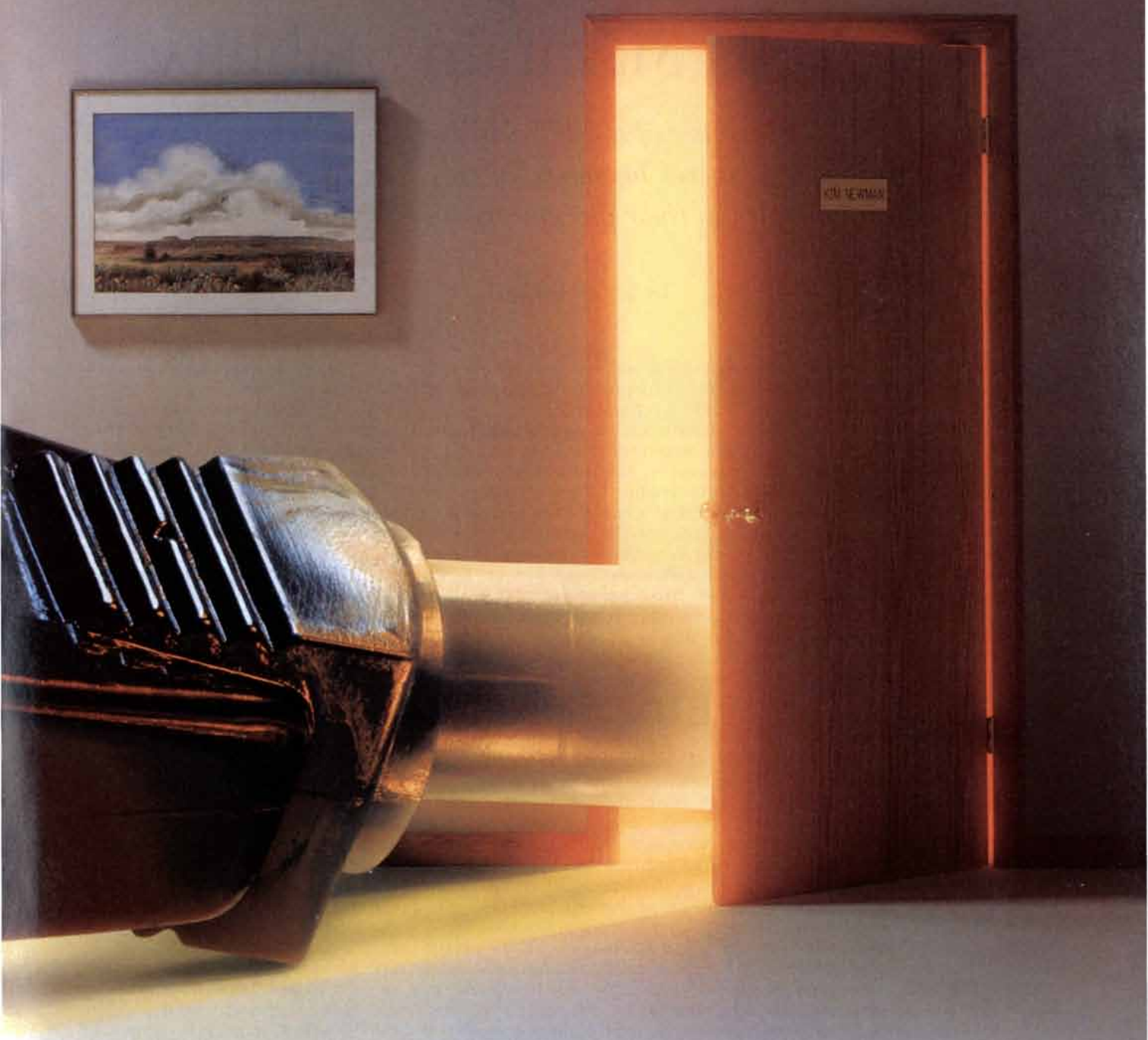

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How Cells Maintain Stability

A member of the U.S.S.R. Academy of Sciences shares his model of how cells recover from blows to their protein-making machinery

by Igor N. Todorov

An organism whose cells cannot make protein is doomed. At the least, the cells must produce appropriate amounts of the proteins needed for their own survival.

For many years, my colleagues and I at the Institute of Chemical Physics in Moscow have studied how resting, or nondividing, cells ensure such protein homeostasis. In addition to identifying a characteristic sequence of responses to the suppression of protein synthesis, we have discovered that profound suppression can trigger an overzealous rebound. The cells not only regain their ability to make crucial proteins, they often go on to grow and divide. Some may also become cancerous.

Our primary window on the restorative strategy is rat hepatocytes, the major cells of the liver. They make ideal subjects because they are continually exposed to many toxic compounds, which means they can be expected to have powerful (and therefore readily detectable) homeostatic mechanisms.

We challenge the hepatocytes by chemically inhibiting translation, the final event in protein synthesis. The first synthetic event, transcription, occurs in the nucleus. Instructions specifying the sequence of amino acids in a given protein are stored in a single gene. When a cell needs that protein, it copies, or transcribes, the instructions from DNA into RNA, which then is modified (without disturbing the instructions) to form messenger RNA. The messenger RNA transcript migrates from the nucleus to the cytoplasm, where it serves as a template for protein synthesis; in other words, it is translated.

Translation is accomplished by globular structures called ribosomes. The ribosomes travel the length of the RNA, "reading" it and directing what are called transfer RNA molecules to add one specified amino acid after another. A number of ribosomes migrate along the same transcript simultaneously, like a mobile assembly line, and together they constitute protein factories called polysomes.

We choose to impede translation rather than transcription because, under normal circumstances, translation is probably disrupted more often. Transcription is insulated from many external influences by the nuclear membrane and by proteins associated with DNA, primarily histones. Translation, in contrast, occurs at the periphery, in the cytoplasm. As a major consumer of energy and materials in cells, the process is thus more vulnerable to any shortages of those commodities.

Our inhibitory agent is the antibiotic cycloheximide (CHI). It interferes with translation by binding to the 60S subunit of ribosomes, the larger of the ribosome's two major parts; the other part is known as the 40S subunit. ("S" stands for a measure called the svedberg unit.) This attachment prevents the molecule guanosine triphosphate (GTP) from binding to ribosomes. Because GTP provides energy for ribosomal migration along a messenger RNA transcript, translation by the affected ribosome—and by those following behind it—stops.

In most of our experiments, rats are exposed to a nearly lethal dose of the drug, which inhibits translation in their hepatocytes by as much as 97 percent. Such strong suppression of protein synthesis reveals the cells' survival strategy most clearly. We have also studied fibroblasts in culture and find that both hepatocytes and the cultured cells respond to the antibiotic in essentially the same way.

A cell's earliest response is an increase in the uptake of nutrients from outside, mainly glucose and amino acids—presumably to augment energy production, in the case of glucose, and supplies of the building blocks of proteins, in the case of amino acids. Soon after, the cell accelerates the internal circulation of proteins, in an apparent attempt to construct new polysomes from readily available, spare materials.

Of particular importance, existing protein constituents of ribosomes are rushed in the first two hours from the cytoplasm to the site in the nucleus where ribosomal RNA, the other component of ribosomes, continues to be made. At this site, called the nucleolus, the proteins and ribosomal RNA combine. Then, according to data collected by John J. Ch'ih and his colleagues at the Hahnemann Medical College in Philadelphia, the cell speeds the resulting complexes to the cytoplasm, where the complexes can be assembled into ribosomes and, if messenger RNA is available, into polysomes.

Concurrently, there is an increase in the flow to the nucleus of proteins involved in gene transcription, reflecting the cell's effort to provide the protein templates needed to restore protein synthesis. For instance, the enzyme RNA polymerase II is hurried to the nucleus, where there is a transitory increase in its binding to DNA. The enzyme is responsible for transcribing DNA into precursors of messenger RNA, and, indeed, the synthesis of messenger RNA increases temporarily.

The increase in protein transport is undoubtedly fueled to a great extent by an elevation in the intracellular level of adenosine triphosphate (ATP), a major carrier of energy. The elevation, which lasts for about three hours, must stem in part from the cycloheximide-induced idling of virtually all the cell's polysomes, which normally use much of the cell's energy. When those struc-

IGOR N. TODOROV is head of the laboratory of molecular biology at the Institute of Chemical Physics of the U.S.S.R. Academy of Sciences. He has studied cell stability since the 1970s and is currently applying his research to an analysis of how various drugs work. Todorov is writing a book on the development of the mechanisms of cell stability in multicellular organisms. In his spare time, he studies music.

tures are quiet, unused ATP becomes free to promote the intracellular circulation of proteins.

This temporary rise in available ATP may be augmented by the early uptake of glucose and the increase in protein movement, which together lead to increased delivery of glucose and mitochondrial proteins to mitochondria. These organelles convert nutrients to ATP and are often referred to as the energy factories of the cell.

Another of the cell's early responses complements those mentioned already. In animal cells, some fraction of ribosomes are unattached to polysomes. Cycloheximide does not interfere with free ribosomes, and so these reserves are pressed quickly into service for making new polysomes.

If translation were depressed only mildly, these relatively simple early responses could reinstate protein homeostasis. In our experiments, however, we suppress translation profoundly, delivering so much cycloheximide that it binds to most of the rapidly formed polysomes, excluding them from the recovery processes. Consequently, the cell is forced to resort to more draconian measures to ensure its survival.

Seeking other material for building polysomes, the cell breaks apart certain existing polysomes and reuses the parts. In particular, it sacrifices those assembly lines devoted to making proteins destined for export to other cells.

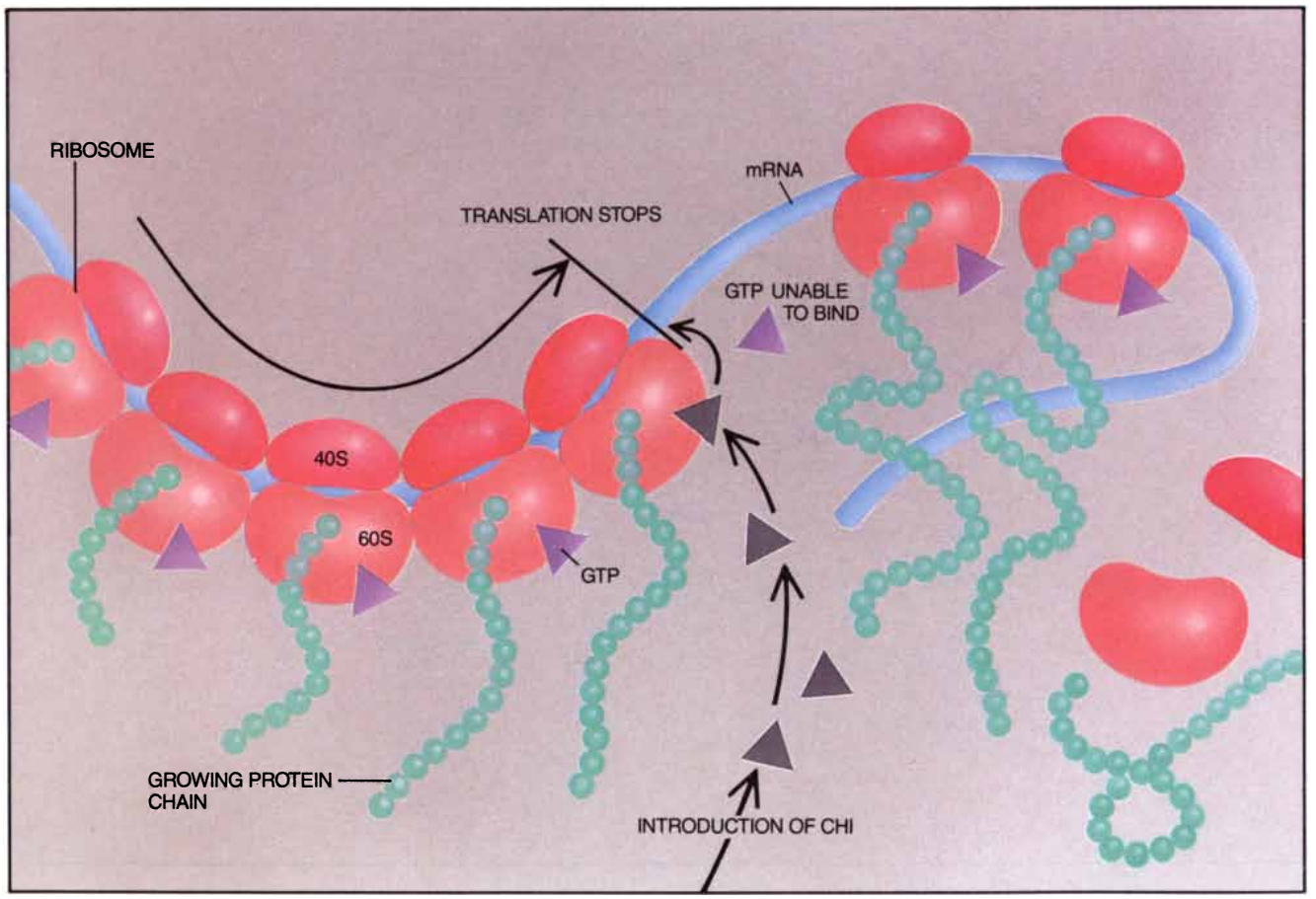
The victims, which are normally found bound to the endoplasmic reticulum (a complex system of membranes), disassemble beginning about an hour after hepatocytes are exposed to a high dose of cycloheximide. The attached membrane also breaks up, releasing fats that can be converted to energy.

Further breakdown of the polysomes and gradual recycling of the pieces succeed where the earlier strategies fail: beginning about six hours after administration of cycloheximide, the cell provides itself with many new, functional polysomes and starts making protein once again. For the most part, these polysomes are unconnected to the endoplasmic reticulum, and they manufacture not export proteins but those required to meet the cell's own needs. Although the cell makes a variety of proteins, it concentrates initially and for many hours on the constituents of polysomes.

Disassembly of existing polysomes and assembly of new ones from the parts are not accomplished easily. When the membrane-bound polysomes are separated into individual ribosomes and subunits, each of the 40S fractions remains linked to the messenger RNA fragment it had been translating; the subunit is therefore unable to act on any other messenger RNA molecules.

Fortunately for the cell, the experimentally induced blockade of translation somehow triggers the enzymatic cleavage of the subunit's ribosomal RNA (the 18S RNA) into several bits. This cleavage, in turn, causes the complete dissociation of the rest of the 40S subunit into its molecular constituents.

Thus, the undesirable remnants of



DRUG CYCLOHEXIMIDE (CHI) was enlisted by the author to reveal how cells respond to threats to protein manufacture. CHI impedes the step in protein synthesis called translation: the assembly of amino acid chains on polysomes. Polysomes consist of many ribosomes that simultaneously travel along a messenger RNA (mRNA) molecule, each stringing together one mRNA-specified amino acid after another. CHI stalls translation by binding to the 60S ribosomal subunit and thus preventing binding by guanosine triphosphate (GTP), which provides energy for ribosomal movement on mRNA.

messenger RNA are released, but the 40S subunits are now shattered and nonfunctional. In contrast, the 60S subunits remain intact, except that they tend to release any bound cycloheximide when they are no longer part of a polysome. The large subunits are also much more abundant in the cytoplasm than their smaller partners. This unsatisfactory imbalance of parts does not last long, however.

Much of the ribosomal protein from the 40S subunits makes its way to the nucleus. There the cell continues to transcribe the genes for ribosomal RNA, many of which are clustered together in the DNA. The genes are copied into a single long transcript called pre-ribosomal RNA, which is then spliced to form smaller pieces, including the 18S ribosomal RNA and the 28S variety, a major RNA constituent of the 60S subunit.

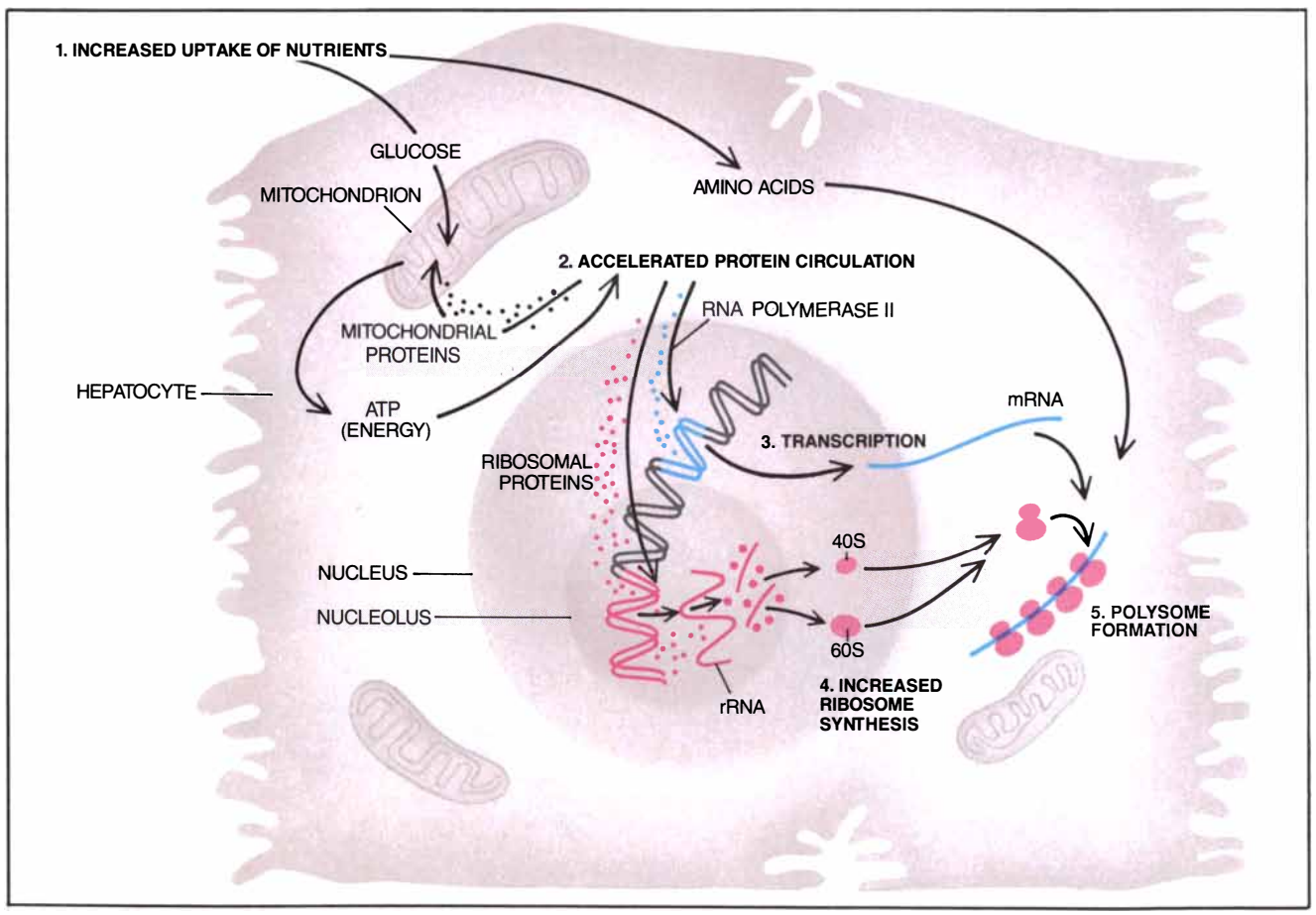
As the concentration of recyclable ribosomal proteins in the nucleus rises, so does the speed with which the proteins combine with 18S transcripts to form mature 40S subunits. Hence, relatively more 40S than 60S ribosomal constituents are delivered to the cytoplasm. Eventually the enhanced delivery of the 40S subunit restores the one-to-one balance of small and large subunits and results in the formation of many new polysomes.

In responding to a sublethal dose of cycloheximide, then, the cell reprograms its translation operation. It tears apart the bulk of its membrane-bound polysomes, which produce mainly export proteins, and builds up a new system of polysomes (mostly unbound) that manufacture proteins required to form still more polysomes and to meet other needs of the cell.

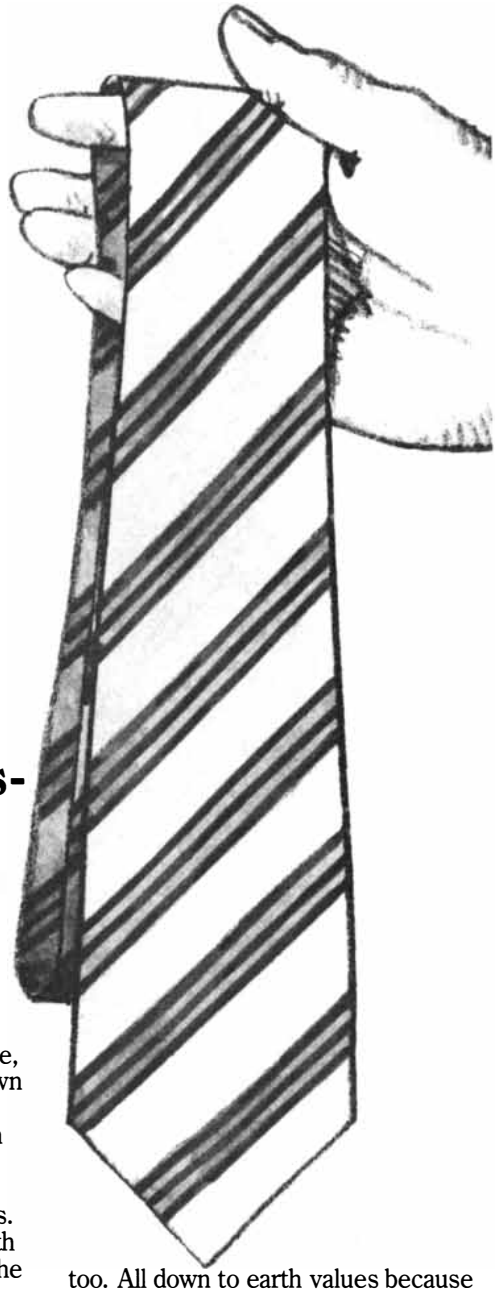
Ribosomes are not the only cellular components that undergo structural change in response to a severe blockade of translation. In the nucleus, chromatin—DNA and associated histones—undergoes changes of its own. Our experiments show that in the first one to two hours after cycloheximide is delivered, chromatin partially decondenses, or uncoils, which facilitates the transcription of genes in that period.

The extensive decondensation is not prolonged, however. The most pronounced response to cycloheximide is actually just the opposite, namely, compaction of the bulk of the chromatin beginning about two hours after drug delivery and lasting for more than 10 hours beyond that. This response was first discovered in 1980 (in cycloheximide-treated animals) by B. B. Stoyanova, P. T. Petrov and M. D. Dabev of the Institute of Molecular Biology of the Bulgarian Academy of Sciences in Sofia.

The compaction probably stems from the gradual decay of short-lived factors that influence chromatin structure; these factors would normally be replenished but cannot be replaced when the translation apparatus is inactivated. When the factors disappear, much of the chromatin condenses. This conformational change would protect



EARLY RESPONSES by liver cells to CHI help to restore normal activity after translation is blocked mildly. Nutrient uptake increases (*1*), providing polysomes with amino acids and providing mitochondria with glucose. Energy from the mitochondria then facilitates an increase in the internal circulation of proteins (*2*). Mitochondrial proteins flow to mitochondria; RNA polymerase II is sped to the nucleus, where it directs transcription of genes into mRNA (*3*); and protein constituents of ribosomes combine with ribosomal RNA (rRNA)—made in the nucleolus—to form the subunits of ribosomes (*4*). In the cytoplasm the mRNA molecules and newly produced ribosomes combine to make new polysomes (*5*).



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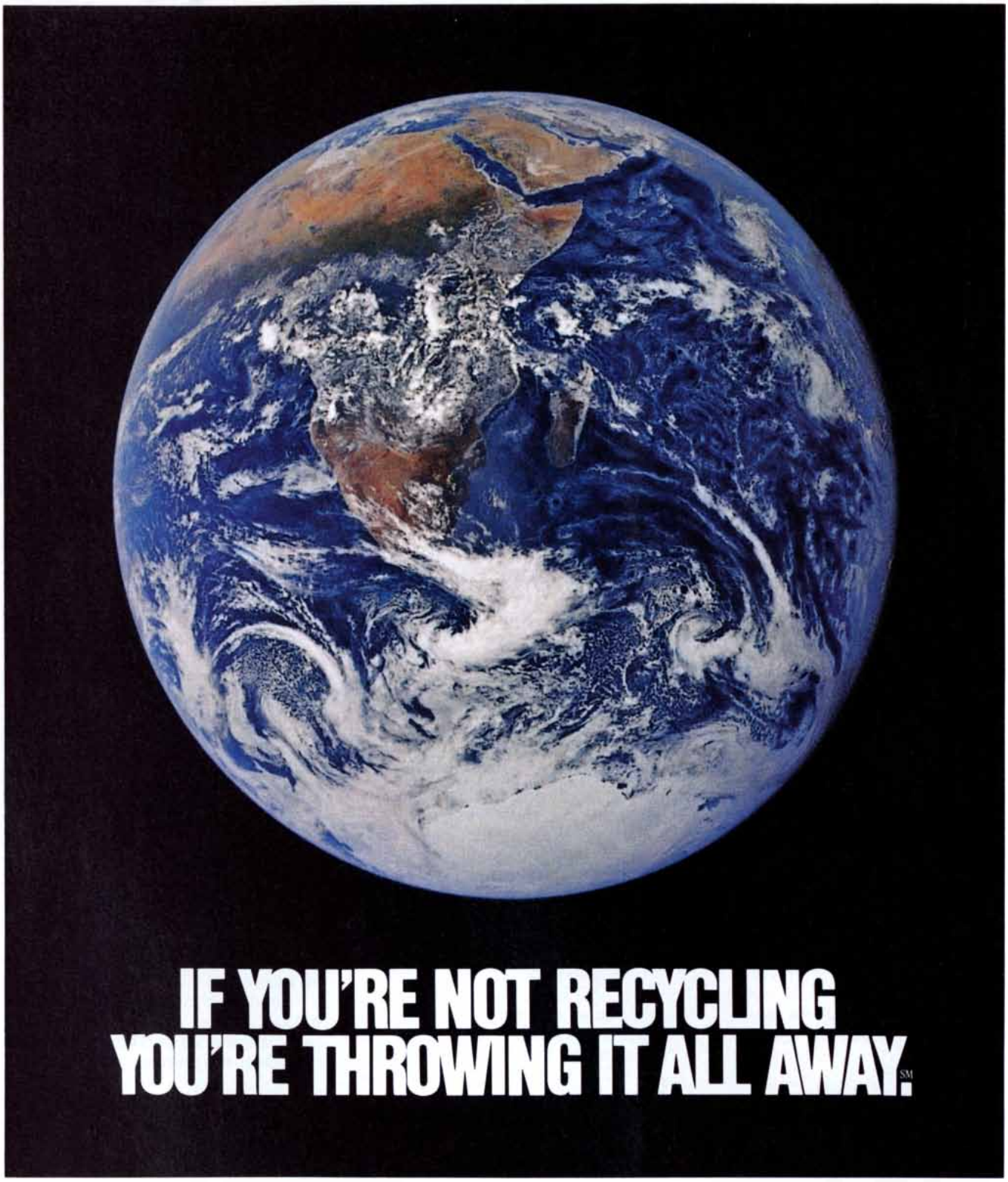

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genes from harmful substances, including those that, from the cell's point of view, already seem to be threatening the translation operation.

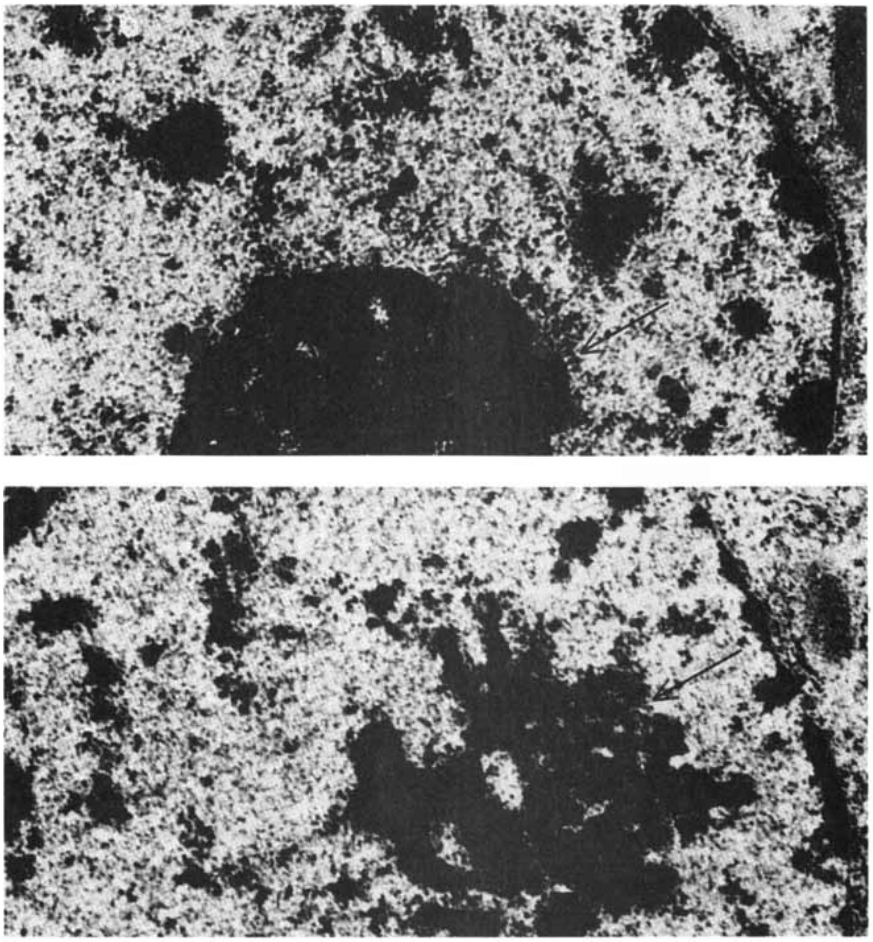
Condensation of one region of DNA can induce decondensation of another region and, indeed, seems to do so in this case. My colleagues Nataly A. Shevchenko, Peter Y. Boykov and I have recently found that decondensation occurs in the nucleolus, where ribosomal RNA and transfer RNA are made. This decondensation undoubtedly helps the cell retain its ability to make ribosomal and transfer RNA and contributes to an eventual increase in their production. Hence, the changes in chromatin facilitate transcription of the genes whose products are needed for protein assembly (by decondensation in the nucleolus). Simultaneously, the changes protect other genes from potentially harmful agents (by condensation of DNA outside the nucleolus).

Together the cell's various responses—the synthesis of messenger RNA and the reconstruction of polysomes with recycled and new components—return protein levels to normal about 18 to 24 hours after hepatocytes are first exposed to cycloheximide. The struggle for homeostasis, it would seem, ends in favor of the cell.

Yet more changes are still to come. Protein production often continues to increase beyond the 24-hour mark. Then, approximately 48 hours after cycloheximide administration, a new wave of synthesis may begin—this time of nuclear proteins, such as histones and constituents of the nuclear membrane. DNA polymerases, enzymes charged with replicating DNA, are also synthesized. Finally, 60 hours after the initial drop in translation, there is a burst of DNA replication.

When the initial suppression of translation is extremely strong, a number of cells then proceed to replicate. They pass through one or more cycles of growth and division before the daughter cells finally come to rest and fully restore both the polysomes on the endoplasmic reticulum and the original balance among the cells' proteins, including specialized proteins (such as export proteins), those involved in translation and those devoted to other aspects of cell survival. In general, then, a disturbance of protein homeostasis leads not only to rapid mobilization of reserves and reconstruction of a protein-synthesizing apparatus but also, in extreme cases, to replication of genetic material and cell division.

The sequential activity of various groups of genes—yielding the synthesis of messenger RNA, then ribosomal and transfer RNA and, finally, new DNA—has led me to propose a model of gene regulation that, combined with other observations, can explain the experimental findings. The model is based on current knowledge about the organization of genes in the nucleus and about cell division. For simplicity's sake, however, my description here omits certain factors known or assumed to be involved in the control and recovery of protein homeostasis, including the molecules cyclic AMP and cyclic GMP, transposable genetic elements and DNA superhelicity.



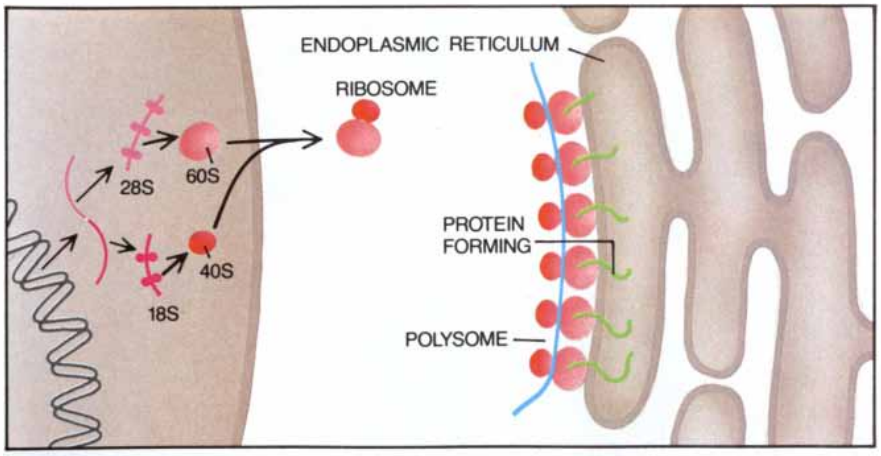
CHROMATIN IN THE NUCLEOLUS of a liver cell (*large black area, top*) undergoes decondensation (*bottom*) after such cells are exposed to CHI. This change in the structure of chromatin—DNA and its associated histone proteins—is thought to facilitate transcription of the genes that specify rRNA and ribosomal proteins.

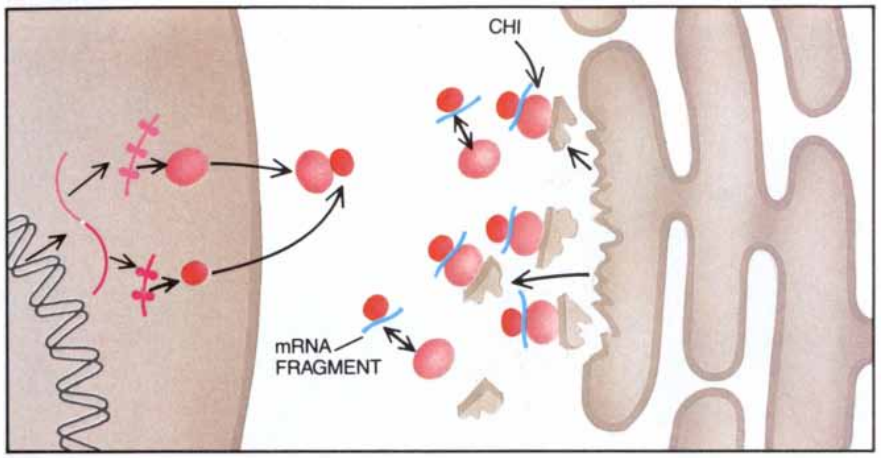
The model assumes that the genome can be divided conceptually into a few large groups, or blocks, of genes according to their function in the cell. It also assumes that the genes within a block are regulated by the same factors. The genes are not necessarily clustered together physically, however.

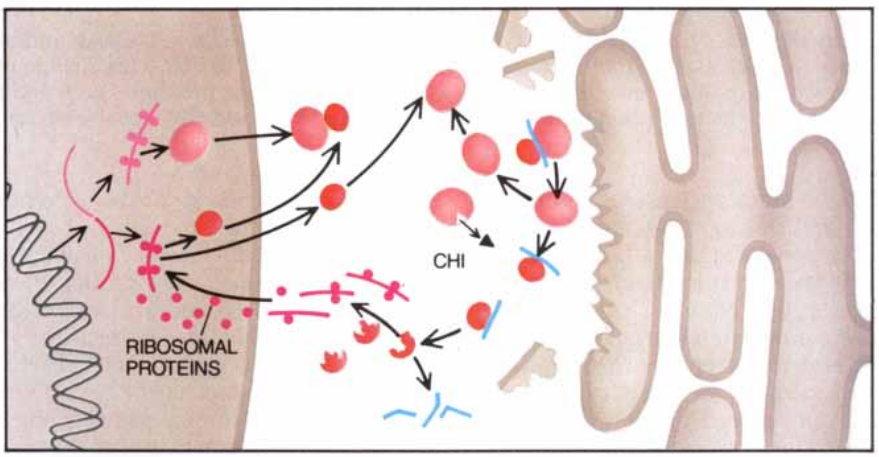
The largest of the groups is the M (metabolism) block. It consists of genes encoding enzymes and other proteins involved in cellular metabolism: the chemical reactions that extract energy from nutrients and synthesize the building blocks of large molecules.

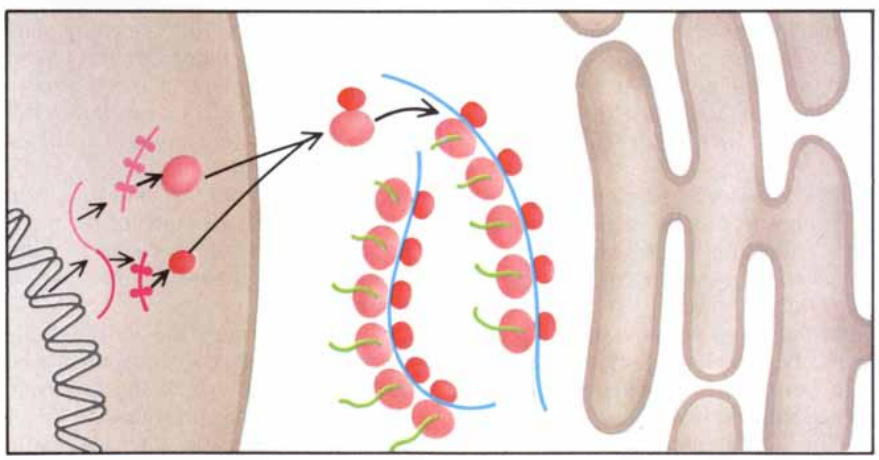
Also part of this block is a subset—the M′ block—which encodes proteins either intended for export or involved in the specialized activities that make, say, a liver cell different from a muscle cell. This subset is influenced by many of the same regulators as the rest of the M block, but its activity also requires signals from extracellular substances, such as hormones. On the basis of experimental findings, the model assumes that the M′ block is suppressed throughout much of the recovery process, largely because the hormones that regulate it are themselves suppressed.

The third group, the R (ribosome) block, specifies the components of the protein-synthesizing machinery, including ribosomal and transfer RNA, ribosomal proteins and other factors im-









CELL RESPONDS TO SEVERE THREAT

When steps aiding recovery from mild suppression of translation are inadequate, cells break down existing polysomes and make others from the parts.

1
TARGETED POLYSOMES, shown in a healthy cell, make proteins destined for export to other cells and not crucial to immediate survival. The polysomes are located on a system of membranes known as the endoplasmic reticulum.

2
CHI TRIGGERS BREAKUP of the polysomes and of the endoplasmic reticulum. Freed 40S subunits remain attached to the fragment of mRNA they were translating, which prevents them from acting on other mRNA molecules.

3
40S SUBUNITS DISSOCIATE, releasing the attached mRNA. Proteins from the subunit migrate to the nucleus, where their elevated concentration facilitates the rapid formation and return to the cytoplasm of new 40S units. The 60S parts remain intact in the cytoplasm and apparently shed any bound CHI.

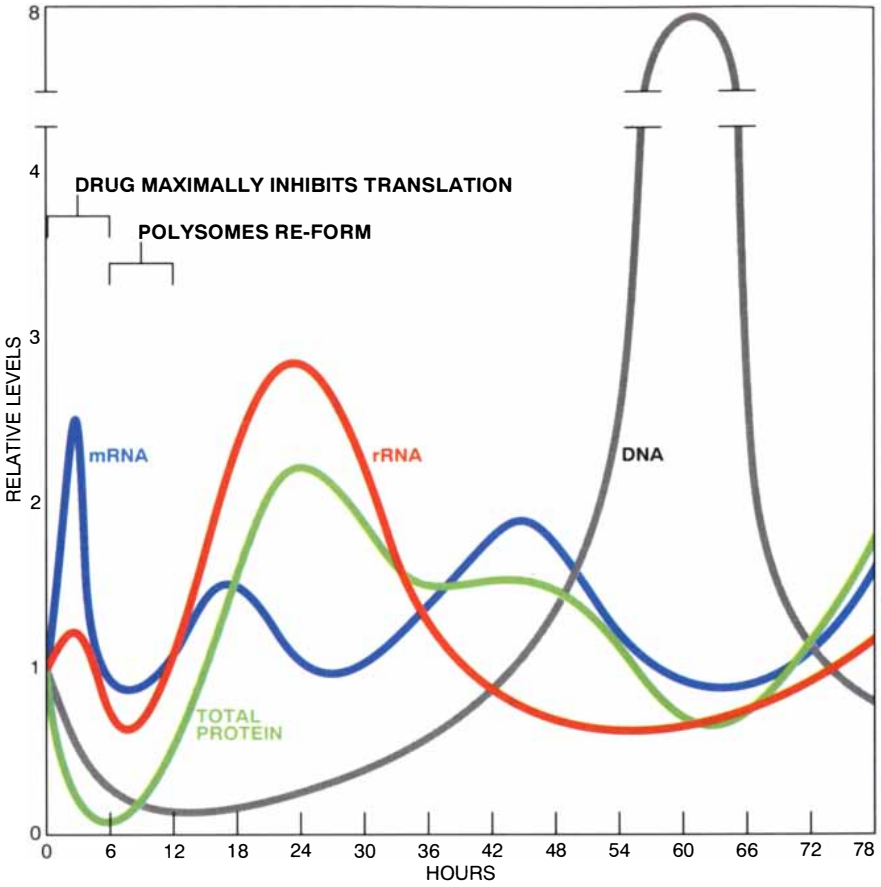
4
POLYSOMES ARE RESTORED eventually, but most are now separate from the endoplasmic reticulum, which is also rebuilt. These polysomes mainly make proteins needed for the cell's own survival, such as ribosomal constituents.

portant in polysome functioning. Each of the R block genes can be repeated many times in the genome (the total DNA in a cell); for example, cells carry hundreds of copies of ribosomal and transfer RNA genes. These genes also tend to be linked together in a line. Finally, the N (nucleus) block includes genes serving the nucleus, such as those encoding histone proteins, DNA polymerases and constituents of the nuclear membrane and matrix.

The model further posits that each block produces activity-modulating regulators of both itself and other blocks; a number of such regulatory molecules have already been identified experimentally. The self-regulators are mainly proteins; the regulators of other blocks are mainly fragments of RNA. Both sets of molecules apparently control gene functioning by binding to a regulatory region—the promoter—of a gene and thereby stimulating or inhibiting the activity of the RNA polymerase that is directly responsible for transcription of that gene.

Evidence suggests that the blocks operate simultaneously and that, as the activity of one block increases or falls, it also causes the activity of the others to change and to do so in a strict sequence. The order of succession is influenced by the life spans of the self-regulators acting on each block and the speed with which the blocks are able to respond to regulatory signals.

It appears that protein regulators (and other proteins) encoded by the M block are short-lived, whereas those of the R block survive longer and those of the N block live longer still. The M block can be brought into heavy operation within about an hour, the R block within a few hours and the N block no sooner than 24 hours.



SUMMARIZED DATA indicate that CHI-induced translation blockade triggers the rapid transcription into mRNA of many protein-encoding genes, followed by transcription of genes encoding rRNA and, later, genes important to DNA replication. Protein synthesis declines in parallel with the rise in mRNA but resumes once polysomes begin to re-form. Proteins needed for metabolism are restored only partially at first, but after DNA replicates, their synthesis and that of export proteins rise markedly. Ribosomal proteins account for most of the protein made between six and 36 hours after delivery of CHI, and histones account for much of the protein made around the time a surge in the production of DNA is observed.

The sequential activation of the blocks is analogous to the performance of a three-part fugue in which high, middle and low voices are featured one after the other. When the cell is in the resting state (the first part of the performance), the M block is most active, the R block is somewhat active and the N block is quiet. In our analogy, the highest, soprano voices (M block) can be heard best; the middle, alto voices (R block) can be heard, but faintly; and the low, bass voices (N block) are almost inaudible.

Now suppose that for some reason the translation mechanism is arrested. The proteins encoded by the M block will fade first, because they are the shortest-lived and cannot be replaced after the polysomes are idled. In particular, imagine that M block–derived inhibitors of the M block, having a shorter life span than the block's stimulators, disappear first, thereby eliminating an important restraint on the transcription of the block's genes. (The model assumes that, for each block, self-inhibitors are shorter-lived than the stimulators.) Transcription of the the block's genes thus increases; the soprano singers become louder.

If the impairment of protein synthesis is not too serious, mobilization of free ribosomal constituents and whole ribosomes, along with the increase in M block transcription, will be enough to restore translation and return protein levels to normal. If the inhibition of protein synthesis persists, however, further events unfold, beginning with stimulation of the R block and the gradual inhibition of the M block; the altos gain prominence, and the soprano section softens.

The R block is stimulated because after a time its self-directed inhibitors finally decay, giving the upper hand to the stimulators. Also, the continuing activity of the M block yields production of RNA fragments that are R block activators. When the precursor of messenger RNA is processed, small pieces of the RNA, called introns, are excised. Strong evidence suggests that introns (or actually fragments of them) serve as major stimulators or inhibitors of transcription and that introns from M block RNA can increase the activity of R block genes.

Once some amount of translation ability has been restored by such measures as the breakup and recycling of polysomes, increased R block activity results in the synthesis of new ribosomal proteins in addition to new ribosomal RNA and transfer RNA. These products lead to the creation of more polysomes, which facilitate translation of some fraction of the newly made M

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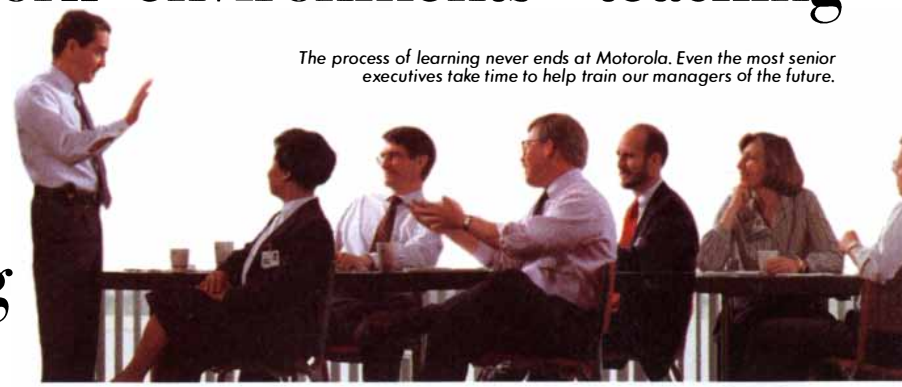

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Building On Beliefs

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block messenger RNA but mainly enable the cell to further shore up the protein-making apparatus.

Yet the cell would not be well served by endless, intense production of messenger RNA and ribosomes, because excessive numbers of polysomes and proteins would eventually surpass the ability of the cell to accommodate them. As the R block becomes aroused, certain of its own introns gradually diminish the activity of the M block. That is, as the alto voices of the fugue gain increased strength, the soprano voices are hushed.

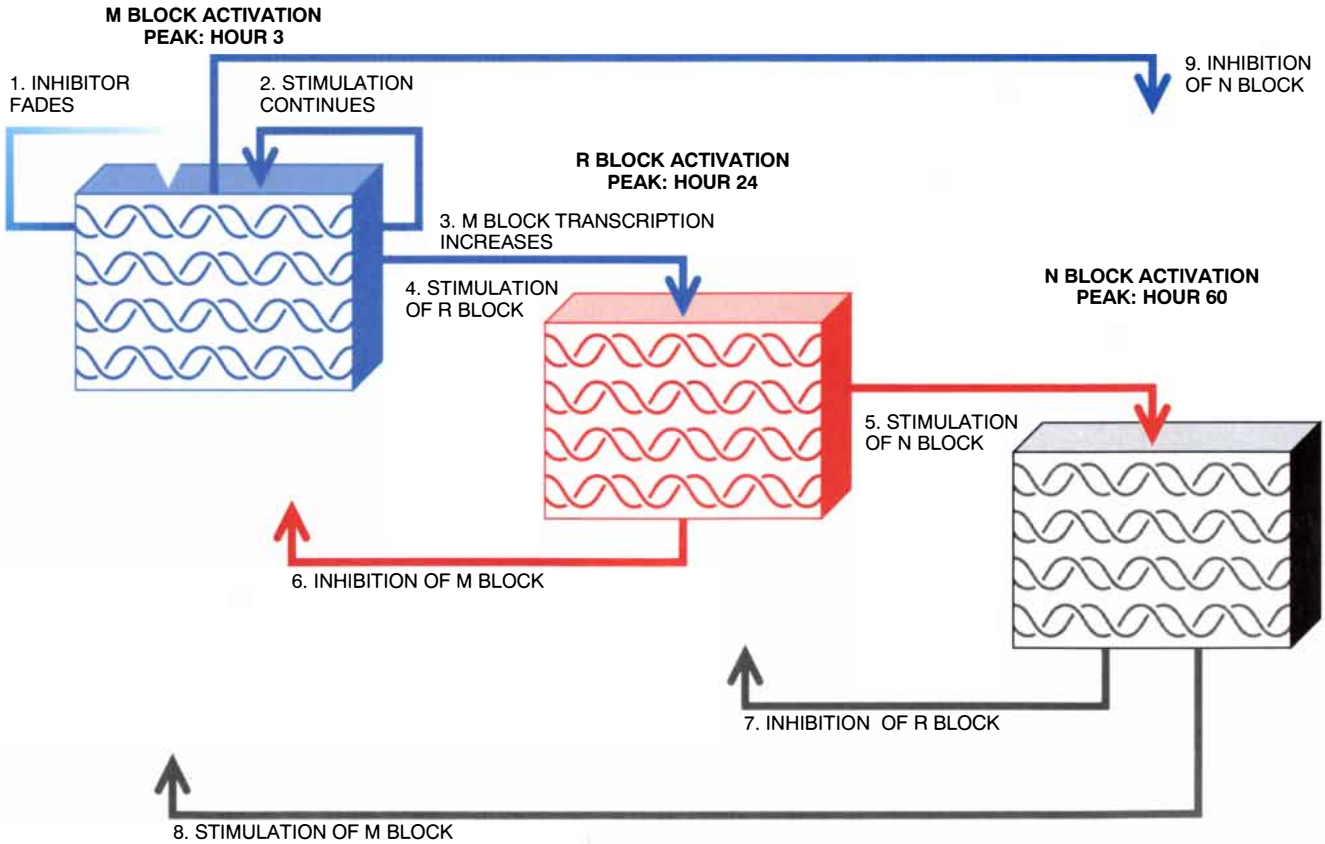
The final part of the model is most speculative. It proposes that, as was true of the R block, the N block and later the M block are stimulated by decomposition of the block's own inhibitors and by introns released from the previously activated block. Hence, it seems likely that, over time, the N block becomes aroused by its own stimulators and by introns freed from R block RNA, leading to the observed surge in histones followed by DNA replication.

As a check on the uncontrolled multiplication of ribosomes, the N block can be expected to gradually inhibit the R block, which in hepatocytes does seem to quiet down as the production of histones rises. Thus, in the finale of the fugue, the bass voices are given full play, and the alto voices become muted. Later, as the M block, under the influence of N block activity, starts to operate normally, it begins to inhibit the N block; the fugue starts again.

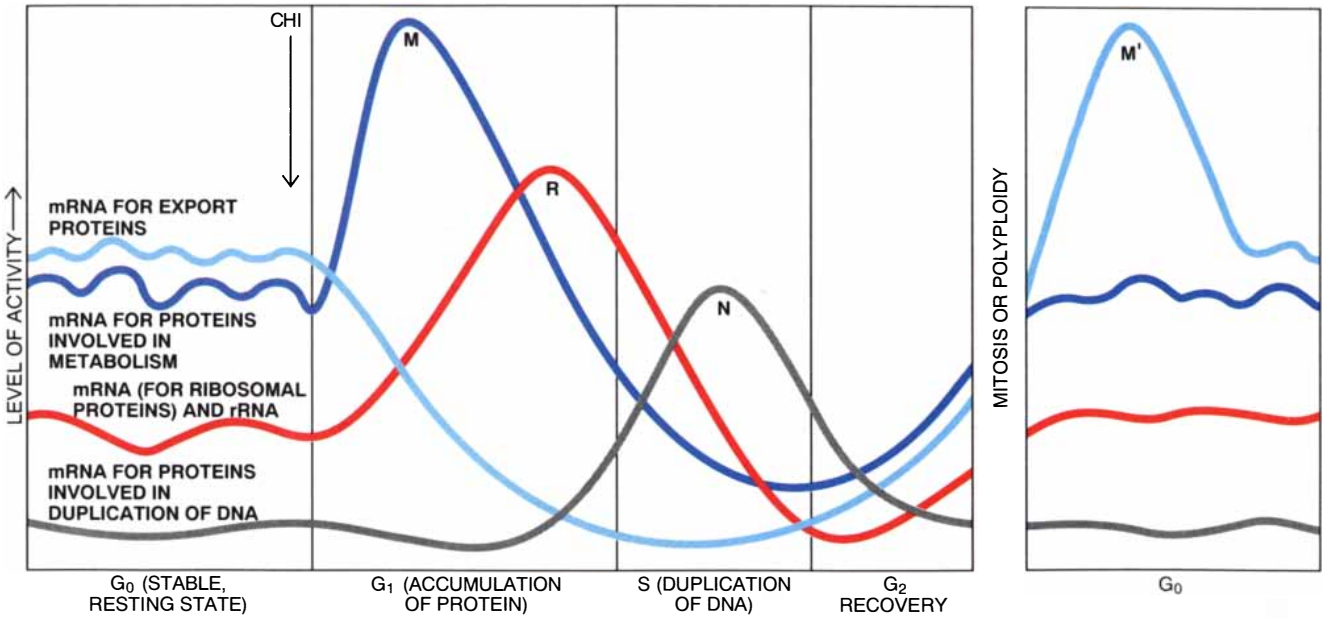
The mechanism by which intron stimulators and inhibitors might influence transcription is worth some explanation. It is straightforward and can be understood by anyone who has a rudimentary knowledge of DNA structure.

The building blocks of DNA are nucleotides, which consist of a sugar, a phosphate group and one of four bases—adenine, guanine, cytosine or thymine. DNA is composed of two helical strands of nucleotides, joined at their bases; adenine always pairs with thymine, and guanine pairs with cyto-

BLOCK NAME	GENE PRODUCTS	AVERAGE LIFE SPAN OF PROTEIN REGULATORS	SPEED OF BLOCK'S ACTIVATION
M (Metabolism)	Mainly proteins required for the cell to extract energy from nutrients and form the building blocks of large molecules	Short (dozens of minutes)	Fast (within an hour)
M′ (subset of M block)	Proteins exported to other cells and otherwise inessential to the cell's immediate survival	Same as above (many regulators are shared)	Same as above
R (Ribosomal)	Ribosomal proteins, factors involved in translation, rRNA, tRNA	Moderate (hours)	Moderately fast (within hours)
N (Nuclear)	DNA polymerases, histones, other proteins of the nucleus (including constituents of the nuclear membrane and matrix)	Long (dozens of hours)	Slow (after a day or more)



MODEL of how genetic activity serves recovery holds that genes with related functions can be grouped (*table*). Each block yields inhibitors and stimulators: proteins that regulate the activity of the same block, and RNA fragments (introns) that act on other blocks. The blocks are aroused sequentially (*diagram*): M; then, more slowly, R; and, much later, N.



PATTERN OF RNA SYNTHESIS in cells passing through the cell cycle resembles that found in cells attempting to cope with exposure to high doses of CHI. In the case of CHI treatment, some cells double their DNA without dividing (a state called polyploidy); other cells may pass through the cell cycle many times before their functioning returns to normal.

sine. In a gene, one strand (the coding strand) specifies the amino acid sequence of a protein, and the other strand is complementary.

Let us assume that an intron excised from virtually all precursor messenger RNA from one block is identical to a part of the coding strand of a promoter for many or all of the genes in another block. That intron would bind to its complement on the strand complementary to the promoter, thereby loosening the double helix at this site. This loosening, in turn, would facilitate the attachment of an RNA polymerase to the promoter and would thus stimulate transcription of the adjacent gene. Similarly, introns that bound to the coding strand of a promoter would inhibit polymerase activity by blocking the enzyme's access to the promoter.

Astute readers will notice that the model's description of the phases of the cell's struggle to restore homeostasis sounds very much like a description of the normal cell cycle. Cells preparing to replicate begin by suppressing the synthesis of export proteins and accumulating other proteins. (They activate the M and then the R block.) Then they synthesize new DNA (by activating the N block) and divide before reestablishing a balance of exported and self-protective proteins (aided by N block–produced stimulators of the M and M′ blocks).

Fortunately for the overall health of the organism, the process of cell division is controlled, not only by internal signals but also by signals generated outside the cell. Hence, cell division generally stops when the organism no longer requires it. Nevertheless, the tendency of hepatocytes in our cycloheximide studies to grow and divide raises the possibility that, when the cell's recovery mechanisms are aroused after a severe damping of translation, the survival response may actually contribute to the development of cancer (which is marked by uncontrolled cell division).

Certain data suggest that activation of the protein-homeostasis machinery in response to cycloheximide may indeed represent a preliminary stage of chemical-induced carcinogenesis in certain cells. For instance, work done in my laboratory and others shows that several oncogenes (cancer inducers) are activated by cycloheximide and that those oncogenes are the very same ones activated by at least two known carcinogens.

If cycloheximide can contribute to cancer, the turning point is probably disassembly of the endoplasmic reticulum and its associated polysomes and the construction, in their place, of assembly lines devoted to the synthesis of intracellular components. Once that changeover occurs, the larger organism loses a certain amount of control over the cell, and the cell ceases to function for the benefit of that organism. Most hepatocytes exposed to cycloheximide do not become cancerous, but transformation of even a single cell can be enough to cause disease.

Where might insights into the mechanisms of cell stability lead? I certainly hope they will hasten the discovery of ways to bolster the body's defenses against agents that suppress translation and will provide clues to preventing the early stages of chemically induced cancer.

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The Birth of Molecules

In less than a trillionth of a second, atoms can collide, interact and give birth to molecules. With lasers and molecular beams, it is now possible to witness the motions of molecules as one substance changes to another

by Ahmed H. Zewail

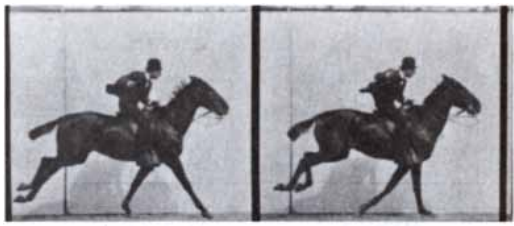
In 1872 railroad magnate Leland Stanford wagered $25,000 that a galloping horse, at some point in its stride, lifts all four hooves off the ground. To prove it, Stanford employed English photographer Eadweard Muybridge. After many attempts, Muybridge developed a camera shutter that opened and closed for only two thousandths of a second, enabling him to capture on film a horse flying through the air [*see illustration at top right*]. During the past century, all scientific disciplines from astrophysics to zoology have exploited high-speed photography to revolutionize understanding of animal and mechanical motions that are quicker than the eye can follow.

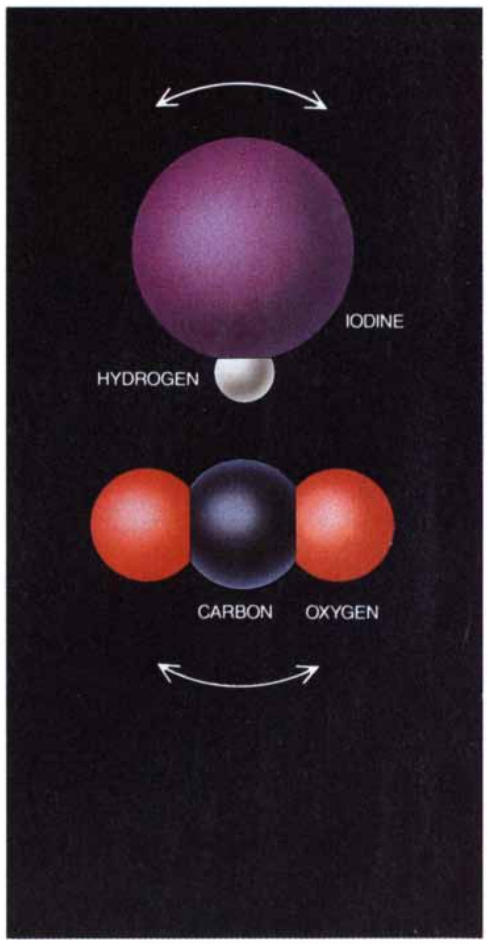
The time resolution, or shutter speed, needed to photograph the ultrafast motions of molecules is beyond any conventional scale. When a molecule breaks apart into fragments or when it combines with another to form a new molecule, the chemical bonds between atoms break or form in less than a trillionth of a second, or one picosecond. Scientists have hoped to observe molecular motions in real time and to witness the birth of molecules: the instant at which the fate of the molecular reaction is decided and the final products are determined. Like Muybridge, they needed to develop an ultrafast shutter, but it had to work 10 billion times faster than the 19th-century model.

For the past decade our research group at the California Institute of Technology has been developing techniques to observe the dynamics of molecules in real time. From 1985 to 1987 we refined our system of advanced lasers and molecular beams to a point at which we can now record the motions of molecules as they form and break bonds. The reaction can be seen as it proceeds from reactants through transition states and finally to products—chemistry as it happens.

Because transition states exist for less than a trillionth of a second, the time resolution should be shorter—a few quadrillionths of a second, or a few femtoseconds (one is equal to 10^{-15} second). A femtosecond is a smaller unit of time than a tick of even the finest atomic clock. A femtosecond is to a second what a second is to 32 million years. Furthermore, whereas in one second light travels nearly 300,000 kilometers—almost the distance between the earth and the moon—in one femtosecond light travels .3 micron—about the diameter of the smallest bacterium.

Alchemists in ancient Egypt, Greece, Arabia and China did not know about the fundamental importance of this time scale to the change of one substance to another, although they certainly did recognize the art of the transmutation. Only in this century have chemists been able to use a variety of tools to understand the sci-





TIME RESOLUTION of high-speed photography has improved 10 billion times as the technology has evolved from filming movements of animals to capturing the birth of molecules. In one second, a horse gallops 10 meters, as shown in photographs (*top*) taken by Eadweard Muybridge in 1887. In five trillionths of a second, hydrogen iodide collides with carbon dioxide, creating carbon monoxide, hydroxide and iodine. The illustration (*bottom*) is based on quantitative observations made at Caltech.

AHMED H. ZEWAIL is the Linus Pauling Professor of Chemical Physics at the California Institute of Technology and has been a faculty member there since 1976. He has pioneered ultrafast laser femtochemistry to investigate the real-time motion of molecules in reactions. He received his B.S. from Alexandria University in Egypt and his Ph.D. from the University of Pennsylvania. Among the awards he has received are the 1989 King Faisal International Prize, the Harrison-Howe Award and the John Simon Guggenheim Fellowship. Zewail is a member of the National Academy of Sciences. This article is dedicated "to the memory of my dear friend Dick Bernstein, a giant in the field of molecular-beam science."

ence of molecular reaction dynamics.

At a molecular level a reaction starts when two molecules—call them *A* and *B*—are brought close enough together so that they begin to interact. As the molecules move even closer, other molecular species, which are neither *A* nor *B,* are formed until a new, stable molecule, *C,* is created.

One of these transitory species represents the stage at which the reaction proceeds irreversibly to products. This stage, technically called the transition state, is here denoted as $A \cdots B$. Hence,

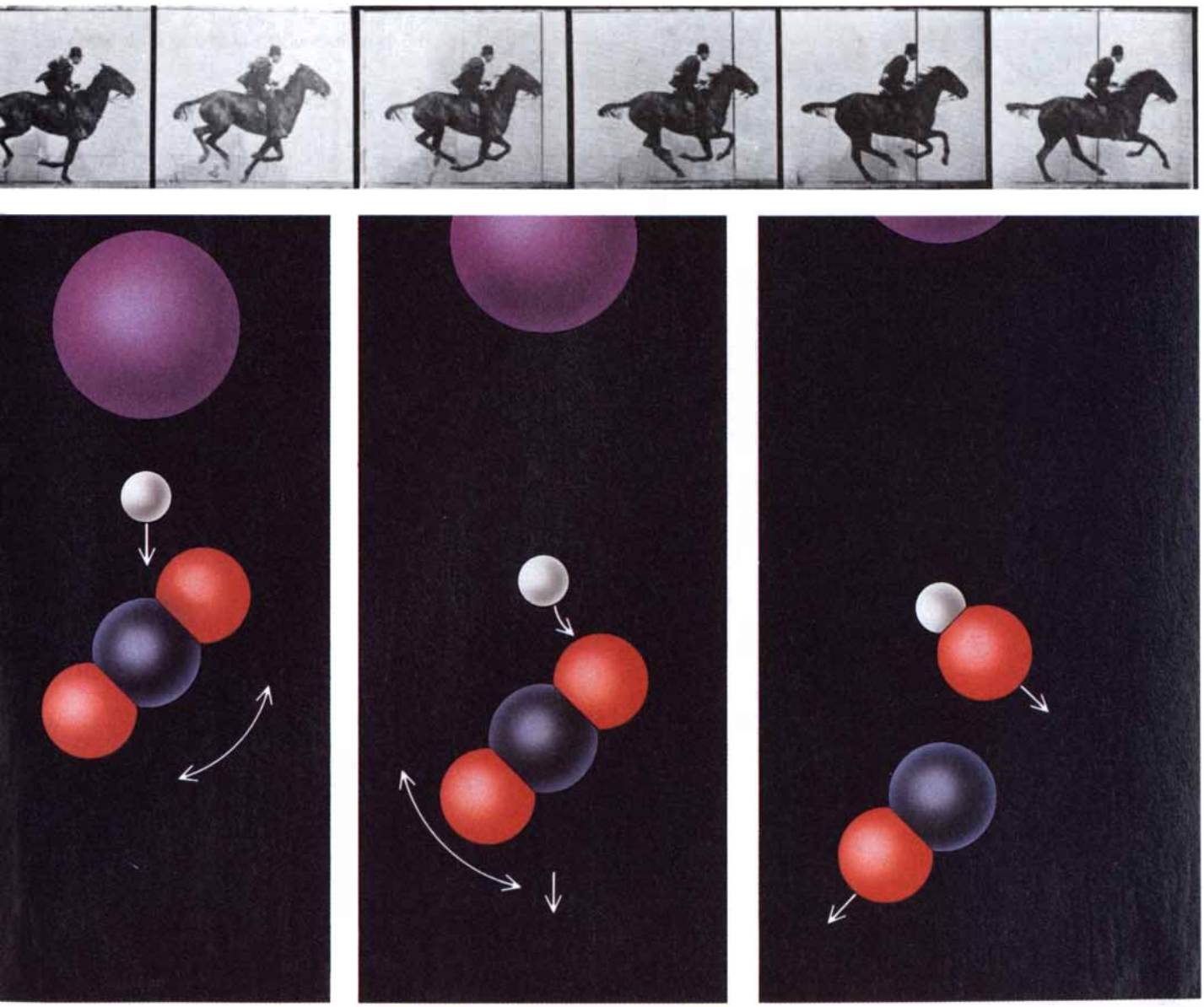
$$A + B \rightarrow A \cdots B \rightarrow C$$

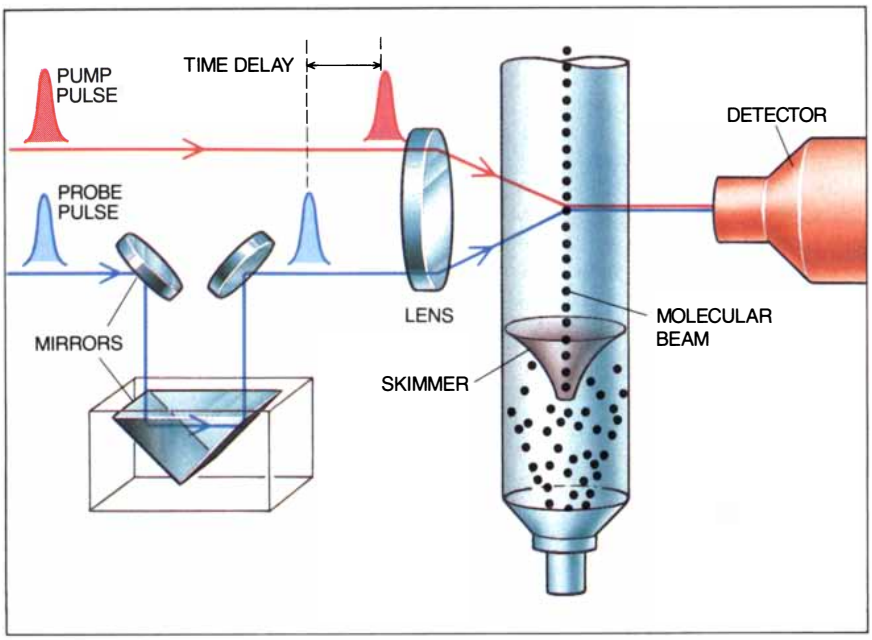
The converse process is also possible: when molecule *C* is energized, it can pass through a transition state to form molecules *A* and *B*.

In any chemical reaction the motions of the electrons and nuclei of atoms determine how the molecules interact, and those interactions in turn create the forces that govern the reaction's dynamics. The molecular motions can be rigorously delineated by the laws of quantum mechanics. In many cases, Newtonian, or classical, mechanics can simply give the transfer of energy and momentum during the course of the reaction, just as effectively as it describes the collision between two objects. If investigators can determine how molecular motions change during the critical transition phase, we can understand how new chemical bonds form and old ones disappear.

In practice, chemists do not keep track of every possible motion of every electron and nucleus in a molecular system. Instead they have discovered clever ways to represent the state of a system. Each state possesses a certain amount of energy. The potential energy of a molecule when the atoms are a certain distance apart can be represented as a point on a graph. When all the states and their corresponding potential energies are graphed, they form a surface that has mountains and valleys. Molecular systems will spontaneously move from high-energy states (mountains) to low-energy states (valleys), but they require energy to move from valleys to mountains. The bottom of a valley indicates a stable state; the slopes around the valley represent the region of transition states, the different configurations for the atoms in proximity. Chemists technically define a transition state as a saddle point on a potential-energy surface.

If a molecular system is composed of two atoms and if the system's potential energy depends only on the distance that separates the atoms, the





FEMTOSECOND PHOTOGRAPHY captures the dynamics of molecular reactions in real time. The laser system (*above*) generates a pump pulse and a probe pulse. As shown in the illustration (*left*), the pump pulse and the probe pulse leave the laser system at the same time. The probe pulse is diverted so that a time delay of a few femtoseconds is introduced between the two pulses. When the pump pulse hits a molecule in the molecular beam, it initiates a chemical reaction. The probe pulse strikes the molecule a few femtoseconds later. The molecule then emits a spectrum of light, which can be analyzed to determine the dynamics of the atoms in real time.

potential-energy surface reduces to a curve. If the system is governed by the attraction of oppositely charged atoms at "long" distances and by the repulsion of atomic nuclei at "short" distances, the curve will have a single well at "intermediate" distances, indicating that the system is stable there.

For molecular systems composed of many atoms that can move in many ways, the potential-energy surface can be complicated and multidimensional. Nevertheless, the surface is very useful for describing every possible path that molecules may follow—from reactants (valleys) through transition states (mountains) to products (valleys).

One can estimate how long it takes for molecular systems to go through the mountains—that is, the duration of the transition state—by applying ideas from Newtonian mechanics. Heavy molecules or atoms typically emerge from chemical reactions at speeds of 1,000 meters per second. If molecules *A* and *B* are close enough to be in a transition state, then the distance between them is on the order of that of a molecular bond, approximately .1 nanometer (10^{-10} meter). The ratio of this distance to the recoil velocity yields the amount of time during which *A* and *B* form a transition state—100 femtoseconds. For the "simplest" of all chemical reactions—a light hydrogen atom approaching a hydrogen molecule—the transition state is very short-lived, about 10 femtoseconds. Thus, the time scales for transition states range from about 10 to 100 femtoseconds.

For more than 100 years chemists have studied reaction mechanisms and molecular kinetics in hope of understanding reactivity. In the late 19th century, Swedish scientist Svante Arrhenius took an important step in describing the macroscopic dynamics of chemical reactions. He determined how the rate of a reaction depends on temperature. His famous exponential equation reveals that the rate of a reaction increases as the amount of applied heat increases.

But such equations, which describe the dynamic properties at the macroscopic level, yield information about microscopic molecular dynamics only if a number of assumptions are made. Nevertheless, many aspects of molecular dynamics can be deduced from macroscopic observations, and Arrhenius's equation remains important to this day.

Some 40 years ago techniques were introduced to study chemical intermediates and fast kinetics for the first time. Ronald G. W. Norrish and George Porter of the University of Cambridge and Manfred Eigen of the Max Planck Institute for Physical Chemistry were able to resolve chemical events that lasted about a thousandth of a second. This time scale was ideal for intermediates but too long for transition states.

To probe the dynamics of molecules as they collide, investigators developed the new methodology of molecular-beam technologies in the 1960s. By releasing molecules into a vacuum and collimating them with a skimmer, chemists created beams of molecules that did not collide with one another. When one beam containing molecules of, say, *A* is crossed with another introducing molecules of *B*, molecules of *A* collide with those of *B* to form a product, *C*. The full collision ($A + B \rightarrow C$) is called a bimolecular reaction. The investigators then detected molecule *C* as it was created in different amounts and in different directions depending on the nature of the forces between *A* and *B*. They used the precollision conditions of the reactants and the postcollision attributes of the products to deduce the dynamics of the collision.

Conversely, a beam of molecules of *C* could be bombarded with light from a laser, energizing the molecules and breaking their chemical bonds to produce fragments *A* and *B*. This dissociation reaction ($C \rightarrow A + B$) could then

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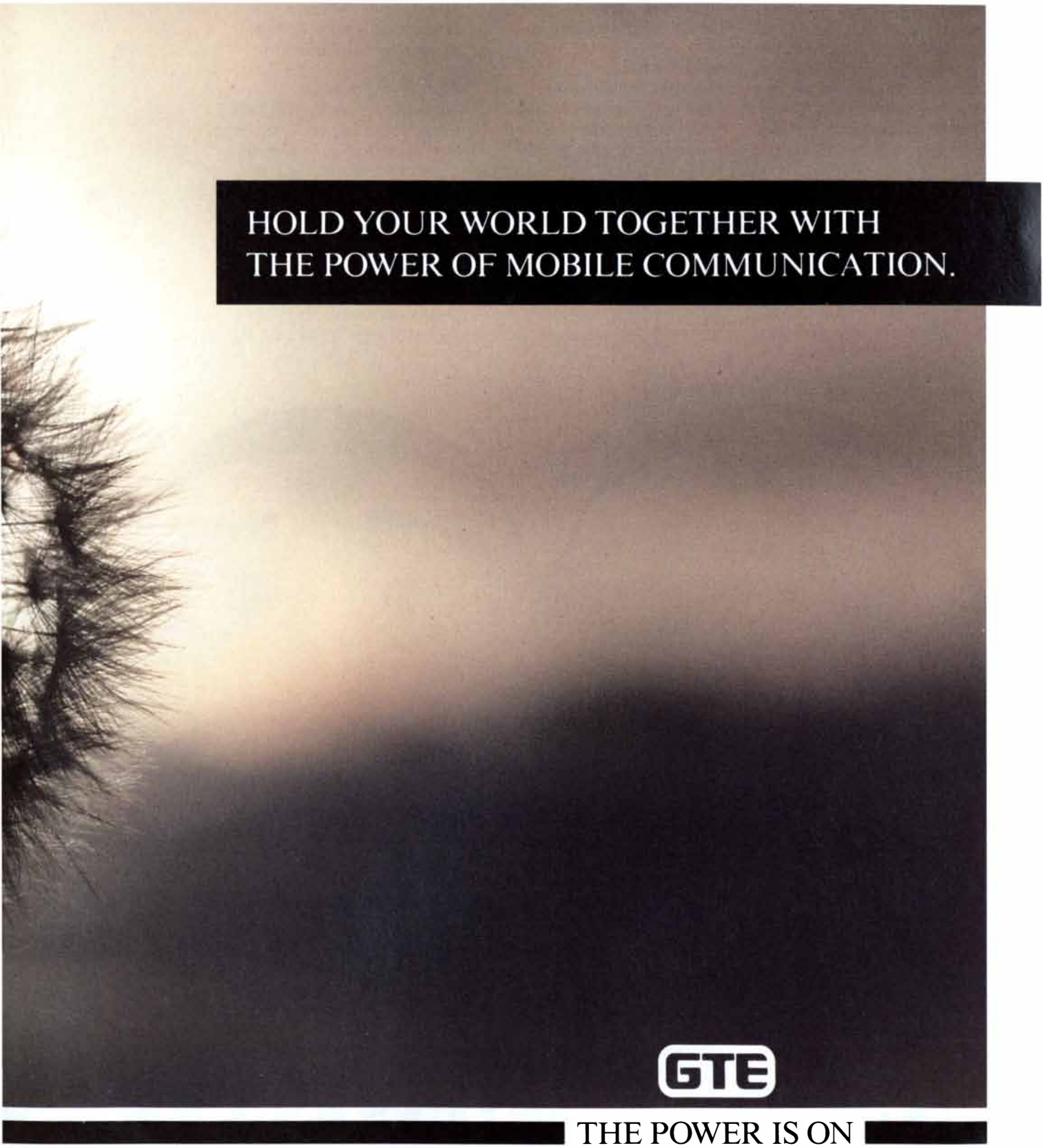

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be analyzed by measuring the attributes of the fragments. Since the development of molecular beams and other techniques that resolve the quantum states of products, chemists have learned much about the elementary dynamics of reactions. As testimony to the importance of molecular-beam science and reaction dynamics, the 1986 Nobel Prize in chemistry and the 1988 Welch Award were given for contributions in these fields.

In molecular-beam experiments, the sequence of events in a reaction, including the transition states, could not be observed in real time. Chemist Sture Forsén of Lund University came up with an insightful analogy that illustrates the importance of understanding transitory stages in the dynamics. He compared the scientific community to a theater audience watching a drastically shortened version of a classical drama. The audience is shown only the opening scenes of, say, *Hamlet* and its finale. Forsén writes, "The main characters are introduced, then the curtain falls for change of scenery and, as it rises again, we see on the scene floor a considerable number of 'dead' bodies and a few survivors. Not an easy task for the inexperienced to unravel what actually took place in between."

In an attempt to probe transition states more directly than can be done with conventional molecular-beam experiments, chemists turned to new time-averaged techniques and developed methods that record the absorption, emission or scattering of light by transition states. Like molecular beams, these methods do not resolve the events in real time, but they do provide more direct possibilities for examining transition states and dynamics.

In 1979 our research team at Caltech first attempted to enter the field of ultrafast chemistry by using lasers and molecular beams. In those days the time resolution was tens of picoseconds, too gross a time scale for viewing the motion of reactions through transition states. We concentrated on developing techniques to study how energy moves in molecules prior to reactions. By 1984 time resolution in molecular-beam experiments had improved to three picoseconds. That advance allowed us to measure directly the rate of reaction as a molecule changed from one quantum state to another. Still, we needed a technology that could record the spectrum of transition states in real time with femtosecond resolution.

To build such a femtosecond, molecular "camera," we combined the technology of molecular beams with that of ultrashort laser pulses. The molecular beams allowed us to isolate the reactions in a vacuum; the ultrashort laser pulses gave us the ability to resolve the dynamics with the needed time resolution. During the past five years, advances in laser technology at AT&T Bell Laboratories and other institutions have made it feasible to reach the critical femtosecond time resolution. At the moment, pulses as short as six femtoseconds can be achieved. With such ultrashort pulses, we can obtain a "shutter speed" of approximately 10 femtoseconds.

The principles involved in ultrafast, molecular photography have some similarity to those applied by Muybridge. The key to his work was a special camera shutter that exposed film for only .002 second. To set up the experiment, Muybridge spaced 12 of these cameras half a meter apart alongside a horse track. For each camera he stretched a string across the track to a mechanism that would trigger the shutter when a horse broke through the string.

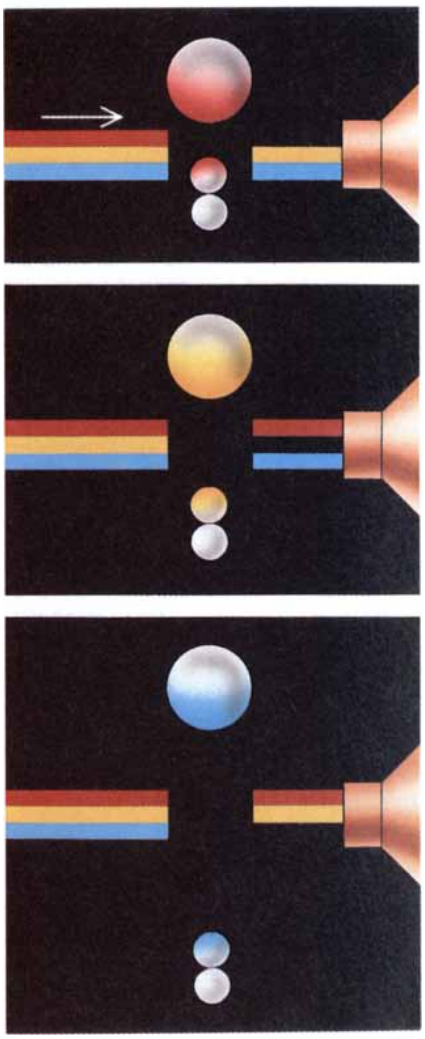
With this system, Muybridge attained a resolution in each picture of about two centimeters, assuming the horse was galloping at a speed of about 10 meters per second. (The resolution, or definition, is simply the velocity of the motion multiplied by the exposure time.) The speed of the motion divided by the distance between cameras equals the number of frames per second—20 in this case. The motion within a picture becomes sharper as the shutter speed increases. The resolution of the motion improves as the distance between the cameras decreases.

Two aspects of high-speed photography are relevant to femtosecond, molecular photography. First, both types of photography break up a continuous motion into a series of snapshots, or frames. Thus, one can slow down a fast motion as much as one likes so that the eye can see it. Second, both methods must produce enough frames in rapid succession so that the frames can be reassembled to give the illusion of a continuous motion. The change in position of an object from one frame to the next should be gradual, and at least 30 frames should be taken to provide one second of the animation.

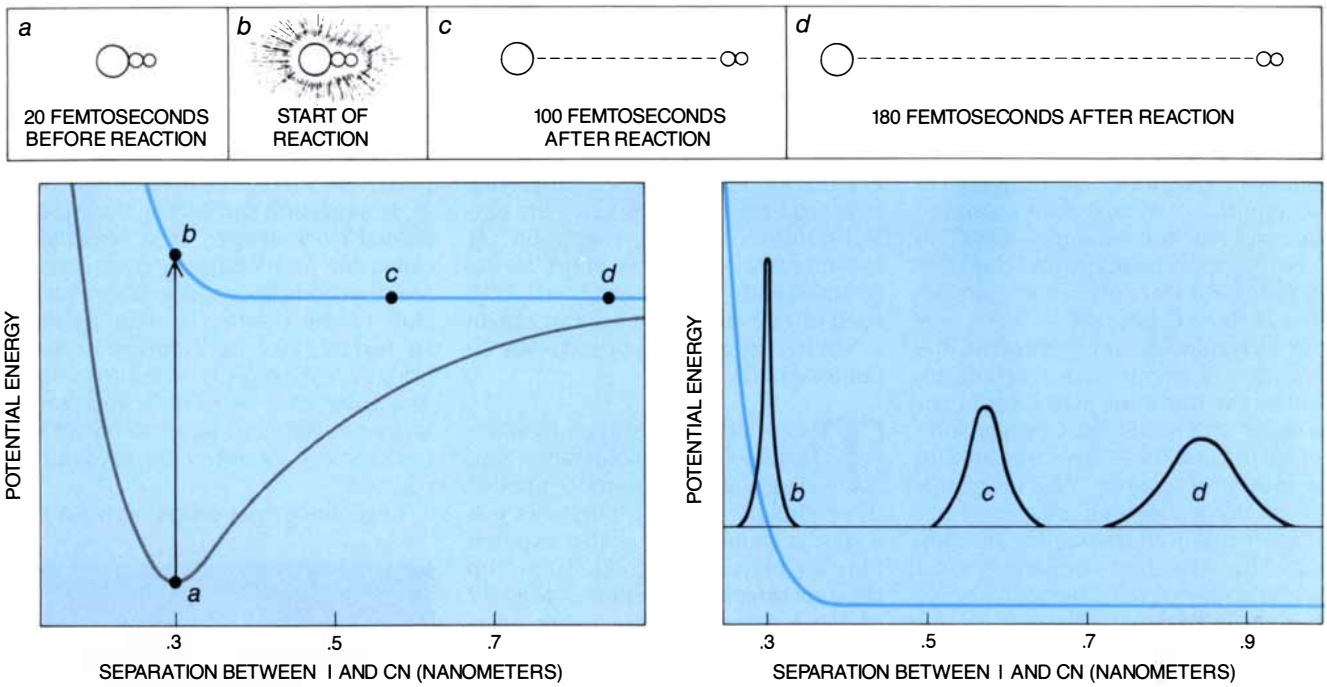
In femtosecond, molecular photography, the definition of the frame and the number of frames per second must be adjusted to resolve the elementary nuclear motions of reactions and, most important, ephemeral transition states. The frame definition must be shorter than .1 nanometer. Because the speed of the molecular motion is typically 1,000 meters per second, the shutter resolution must be in a time range of better than 100 femtoseconds.

The conceptual idea behind these femtosecond experiments is rather simple. A first laser flash, called the pump pulse, hits a molecule in isolation, initiating a reaction and setting the experimental clock at zero. A second flash, called the probe pulse, arrives several femtoseconds later and records a snapshot of the reaction at that particular instant. Like the cameras in Muybridge's experiment, a femtosecond, molecular camera records successive images at different times to obtain information about different stages of the reaction.

To produce time delays between the



STATE OF MOLECULAR SYSTEMS can be identified by the light that the molecule absorbs. When atoms in a molecule are relatively close together, they tend to absorb long wavelengths of light (red, for example). When the atoms are farther apart, they tend to absorb short wavelengths of light (blue, for instance). The change in the spectrum is the fingerprint of the atoms in motion.



FEMTOSECOND DYNAMICS of cyanogen iodide (ICN) can be best described in terms of potential-energy curves. In classical mechanics, when molecules of ICN in a low-energy state (*a*) interact with a laser beam, light excites ICN to a high-energy state (*b*). The molecule then dissociates into iodine and cyanide, and the distance between iodine and cyanide increases (*c* and *d*). The diagram at the left is a simplification, because the exact momentum and position of the atoms cannot be determined simultaneously, as specified by quantum mechanics. As shown in the diagram at the right, it is most likely, for example, that iodine is separated from cyanide by about .85 nanometer at 180 femtoseconds (*d*). At that instant, however, there is a small chance that they might be separated by .7 nanometer or even 1.0 nanometer.

pump pulse and the probe pulse, our research group takes advantage of the large but finite speed of light. Initially we tune the optical system so that both pulses reach the apparatus at the same time. We then divert the probe pulse so that it travels a longer distance than does the pump pulse before it reaches the molecular beam. If the probe pulse travels one micron farther than the pump pulse, it will be delayed 3.33 femtoseconds, because light travels at 300 million meters per second.

Accordingly, pulses that are separated by distances of from one to 100 microns resolve the motion during periods of from 3.33 to 333 femtoseconds. Hence, a spatial detour of microns, which can be easily accomplished in the laboratory, can be used to obtain a delay of femtoseconds. (A shutter speed of a few femtoseconds is beyond the capability of any camera based on mechanical or electrical devices.)

When the probe pulse hits a molecule, it does not then transmit an image to a detector, like light reflecting off a scene into a camera. Instead the probe pulse interacts with the molecule, and then the molecule emits a spectrum of light. The spectrum varies in intensity and color. The variation depends on the wavelength of the original probe pulse, the atoms in the original molecule and the state of the molecule when it was hit by the probe pulse. Free molecules A and B have a different spectrum from that of $A \cdots B$ in the transition state, and the transition state's spectrum differs from that of the product, C.

We could therefore distinguish the spectral signals from each of these states. We could determine the timing of these signals by knowing the time that had elapsed between the impacts of the pump pulse and the probe pulse. Based on these principles, we were able to reconstruct and study an image of elementary reactions in real time.

When my colleague and friend Richard Bernstein of the University of California at Los Angeles learned about the femtosecond, molecular camera, he was very enthusiastic about the development, and we discussed the exciting possibilities the technique created. Over champagne at his house in Santa Monica, he suggested the designation "femtochemistry."

Since 1985 we have investigated the femtochemistry of cyanide reactions, atmospheric reactions and salt reactions. These examples illustrate the broad scope of the method and the potential for gaining insights into the dynamics of various chemical processes.

We began work five years ago on the dissociation of cyanogen iodide:

$$ICN \rightarrow I \cdots CN \rightarrow I + CN$$

The goal was to detect the fragment CN (cyanide) as a nascent product. Our graduate students and postdoctoral fellows were working hard to reach this goal, and we were all determined to achieve results by the end of 1985. We built a two-pulse laser system, and by borrowing some equipment to help compress the pulses, we were able to get the experiment running. In December we reported that we had detected nascent cyanide molecules. We realized that the transition states of cyanogen iodide were just beyond the time resolution of our apparatus.

To improve the time resolution, we decided to build a better system of molecular beams and lasers. We set up our experiment in a newly rehabilitated, dust-free room that once housed the X-ray machines from Linus Pauling's days at Caltech. Shortly after Thanksgiving in 1986, we opened the facility. We were very excited about the possibility of being able to observe transition states directly.

A key feature of these experiments was the ability to make the definition of the frame adequate enough to re-

solve the motion. The detector was made sensitive enough to probe the cyanide molecule when it was free or in the process of separating from the iodine atom. The sensitivity was achieved by using probing laser pulses of different colors in accordance with the spectrum of the molecules. We were thus able to observe the spectral frames changing with time as the reaction progressed from an intact ICN molecule to an iodine atom and molecular fragment, cyanide. We enjoyed discussing the results late into the night.

In 1987 we reported on the probing of the reaction of ICN to iodine and cyanide with enough time resolution to be able to observe the transition state {I•••CN} directly. We obtained the real-time dynamics of the reaction and then deduced detailed features of the potential-energy surface [*see illustration on opposite page*].

That experiment made it possible to clock the breaking of an elementary chemical bond on a femtosecond time scale. The findings generated enthusiasm in the scientific community and inspired many more theoretical and experimental studies. The science writer Isaac Asimov provided an interesting description of the experiment. He compared the experiment with sticking a pin in a balloon only four billionths of an inch across—the size of an average molecule.

While we were still building the new femtosecond laser facility in 1986, Bernstein visited us at Caltech, and we planned to probe the collision and bonding of two molecules, that is, a bimolecular reaction. At first we could not find a way to detect the start of these reactions: the time zero. Although bimolecular reactions last less than a picosecond, the two reactant molecules must first travel to meet each other—a journey that lasts about a million times longer than the reaction itself.

We found a solution to this problem when we studied the investigations of our colleagues at Orsay, France, and at the University of Southern California. By anchoring the two reagents together with a weak van der Waals bond, we could avoid the long time journey and establish the time zero. Fortunately, we had guidance from investigators at U.S.C. who had performed time-integrated studies on the reaction of hydrogen bromide and carbon dioxide.

For our first real-time experiments on these types of bimolecular reactions, we combined hydrogen iodide with carbon dioxide to produce iodine, carbon monoxide and hydroxide:

$$HI + CO_2 \rightarrow I + HOCO \rightarrow I + OH + CO$$

We wanted to understand this reaction at the elementary level. We broke the bond between hydrogen and iodine with a pump pulse. We then observed with probe pulses that the hydrogen attacks the carbon dioxide and sticks to it for hundreds of femtoseconds. The hydrogen atom then strips one of the oxygen atoms from the carbon. The hydroxide molecule finally emerges five picoseconds after the start of the reaction, as we reported in 1987 and earlier this year.

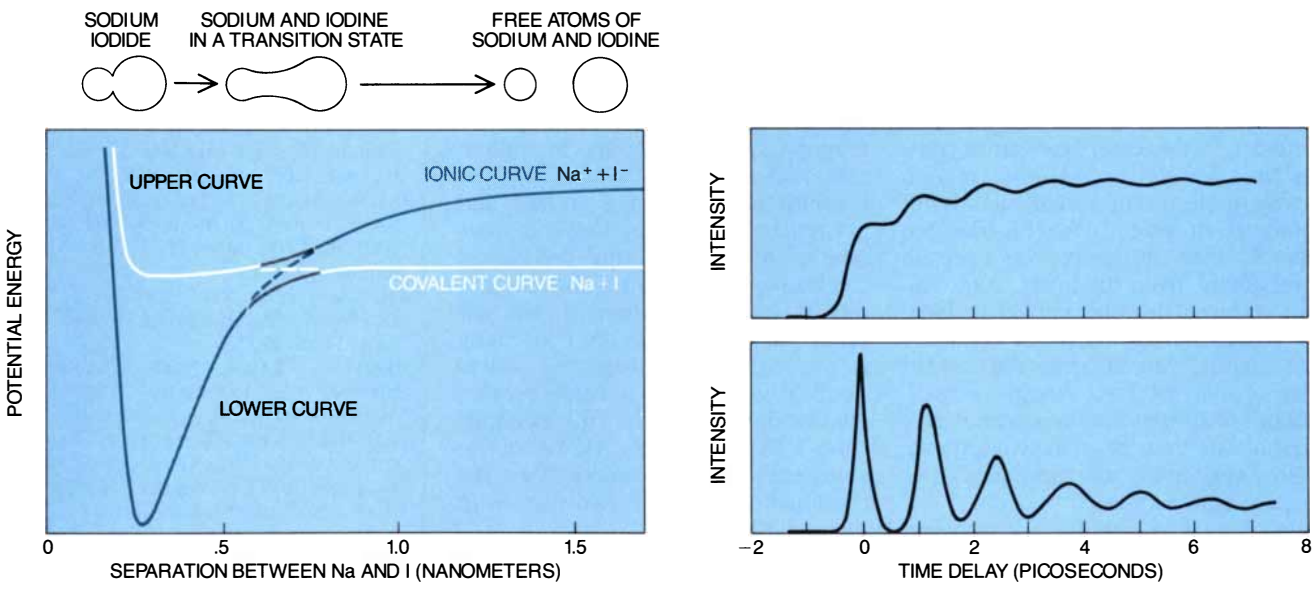
The technique also allowed us to view the dynamics of the transitory collision complex HOCO in real time. We were able to relate this complex to the potential-energy surface representing hydrogen's approach to carbon dioxide. We are still examining the many subtle differences between our results and theory.

Just as physicists like to deal with the hydrogen atom for simplicity, chemical physicists like to understand elementary molecular systems. The simplest of all chemical reactions is that involving two atoms. I thought it would be interesting to direct some efforts at unraveling the dynamics of salt molecules such as sodium iodide:

$$NaI \rightarrow Na \bullet\bullet\bullet I \rightarrow Na + I$$

Alkali halide reactions were the prototype for the "alkali age" of molecular-beam experiments, and it is insightful to study them in the "femtosecond age." Furthermore, researchers at the University of Toronto had investigated the emission spectra of the sodium iodide molecule during its transition to atoms of sodium and iodine.

What intrigued us about sodium iodide is a rather interesting potential-energy surface for the interaction of



FEMTOSECOND MOTIONS of the salt sodium iodide (NaI) reveal the molecular dynamics of the chemical bond linking sodium and iodine. In the potential-energy diagram at the left, the ionic (attractive) curve intersects the covalent (repulsive) curve. As a result, sodium iodide can break up into sodium and iodine, acting in a covalent manner, or sodium iodide can exist in a high-energy bound state, alternating between covalent and ionic behavior. If sodium iodide dissociates into atoms, then the intensity of part of the spectrum will jump in steps, as shown in the experimental results (*top at right*). If sodium iodide is in its high-energy bound state, then the intensity of part of the spectrum will oscillate (*bottom at right*).

sodium and iodine atoms. If these atoms are brought together, they repel one another, particularly at short distances. On the other hand, if the same elements are brought together as oppositely charged ions of sodium and iodine, they attract each other. In fact, at a short enough distance, a stable salt composed of sodium and iodine ions will be formed. When the sodium and iodine form a covalent bond, they share electrons to create a stable energy state. When the atoms form an ionic bond, the sodium atom donates an electron to the iodine atom to create charged ions that attract.

Nature, however, does not work exactly in this way. Actually, the atoms behave as if they are both ionic and covalent. The true potential-energy curves are therefore composed of an ionic and a covalent curve [*see illustration on preceding page*]. The ionic curve crosses the covalent curve at a certain distance. In this region of interaction, the molecular system has a mixture of covalent and ionic characteristics; in other words, the molecule has a certain probability of being covalent and a certain probability of being ionic.

Theorists have divided the potential-energy curves into two parts: a lower and an upper. The lower curve, which represents low-energy states, is composed of the ionic curve at short distances and the covalent curve at long distances. The upper curve depicts the opposite situation: it is covalent at short distances and ionic at long distances. The upper curve also represents a state high in energy.

The behavior represented by the lower surface usually dominates when the sodium and iodine atoms are brought together slowly so that they begin to interact. In this case, an electron passes from sodium to iodine to create a stable molecule of sodium iodide. If, however, the atoms come together too rapidly, they can jump, with a certain probability, from the lower to the upper surface. The upper surface no longer represents the covalent repulsive (or slightly bound) curve and instead has a point of least energy (a minimum). Molecules in this potential minimum will thus be somewhat stable. (More specifically, the molecules enter a quasi-bound state.)

We hoped to view the femtosecond dynamics of the bond in sodium iodide as it breaks to form atoms of sodium and iodine. In particular, we focused on the jump from the upper potential surface to the lower one, or vice versa. We observed the motion as the molecules change from being covalent to being ionic and as they go through the crossing region. The sodium atom gave an electron to the iodine atom at a distance of .7 nanometer. The sodium atom had, in effect, employed its electron as a harpoon to reel in the iodine atom.

To perform the experiment, we first sent a laser pulse to excite the NaI molecules. When the sodium separates about .25 nanometer from the iodine, the bond begins to break. A second pulse is then released to probe the reaction at a point when the sodium iodide bond is completely broken and a sodium atom and an iodine atom are formed. The probe pulse excites the sodium atom and causes it to emit yellow light. By probing the motion from the moment the bond breaks—time zero—until the birth of free sodium atoms, we can count, in real time, the number of sodium atoms that have appeared on the lower curve. But, more important, by detecting the quasi-bound transition species, Na•••I, which has different spectral properties from those of free sodium, we can observe the transition from Na•••I to free sodium and iodine atoms.

Some of the sodium iodide molecules on the upper curve, when reaching the crossing area, will jump to the lower curve, and their bond will break to form sodium and iodine atoms. The molecules that do not jump but instead remain on the upper curve do not break a bond. They continue to vibrate until they do jump. Hence, pulses of sodium atoms should be evident only after each round-trip in the well of the upper curve. This phenomenon is exactly what we have observed. The results show the motion of the molecule during the breaking of a chemical bond and give the details of the potential energy governing the motion of sodium and iodine atoms.

Laboratories in the U.S. (at IBM) and in Germany (at Freiburg University) are now applying femtosecond techniques to observe the dynamics of many different types of reactions in the gas phase. At Caltech, we are continuing to probe elementary reactions and to examine more complex reactions that involve multiple births (for example, $ABA \rightarrow AB + A \rightarrow A + B + A$). We hope to study the simplest of all reactions, the combination of atomic hydrogen with molecular hydrogen.

We are also exploring large molecular systems with the aim of answering questions about selective reactivity. For example, if a molecule with two identical bonds is energized, do the two bonds break simultaneously or consecutively? To address this general and important question, we studied the dissociation of $C_2I_2F_4$ into iodine and C_2F_4. (In C_2F_4, a double bond forms between the carbon atoms.) From real-time studies we found that the reaction proceeds consecutively, despite the molecular equivalence of the two carbon-iodine bonds. Even more remarkable is the discrepancy in the time scale for bond breakage—the first bond breaks in less than half a picosecond, whereas the second bond takes 100 times longer to break!

The ability to view molecular dynamics also suggests new ways of controlling reactions. There are several theoretical schemes for achieving control, and already experimentalists are exploring some new possibilities. The prospect exists for fine-tuning the motion and reactivity of molecules. If successful in the coming decades, laser-customized chemistry may be developed.

Muybridge invented high-speed photography for the fun of it, and today the technique has gone far beyond what he or Stanford could imagine. Although one cannot predict the future, we are certain of the importance and beauty of understanding the science of molecules and their reactions. The door is open for much experimental and theoretical research and for unexpected findings. It is my hope that readers will share in the fun and excitement that we have experienced in learning about the basics of alchemy—the transmutation of one substance to another—by observing the ultrafast motions of molecules.

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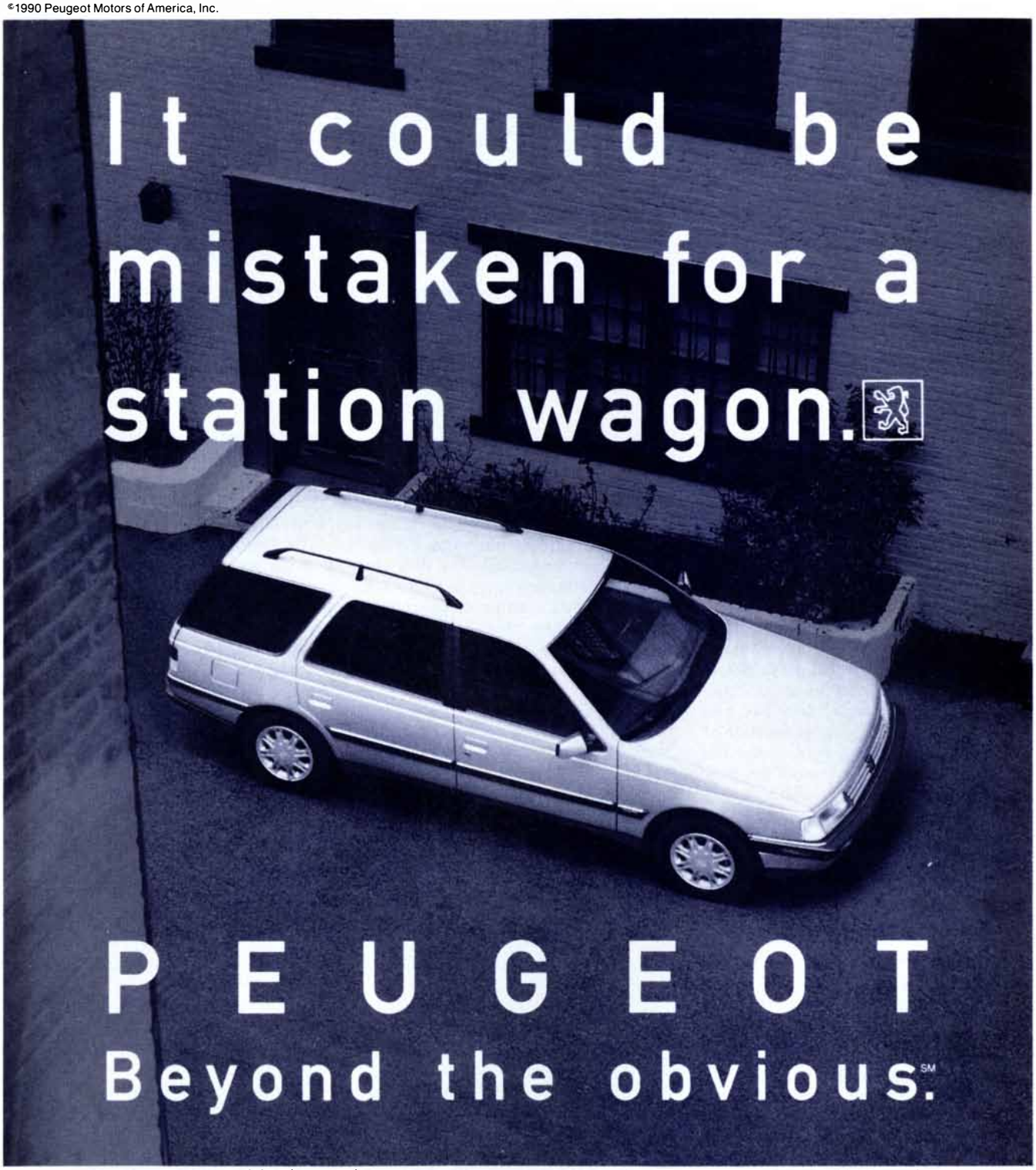

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The Legacy of Gestalt Psychology

Since its inception early in this century, Gestalt theory has made significant contributions to the study of perception, learning and social psychology. These contributions remain influential today

by Irvin Rock and Stephen Palmer

Like many important movements in science, Gestalt psychology was born of a revolt against the intellectual establishment of its time. Today several concepts that Gestalt theorists proposed early in this century have been incorporated into modern understanding of perception, learning and thought—indeed into our very language and culture. Many people have heard the phrase "the whole Gestalt" or have seen pictures that demonstrate Gestalt principles, such as the one that looks now like a vase, now like two profiles face to face. But few outside of academic psychology know what the movement was about or what has happened to the ideas on which it was based.

Gestalt psychology started in Germany, but after the rise of Nazism its founders—Max Wertheimer, Wolfgang Köhler and Kurt Koffka—moved to the U.S., where some of their students remain active. The Gestaltists contributed more to the study of perception than to other areas of psychology—*Gestalt* is German for "pattern" or "shape," although "configuration" comes closer to its intended meaning—but they also made important advances in education, learning, thinking and social psychology. Some of their ideas have not survived, but others continue to influence the work of modern psychologists.

IRVIN ROCK and STEPHEN PALMER, both at the University of California, Berkeley, collaborate on studies of visual perception. Despite their different backgrounds, they share an interest in many phenomena uncovered by Gestalt psychologists. Rock received his training at the New School for Social Research under students of the founding fathers of Gestalt, including Solomon Asch, Hans Wallach, Mary Henle and Martin Scheerer. He completed his Ph.D. there in 1952. Palmer was trained at the University of California, San Diego, in the more modern tradition of information processing, under the guidance of Donald Norman and David Rumelhart. His doctoral dissertation, completed in 1975, attempted to investigate Gestalt ideas in terms of information processing. Rock and Palmer are currently pursuing several research projects that extend and revise Gestalt theories of perceptual grouping and frame of reference.

Gestalt psychology was launched in 1912 when Wertheimer, then at the Institute of Psychology in Frankfurt am Main, published a paper on a visual illusion called apparent motion. Apparent motion is the perception of movement that results from viewing a rapid sequence of stationary images, as in the movies [*see illustration on page 86*]. This phenomenon indicated to Wertheimer that the perception of the whole (movement) was radically different from the perception of its components (static images).

The idea that the whole is different from the sum of its parts—the central tenet of Gestalt psychology—challenged the then prevailing theory of Structuralism. In particular, the Gestaltists rejected elementarism, a basic Structuralist assumption that complex perceptions could be understood by identifying the elementary parts of experience. Structuralists believed a trained observer could break down the fundamental elements of perception into primitive sensations, such as the points that make a square or the particular pitches in a melody. They maintained that a square was just the experience of a particular set of points stimulating the retina; a melody was just the experience of a sequence of distinct tones that became associated with one another in the listener's mind. Their view has been described as "mental chemistry" because it assumes that perceptions can be analyzed component by component, much as molecules can be broken down into atoms.

The Gestaltists attacked this theory. What people perceived, they held, is not merely a sum or sequence of sensations but the whole configuration of which they are part. The location or size of a square's image can be altered so that entirely different retinal sensations are produced, yet the perception is still that of a square. How else could people experience the same melody when it is transposed in key? All the corresponding pitches are now different, yet only a few musicians with perfect pitch would notice any change.

Gestalt theorists maintained that the parts of a square—or the tones of a melody—interact with one another and in so doing produce a perceived whole that is distinct from the sum of its parts. Shape and melody are examples of what they called emergent properties: overall qualities of an experience that are not inherent in its components. Emergent properties are not unique to mental phenomena, however. The properties of table salt, for instance, are very different from those of its constituents, sodium (a corrosive metal) and chlorine (a poisonous gas). Even the characteristics of a society are distinct from those of the individuals who compose it.

Emergent quality illustrates one meaning of the Gestalt concept of organization. The Gestaltists also believed organization was necessary to explain why human beings see the world as

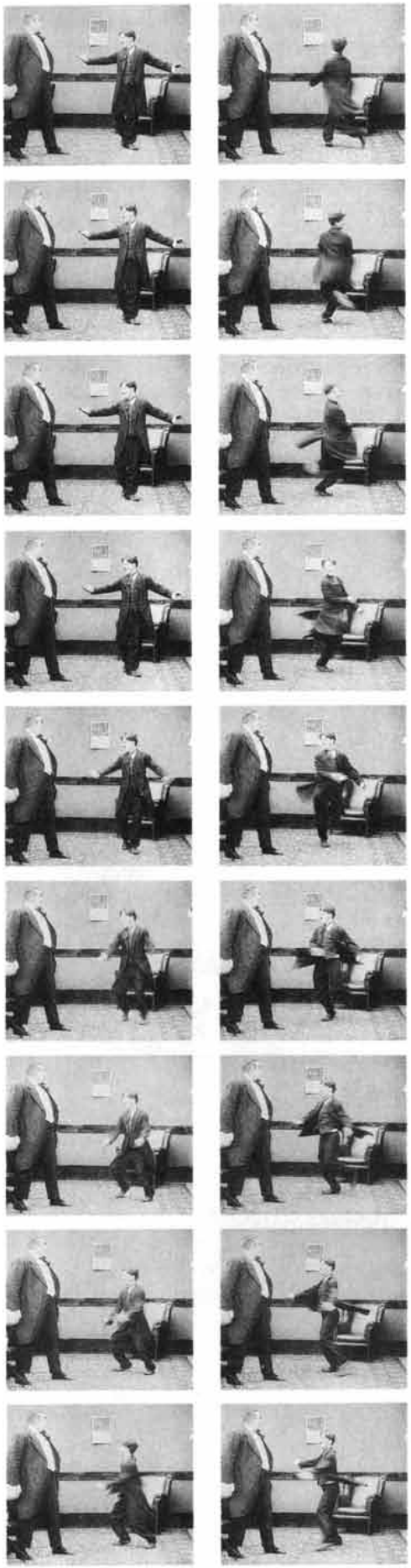
NATURAL CAMOUFLAGE shows how the laws of grouping, such as similarity, proximity and connectedness, can conceal animals. The ponies cannot easily be distinguished from the background.

composed of distinct objects. They pointed out that because the retinal image is nothing but an array of varying intensities and frequencies of light, the rays coming from different parts of the same object have no more affinity for one another than those coming from two different objects. It follows that the ability to perceive objects—such as stones, trees and houses—must be an organization achieved by the nervous system. The realization that the perception of separate objects was not achieved solely by the "picture" focused on the retina was one of the Gestaltists' most important contributions.

To explain how perceptions of individual objects are formed, Wertheimer proposed that the visual system organizes parts into wholes based on laws of grouping. Elements tend to be grouped perceptually if they are close together, similar to one another, form a closed contour or move in the same direction [*see illustration on page 89*]. Most often these laws lead to an accurate representation of the objects in a scene, but they can also lead to inaccurate ones, as in the case of camouflage.

Another important aspect of organization, called figure-ground perception, was discovered in 1921 by Danish psychologist Edgar Rubin. Rubin pointed out that even if all the parts of a connected region are grouped together properly, it can be interpreted either as an object (figure) or as the surface behind it (ground) [*see lower illustration on page 87*]. He formulated a set of laws that describe the conditions under which a region would tend to be seen as figure rather than as ground.

The Gestaltists further discovered that certain structures determine a frame of reference with respect to which other objects are perceived. Many people have reported experiencing an instance of this phenomenon, called induced motion, when a neighboring train slowly pulls out of the station, producing the impression that one's own train has begun to move in the opposite direction, although it is actually stationary. Another example of this phenomenon occurs when an observer is inside a tilted room. The walls of the room define the vertical and horizontal axes of the frame, causing a chandelier to look strangely askew and



MOVIE FRAMES of Charlie Chaplin illustrate how the illusion of apparent movement is created. The still frames give the impression of motion if they are viewed successively at rapid speed.

the observer's own body to feel tilted, despite the fact that both are perfectly aligned with gravity. In each case, the visual system takes a large, surrounding structure to define the perceptual standard—stillness or uprightness—and construes other objects, including one's self, in terms of these standards.

A final aspect of the Gestalt concept of organization deals with what they called the principle of *Prägnanz,* which states that when stimuli are ambiguous, the perception will be as "good" (meaning simple, regular and symmetric) as the "prevailing conditions" allow. The prevailing conditions refer to the information being registered by the retina. Obviously, the visual system does not convert any pattern into the simplest shape. An irregular triangle, for example, is not seen as a circle, because perception must account for the nature of the retinal image. But in cases where the image is ambiguous, such as a partly hidden figure [*see lower illustration on page 88*], the viewer tends to perceive the simplest shape consistent with the information available.

Gestalt theorists sought to understand these and other perceptual phenomena in physiologic terms. They posited a very direct connection between experience and physiology in their doctrine of isomorphism, which states that a subjective experience and its underlying neural event have similar structures. Wertheimer's analysis of apparent movement illustrates this idea. When two lights in nearby locations are turned on and off at the proper alternation rate, the observer sees a single light moving back and forth [see "The Illusion of Movement," by Paul A. Kolers; SCIENTIFIC AMERICAN, October, 1964]. Wertheimer argued that this perception was caused by electric energy in the brain flowing between the two locations stimulated by the lights—in other words, the physiological event had the same structure as the perception it gave rise to.

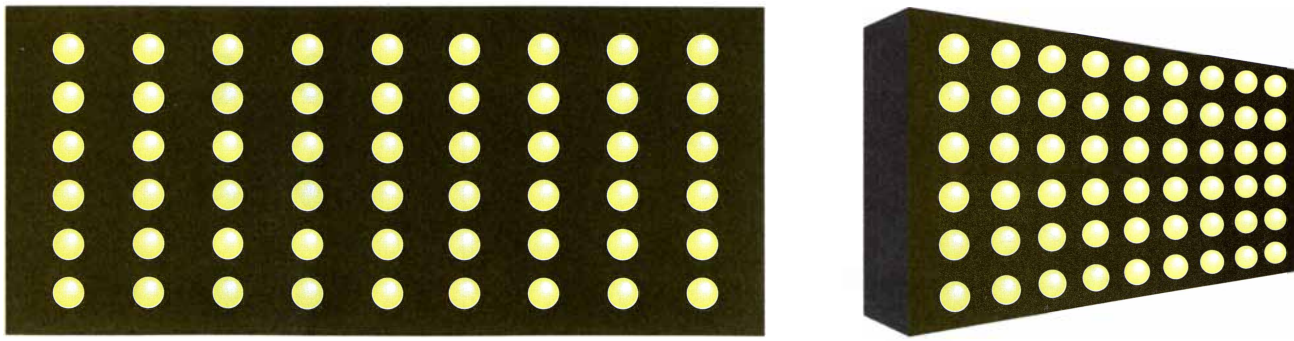
The flowing of electric energy in the brain did not refer to the transmission of electric signals along individual neurons, as dictated by the standard view of neurophysiology. Such a neuronal system did not seem capable of explaining the kind of interaction and organization Gestalt theorists had in mind, so they suggested that direct current flowed through brain tissue. They held that stimuli created electric fields in the brain that interacted with one another and converged toward a state of minimum energy. Köhler, who was well versed in the physics of the day, argued that the brain was only one example of many physical systems—which he called physical *Gestalten*—that evolve toward a state of equilibrium. Soap bubbles, for instance, start out in various shapes, but they always change over time into perfect spheres because that is the minimum energy state for a soap film.

Consistent with their doctrine of isomorphism, the Gestaltists believed that the convergence of electric brain fields toward a minimum energy state provided the mechanism for *Prägnanz:* perceptions were simplified when the underlying brain event reached a state of equilibrium.

Although Köhler's theory of electric brain fields is no longer taken seriously, many other ideas that emerged from Gestalt psychology continue to influence today's perception theorists. In some cases, Gestalt views have been extended and in others revised, but one cannot read a contemporary perception textbook without finding a wealth of ideas that originated with the Gestalt movement.

Wertheimer's laws of grouping have withstood the test of time. In fact, not one of them has been refuted, and no new ones have been added to his original list, until our own recent proposals. One of us (Palmer) suggested a law of enclosure, or common region, referring to an observer's tendency to group elements that are located within the same perceived region [*see illustration on page 89*]. The second law, connectedness, which we postulated jointly, may be the most fundamental principle of grouping yet uncovered. Connectedness refers to the powerful tendency of the visual system to perceive any uniform, connected region—such as a spot, line or more extended area—as a single unit. Connectedness is a particularly good candidate for a law of grouping because it is perhaps the most diagnostic property of objects in the environment. We suspect Wertheimer missed this important principle because he failed to realize that an explanation was required for why each element in his configurations was itself perceived as a single entity.

Although the validity of the laws of grouping has not been seriously challenged, the stage at which they operate in the visual system is being reassessed. The Gestalt position implic-



LATTICE OF GLOWING BEADS is organized vertically into columns (*left panel*). When it is tilted backward (*right panel*), observers still perceive columns even though the retinal images of the beads are now closer together horizontally.

itly assumes that grouping must occur early in visual processing. So when Wertheimer discussed principles such as proximity, he presumably referred to retinal proximity: how close the stimuli were to one another on the retina. It is possible, however, that these grouping principles operate later in visual processing, after depth and lighting conditions have been perceived.

To disentangle these two hypotheses, one of us (Rock) performed an experiment with Leonard Brosgole some years ago. Luminous beads were strung on parallel strings and suspended in the dark so that they appeared as a lattice of glowing dots. Because the beads were closer to one another vertically than horizontally, observers saw them as organized into columns [*see illustration above*]. We then tilted the display backward so that the retinal images of the beads were closer together horizontally, although the beads themselves of course remained closer vertically. When observers viewed this display, they continued to see the beads in columns, indicating that grouping was based on perceived proximity in three-dimensional space rather than on actual proximity on the retina. Grouping by proximity must therefore occur after depth perception. We have reached similar conclusions for the principles of common region and connectedness, as well as for similarity grouping by lightness.

New experimental methods have further advanced the understanding of grouping and have also suggested links to the underlying physiology. Jacob Beck of the University of Oregon pioneered the study of texture segregation, a form of grouping elements by similarity when they are perceived as a pattern rather than as individual forms. In one experiment he presented observers with a field of three different types of elements side by side: L's (or reversed L's), T's and tilted T's [*see top illustration on page 90*]. The observers were to say at which boundary there was a more natural break in the pattern.

Beck found that the boundary between the upright and tilted T's was much more evident than the one between the L's and the T's. This reveals—somewhat surprisingly from the Gestalt point of view—that the orientation of the elements is a more powerful factor than their overall shape. These and related findings have forged theoretical connections between the separation of textures and the activity of cells in the visual cortex that respond strongly to differences in the orientation of component lines and edges [see "Brain Mechanisms of Vision," by David H. Hubel and Torsten N. Wiesel; SCIENTIFIC AMERICAN, September, 1979].

Other techniques have provided ways of testing the Gestalt idea that wholes are perceptually dominant. David Navon, now at the University of Haifa in Israel, performed a study to determine whether wholes are perceived before parts, or vice versa. Using large letters composed of small letters, he measured the time observers needed to identify the large (global) or small (local) letters [*see middle illustration on page 90*]. In some cases, the large and small letters were the same (consistent); in others, they were different (conflicting).

If whole figures are perceptually primary, as the Gestaltists held, global letters should be identified faster than local ones; if parts are primary, as others believe, the reverse should be true. Another prediction of the Gestalt view-

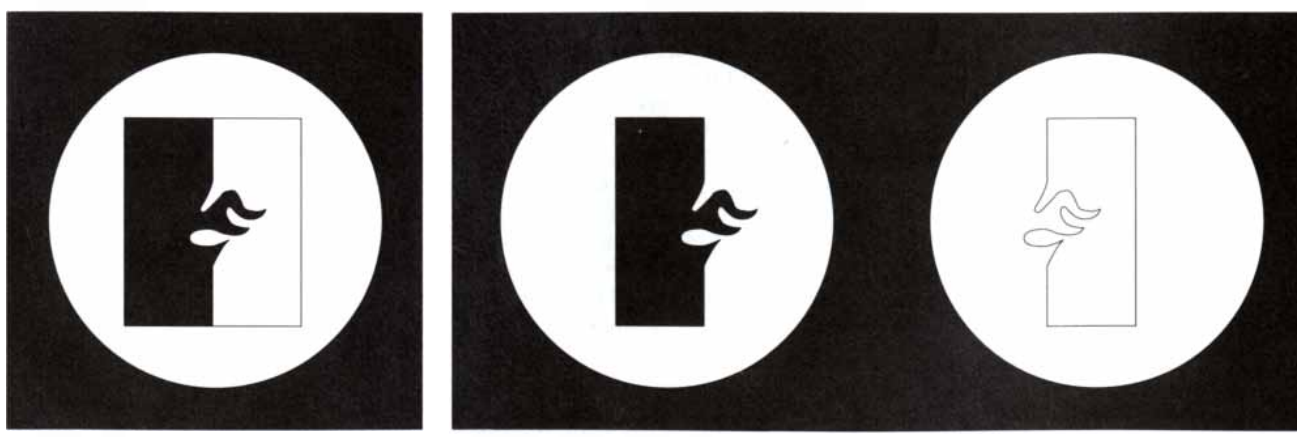
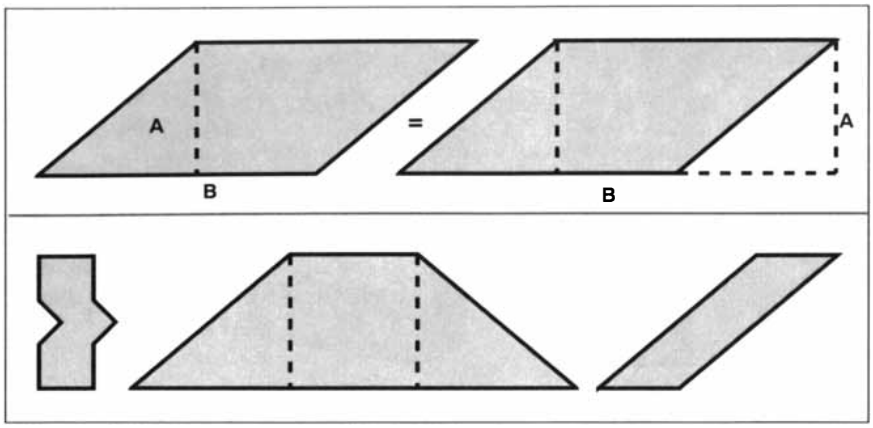
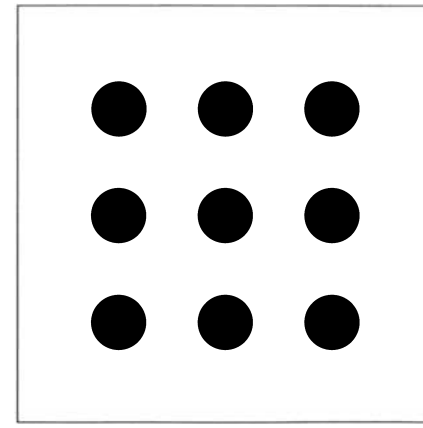


FIGURE-GROUND ORGANIZATION is fundamental to perception. Either side of the pattern on the left can be perceived as figure or as ground. Although the two shapes on the right share the same contour, they seem very different.



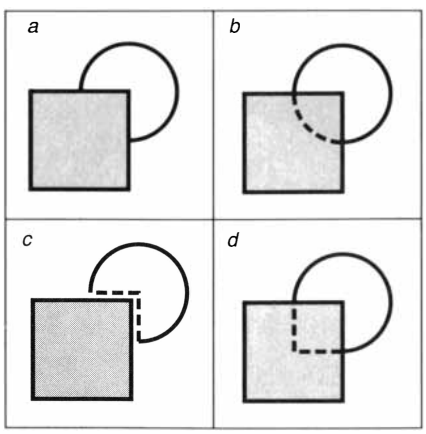
UNDERSTANDING that a parallelogram's area is equivalent to that of a rectangle's (*top panel*) makes finding the areas of other shapes (*bottom panel*) easier. Learning by understanding allows insights to be transferred to analogous situations.



CONNECT the dots by drawing four straight lines without lifting pencil from paper. (Solution on page 90, at bottom.)

point is that if the whole is perceived first, conflicting local letters should not affect the naming of the global ones, but conflicting letters at the global level should slow naming of the local ones. Again, part-to-whole theorists predict the opposite. Navon's results supported the Gestalt predictions on both counts. Later investigators have found these results to be less pervasive than Gestalt theory would suggest by showing that responses depend on factors like the absolute and relative size of the letters.

Another concept of Gestalt theory that is very much alive is the principle of *Prägnanz*—the idea that the visual system converges on the most regular and symmetric perception consistent with sensory information. The vague Gestalt notion of "goodness" has now been clarified. Emanuel Leeuwenberg and Hans Buffart, then at the University of Nijmegen, advanced a theory that specifies the amount of information in various perceptions—"good" ones contain little information, and "bad" ones contain a lot—and have predicted how people will perceive partly hidden figures, among other phenomena. Wendell R. Garner of Yale University has shown that good patterns can be matched more quickly, remembered better and described more succinctly than bad ones.



OBSCURED FIGURE illustrates the idea of *Prägnanz*. Given an ambiguous pattern (*a*), observers perceive simple shapes (*b*) instead of complex ones (*c, d*).

In contrast to their theories of perception, Gestaltists' ideas about electric fields in the brain have been resoundingly rejected by modern physiologists. Concepts similar to Köhler's notions about physical *Gestalten,* however, have resurfaced under the guise of neural networks. According to neural-network theorists, mental processes result from the dynamic behavior of many interconnected computing units, which can be thought of as neurons. Each unit's behavior can be characterized by its state of activation—much like a neuron's firing rate—and units affect one another by excitatory or inhibitory connections—much like synapses. The entire system is initially activated by an external stimulus that affects some subset of the units. Activation then propagates through the network until it reaches an equilibrium state of minimum energy [see "Collective Computation in Neuronlike Circuits," by David W. Tank and John J. Hopfield; SCIENTIFIC AMERICAN, December, 1987]. In short, these networks can be thought of as examples of physical *Gestalten.* Although this work is still in its infancy, neural-network models of perception promise to open a whole new chapter of Gestalt theory.

Beyond revolutionizing the study of perception, Gestalt theorists enriched the fields of learning, memory and thinking—with important implications for education—and social psychology. Early Gestalt ideas about thinking clashed with those of the emerging Behaviorist movement. A forerunner of that school, Edward L. Thorndike, concluded from his studies that animals solved problems by trial and error rather than by thought or understanding. In one now famous experiment, he placed a cat in a cage from which it could escape by pulling a hanging string that opened the door latch. In the process of thrashing about, the cat would inadvertently tug the string and be released. After many such trials, it would pull the string the moment it was returned to the cage. Thorndike concluded that the cat did not use intelligence but gradually developed an association.

Gestalt theorists vehemently denounced this kind of experiment and the conclusions drawn from it. They objected that the situation actually prevented any display of intelligence in problem solving because the cat could hardly be expected to understand the hidden mechanism that related tugging on the string to opening the door. In contrast, Köhler performed experiments with chimpanzees while he was isolated on the island of Tenerife during World War I in which both the requirements for a solution and the means to achieve it were perceptually evident. Köhler observed chimps discovering how to retrieve bananas from outside their cage with a stick.

These findings conflicted with Behaviorist dogma in at least two important ways. First, the chimps arrived at the solution suddenly, in a flash of "insight," rather than gradually. This was possible, Köhler argued, because the nature of the problem was perceptually apparent, unlike the string-latch mechanism. Second, the errors made by the

chimps were not random, as predicted by Behaviorist theory, but displayed intelligence and comprehension.

Although no one has explained how insight occurs, the Gestaltists did illuminate certain aspects of how understanding could be achieved. One way humans can do it, unlike animals, is by having something explained to them. Mere listening is not enough, of course, for the listener must achieve the same cognitive structure as the explainer in order to become aware of the essential connections among the relevant facts. Listeners do not have to go through the same creative process as did the original problem solver to arrive at the solution, but their final state of comprehension must be similar.

The educational implications of achieving insight through explanation cannot be overestimated. Not only is it satisfying to grasp the solution to a problem, but it is far less likely to be forgotten than rote memorization, and it can be readily transferred to related new problems. Wertheimer showed, for instance, that once children realize why the area of a parallelogram equals its base times its altitude [*see upper left illustration on opposite page*], they can find the areas of other geometric figures without having to memorize the formulas. Many modern educators critical of rote learning advocate teaching students to think creatively to achieve insight. Few realize that these "revolutionary" ideas about education originated with Gestalt psychologists.

Gestalt theorists also struggled to describe the creative process through which a person achieves original insight in everyday life. They proposed that problems have certain demands that are readily grasped, which lead people to attempt nonrandom solutions [see "Problem-Solving," by Martin Scheerer; SCIENTIFIC AMERICAN, April, 1963]. Becoming fixated on one hypothesis or one function of an object—often without realizing it [*see upper right illustration on opposite page*]—is the chief obstacle to insight. When people let go of implicit assumptions, their understanding of a problem is sometimes dramatically reorganized, enabling them suddenly to "see" the solution, complete with the accompanying "aha!" experience.

Modern researchers on human problem solving have not yet explained insight, but they have abandoned the Behaviorist idea of blind trial and error in favor of one more consistent with Gestalt ideas about the value of comprehension. One promising focus of recent research has been the use of analogies in problem solving: those who understand one topic can apply this knowledge elsewhere through analogy.

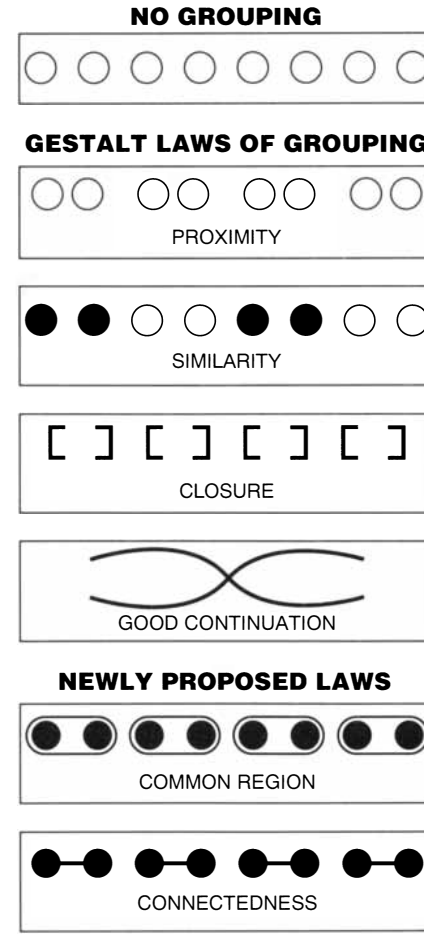
The Gestaltists made further inroads against the Behaviorist approach in the realm of social psychology. Beginning in the late 1930s, three investigators—Kurt Lewin, Fritz Heider and Solomon E. Asch—rejected the idea that social behavior could be explained solely as a response conditioned by societal rewards, such as approval or praise. Rather, they argued, people make sense of the behavior of others by attributing to them feelings, perception, goals, beliefs and intentions—a view known as attribution theory. As obvious as this idea sounds, it was a radical departure from the prevailing Behaviorist approach, which minimized or denied subjective states of mind. Attribution theory has since displaced Behaviorism as the dominant view in social psychology.

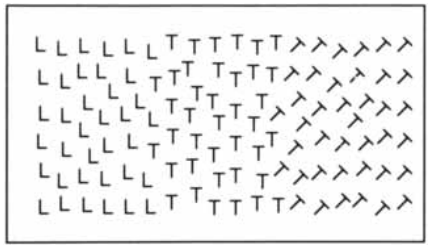
Few of Lewin's ideas have survived in contemporary psychology, but the work of Heider and Asch has had lasting influence. Heider applied Gestalt ideas about object perception to the perception of others. One cornerstone of his theory was the idea of attribution: that people try to account for one another's behavior in terms of deeper causal explanations, such as motives and intentions, using context and behavioral consistencies. Heider also developed the concept of balance: the idea that individuals prefer harmonious cognitive relations. For instance, if Jane likes person *X* and thinks *X* likes person *Y,* then the system of beliefs will be balanced if Jane also likes *Y*—and imbalanced if she does not. This idea echoes the principle of *Prägnanz:* the tendency to achieve the best or most basic organization.

Heider's seminal work on balance theory is related to the late Leon Festinger's theory of cognitive dissonance. Because Festinger believed people seek to reduce inconsistencies in their beliefs, feelings and behavior, he studied how people's choices affect their subsequent beliefs and attitudes. He reasoned that when a rejected alternative (say, a sporty but temperamental car) is in many ways more desirable than the chosen one (a staid but reliable car), the fact that it was not chosen will produce an inner state of disharmony—or dissonance, as Festinger called it—which produces pressure toward eliminating it. One way to reduce dissonance is to reevaluate the relative attractiveness of the alternatives, such as devaluing the unchosen one (sporty cars are too dangerous anyway), thereby enhancing the chosen one.

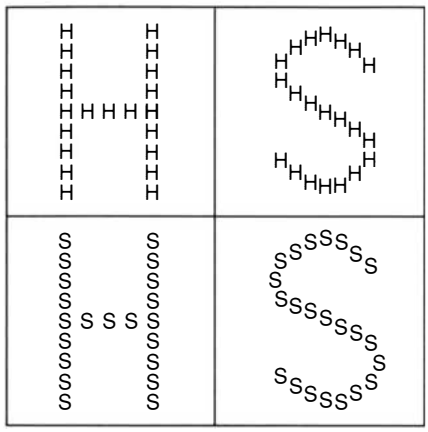
Asch, who worked with Wertheimer at the New School for Social Research, directly extended Gestalt theory to social psychology. He contended that attitudes are rooted in beliefs, that beliefs are rooted in information and that beliefs tend to be rational rather than molded by "suggestion," as early social psychologists thought. His emphasis on human rationality conflicted with the seeming irrationality of phenomena such as racial prejudice. Asch argued, however, that even prejudice can be understood as being reasonable and rooted in information, albeit misinformation. For example, if children depend on parents and other respected adults and have little reason to mistrust them, accepting adult opinions about an ethnic or racial group is a reasonable thing to do. Moreover, children get little if any information from other sources to contradict what they have been told by their parents.

Asch also challenged the Behaviorist assumption that beliefs and attitudes result from suggestions based on the prestige of the source. For instance, American college students were known to change their opinion of a statement depending on who they believed had made it. When told Thomas Jefferson

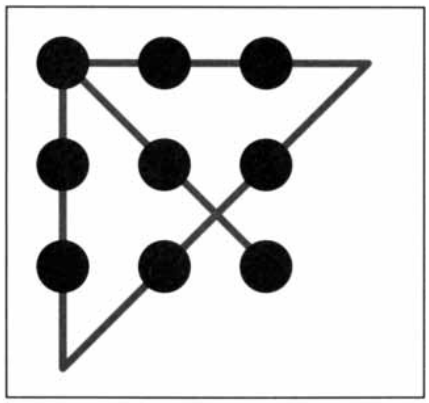




TEXTURE SEGREGATION is based on the dissimilarity of elements. The boundary between upright and tilted T's is clearer than between upright T's and L's.



GLOBAL PRECEDENCE allows larger letters to be recognized more rapidly than smaller ones, whether or not the latter are consistent. Identifying small letters, in contrast, takes longer when they conflict with the global letter.



DOTS can be connected by extending the lines beyond them. People assume incorrectly that they may not do this.

had said "a little rebellion, now and then, is a good thing, and as necessary in the political world as storms in the physical," they often strongly agreed. If the same statement was attributed to Lenin, their agreement with the statement diminished considerably.

These results superficially support the idea that the acceptability of the source strongly influences a person's opinions. But Asch believed there was a rational basis for such decisions. He proposed that people understood the statement differently depending on who was thought to have said it. Indeed, Asch found that students who attributed the statement to Lenin interpreted "rebellion" to mean the complete overthrow of the socioeconomic system. Those who attributed it to Jefferson usually had a less violent interpretation, such as moderate social or political reform [see "Opinions and Social Pressure," by Solomon E. Asch; SCIENTIFIC AMERICAN, November, 1955].

This aspect of Asch's work represents an extension of the Gestalt concept of part-whole contextual effects that was developed to explain perceptual phenomena. The part in this case was the statement, which had different meanings when embedded within the whole (all that one knows about the author, be he Jefferson or Lenin). The idea of the whole resulting from the organization of parts is illustrated by Asch's experiment on how people form impressions of personalities from lists of traits. Asch found that when people arrive at a unified impression of a person, certain traits are pivotal: substituting one for the other in a list of otherwise identical traits would entirely change the overall impression. Even the same trait will be perceived differently as a function of another trait. Thus, the meaning of being "determined" in a warm person is not quite the same as being "determined" in a cold person.

In some ways, the Gestalt movement, despite its acknowledged impact on several areas of psychology, has always been regarded rather skeptically by the scientific establishment. This opinion was certainly true in the 1920s and 1930s when the dominant theories were Structuralism and Behaviorism, schools that the Gestaltists attacked vehemently—and successfully. Yet such skepticism persists today for several reasons. First, Gestalt psychology sought to investigate subjective experience, as in perception, which Behaviorists rejected as an improper subject for scientific inquiry. Second, although Gestaltists did perform many well-controlled experiments, their best-known phenomena were often presented as straightforward demonstrations, such as the figures illustrating the laws of grouping. Third, their theories were usually expressed qualitatively and fell short of current standards of precision. Moreover, their views about brain function have been largely discredited by modern neurophysiologists. And last, but certainly not least, the theoretical approach they advocated seems to deny one of the most basic tenets of the scientific method—that wholes can be understood by reducing them to a set of parts.

These formidable obstacles to the acceptance of Gestalt ideas should be weighed against their considerable accomplishments. The list of major perceptual phenomena they elucidated—grouping, figure-ground organization, frames of reference, figural goodness and apparent motion, just to name the ones mentioned in this article—is impressive. Although it is logically possible that these discoveries could have been made independently of their methods and theoretical beliefs, it seems unlikely. The Gestalt attack against Structuralism was devastatingly effective.

In addition, the Gestaltists were victorious over the Behaviorists in their clash regarding the nature of learning, thinking and social psychology. Although behavioral methods are adhered to by modern psychologists, Behaviorist theory has been abandoned in favor of a cognitive approach more in line with Gestalt thinking. The theoretical problems they raised about perceptual organization, insight, learning and human rationality remain among the deepest and most complex in psychology.

Even though Gestalt ideas about electric brain fields were erroneous, the more general proposal that the brain is a dynamic system converging toward equilibrium in an energy function—physical *Gestalten* in Köhler's terminology—may turn out to be correct. The remarkable surge of interest in neural-network models attests to the fact that Gestalt theories are very much alive today and that their place in psychological history is assured.

FURTHER READING

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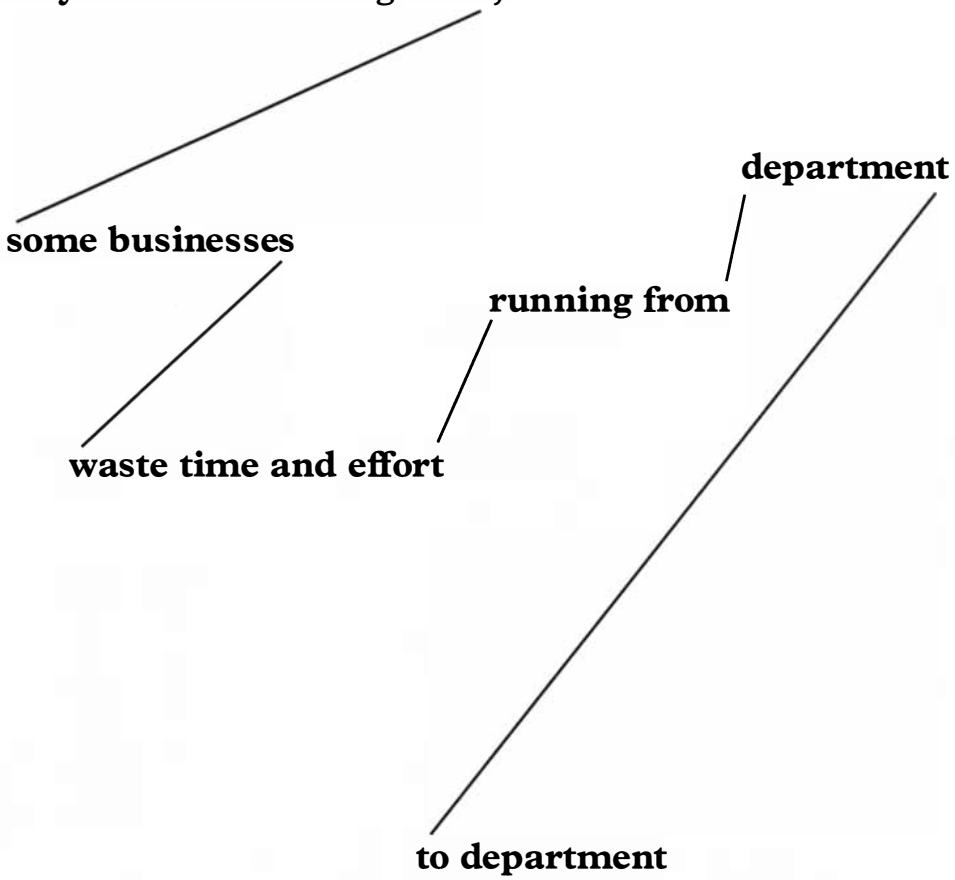
When their systems aren't integrated,



until finally they learn to integrate their systems the Intelligent way.

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Frozen and Alive

A variety of animals freeze solid during the winter months and thaw in the spring. This natural ability to survive freezing may yield clues to the cryopreservation of human tissue

by Kenneth B. Storey and Janet M. Storey

When the mercury dips below zero degrees Celsius, we retreat to our warm houses, don parkas if we venture outdoors and perhaps look forward to a vacation somewhere tropical. Few animals remain active during the winter months. Birds have flown south, and many terrestrial animals hibernate in dens or on lake bottoms. But what happens to ectothermic, or cold-blooded, animals—frogs and turtles, beetles and spiders—that cannot find a relatively warm haven? How do they endure when environmental temperatures fall below the freezing point of their body fluids? Some species avoid freezing through biochemical changes in their bodies. But, remarkably, the answer for many other animals is that they freeze solid and survive.

Hundreds of species of terrestrial insects survive long periods of freezing while they overwinter. At the extreme, insects of the high Arctic, such as the woolly bear caterpillars (*Gynaephora groenlandica*), may spend 10 months of the year frozen solid at temperatures that descend to –50 degrees C (–58 degrees Fahrenheit) or even lower. A variety of invertebrate animals that colonize the intertidal zone of northern seashores, such as barnacles, mussels and periwinkles, also freeze when exposed to subzero air temperatures at low tide. But of greatest interest to our laboratory at Carleton University in Ottawa, Ontario, are a group of amphibians and reptiles that survive freezing during their winter hibernation.

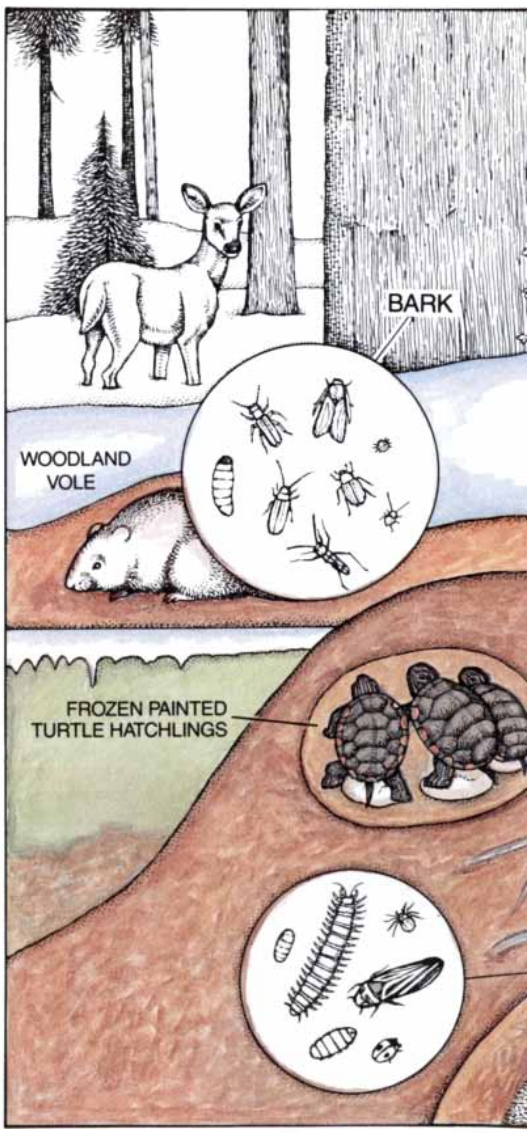
KENNETH B. STOREY and JANET M. STOREY explore the biochemical adaptations of animals at Carleton University in Ottawa, Ontario. Kenneth Storey received his B.Sc. from the University of Calgary and a Ph.D. from the University of British Columbia. Recently elected as a Fellow of the Royal Society of Canada, he is currently professor of biochemistry at Carleton. Janet Storey received her B.Sc. from the University of Manitoba and her M.Sc. from the University of British Columbia. Now a research associate at Carleton, she spends her time with her husband researching as well as raising two daughters, who think it is perfectly normal to have jars of frogs in the kitchen fridge.

William D. Schmid of the University of Minnesota at Minneapolis stimulated our work on this striking adaptation with a 1982 report on frogs that survive freezing. Following up on Schmid's study, we have shown that four common species of frogs—the wood frog (*Rana sylvatica*), the spring peeper (*Hyla crucifer*), the gray tree frog (*Hyla versicolor*) and the striped chorus frog (*Pseudacris triseriata*)—that hibernate on the forest floor can survive days or weeks of freezing with as much as 65 percent of their total body water as ice. Scientists in the U.S.S.R. have also reported that the Siberian salamander (*Hynobius keyserlingi*) can survive freezing. This species, the only land-hibernating amphibian found on the tundra, may survive exposure to –35 degrees C.

Then, in 1988, we identified a reptile that freezes during the winter. Our colleague Ronald J. Brooks of the University of Guelph told us about the unusual behavior of newly hatched painted turtles (*Chrysemys picta*). Instead of leaving their nests after hatching in late summer, the young turtles stay put, safely hidden from predators, until spring arrives. Their nests, only three to four inches deep and placed on exposed banks of lakes and rivers, offer little insulation.

Brooks recorded nest temperatures of –6 to –8 degrees C during January and February of 1988, but our laboratory tests showed that the turtles froze whenever the temperature fell below –3 degrees C. Therefore, the hatchlings must freeze and thaw repeatedly over the winter before emerging in the spring. Studies by Jon P. Costanzo, Dennis L. Claussen and Richard E. Lee, Jr., of Miami University in Oxford, Ohio, also showed that adult box turtles and garter snakes have some ability to survive freezing.

While frozen, all these animals show no movement, respiration, heart beat or blood circulation, and our latest ex-



periments show barely detectable neurological activity. Ice accumulates in all extracellular fluid compartments and fills the abdominal cavity and the bladder; crystals run under the skin and in between muscles. These animals have mastered the tricks of organ cryopreservation—the freezing of live tissue for storage and subsequent use—and our studies of frozen frogs and turtles are revealing the molecular mechanisms essential to life in a frozen state.

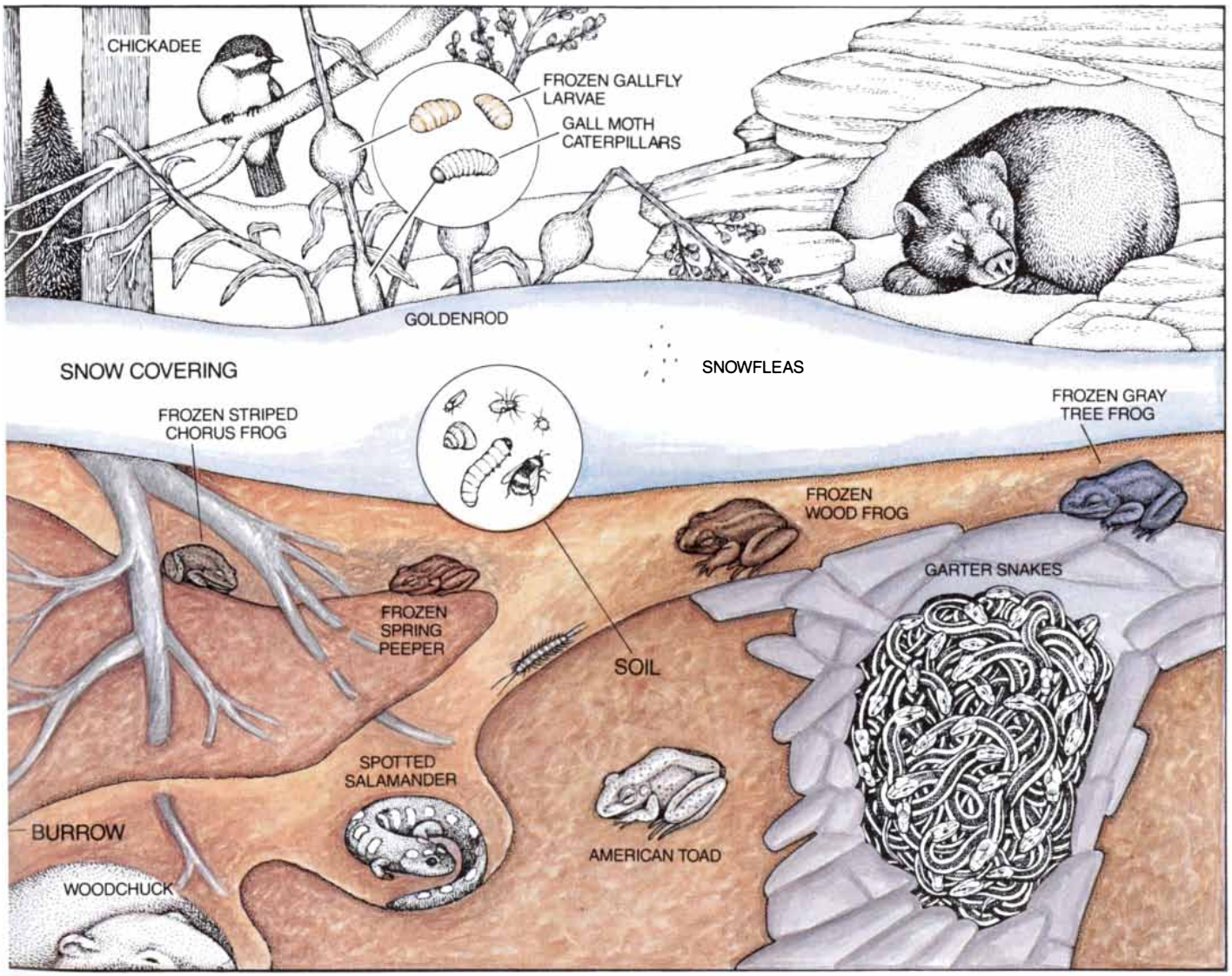
Spending the winter frozen seems to be an incredibly dangerous adaptive strategy—freezing is lethal for most cells. As any gardener knows, the first hard frost will transform a lush autumn flower bed into a pile of brown mush. Ice crystals rip through cell membranes and damage subcellular organelles; cell contents spill out, and the discrete localization of individual metabolic processes within the cell becomes scrambled. And even if ice formation can be controlled, freezing stresses cells in other ways. For example, because freezing halts breathing and blood circulation, all organs are cut off from access to oxygen and blood-borne fuels for the duration of the freeze. Instead of tolerating the frozen state, are there not easier ways for cold-blooded animals to deal with subzero temperatures?

In fact, two alternatives exist. The first—and most familiar—strategy is to avoid exposure to temperatures below the freezing point of body fluids. Animals simply "choose" relatively warm hibernation sites under water or deep underground. Numerous insect species overwinter as aquatic larvae, and many types of frogs and turtles hibernate at the bottom of ponds, where they are safe unless the body of water freezes completely. On land, toads may dig into the earth to remain below the frost line, and snakes may congregate in underground communal dens.

The second alternative to freezing is to use specific adaptations that stabilize the liquid state at subzero temperatures. All water solutions, including body fluids, have an equilibrium freezing point, or the temperature at which an ice crystal placed in the solution will begin to grow. But all water solutions can also be supercooled—that is, they can be chilled well below the equilibrium freezing point before the water crystallizes spontaneously into ice. Human plasma, for example, has a freezing point of –.8 degree C but, if chilled in a controlled manner, can be supercooled to –16 degrees C.

The presence of nucleators, however, limits the extent of supercooling. Nucleators are compounds that seed ice

STRATEGIES FOR WINTER SURVIVAL IN A TEMPERATE ZONE FOREST



growth by providing binding sites that can order water molecules into the ice-lattice structure. Ice itself is the best nucleator, but plasma proteins, foreign bacteria and food particles also act as effective nucleators. To stabilize the liquid state, then, animals must eliminate nucleators or prevent the nucleators from triggering widespread crystallization—in effect, animals must lower the supercooling point of their body fluids.

Arthur L. DeVries and his colleagues at the University of Illinois at Urbana-Champaign discovered that polar marine fish use such a strategy. The fish avoid freezing because they have antifreeze proteins in their body fluids. When embryonic ice crystals form within the fish, the proteins quickly bind to the crystal and effectively impede the further addition of water molecules to the crystal growth plane [see "Antarctic Fishes," by Joseph T. Eastman and Arthur L. DeVries; SCIENTIFIC AMERICAN, November, 1986]. Many terrestrial arthropods, including spiders, ticks, mites and numerous insects, have also developed antifreeze proteins. In many cases, insect antifreeze proteins are so potent that they can prevent ice formation at temperatures as low as –15 degrees C, enabling many insects to remain active under the winter snowpack.

Other insects require greater winter protection and have developed an additional antifreeze besides proteins to depress the supercooling point. These insects load their body fluids with an antifreeze made of low molecular weight polyhydroxy (sugar) alcohols. A solution of 50 percent ethylene glycol, providing protection to –30 degrees C, is the standard level of antifreeze added to the radiators of cars in southern Canada. By comparison, our studies of caterpillars of the gall moth (*Epiblema scudderiana*) found that they have body fluids that are about 40 percent glycerol in midwinter, representing an enormous 19 percent of the total body weight of the animal. This amount allows the insects to supercool to –38 degrees C.

Given that a variety of terrestrial animals can successfully avoid freezing by deep supercooling, it may seem odd that other animals have become tolerant to freezing, taking on the much more difficult job of regulating and surviving the freezing of body fluids. But avoiding freezing has its risks. The supercooled state is metastable, and the probability of spontaneous nucleation below the freezing point increases as the period of cooling lengthens and the temperature continues to drop. Cooling below the supercooling point or contact with nucleators (for example, as a result of injury to the skin) results in instant and lethal flash freezing. Many freeze-tolerant animals may have opted to forgo the probabilistic nature of supercooling in favor of a slow and controlled freezing that, if done properly, is readily survivable.

To some extent the rationale for "choosing" to freeze rather than to supercool is lost in the evolutionary history of each species. For instance, the gall moth caterpillars that we study share their winter home on goldenrod stems with larvae of the gallfly (*Eurosta solidaginis*). The caterpillars supercool and avoid freezing, but the gallfly larvae freeze when temperatures drop below about –8 degrees C. Both experience the same winter weather conditions but use opposite strategies to survive.

We have no good answer to this dichotomy except the following obvious observation: one species has evolved mechanisms to avoid freezing, the other to tolerate it. The gall moth caterpillars succeeded in eliminating internal nucleators from their bodies, spun a waterproof cocoon to prevent seeding by environmental ice and then perfected the supercooling strategy. In contrast, the gallfly larvae cannot or do not block the action of nucleators and have perfected ways to tolerate freezing instead.

How, then, do animals such as the gallfly larvae survive freezing? We noted earlier that ice crystals can cause extensive physical damage to the internal structure of cells as well as to the greater organization of connections between cells or the integrity of capillaries. Indeed, the destruction caused by ice inside cells is so massive that even freeze-tolerant animals do not survive intracellular ice. The same is true, for all practical purposes, for all types of mammalian cells and tissues that have been successfully cryopreserved to date. Freeze tolerance in nature consequently means a tolerance for ice growth in extracellular fluid spaces coupled with mechanisms that keep the cytoplasm liquid.

To survive freezing, animals must use specific biochemical adaptations that satisfy three basic conditions. The first condition is that ice formation must be controlled. Ice growth must be initiated in extracellular fluids (for example, blood plasma, abdominal fluid and urine) in a way that keeps the rate of freezing slow and the size of the crystals small. To accomplish these tasks, freeze-tolerant animals add specific nucleating agents to their extracellular fluids. By providing binding sites that order water molecules into an ice-lattice structure, the nucleating agents stimulate crystallization and enable it to occur more easily.

Biological nucleators in freeze-tolerant animals are most often specific blood proteins (called ice-nucleating proteins) that are synthesized during the autumn months. The regulation of their production probably comes from the same types of photoperiod cues and hormonal stimulation that control the synthesis of antifreeze proteins in insects that avoid freezing. Ice-nucleating proteins seed ice formation, generally initiating crystallization at a temperature less than two degrees C below the freezing point of body fluids.

Such a process minimizes the extent of supercooling, so that freezing becomes a relatively slow and controlled event that allows plenty of time for cells to adjust both physically and metabolically during the transition to the frozen state. Our studies of ice-nucleating proteins in the blood of wood frogs (done in collaboration with Jan P. Wolanczyk and John G. Baust of the State University of New York at Binghamton) have shown that these proteins are quite potent. As little as .5 percent by volume of frog blood added to human plasma effectively raises the nucleation temperature of the plasma by seven degrees C.

The action of ice-nucleating proteins ensures that the initial freezing process results in the dispersal of thousands of small ice crystals throughout the extracellular spaces of the animal. Small ice crystals, however, are thermodynamically unstable, and they tend to re-form over time into larger and larger crystals, much as sizable ice crystals appear in ice cream kept too long after opening. For animals, such recrystallization could do physical damage, especially in delicate spaces such as the lumina of capillaries; therefore, freeze-tolerant animals require a mechanism that controls the size of ice crystals.

John G. Duman and his colleagues at the University of Notre Dame identified such a mechanism. They noted the puzzling presence of both ice-nucleating and antifreeze proteins, which apparently perform opposite functions, in freeze-tolerant insects. Experiments soon showed, however, that the same molecular actions that enabled antifreeze proteins to block the growth of embryo ice crystals were equally effective in blocking the recrystallization of existing crystals. Together, then, the two proteins control ice structure: ice-nucleating proteins seed the formation of extracellular ice, and antifreeze pro-

teins stabilize the ice crystals at a small, harmless size.

The second condition for freezing survival involves the protection of cell structure and function. The semipermeable cell membrane, which separates the extracellular and intracellular compartments, allows the free passage of water and some solutes but restricts movement of other compounds. So when ice forms outside cells, it immediately changes the water and solute balance inside cells.

Ice is a crystal of pure water, and as extracellular ice forms, it excludes from its structure solutes such as salts, sugars and proteins. Thus, the remaining extracellular fluid becomes more and more concentrated. This process places osmotic stress on the cell because the total concentration of solutes on either side of the cell membrane must always balance. In response to such stress, water flows out of the cells, and the solutes move in. The process stops when the concentration of solutes becomes great enough to prevent the further loss of water into ice.

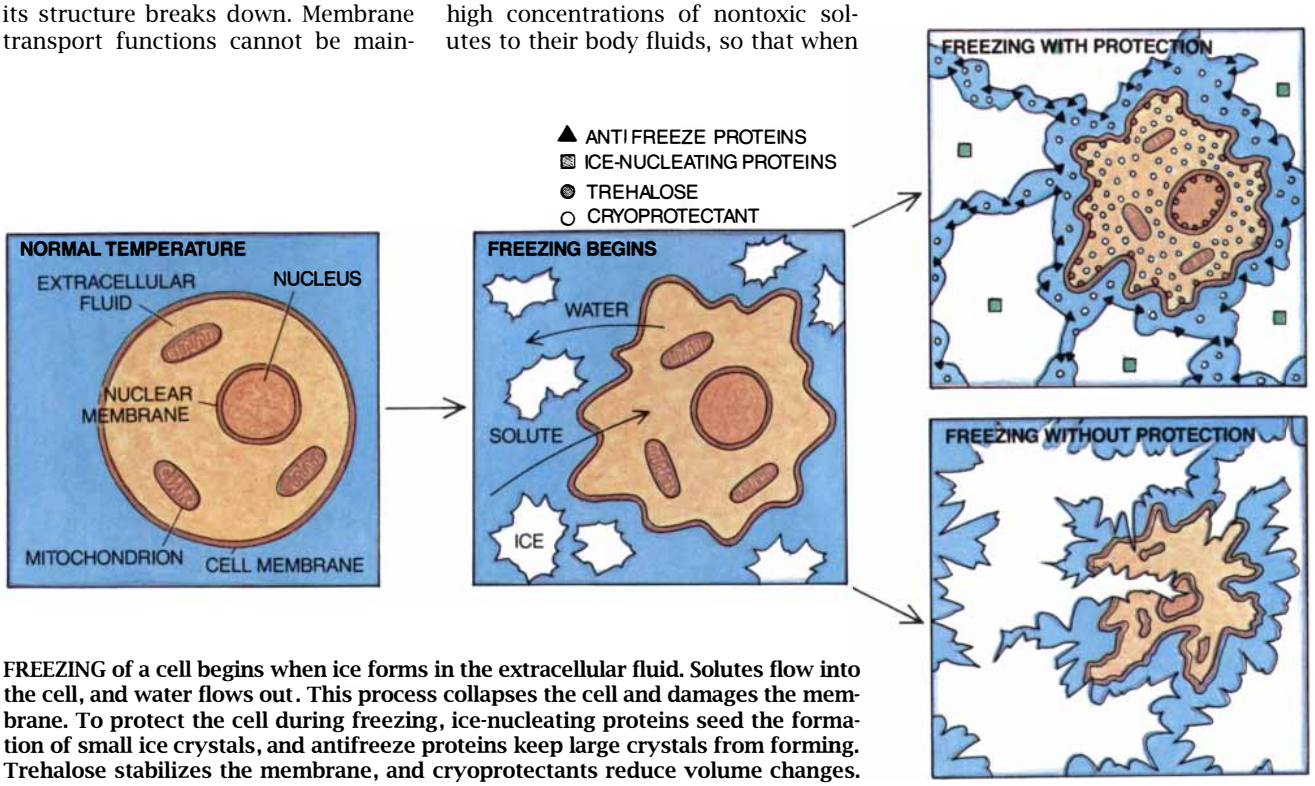
The most serious injury that can potentially occur during freezing is to the cell membrane. The outflow of cell water caused by extracellular ice formation rapidly reduces cell volume, and the cell membrane collapses inward. If the cell volume falls below a critical minimum, then the bilayer of phospholipids in the membrane becomes so greatly compressed that its structure breaks down. Membrane transport functions cannot be maintained, and breaks in the membrane spill cell contents and provide a gate for ice to propagate into the cell. Most freeze-tolerant animals reach the critical minimum cell volume when about 65 percent of total body water is sequestered as ice.

To counter these stresses on cell structure, freeze-tolerant animals use both membrane and colligative cryoprotectants—low molecular weight compounds that in various ways prevent the injuries that would result from massive cell volume changes during freezing. Membrane cryoprotectants interact with the membrane phospholipids to spread the bilayer and stabilize membrane structure as the cell volume collapses. Trehalose, a disaccharide, and proline, an amino acid, are the natural compounds known to perform this function. Not surprisingly, freeze-tolerant animals such as the gallfly larvae accumulate substantial amounts of both compounds during the autumn months prior to their first exposure to freezing temperatures.

Colligative cryoprotectants help to limit by osmotic action both the amount of ice that can form and the degree to which cells lose water and hence the extent to which cell volume decreases during freezing. The higher the concentration of solutes in a fluid, the less ice forms at any given temperature and the lower an animal's temperature can be pushed before the lethal 65 percent ice content is reached. Therefore, freeze-tolerant animals add high concentrations of nontoxic solutes to their body fluids, so that when extracellular freezing occurs the resulting reduction of cell volume can be minimized.

For this purpose freeze-tolerant insects use the same polyhydroxy alcohols that freeze-avoiding species use for antifreeze protection. Gallfly larvae build up a huge reserve of carbohydrate in their fat body (the insect equivalent of a liver) during the final weeks of summer feeding. During the autumn months this stored glycogen, making up about 8 to 12 percent of the total body weight of the larvae, is completely converted into two polyhydroxy alcohols: glycerol and sorbitol.

Key enzymes involved in the synthesis of these compounds respond uniquely to low temperatures. Whereas the activity of most enzymes and other metabolic processes lessens with decreasing temperature, temperatures between zero and five degrees C actually raise the activity of an enzyme called glycogen phosphorylase by stimulating it to convert from its inactive to its active form (the enzyme chops hexose sugar units off glycogen to begin synthesis). In addition, low temperatures inactivate other enzymes, resulting in a redirection of the flow of carbon from the normal routes of carbohydrate catabolism (used to produce cellular energy) to special pathways that lead to cryoprotectant syn-



FREEZING of a cell begins when ice forms in the extracellular fluid. Solutes flow into the cell, and water flows out. This process collapses the cell and damages the membrane. To protect the cell during freezing, ice-nucleating proteins seed the formation of small ice crystals, and antifreeze proteins keep large crystals from forming. Trehalose stabilizes the membrane, and cryoprotectants reduce volume changes.

thesis. Cryoprotectants persist throughout the winter, and then as spring begins they are converted back into sugars to fuel the continued development of the insects through the pupal and adult stages.

Glycerol, sorbitol and related compounds represent excellent choices of cryoprotectant in biochemical terms. Not only do these compounds provide the osmotic actions needed to regulate cell volume during freezing, but they also remain nontoxic to cells even at very high concentrations. They do not crystallize spontaneously from aqueous solutions at low temperature, and they pass freely across membranes. In addition, these polyhydroxy alcohols stabilize the structure of proteins and enzymes and protect them from the denaturing effects of low or freezing temperatures.

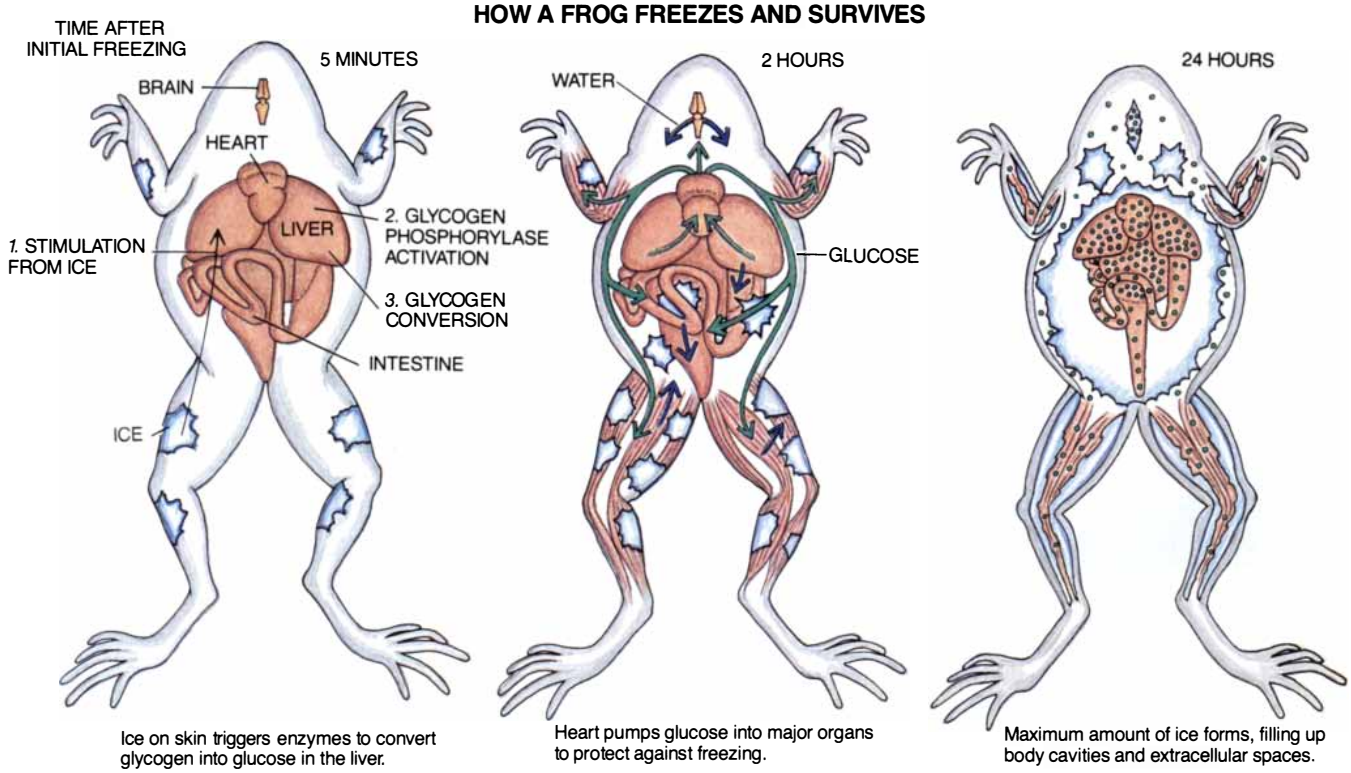
Our studies of freeze-tolerant frogs have revealed a system unlike the one insects employ. Frogs use a different cryoprotectant and an unusual way of triggering its synthesis. Wood frogs, spring peepers and striped chorus frogs all accumulate massive quantities of glucose, the normal blood sugar of vertebrate animals, during freezing episodes (gray tree frogs use glycerol). Whereas human blood has a normal glucose content of about 50 to 100 milligrams per 100 milliliters (in diabetics, glucose levels may be three to four times higher), wood frogs after freezing have blood glucose levels that average 4,500 milligrams per 100 milliliters. All the organs of the frog body also contain glucose in concentrations that seem optimal for the protection of each organ.

But frogs do not gradually build up cryoprotectant pools over the autumn months as insects do. Instead they wait until actual freezing begins on their skin surface. Ice on the skin triggers a hormonal or nervous response that instantly activates glycogen breakdown in the liver, flooding glucose into the blood. Indeed, we have detected rising blood glucose levels within as little as five minutes after initial ice formation, and organs become well packed with glucose in less than eight hours—well before the approximately 24 hours required to reach maximum survivable levels of ice in the body. The rapid synthesis of cryoprotectant during freezing, and the similarly rapid reconversion to liver glycogen when the frogs thaw, may be the key to circumventing various negative effects of sustained high glucose levels that are associated in humans with, for example, diabetes or the aging process.

But if high levels of glucose can be damaging, why do frogs use the sugar for cryoprotection? One reason is that glucose can be produced quickly from liver glycogen. Cryoprotectant synthesis in frogs appears to be an extreme exaggeration of the adrenaline-mediated "fight or flight" response that occurs in all vertebrate animals and that rapidly increases blood glucose during stress. Indeed, compounds that block the action of adrenaline on the liver, such as propranolol, also effectively block the synthesis of glucose by the frog liver during freezing.

Our studies with heart strips and liver cells from the wood frog, however, suggest a more crucial reason for the choice of glucose: the sugar has specific, beneficial effects for the cryopreservation of vertebrate organs. For example, ventricle strips regained their ability to contract after thawing if they were frozen in the presence of high glucose levels but not if they were frozen in an equivalent concentration of glycerol. Because both glucose and glycerol should provide the same osmotic effects to control the decrease in cell volume during freezing, the superiority of glucose must result from other specific actions that aid cell survival.

One of these actions may be the use of glucose as a fuel to provide adenosine triphosphate (ATP) energy in cells that have no access to blood-borne oxygen while frozen. In addition, we have observed that high levels of glucose (but not glycerol) can depress the biosynthesis of urea in the frog liver. This evidence suggests that high glucose levels may help arrest the metabolism of frozen organs, limiting cellular ener-



gy needs and thereby enhancing long-term survival.

The third and final condition to surviving freezing is the maintenance of cell viability. Although the low body temperature of frozen animals automatically lowers their metabolic rate, the cells of freeze-tolerant animals must have a well-developed ability to survive without oxygen, without access to blood-borne fuels and without being poisoned by a buildup of the metabolic end products that are normally carried away by the blood. A human brain can survive perhaps three minutes of interrupted blood flow before tissue necrosis begins; a kidney or heart removed for transplantation can be stored for about six to 12 hours if packed in ice. But in our laboratory we routinely revive wood frogs after one to two weeks of constant freezing.

Such animals must continue to generate cellular energy in the absence of oxygen. We found that frozen gallfly larvae showed no disruption at all of their cellular levels of ATP when frozen for one week, and energetics in frog organs remained stable over at least three days of freezing. Even when ATP levels fell during prolonged freezing, both gallfly larvae and frogs could rapidly restore cellular energy levels after thawing. Consequently, freeze-tolerant animals can survive without oxygen for long periods. They have mechanisms for generating sufficient ATP from the fermentation of glycogen or glucose, and all organs tolerate quite well the prolonged periods of low energy levels.

The metabolic arrest that occurs during freezing may also figure highly in subsequent recovery. The ability to reduce metabolic rate greatly, frequently to as low as 1 to 10 percent of the normal resting rate, is a key adaptive strategy used by many animals to survive environmental extremes. A tenfold drop in metabolic rate, for instance, gains for the animals a tenfold extension of the time that a fixed store of body fuels can sustain life. The most familiar example is mammalian hibernation: by entering a dormant state and dropping body temperature to near zero degrees C, small mammals can save up to 88 percent of the energy that would otherwise be expended for winter survival. Numerous insects overwinter in diapause (a state of arrested development), and turtles hibernating at the bottom of ponds drop their metabolic rate to survive the whole winter without breathing. For freeze-tolerant species, then, the ability to lower their metabolic rate while frozen can greatly enhance the prospects for long-term survival.

GRAY TREE FROG (*left*) freezes beneath the winter snowpack, where temperatures fall to –8 degrees Celsius. Its skin pigments turn blue in the frozen state (*right*).

To us, the adaptive strategies that animals use to survive freezing are marvelous in themselves, but we are always asked about the application of our studies to medical cryopreservation, particularly for organs used in transplants. The first successful cryopreservation occurred in 1949, when sperm were revived after having been frozen in a glycerol solution. Since then, techniques have been developed for freezing many single-cell suspensions (sperm, red and white blood cells, platelets) and simple tissues (embryos, skin, cornea, pancreatic islets).

Physical problems remain, however, for complex tissues, and researchers do not yet have adequate technology to restore a functional organ after freezing. Obstacles to organ freezing include the difficulty of evenly chilling or warming a large organ mass to prevent physical damage by ice and the problem of infusing or removing large amounts of cryoprotectants from cells that are not naturally adapted to dealing well with major osmotic stresses. Furthermore, metabolic problems exist. Unnatural cryoprotectants (such as the commonly used dimethyl sulfoxide) offer excellent physical protection but have toxic effects on cell metabolism. In addition, metabolic decay occurs within minutes after an organ is removed from its blood-oxygen supply, and the chilling process further damages mammalian organs that are not designed to function at temperatures far lower than their normal 37 degrees C.

But the injuries caused by freezing and the principles of circumventing them are the same in cryopreservation as in natural freeze tolerance, and some answers are identical. For instance, glycerol and other low molecular weight alcohols and carbohydrates are commonly used for medical cryopreservation because they are relatively nontoxic and can move rapidly across membranes. Workers also lower the temperature in stages to trigger extracellular nucleation at a mild subzero temperature and to avoid spontaneous crystallization in a supercooled cytoplasm. Some of the newest studies in the field are investigating whether membrane stabilizers or metabolic inhibitors (which impose metabolic arrest by inhibiting ATP-using processes) can improve survival during freezing.

Our studies suggest additional approaches. Synthetic compounds that mimic the actions of ice-nucleating or antifreeze proteins could be developed to regulate extracellular ice formation more effectively, and a careful choice of cryoprotectant (such as glucose) could provide both physical and metabolic protection during freezing. Research should also examine other metabolic arrest strategies to preserve the viability of an organ while frozen. We are beginning to test these ideas by comparing freezing survival in wood frog and rat tissues. We already know some secrets of freeze tolerance; we hope to continue to unravel more.

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The Emergence of Modern Humans

The theory that all humans are descended from a recent African ancestor was promoted by geneticists who study living populations. The fossil record provides independent support for this model

by Christopher B. Stringer

In the 1970s a series of extraordinary anthropological finds in East Africa transformed the scholarly understanding of early human evolution and quickly captured the public imagination. The media followed each step in the dramatic discoveries of extremely ancient hominid remains, such as the Kenyan fossils attributed to the early human species *Homo habilis* and *Homo erectus,* the Tanzanian footprints dated to 3.7 million years ago and the Ethiopian bones of "Lucy" and her fellow australopithecenes.

The same period saw the beginning of another revolution in human paleontology whose import is only now becoming generally known. This quiet revolution concerns the latest phase in human origins—the emergence of people like you and me, our species, *Homo sapiens,* with its widespread varieties of physique and color.

At the heart of the matter lies the question of how special are modern humans. Did our small-browed skull and lightly built skeleton develop in unique circumstances in a single localized ancestral population, or were they the culmination of ancient evolutionary trends inexorably leading to the appearance of modern humans throughout the world? The controversy is likely to continue for several more years, as the latest evidence is tossed back and forth among the opposing schools of thought. It is clear, however, that the debate will center on the pattern of evolution of geographic variants—commonly called races—of *H. sapiens*. Three main theories can be distinguished.

The multiregional model holds that racial features evolved over very long periods in the regions where they are found today, except when comparatively recent migrations occurred. Such an exception is found in North America, where Amerindians, Inuit, Europeans and Africans in turn brought their distinctive features with them during the past 20,000 years. The multiregional model has been advanced by a number of paleoanthropologists over the years and is now championed by Milford H. Wolpoff of the University of Michigan at Ann Arbor and by some geneticists, such as James N. Spuhler of Los Alamos National Laboratory.

If this account is correct, then the features generally described as racial must be very old indeed. The large noses of Europeans and the robust cheekbones of Australian aborigines, for example, would derive, respectively, from the Neanderthals, who lived in Europe for at least the 200,000-year period that ended about 30,000 years ago, and Java Man, a variety of *H. erectus* who lived on the Indonesian island of Java about 700,000 years ago.

The out-of-Africa model proposes that a racially undifferentiated stock of modern humans evolved in Africa and spread throughout the world, developing racial features in the process. This hypothesis, propounded by a group of geneticists led by Allan C. Wilson of the University of California at Berkeley, implies that archaic lineages, such as the European Neanderthals and the East Asian Solo Man (a probable local descendant of Java Man who lived about 100,000 years ago), mixed little or not at all with early modern humans but were replaced by them.

The gene-flow, or hybridization, model traces modern populations back to a web of ancient lineages whose genetic contributions varied from region to region, the rate of intermixture perhaps gradually increasing as modern humans evolved. Proponents of this view, who include Erik Trinkaus of the University of New Mexico and Fred H. Smith of Northern Illinois University, regard present-day genetic and fossil samples as still inadequate to resolve such a complex pattern of origin.

Although all the models predict that modern characteristics evolved late and that racial characteristics evolved locally, they disagree fundamentally in the timing of racial differentiation. In the multiregional and gene-flow models, racial features preceded the appearance of modern ones, whereas the African model reverses the order.

Recent discoveries appear to have raised the pitch of the debate without resolving it, yet certain points already seem settled, and others offer the hope of rapid progress. I shall highlight both the promise and the difficulties of interpreting the two bodies of evidence concerning the emergence of modern humans—that of the paleontologists and that of the geneticists. Paleontologists study the external evidence manifested in bones and teeth of the fossil record; geneticists rely on the evidence internal to living cells. I believe

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THE RACES constitute regional variants whose origins must be explained by theories of the evolution of modern humans. Here the races are traced to Noah's sons, Ham, Shem and Japheth, in a French illustration from the 1940s.

the order presented in the African model gives the best account of the facts deduced by both groups of workers. Let us first look at the contributions of the geneticists.

Geneticists began studying the history of genes by reference to features (such as eye color) or proteins (such as blood groups) that the genes encode, but new techniques have made it practical to analyze the code on the DNA itself. In animal cells, DNA resides in the nucleus (nDNA), where it controls most aspects of organismal structure, or phenotype, and in the tiny organelles called mitochondria, which convert glucose into a more readily usable form of energy. The mitochondrial DNA (mtDNA) may be a vestige of a free-living phase in the organelle's history, one that is thought to have preceded a symbiosis that formed modern cells [see "Symbiosis and Evolution," by Lynn Margulis; SCIENTIFIC AMERICAN, August, 1971].

For our purposes, the major difference between the two kinds of DNA lies in their modes of inheritance. Nuclear genes are inherited from both mother and father and are shuffled at random in sexual reproduction; that is why children are not identical to one parent or the other. Mitochondrial genes, however, are handed down by the mother alone. Alterations can be ascribed to copying mistakes, or mutations, in the DNA, and such mutations occur much more frequently in mtDNA than in nDNA. These features make mitochondrial genes by far the simpler to track through the generations and to use as a molecular clock (one, however, that shows only part of the organism's genetic history). Such a clock could assign a date to every branching point on the genealogical tree.

But molecular clocks can be reliable only if two assumptions hold true: the genetic similarities of organisms must be a function of their relatedness and directly proportional to the recency of their divergence from a common ancestor. Both conditions require that the genetic material under study mutate at a constant rate and that the mutations neither be culled nor favored by natural selection. Culling would tend to conserve a gene in its pristine state, so that the common ancestor seems much more recent than it really is. Selection for particular mutations would accelerate change, making divergence seem more ancient.

Fortunately, some portions of mtDNA appear to fit these requirements because, as one form of so-called junk DNA, they seem not to affect the phenotype at all. Yet another requirement for the development of a valid molecular clock is that the lineages should not have mixed significantly after they diverged. Otherwise they will seem to have split more recently than they did.

One attempts to make a molecular clock by comparing genetic differences among various species or varieties within species and expressing their re-

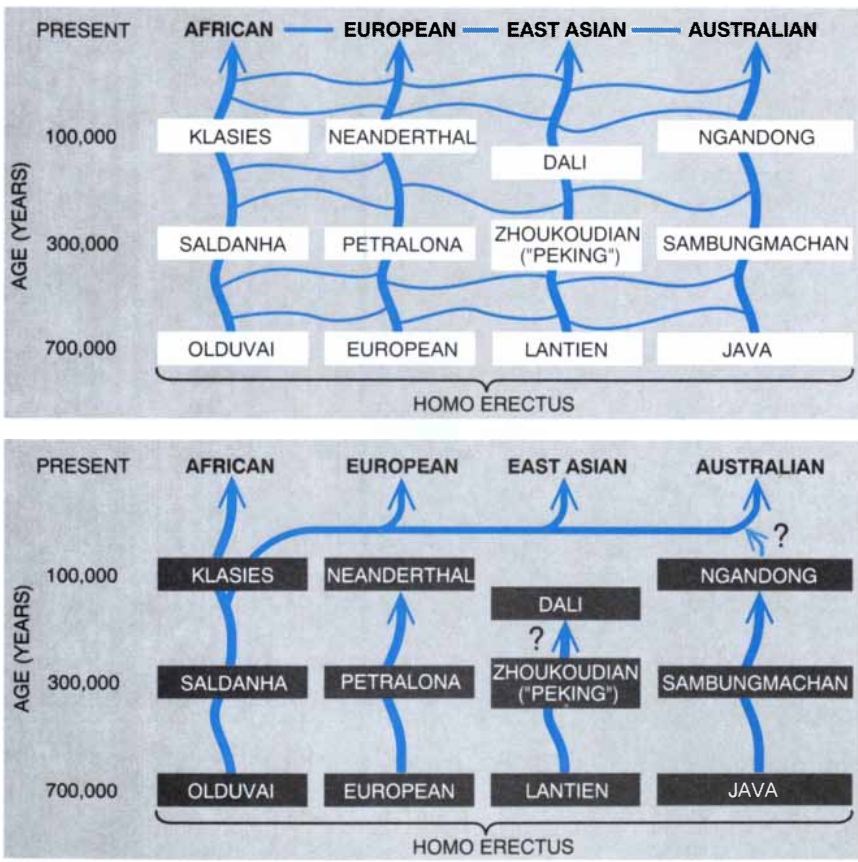
latedness in a tree. One then calibrates (or "dates") the tree by comparing it with another group that diverged from the tree at a known date. Calibration allows workers to assign dates to other divergences in the tree. It is important to remember that such trees are not necessarily true genealogies but rather groupings that reflect resemblances and differences among the populations in question. Evolutionary patterns are not demonstrated by the trees but must be inferred from them.

A number of genetic trees representing the relatedness of modern humans reflect two fundamental unities: sub-Saharan Africans and all other human populations. Calibration of genetic evolution from such trees can be problematic (a few would say impossible). Some experts contend that all the genetic differences found among living human beings could have developed in 100,000 to 200,000 years, whereas others argue for a much longer time scale on the grounds that gene flows among populations would have made their differences seem older than they really are.

It can be as difficult to locate a tree's ancestor in place as in time. An early study of human mtDNA, for example, could have been interpreted as favoring either Asia or Africa as the homeland of modern humans. If one prefers the continent whose population carries DNA types that are closest to the average for all populations, then Asia emerges as the likely homeland. In that case, the great genetic difference of the Khoisans (or Bushmen) would have to be explained as the result of a locally accelerated mutation rate.

If, on the other hand, one begins with the assumption that mtDNA mutates at a consistent rate throughout all human populations, then Africa gets the nod (and the greater differentiation of African populations makes sense). This conclusion can certainly be drawn from a subsequent mtDNA study, which used chimpanzees as an out-group to root humans in a more ancient and inclusive tree [*see illustration on opposite page*]. This, then, is the first item in support of African monogenesis.

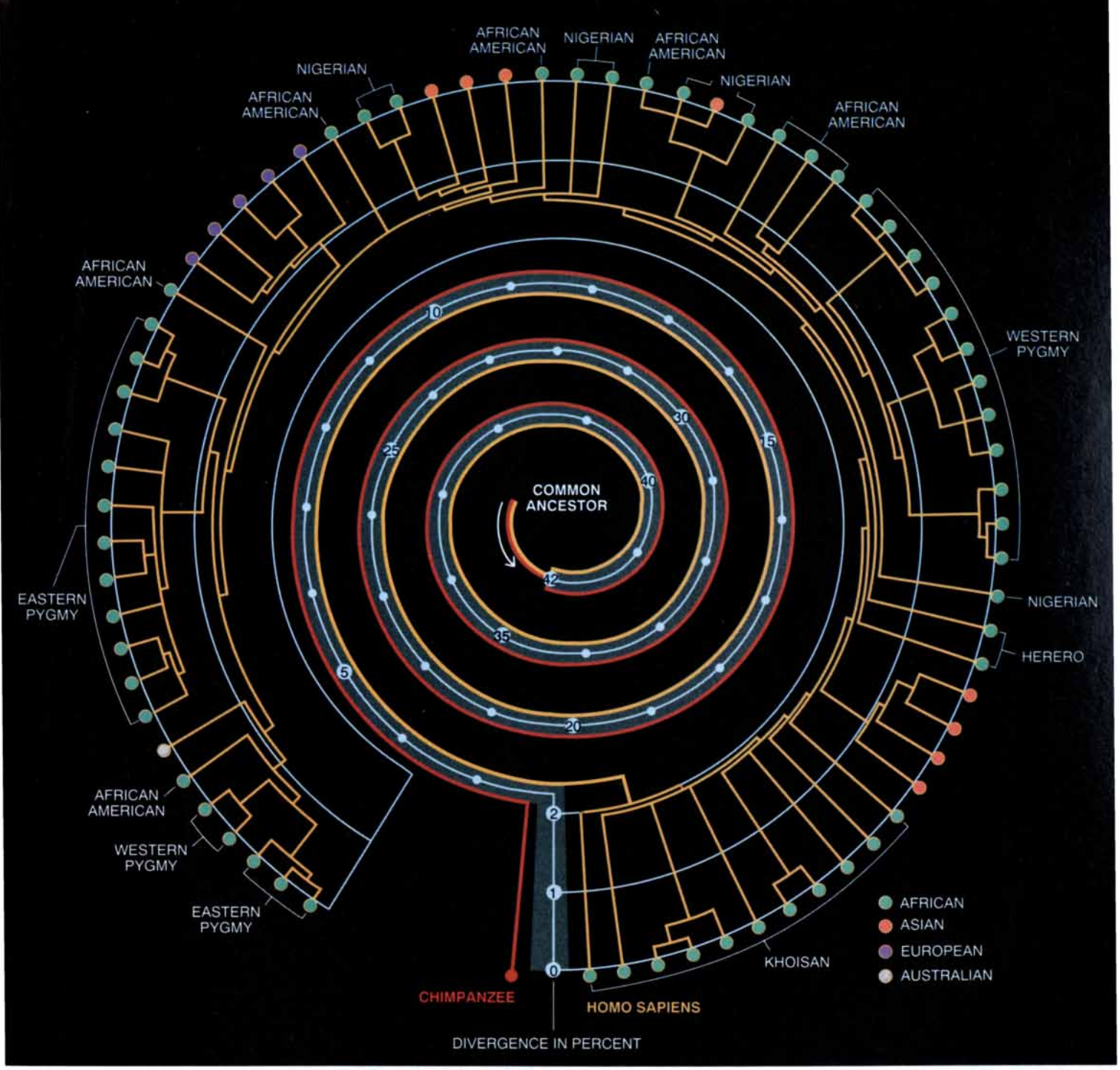
GENETIC DISTANCES among populations are charted according to mutations that have accumulated in a rapidly evolving segment of mitochondrial DNA. The diagram covers a worldwide sample of humans. A chimpanzee sample is included for reference (*red line*). The greatest intrahuman divergence, 2 percent, appears among Khoisans and other Africans. This measurement can be ascertained by tracing the yellow line that leads from the green circle closest to the bottom, representing one of the Khoisan samples, to the node that links it to other branches and comparing the distance with the index (*gray bar at the six o'clock position*). The human and chimpanzee lines split from a common ancestor about five million years ago, during which time they diverged by 42 percent (*center*). The chart is adapted from a study headed by Linda Vigilant at the University of California at Berkeley.



MULTIREGIONAL MODEL (*top*) argues that regional features were inherited from ancient hominids whose remains were found at sites in Africa, Europe, East Asia and Australasia. It attributes the unity of the modern species to inferred gene flows among contemporaneous populations (*horizontal lines*). The monogenesis model (*bottom*) holds that regional variants arose more recently, after modern humans emerged from Africa to replace other hominids without interbreeding, except perhaps in Australasia. The gene-flow (hybridization) model resembles the multiregional model but places the main gene flow in the more recent evolutionary stages.

Disagreement and simple misunderstanding have marked the controversy over the rate of mutation in mtDNA. Yet here, too, a reasonable resolution of the issue favors the monogenesis theory. Some workers have argued that the average rate of change, based on many different organisms, is about .7 percent (that is, about 115 mutations in the mtDNA molecule) per million years. Others have estimated the change at between 2 and 4 percent (or about 330 to 660 mutations) per million years. What is not always appreciated is that the two estimates are not measuring the same thing. The slower rate measures change along a given lineage; the faster measures cumulative changes between different lineages. The latter rate should therefore be twice the former. Additionally, some parts of the mtDNA molecule seem to evolve faster than others, and the faster rates of change are calculated mainly from these parts. Together these considerations account for much of the discrepancy between the two figures.

Such variations in rate constants can produce a difference of several hundred thousand years in the estimated date of a common ancestor of humanity. A slow or inconsistent rate could position the ancestor more than 500,000 years ago, during the time of *H. erectus*, whereas a faster, steadier rate would place the ancestor within the past 150,000 years, when modern *H. sapiens* probably already existed.

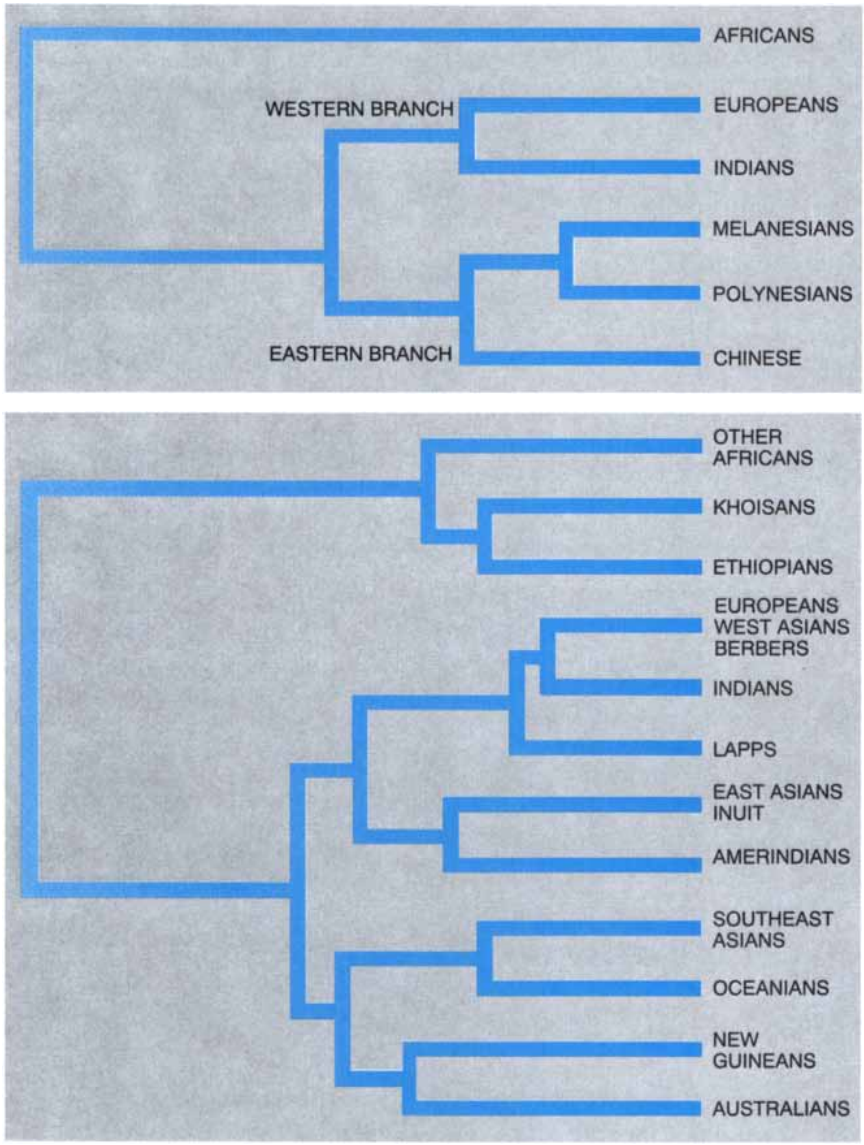


The more recent date seems preferable because it makes more evolutionary sense. If modern humans had begun differentiating during the time of *H. erectus,* some of their subgroups would have had to develop modern skeletal features independently of one another. Instead it seems more likely that the mtDNA tree reflects evolution within a gene pool of humans who already shared many modern-looking characteristics.

A further implication of the genetic reconstructions based on nuclear DNA is that modern Europeans, Asians and Australasians are more closely related to one another than to sub-Saharan Africans. This pattern is difficult to reconcile with the hominid fossil record from about 300,000 years ago, which shows a close relation between the populations of Europe and Africa on the one hand and China and Indonesia on the other. Moreover, differentiation increased so much that by about 100,000 years ago, hominid populations in each region looked quite different from one another: there were Neanderthals in Europe and western Asia, modern humans in Africa and western Asia, archaic hominids of uncertain affinities in China and peoples of the *H. erectus* type in Java. Yet we know that today's populations of Europe, Asia and Australia are quite closely related genetically and that the early modern populations that inhabited these areas 20,000 to 30,000 years ago also closely resembled one another.

I believe that these observations support the monogenesis hypothesis: modern demographic patterns most probably began with the dispersal of early modern humans from Africa within the past 100,000 years.

My evaluation of the fossil record 10 years ago supported the out-of-Africa



TREES OF RELATEDNESS derived from variations in nuclear DNA (*top*) and its products (*bottom*) give additional support to the theory of African origins. The top tree is adapted from a study led by Jeffrey C. Long of the University of New Mexico, the bottom from a study led by Luigi L. Cavalli-Sforza of Stanford University.

hypothesis. But this conclusion seemed speculative until recently, because radiocarbon techniques cannot reliably date materials older than 30,000 to 40,000 years. Now this impediment is slowly being overcome by the development and wider application of the uranium series (U-S), thermoluminescence (TL) and electron-spin resonance (ESR) techniques. The first method can be used on cave sediments such as stalagmites; the second on sediments or on flints that have been burned by ancient fires; and the third on a variety of materials, particularly animal teeth.

In each case, one assigns a date to hominid remains by determining the age of the materials with which the remains are associated. Although all three techniques have limitations, together they have confirmed that modern humans were present in the Middle East and Africa when Neanderthals still lived in Europe and western Asia and Solo Man probably still occupied Java.

Suspicions that this might be so had been provoked years earlier by the discovery of modern-looking fragments of skulls, jaws and limb bones in the caves at Klasies River Mouth and Border Cave, both in South Africa. In each site the remains were associated with artifacts from the African Middle Stone Age (the era between about 130,000 and 35,000 years ago). At Klasies, U-S and ESR dating recently placed the early Middle Stone Age levels and most of the hominids at more than 90,000 years ago. At Border Cave, the situation is complicated by the unsystematic excavation of the first two hominid finds. Several anthropologists have argued, however, that three fossils came from a level that ESR has since dated to about 75,000 years ago and that a fourth comes from a level now dated to about 60,000 years ago. Sites in Kenya, Ethiopia and Morocco have also yielded pieces of anatomically modern bones, which some workers say may be even older than those from South Africa.

More evidence that early modern humans did not evolve from later archaic populations comes from recent reinterpretations of findings in Israeli caves. It is instructive to review the history of scholarly opinion on these findings.

In the 1930s the caves of Skhul and Tabun on Mount Carmel produced partial human skeletons, probably the result of deliberate burials. Many theories were offered as to the populations represented in the two caves, but it gradually became accepted that Tabun had been inhabited by Neanderthals and Skhul by primitive-looking moderns. Between 1935 and 1975 an even larger sample of primitive moderns were excavated at Jebel Qafzeh near Nazareth, and more Neanderthals were found in caves at Kebara, also on Mount Carmel, and Amud near the Sea of Galilee. In the Middle East as in Europe, therefore, it was assumed that modern humans came after the Neanderthals and so may be descended from them.

This view was shattered in 1987–1988, when workers using TL and ESR dated a Neanderthal from Kebara to about 60,000 years ago (much as expected) but dated early modern humans at Qafzeh about 40,000 years earlier still. The new estimates suggested that two human lineages existed in the Middle East. One, leading from African or poorly known local ancestors to the people whose remains were found at Qafzeh, appeared to have given rise to fully modern humans. The other, Neanderthal line seemed to appear about 70,000 years ago, perhaps as the result of a migration from an increasingly glaciated Europe. The Neanderthals would then have occupied the area until modern humans took over again at the time of the Skhul people, perhaps 40,000 years ago.

The last word has not been said, for the most recent ESR measurements, made in 1988–1989, date mammal teeth from the levels of the human burials at Skhul and Tabun to about 100,000 and 120,000 years ago, respectively. The new dates seem to confirm the ear-

ly presence of modern humans but add the complication that early Neanderthals were apparently there, too. The Neanderthals (at Tabun) either immediately preceded the moderns of Qafzeh and Skhul after all or were their approximate contemporaries.

The revised dating schemes provide important supporting evidence that modern humans constitute a branch separate from the Neanderthals—a branch that evolved in Africa or the Middle East, or both. Moreover, if Neanderthals both preceded and succeeded early moderns in the Middle East, it would be more likely that the early moderns immigrated into that area from another place. Because the oldest-known records of modern humans are found in southern Africa and Israel and are dated to approximately 100,000 years ago, it is probable that a still earlier ancestral population had lived in an intermediate area, perhaps northern or eastern Africa.

The new dates also support the view of a minority of workers, including myself, who believe that Neanderthals may have constituted a separate species (*H. neanderthalensis*). Other evidence of a clear biological separation of Neanderthals and moderns is provided by the persistence of the two populations' separate identities over a long period. The Kebara Neanderthal may have lived 40,000 years after the two populations could have come into contact, yet this specimen shows no signs of hybridization with modern humans—in fact, it is one of the most robust and characteristic of Neanderthal skeletons. By the same token, early modern fossils from Israel and Lebanon dated to between 30,000 and 40,000 years ago show no features that might be ascribed to previous hybridization with Neanderthals.

Modern humans and Neanderthals therefore seem to be distinct lines that diverged from a common ancestor more than 200,000 years ago—the Neanderthals evolving in Europe, the moderns in Africa. The moderns' ultimate progenitors cannot yet be discerned in the fossil record, although various workers have proposed materials found in different parts of Africa. But these samples differ greatly from one another; some of them also seem to be too recent to have been actual ancestors of the earliest modern humans.

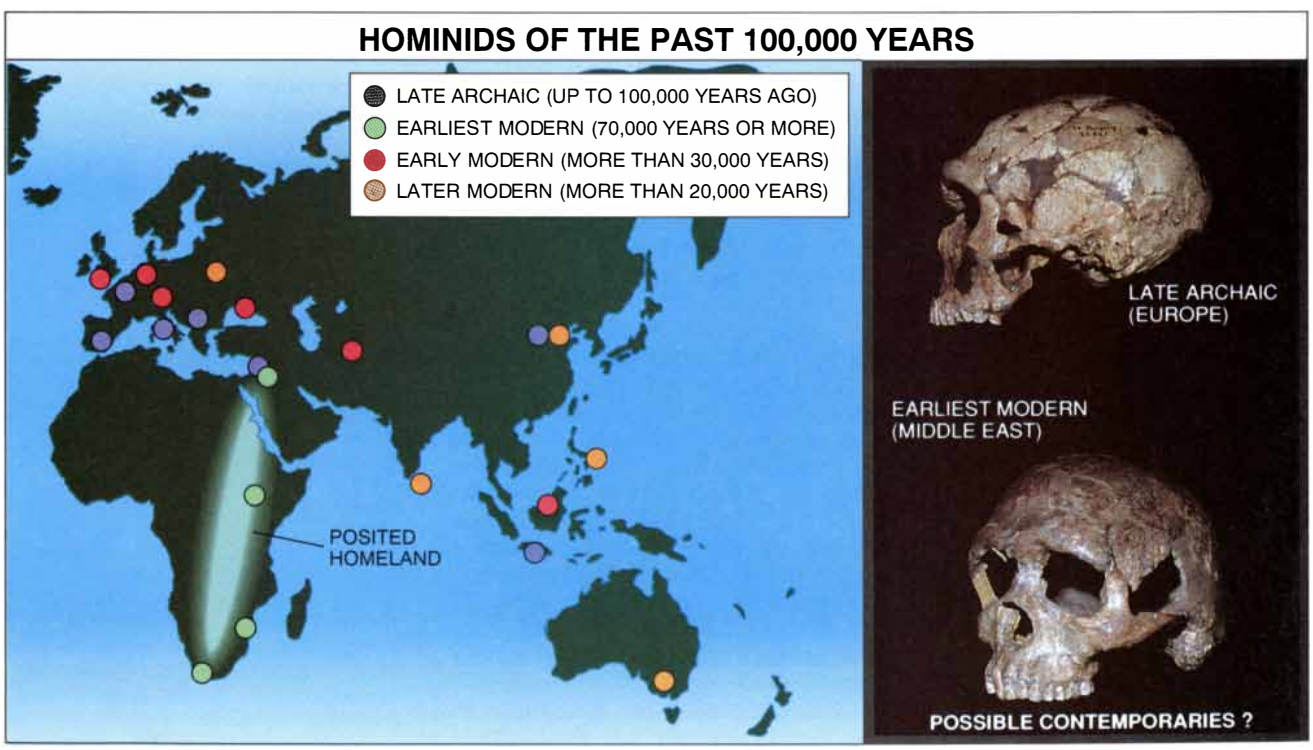
Recent advances on many fronts make this an exciting time for students of the emergence of modern humans. Some progress is being made in relating the evolution of the brain and vocal system to the emergence of cultures based on symbols and abstractions and in reconstructing aspects of the earliest languages. It is possible that we are in sight of a kind of unified theory that will bring together the fossil, archaeological, genetic and linguistic evidence bearing on the African monogenesis hypothesis. A number of questions must be answered, however, if this comprehensive synthesis is not to collapse like a house of cards. Here are some of the most important ones:

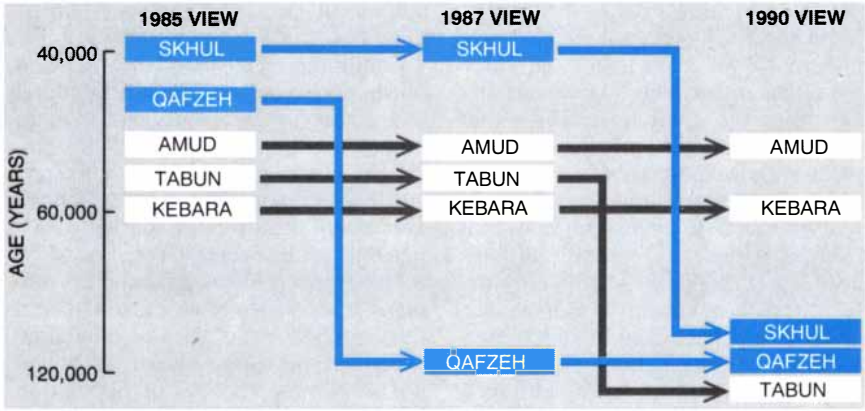
Conditions that existed in Africa and nowhere else must eventually be found to account for the evolution of modern humans on that continent. These conditions might have to do with ecology and human behavior, about which we know very little for this period in Africa (and many other places).

Proliferation of early modern humans from Africa to western Asia and thence to the rest of the world must be explained, perhaps by linking this exodus to climate changes or population growth, coupled with the humans' increasing adaptive abilities. The causes of proliferation must have been operating between 50,000 and 150,000 years ago, and these or additional factors must have persisted for as long as modern people continued to spread in the period up to 10,000 years ago.

Advantages of body, brain or behavior, perhaps associated with the emergence of modern language, need to be demonstrated to explain why the moderns replaced earlier hominids. One would like to know why the advantages took 70,000 years, by some estimates, to achieve this evolutionary success. Many archaeologists say there is no evidence that early moderns possessed any clear advantages and that their cultural sophistication developed only in the past 30,000 years, *after* they had replaced earlier hominid lines.

Interbreeding of archaic and early modern humans must be demonstrated or ruled out to resolve the clash be-





DATING REVOLUTION has upset the order traditionally assigned to the remains of early modern humans (*blue*) and Neanderthals (*white*) found in Middle Eastern caves. Until recently, paleoanthropologists had believed that moderns succeeded Neanderthals and thus may have evolved from them (*left*). Early results of thermoluminescence, electron-spin resonance and uranium series dating, however, placed moderns both before and after Neanderthals (*center*). The latest interpretation of the evidence suggests that the two groups may have been contemporaries (*right*).

tween the multiregional and hybridization models on the one hand and the African model on the other. In the most extreme statement of the African hypothesis—suggested by some interpretations of the mtDNA evidence—the replacement would have been total. Could one group of hunter-gatherers have replaced another throughout a whole continent without the slightest interbreeding? Some workers contend instead that there are signs of breeding between the last archaics and the earliest moderns in areas such as eastern Europe. Also, it is generally agreed, Neanderthals in western Europe changed long-established toolmaking techniques to parallel those of contemporary early moderns. Could they have learned from the newcomers or even have interbred with them?

There are serious problems here about the reliability with which the fossil record can be interpreted for signs of hybridization. Moreover, even if hybridization occurred, it could have been so localized that the genes of the hybrids might have been passed on to modern populations only at very low frequencies or not at all. In that case, one might discover fossils indicating hybridization even though modern genetic studies could find no trace of it.

Far Eastern evidence must also be reconciled with the emerging unified theory of human origins. Fossils discovered in China over the past 15 years appear to represent a line distinct both from the contemporaneous Neanderthals to the west and from such local predecessors as Peking Man (of circa 350,000 years ago). This putative line might provide an alternative to the African hypothesis or perhaps be linked with it to form a theory of dual African-Asian ancestry. Fossils from the same region dating to only 20,000 years ago tend, however, to reinforce the purely African theory because they seem to be from a time when specifically Asian features were still developing. If this judgment stands, then the features could not have been inherited from Peking Man.

Comparisons of modern dental variations show that features of the teeth of people in southeast Asia come closest of all to the average human condition. But, as in the case with the mtDNA work discussed earlier, the dental evidence cannot be taken as proof of an Asian homeland for modern humans. Asians would be expected to approach the mean in most respects if humans originated in Africa and spread first to Asia and then to Europe, Australasia and the Americas.

Australia poses particularly intractable problems because the remains of its early population show a marked diversity in appearance. It seems likely that the first Australians arrived about 50,000 years ago, having embarked from somewhere in southeast Asia. Yet the physical type of the earliest inhabitants is unknown. In any case, within 25,000 years some Australian skulls were built more lightly and others much more heavily than the vast majority of their early modern counterparts in Europe and Asia. The appearance of the robust varieties is especially perplexing, because it seems to contradict the global trend toward a more gracile skull.

One can explain the appearance of such wide differences in skull form—including that of the robust varieties—as the result of local microevolution caused by environmental or behavioral factors within Australia. Alternatively, some multiregionalists, such as Wolfpoff, attribute the variation to the influence of the Archaic Solo (Ngandong) people, whose remains have been found in Java. In this view, their interbreeding with early modern populations left vestiges in Australia and hence in the genes of living Australian aborigines. The success of the African-origins model depends on how these questions are resolved.

The next few years are likely to hold many surprises for paleoanthropologists and geneticists alike, as techniques of investigation improve. There is an emerging consensus that modern humans existed in Africa and the Middle East before they appeared in Europe and Australasia. There is also increasing agreement about the pattern of genetic relationships among modern populations, which favors an ultimate African origin, although the dating of such an origin is still controversial.

New fossils will come to light, and new information may be teased from bones, stones and genes. In the not too distant future it may even be possible to study DNA extracted from fossil human remains and to compare it with ancestral patterns now being reconstructed from the living. These and other as yet unavailable data from ancient times should one day allow workers to explain present discrepancies in the results found by those who study the living and those who study the ancient dead. Such breakthroughs in our knowledge will be necessary to reconstruct and understand the vast migrations that apparently intervened between the origin of modern humans and their conquest of the earth.

FURTHER READING

RECONSTRUCTION OF HUMAN EVOLUTION: BRINGING TOGETHER GENETIC, ARCHAEOLOGICAL, AND LINGUISTIC DATA. Luigi Luca Cavalli-Sforza, Alberto Piazza, Paolo Menozzi and Joanna Mountain in *Proceedings of the National Academy of Sciences,* Vol. 85, No. 16, pages 6002–6006; August, 1988.

THE HUMAN REVOLUTION: BEHAVIORAL AND BIOLOGICAL PERSPECTIVES ON THE ORIGINS OF MODERN HUMANS. Edited by Paul Mellars and Chris Stringer. Princeton University Press, 1989.

MITOCHONDRIAL DNA SEQUENCES IN SINGLE HAIRS FROM A SOUTHERN AFRICAN POPULATION. Linda Vigilant et al. in *Proceedings of the National Academy of Sciences,* Vol. 86, No. 23, pages 9350–9354; December, 1989.

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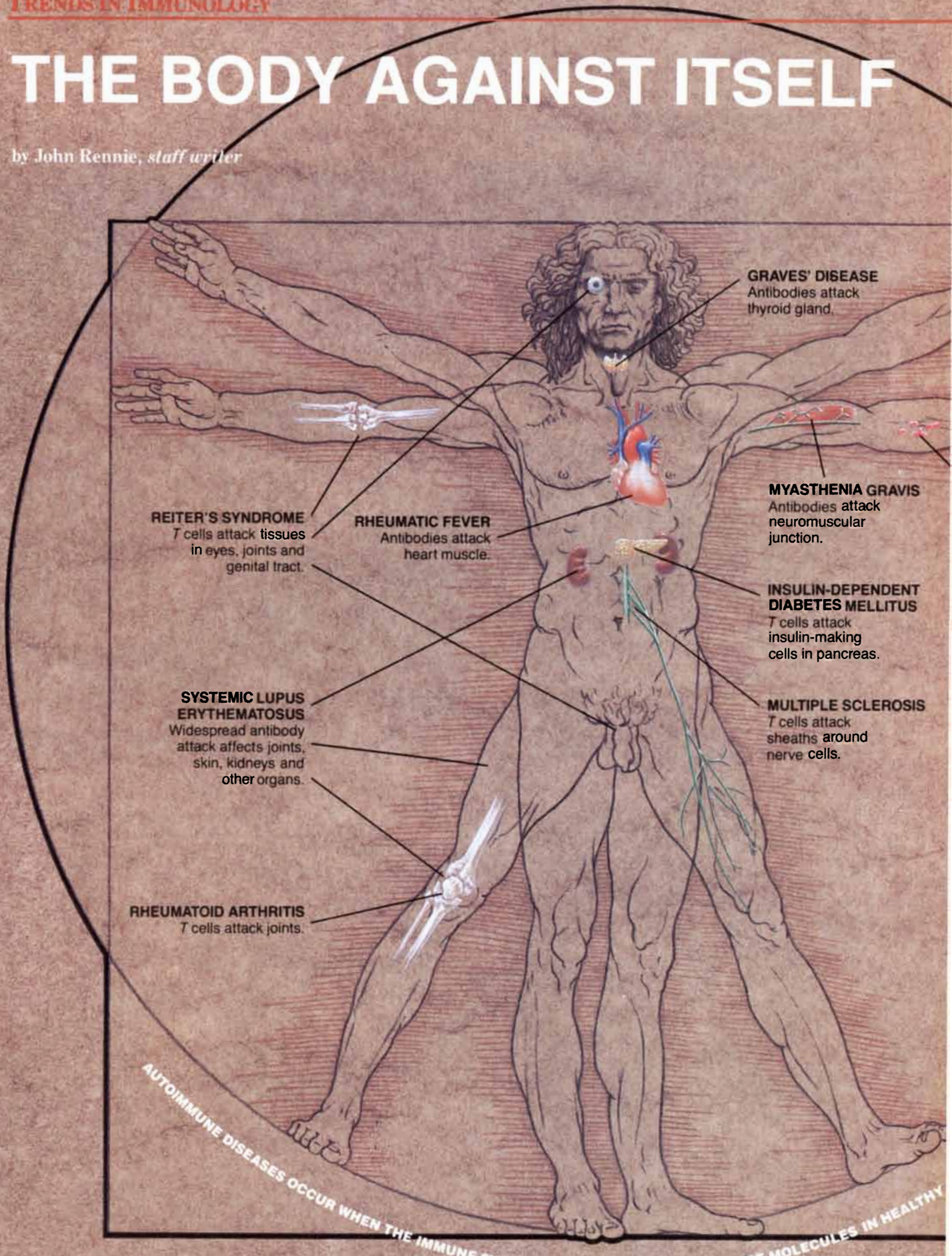
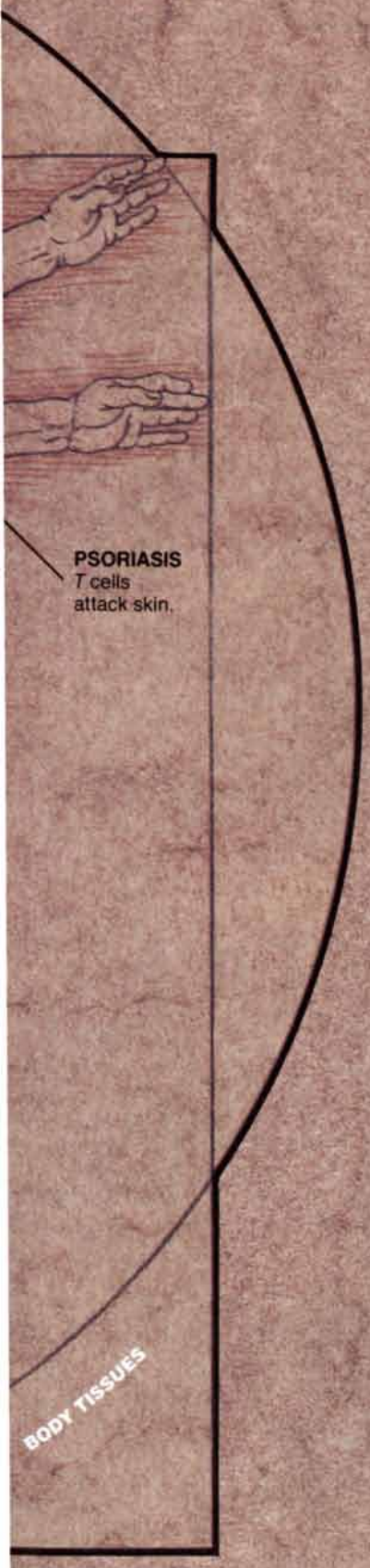
THE BODY AGAINST ITSELF

by John Rennie, *staff writer*



Better therapies for autoimmune diseases are on the horizon, but researchers are still split over how the immune system works.



Gleefully, immunologist David A. Hafler leads the way back to his laboratory to show off his cells. Spotlighted under the microscope, the golden cells in the bottom of the culture dish look tender and innocent. Nevertheless, Hafler explains, they react aggressively to substances in the fatty myelin sheath encasing nerve cells. "They go crazy when they see myelin basic protein," he boasts. At times Hafler sounds like a proud father, which is appropriate because the cells in the dish are literally his own: the originals came from his blood.

Their presence could have ominous overtones. Cells like those in Hafler's blood, called myelin-reactive *T* lymphocytes, are suspected of causing multiple sclerosis (MS), a degenerative condition that occurs when the body's immune system attacks the central nervous system. MS can sometimes blind, weaken or even paralyze its sufferers. Yet Hafler seems unconcerned.

To Hafler, the fact that he—and other healthy people—routinely harbor such cells without acquiring MS is a hopeful sign. He and his colleague Howard L. Weiner, head of the MS program at the Brigham and Women's Hospital in Boston, where Hafler works, believe that as yet unidentified suppressor cells and other mechanisms may allow the immune system to keep these potentially dangerous cells in check.

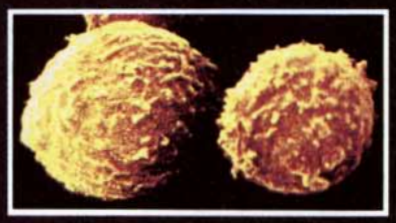
The Boston researchers are attempting to use those mechanisms to treat MS and other autoimmune diseases, in which a renegade immune system attacks the "self" of the body instead of the "nonself" of invading microorganisms. So far they have vaccinated a small group of MS patients with inactivated *T* cells. Their hope is that these inoculations will boost the patients' suppression reactions.

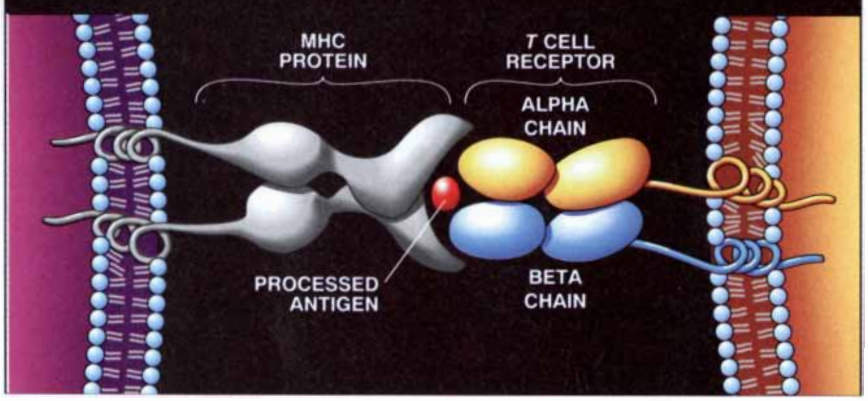
Hafler and Weiner are among a group of scientists pioneering better treatments for autoimmune diseases. Others are bringing to clinical trials a spectrum of tailor-made antibodies that seek and destroy troublesome cells. Still other therapies, at much earlier stages of development, involving special transplants and protein medications taken orally are being explored as well.

Aside from MS, many ailments are classified as autoimmune diseases: rheumatoid arthritis, insulin-dependent (Type I) diabetes mellitus and systemic lupus erythematosus, to name only a few of the most common ones. Ideally, a treatment for such diseases should safely and permanently restore a patient's tolerance for the besieged tissues. Current protocols have serious drawbacks. They usually involve anti-inflammatory drugs or general immune system suppressants, such as steroids and cyclosporine. Most of these drugs are expensive and their frequent side effects unpleasant. Moreover,

KILLERS AND THEIR HELPERS

T lymphocytes (*right*) destroy infected and foreign cells in the body and generally oversee most immunologic reactions—including many of the ones that cause autoimmune diseases. Cytotoxic ("killer") *T* cells attack their targets directly. Helper *T* cells produce a variety of substances that enhance the immune responses of the killer cells and other parts of the immune system. The *T* cell antigen receptor (*below*) is the key to the cells' activity. The receptor consists of one alpha-chain protein and one beta-chain protein. The receptor is fussy: it can bind only with a single type of antigen, which must be held by specific major histocompatibility (MHC) proteins on the surface of cells.





the harshness of these remedies often discourages physicians from prescribing them for patients in the early stages of autoimmunity, when they might do the most good.

The new strategies have great promise, but in some respects the clinicians are working in the dark. Many of the treatments are based on the presumption that some type of cell suppresses the self-reactive cells that cause autoimmune disease. Yet no one has been able to positively identify such a suppressor cell.

In fact, most immunologists, particularly those in the U.S., strongly doubt the validity of the suppressor cell theory. Instead they favor two alternative ideas that have accumulated a wealth of evidence from molecular biology—clonal deletion and clonal anergy. According to these theories, the immune system becomes tolerant of the body's molecules because mechanisms either eliminate self-reactive cells (deletion) or turn them off (anergy).

"Ten years ago most people thought all forms of self-tolerance were due to suppression," comments Harald von Boehmer, a senior researcher at the Basel Institute for Immunology, who was one of the first to prove that clonal deletion occurs. "But the suppressor cells could never be identified rigorously." Philippa Marrack, a clonal deletion pioneer at the National Jewish Center for Immunology and Respiratory Medicine in Denver, concurs: "All the basic experiments on suppression were done 10 years ago, and the story hasn't changed much since then."

Yet the advocates of some form of suppression are not giving up. They point to recent clinical and animal data as evidence that suppression is far from being an idea that has had its day. Irun R. Cohen of the Weizmann Institute of Science in Israel, a champion of suppression, insists that both clonal deletion and clonal anergy "leave much of what we know unexplained." He argues that the behavior of the immune system as an organized whole, and not just the biochemical activity of individual cells, is crucial to the understanding of autoimmune diseases. "Nobody wants to invoke 'behavior' when you can hang everything on a molecule, but I'm sorry—that's the nature of the beast," he contends.

Indeed, the theoretical controversy may turn out to be comparable to the story of the three blind men examining an elephant, in which each one pictures the animal differently. Immunologists asking questions about the molecular biology of self-tolerance find clonal deletion and clonal anergy, and those looking at the behavior of cells find suppression.

As with the elephant, all explanations may be at least partly true. And the clinical researchers, in any case, are not waiting for the debate to be resolved. In fact, a perfectly correct theory may not be essential for finding cures for autoimmunity. Ideas that are even partly right can point the way to successful approaches. As Judith Kapp, a suppression researcher at Washington University in St. Louis, remarks: "That's the way clinical medicine works. They don't always wait for the theories. Sometimes they develop a treatment, and we scurry around trying to figure out why it worked."

Birth of a Notion

If the U.S. has a central headquarters for research aimed at deciphering the why and how of autoimmune diseases, it resides in the smallest red-brick research building on the Bethesda, Md., campus of the National Institutes of Health. That building is the home of the National Institute of Allergy and Infectious Diseases (NIAID).

Sitting in his tidy office on the first floor, Ronald H. Schwartz, chief of the laboratory of cellular and molecular immunology, describes how the theories explaining the recognition of self and nonself have seesawed for decades. "During the 1930s and 1940s and 1950s, people were asking the right questions about self-tolerance," Schwartz explains. "But they weren't getting the right answers, probably because they didn't understand the basic system."

Even then immunologists knew that the blood and lymph contained protein molecules called antibodies that could recognize specific antigens, or molecular targets. They also suspected that white blood cells, such as lymphocytes and macrophages, played an important part in the immune response, probably by producing antibodies and ingesting bacteria. But no one knew precisely how the cells and antibodies in the immune system recognized antigens, let alone distinguished self-antigens from foreign ones.

The turning point came in 1955, when F. Macfarlane Burnet of the Walter and Eliza Hall Institute of Medical Research in Australia framed the hypothesis that eventually brought him the Nobel Prize. Burnet proposed that each lymphocyte could react with only one type of antigen but that the tremendous variety of lymphocytes randomly generated by the immune system provided coverage against every

conceivable antigen. He then suggested that immune responses depended on the selective multiplication of clones (genetically identical sets) of lymphocytes. When a cell encountered its antigen, it proliferated, thereby increasing the immune system's ability to attack that antigen in the future.

If the immune system produced cells against antigens randomly, it would inevitably make cells against self-antigens. Burnet pointed out, however, that if such a mechanism existed for deleting self-reactive clones, it could induce tolerance to self-antigens by, in effect, tearing a strategically placed hole in the body's natural defenses.

The great strengths of Burnet's so-called clonal selection hypothesis were its explanatory power and its simplicity. These traits became increasingly precious in subsequent decades because immunology soon became a field badly in need of simple, unifying ideas. The problem was that the closer experimenters looked at the immune system, the more complex and intricate it appeared.

Lymphocytes, immunologists realized, came in two varieties. Some were *B* cells, which matured in the bone marrow, recognized antigens in the blood and changed into antibody factories. Other lymphocytes were *T* cells, which matured in the thymus (a glandular organ above the heart in humans) and reacted only to antigens that protruded from the surfaces of infected or abnormal cells. Making matters worse, there were at least two types of *T* cells: cytotoxic, or "killer," cells that attacked infected tissues and helper cells that somehow promoted immune responses [*see box on opposite page*]. Because Burnet's theory imposed some order on this unruly mob of cells, it was welcome.

Yet proof of Burnet's idea that self-tolerance was caused by the deletion of *T* cell clones was slow in coming. To verify that cells against self-antigens were being deleted, immunologists needed to know the fate and antigen affinity of individual cells in the body—a feat far beyond the reach of biological techniques in the 1950s and 1960s.

Indeed, as Schwartz points out, the earliest tests of the clonal deletion explanation for tolerance were unsettlingly negative. Clinical immunologists began finding antibodies against normal body proteins, such as insulin, in the blood of healthy people. Several research groups injected radioactive self-antigens into animals and found that some antibodies and lymphocytes did react with them—a consternating sign that self-reactive cells had not been deleted. Obviously, some self-reactive cells were surviving, at least occasionally.

"Because the major theory had taken a blow on the chin," Schwartz comments, "the way was open for another view of tolerance. That began the era of suppression." In 1971 Richard K. Gershon, an immunologist at the Yale University School of Medicine, proposed the existence of specialized suppressor *T* cells that patrolled the body and subdued the responses of self-reactive cells. Hypothetical suppression networks were invented to explain how the multitudes of killer, helper and suppressor cells might carefully counterbalance one another. All immune responses—whether against self or nonself—were interpreted as disruptions of the normal cellular equilibrium.

Suppression reigned supreme until the biotechnology revolution of the late 1970s and early 1980s. Then suppressor cell theories suffered a more ringing defeat than clonal deletion had previously—and clonal deletion suddenly regained its prominence.

Three important methodological developments effected the change. The first was the discovery of techniques for growing clones of *T* cells in the laboratory. More could be learned about the chemical interactions of *T* cells by studying these homogeneous populations than by studying mixtures of *T* cells. The second breakthrough, related in some ways to the first, was the ability to produce monoclonal antibodies. These identical antibody probes could locate target proteins anywhere in the body. The third was recombinant DNA technology, which made it possible to isolate and manipulate genes.

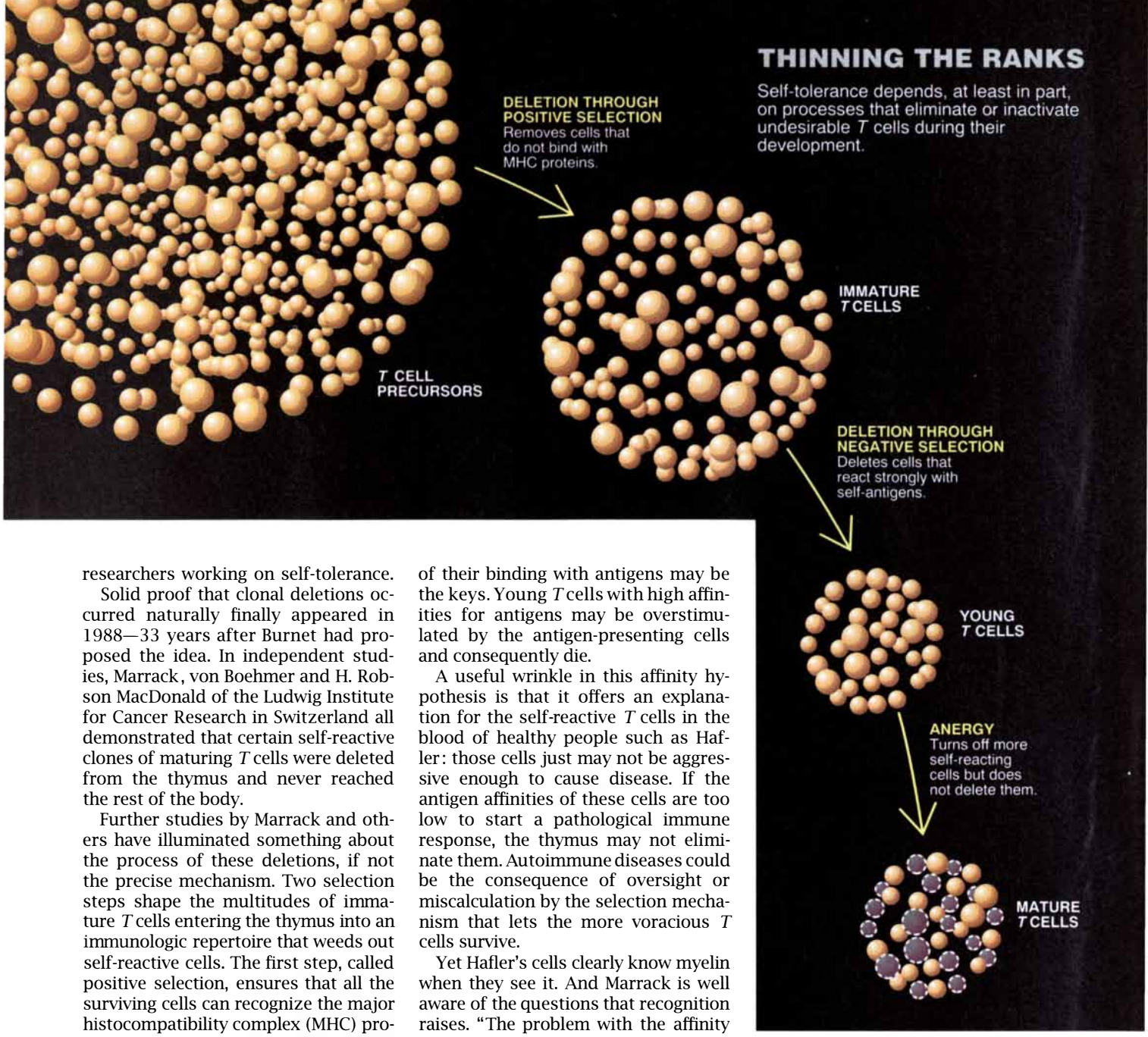
These techniques opened the way for a flood of discoveries, continuing to this day, about the mechanisms of antigen recognition and immunologic response. The receptor molecules that made *T* cells behave in specific ways could be identified and then analyzed structurally and genetically. For the first time, biochemical technology made it possible to study self-tolerance at the molecular level.

Under that close scrutiny, suppression ran into trouble. Gershon and others had predicted that suppressor cells would have unusual receptor molecules and other features, but no sign of those molecules could be found. Distinct sets of suppressor cells began to look less likely. Without them, suppression theories fell into disarray during the early 1980s. As Schwartz puts it, "A new generation of people with a molecular bent were coming into immunology who felt that 'if we can't find it there, it ain't there.' "

Screening Out Cells

Yet the same methods that were sinking suppression were a boon to clonal deletion studies. Researchers could study the fate of particular cells, for example, by inserting the genes for a specific *T* cell receptor into a mouse. In the resulting transgenic mouse, all the *T* cells would respond to a single type of antigen, which made it easy to study what happened to them. Deletion once again became the focus of

MULTIPLE SCLEROSIS RESEARCHERS David A. Hafler (*left*) and Howard L. Weiner hope to treat autoimmunity by suppressing immune system cells attacking the body.



researchers working on self-tolerance.

Solid proof that clonal deletions occurred naturally finally appeared in 1988—33 years after Burnet had proposed the idea. In independent studies, Marrack, von Boehmer and H. Robson MacDonald of the Ludwig Institute for Cancer Research in Switzerland all demonstrated that certain self-reactive clones of maturing *T* cells were deleted from the thymus and never reached the rest of the body.

Further studies by Marrack and others have illuminated something about the process of these deletions, if not the precise mechanism. Two selection steps shape the multitudes of immature *T* cells entering the thymus into an immunologic repertoire that weeds out self-reactive cells. The first step, called positive selection, ensures that all the surviving cells can recognize the major histocompatibility complex (MHC) proteins. These proteins, which are found on almost all body cells, hold antigens and present them to *T* cells. Because these proteins differ among individuals, recognizing them is essential to *T* cell function.

The second step, called negative selection, is critical for self-tolerance. It weeds out dangerously self-reactive *T* cells by exposing them to a potpourri of self-antigens in the thymus. Young *T* cells that take this bait, by binding aggressively to the self-antigens, die.

Now Marrack and others are trying to solve the mystery of exactly what kills the *T* cells during negative selection. After all, recognizing antigens is what *T* cells are supposed to do. Marrack's tentative explanation is that the age of the cells and the strength of their binding with antigens may be the keys. Young *T* cells with high affinities for antigens may be overstimulated by the antigen-presenting cells and consequently die.

A useful wrinkle in this affinity hypothesis is that it offers an explanation for the self-reactive *T* cells in the blood of healthy people such as Hafler: those cells just may not be aggressive enough to cause disease. If the antigen affinities of these cells are too low to start a pathological immune response, the thymus may not eliminate them. Autoimmune diseases could be the consequence of oversight or miscalculation by the selection mechanism that lets the more voracious *T* cells survive.

Yet Hafler's cells clearly know myelin when they see it. And Marrack is well aware of the questions that recognition raises. "The problem with the affinity hypothesis is that you have to look at whether an animal has a way of changing the affinity that we don't know about," she says.

Jonathan Sprent, who investigates tolerance at the Research Institute of the Scripps Clinic in La Jolla, Calif., says, "When people like me start talking about affinities, it's just handwaving." Because *T* cell receptors have complex structures and functions, no one can characterize their relative activity in simple biochemical terms.

A more fundamental problem also stands in the way. For clonal deletion to explain all tolerance, every potential self-antigen in the body must somehow manifest itself in the thymus so that *T* cells can be screened. Some researchers think this idea is credible because the thymus is a crossroads for macrophages and many other antigen-presenting cells circulating through the body. Macrophages, which scavenge the tissues for dying cells, could pick up a representative sampler of self-antigens. Soluble molecules in the blood and lymph also flow through the thymus. Sprent, for one, believes that the thymus is probably efficient enough at accumulating self-antigens to screen *T* cells effectively.

But even Marrack, who has great faith in clonal deletion, acknowledges that something may still be missing. "In some cases, the antigens may not be able to get to the thymus—they're stuck in your brain or your big toe or

wherever," she says. "You need to develop another mechanism for dealing with them."

Clonal anergy has therefore emerged as a possible backup or alternative mechanism for self-tolerance. The term "anergy" was coined by the immunologist Gustav J. V. Nossal of the Hall Institute, who first noticed the phenomenon in the mid-1970s while studying *B* cells in culture. Under some circumstances, he noticed, antigens did not activate the cells to produce antibodies but instead had the opposite effect: they rendered the cells unresponsive. The cells did not die but persisted in this lazy, or anergized, state unless exposed to large quantities of helper *T* cells or interleukin-2, a lymphokine or growth-hormonelike substance that is secreted by helper *T* cells.

Almost a decade later Schwartz and Marc K. Jenkins, who is now an assistant professor at the University of Minnesota at Minneapolis, discovered the same phenomenon in *T* cells growing in culture. To explain their results, Jenkins and Schwartz proposed a two-signal model for the activation of *T* cells.

On Again, Off Again

The essence of the two-signal model is that simply binding a receptor to an antigen is not enough to trigger a response in *T* cells. The cells must also receive an additional signal of some kind from the antigen presenters. Without this second signal, a *T* cell becomes anergized and stays that way unless "reset" by helper cells.

Only a few types of specialized cells in the body—macrophages, for example—may be able to send the second signal needed to give *T* cells a full push into an active, proliferative state. Most cells would only be able to present antigens. Clonal anergy could therefore reinforce deletion for self-tolerance: self-reactive *T* cells that escaped deletion in the thymus would be turned off the first time they recognized an antigen on a typical body cell.

Since 1987 many experimenters have argued persuasively that clonal anergy does take place among *T* cells and *B* cells in whole animals and not just in the test tube. But even if most immunologists now generally accept clonal anergy in principle, they are not precisely sure of what it is.

Everyone agrees that anergy is not the same as suppression, despite some superficial similarities in their effects. Suppression depends on an inhibitory effect that one cell imposes on another. Anergy is a reaction that a cell has when it does not receive all the essential cues to proliferate. Some suppression workers do theorize, however, that cell-mediated suppression might take advantage of the biochemical mechanism causing anergy.

The mushiness in the description of the anergy phenomenon also makes it hard to grasp. In different investigators' hands, clonal anergy seems to show different characteristics. Schwartz, for example, believes that *T* cells may be anergized primarily outside the thymus, in the peripheral lymph nodes. Yet B. J. Fowlkes and Fred Ramsdell, senior immunologists who work two floors above Schwartz at the NIAID, have found evidence in animal studies that anergy occurs inside the thymus. In Schwartz's studies of cultured cells, those that were anergized tended to remain that way unless activated by helper cells. On the other hand, experiments Fowlkes and Ramsdell are now performing on mice suggest that anergized cells eventually recover on their own if they stop encountering their antigen target.

Of course, as Fowlkes is quick to point out, no one knows whether the anergy that she and Ramsdell have studied is the same thing that Schwartz and Jenkins observed in cell cultures. If several different forms of anergy can occur in the immune system simultaneously, everyone could be right. Schwartz cheerfully admits that anergy has become a buzzword to describe unresponsiveness in *T* cells. "The problem with buzzwords," he adds, "is that they gloss over the differences in the individual systems."

Meanwhile, a continent away from Bethesda, in his laboratory in La Jolla, Sprent draws on his pipe and remains unimpressed by the whole idea of anergy. "You have a cell and you expose it to an antigen and it doesn't respond, but it starts responding if you add lymphokines. That's more or less the current definition of anergy." He shakes his head doubtfully.

Sprent has found cells that act as though they are anergized even though they have never been exposed to their antigen. He believes anergy becomes "sort of absurd" if it relies solely on unresponsiveness as a criterion. "My point is you can take some *T* cells that probably have a low affinity for an antigen, and they will behave in exactly the same way."

But such reservations do not faze Fowlkes. "We know that the cells are there and that they're not responding when the controls are still responsive," she says. "You have to think that the cells have gone through some kind of redifferentiation." Ramsdell reinforces

SUPPRESSION SUPPRESSED?

"Two years ago, almost as a joke, I was asked to chair a session on suppressor cells, at a time when 98 percent of the field did not want even to hear about their potential existence," recalls Ronald Germain, an immunologist at the National Institute of Allergy and Infectious Diseases. With a grim chuckle he says, "I think people felt that because I had worked on suppression previously, I was now going to get my comeuppance."

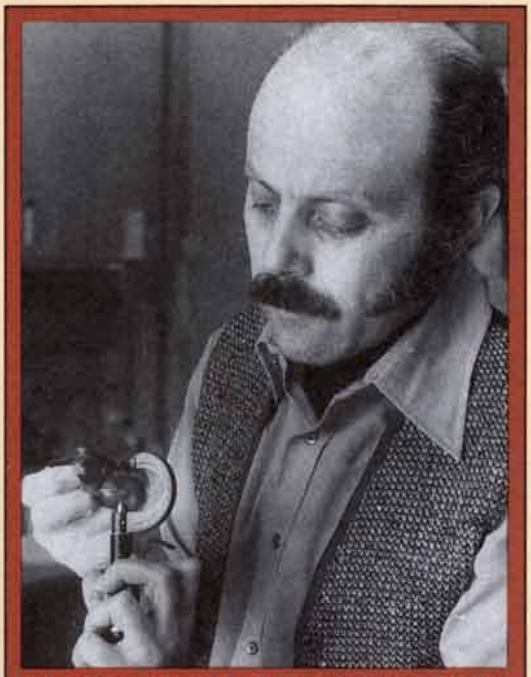
Instead Germain began the session with slides of old published papers on suppression—all authored by respected immunologists, many of whom had since distanced themselves from the theory. "I reminded people of the history of suppression and that we're not talking about a bunch of weirdos out in the boondocks."

Suppression theories of immunotolerance are clearly out of vogue. According to several researchers, it is currently difficult to get funding for a research grant on suppression because of the strong peer-review resistance to the idea. Some investigators in the area now couch their work in terms of "immunoregulation" rather than suppression.

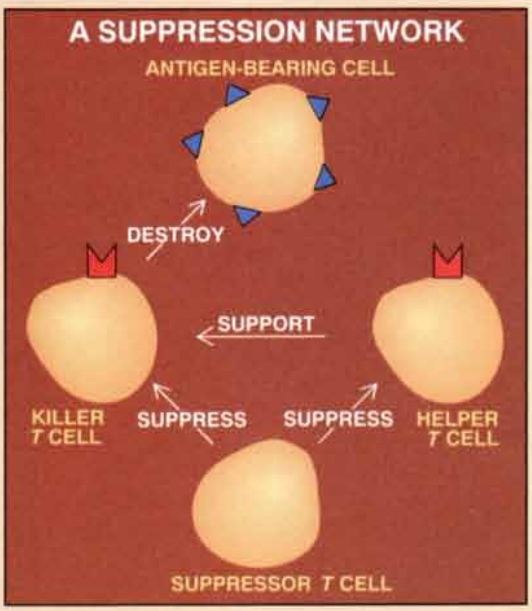
How did a theory that dominated immunologic discussions a decade ago fall into such disfavor? "Suppression became very fashionable at a time when it had a rather flamboyant, persuasive spokesman named Dick Gershon," Germain explains. The late Richard K. Gershon, a medical immunologist at Yale University, performed many experiments indicating that active suppressor cells in the body limited the activity of other *T* cells. During the 1970s, he advocated the idea that the immune system suppressed itself through an elaborate network of such cell interactions. As Jonathan Sprent of the Research Institute of the Scripps Clinic recalls, "Everybody went along with it, but it was all incredibly complicated."

The sheer intricacy of suppression theories was part of their problem. Relatively few laboratories could get experimental suppression systems to work, and many experiments proved difficult to reproduce reliably. As discrepant results accumulated, the proposed regulatory networks became "more and more baroque," Germain says. As time passed, investigators began questioning whether suppressor cells existed at all.

"People started to feel conned," Germain recollects. "In a sense [suppression theory] represented the worst of immunology: all this black box imagination and lousy experiments, none of which could be confirmed by hard science. Immunologists didn't like being cast as something other than real scientists." Eventually, he adds, "people felt like 'Enough is enough, this isn't how you do immunology anymore.'" When Gershon died in 1983, suppression theory lost its most ardent and eloquent defender.



The late Richard K. Gershon proposed the now controversial idea that suppressor cells regulate other cells in the immune system (as below).



Without a theory for inspiration and faced with shortages of funding, "a lot of people left the field, and the energy of the competition of several labs working on suppression disappeared, and the progress fell to near zero," comments Judith Kapp, a suppression researcher at Washington University. Yet, Kapp insists, "the data and the phenomena are still there."

But suppression theories are by no means extinct. Outside the U.S., they are still taken seriously by many mainstream immunologists. "I think it suits the European mind more. It's more philosophical," says Irun R. Cohen, who studies tolerance at the Weizmann Institute of Science. Suppression theories underlie his work on the therapeutic effects of *T* cell vaccinations on animals with autoimmune disorders. "It's not attractive to people who are trained to believe in reductionism as the holiest element of science," he says.

Harald von Boehmer of the Basel Institute for Immunology has doubts about suppression but allows that "there are some phenomena that are best explained in this way." When asked whether he thinks his European colleagues are more open to the idea of suppression than those in the U.S., he is diplomatic: "There are some Americans who have made strong statements [against it], but some of them have also changed their minds quite often in the past. Maybe it's just that their statements are more forceful."

Indeed, almost all immunologists accept that some complex regulatory phenomena guide the immune system, and some of these concepts hedge against the broadest statements of suppression theory. It is the existence of unique suppressor cells that is most controversial.

"Ultimately, I'm sure suppressor cells will be shown to exist," Sprent comments. "Whether they are a separate lineage of cell is debatable. My own view is that it is just an ordinary *T* cell that is probably doing something like killing another *T* cell by recognizing its receptor. The time is probably right to reinvestigate suppression, but it's just not a very popular thing to do at the moment."

the point. "There's no universally accepted molecular definition for anergy yet," he notes, "but it's a useful term."

Yet the lack of a molecular definition is exactly the shortcoming that seems to deny respectability to suppression theories. Indeed, to an outsider, there seems to be little reason why anergy should be much more acceptable than suppression to most immunologists. Both anergy and suppression may cover a range of mechanisms with the same net effect: stopping *T* cells from attacking the body.

"The phenomenon of suppression undeniably exists," Hafler insists. "You can transfer biological responses with populations of *T* cells. What we haven't been able to do is isolate a stable population of suppressor cells to define them at the molecular level." The reason no one has been able to clone a suppressor *T* cell, he suspects, is that suppressiveness is a transient state. "All our work with human *T* cell cloning suggests that cells can give some kind of suppressive signal at one time in their lives and that at other times they can't," he says.

In spite of discouraging opposition, some researchers continue to try to redefine the suppression effects they observe in the biochemical terms respected by the immunology establishment [*see box on opposite page*]. One of these scientists is Kapp in St. Louis, much of whose recent work concerns the natural mechanisms that create immunologic tolerance for insulin—a faculty that is usually missing in people with insulin-dependent diabetes.

In her studies on mice, Kapp has identified clones of *T* cells that react to insulin as an antigen, as well as other *T* cells that seem to confer tolerance to insulin: the presence of the second cells seems to discourage attacks on insulin by the first. These putative suppressor cells do not have unusual receptor molecules and cannot be distinguished from killer *T* cells on the basis of their molecular markers.

Kapp and her colleagues are now studying tolerance in transgenic mice that make human insulin. They have already established that the transgenic mice are tolerant of human insulin even though they have insulin-reactive *T* cells in their peripheral organs. "We haven't nailed down the mechanism of tolerance for those cells. They're certainly not irreversibly anergized," Kapp says. "And we do know that clonal deletion doesn't contribute much, if at all, to the nonresponsiveness."

She believes clonal deletion, clonal anergy and suppression operate side by side in the immune system, possibly inducing tolerance to different antigens. The concentration of an antigen in the thymus may determine which mechanism takes effect: membrane-bound proteins expressed on most cells, such as the MHC proteins, may be tolerated because of deletion, whereas insulin and other soluble proteins that reach only fairly low concentrations in the blood may be tolerated by suppression.

Building a Bridge

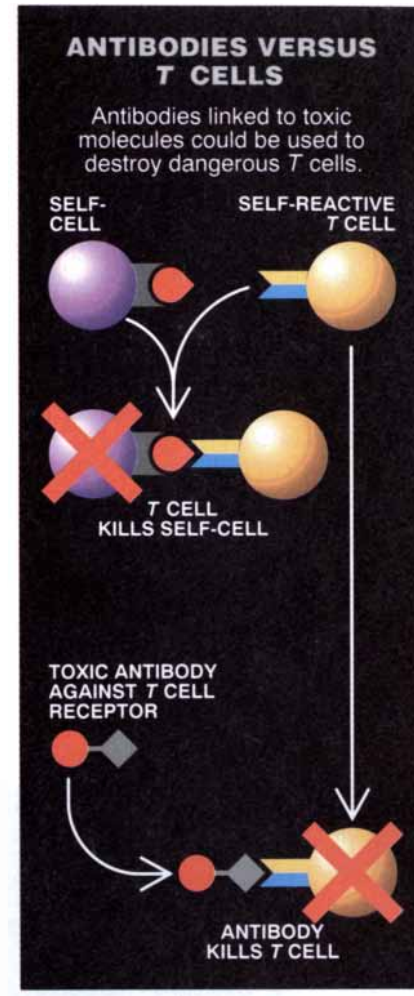
If Kapp's theory is correct, then by gradually raising the amounts of insulin expressed in transgenic mice, "we should reach a point at which we will cause clonal deletion. And if we can do that, I think we will learn a lot about what the rules are," Kapp says.

Other immunologists echo Kapp's thoughts. "I'm not sure that [clonal deletion] explains why we don't react to our own myelin, our own thyroglobulin, our own acetylcholinesterase receptor," muses Lawrence Steinman of the Stanford University School of Medicine. "I think a bridge is going to have to be built between the very elegant studies now being done on thymic selection and these tissue-specific autoimmune diseases."

While immunologists generally agree with Steinman that their understanding of self-tolerance still falls short of explaining how autoimmune diseases develop, researchers are nevertheless rushing to leap that gap by applying what they have already learned to therapies. A major part of this effort involves zeroing in on the specific *T* cells associated with diseases.

Early this past summer Steinman's group and Hafler and Weiner independently announced that they had identified a narrow set of *T* cells responsible for MS. The antigen receptors on these cells always seem to contain one of only four slightly different proteins called beta chains. (*T* cell receptors consist of an alpha-chain protein and a beta-chain protein, both of which can exist in many different genetically determined forms.)

Knowledge of the specific *T* cells associated with autoimmune diseases should enable immunologists to take aim at the cells with therapies that will delete or suppress them selectively. Such treatments include highly specific monoclonal antibodies and customized peptides that bind only with the active *T* cells or with the MHC proteins on the antigen-presenting cells. To pack more wallop into such therapies, antibodies against self-reactive *T* cells are sometimes being linked with toxic molecules to form so-called immunoconjugates that will kill, not just incapacitate, the targeted cell.



Ideally, such therapies will halt the autoimmune conditions without causing other complications or weakening the immune system generally. A number of companies are already trying to develop pharmaceutical products along these lines, including Xoma Corporation in Berkeley, Calif., Centocor Corporation in Malvern, Pa., and T Cell Sciences in Cambridge, Mass.

A good example of the successes and possible hurdles faced by the monoclonal antibody approach is the work on experimentally induced allergic encephalomyelitis (EAE), an artificial disease often used to model MS in animals. To induce EAE, workers inject myelin protein into mice or rats. The rodents' immune systems, perhaps sensitized to the protein as an antigen, then attack their own nervous systems, with debilitating consequences.

In 1988 two groups—one led by Steinman and one by Leroy E. Hood, a leading immunology researcher at the California Institute of Technology—in-

dependently showed that the antigen receptors of *T* cells involved in EAE always contained one of two beta-chain proteins. Steinman's group then injected an antibody against one of these receptors into mice with EAE.

The results were dramatic. Most of the mice that had been partly or totally paralyzed by EAE regained their mobility. The antibody also seemed to be able to prevent EAE in many mice that subsequently received myelin injections. This past June, Hood announced that he and his colleagues had carried the work still further by injecting EAE mice with a combination of two antibodies against the *T* cell receptors. Four out of five mice with advanced EAE recuperated, and the combined treatment seemed to prevent EAE in 19 out of 20 others. The one mouse that did develop EAE showed mild symptoms.

The clear success of these antibody treatments raises the hope of eventually extending similar work to humans with MS and other autoimmune diseases. But many more questions must first be answered. "There was still that one animal that got sick," reflects Dennis M. Zaller, one of Hood's collaborators. "I kept trying to figure out why." He has since found that two rare sets of closely related *T* cells with different antigen receptors seemed to expand and attack the nervous system.

"I think that normal animals have some of these *T* cells. The question is, Is there a finite end?" Zaller asks. It is possible that once the immune system has become sensitized to an antigen, rare clones of cells may keep proliferating to fill the void left by those that have been neutralized by therapies.

Active Vaccination

Stopping an errant immune system from overcoming the treatments meant to correct it may therefore prove to be a problem. Hafler and some other investigators believe the best hope for lasting cures rests with helping the immune system to police itself—either by enhancing the suppression networks in the body, if any, or by creating some.

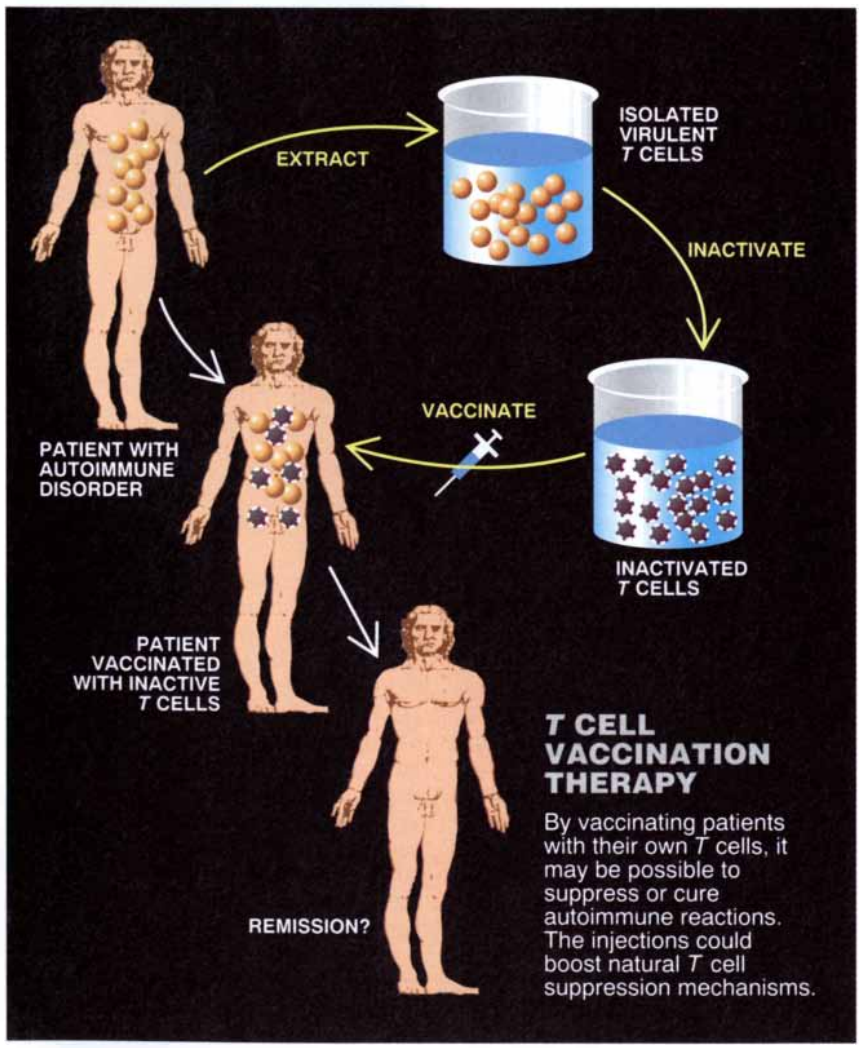
So far the best established way of achieving that end is active vaccination, which Cohen and his colleagues pioneered in Israel during the early 1980s. Cohen showed he could cure rats of EAE by injecting them with harmless clones of myelin-reactive *T* cells taken from their bodies; the clones had been inactivated by chemicals or radiation. Presumably, the vaccinations raised the animals' sensitivity to the myelin-destroying *T* cells causing the EAE, and their immune systems suppressed the dangerous reaction. "The immune system seems to be receptive to *T* cell vaccination," Cohen says, which he takes as evidence that suppression mechanisms are native to the body.

Two years ago Hafler and Weiner became the first to test those ideas in humans when they began a small clinical study involving four MS patients to see whether active vaccinations were safe enough for humans. (The patients were in the most advanced stages of debilitation from MS and did not respond to conventional protocols.) After finding certain clones of *T* cells that seemed to have multiplied in the blood and nervous systems of these patients, the investigators grew the cells in the laboratory. They then rendered the cells harmless with chemicals and injected them back into the patients.

So far no side effects have emerged, although Hafler emphasizes that the study group is too small to reveal whether the treatments would do the patients any good. Earlier this year René de Vries of the University Hospital in Leiden, the Netherlands, began a similar study on four rheumatoid arthritis patients, using clones of *T* cells taken from their inflamed joints.

For Hafler and Weiner, the trials are important not just as precursors for more clinical studies but as basic scientific inquiries into the mechanisms of MS. "You can never know whether an antigen is the target antigen from in vitro studies," Hafler asserts. "You have to go back to the patients and make them tolerant of the antigen to see the effects on the disease."

Despite its promise, active vaccination with whole *T* cells has some drawbacks as a prospective therapy. The process of producing enough cells for a treatment is slow, expensive and labor intensive: they must be extracted from individual patients, purified, grown in culture, inactivated and chemically altered to raise their antigenicity. "Considering the hundreds of thousands, if not millions, of people who may need to be treated with these approaches, I



think it won't be feasible on a large scale to use cellular vaccines," Steinman comments.

Consequently, researchers involved in active vaccination are also interested in refining the technique to use specific *T* cell peptides (protein fragments) instead of whole cells. These molecules could be chemically synthesized in large quantities and distributed to many patients.

Steven W. Brostoff heads a group investigating the peptide vaccination approach for the Immune Response Corporation in San Diego. Brostoff and his co-workers have created short peptide snippets of the antigen receptors found on the myelin-reactive *T* cells that cause EAE. They reported in November, 1989, that if they injected those peptides into rats, the animals became resistant to EAE.

Brostoff's explanation is that the injections cause the rats to develop a cadre of killer *T* cells capable of recognizing and selectively suppressing myelin-reactive cells. He says that although final products are a long way off, his company hopes to begin toxicity trials of peptides for rheumatoid arthritis in 1991.

The idea of treating human autoimmune disease with peptides, however, is not yet foolproof. This past summer some as yet unpublished data showing potential hazards were discussed: when some researchers injected *T* cell peptides into animals, the animals' symptoms became worse. No one knows why the procedure might be safe in one case and dangerous in another. As such issues are being settled, clinical applications will no doubt advance cautiously.

Two other possible approaches to treating autoimmunity take advantage of the new understanding of the natural systems for inducing tolerance. One was announced this past September, when Ali Naji, a surgeon at the Hospital of the University of Pennsylvania, described how he and his co-workers had induced tolerance to insulin in rats with a novel type of transplant.

The Pennsylvania group was working on overcoming the problem of organ rejection, which is the body's refusal to tolerate tissues with foreign MHC proteins. Transplants have been suggested as a cure for patients with insulin-dependent diabetes, whose insulin-secreting pancreatic islet cells have been destroyed by autoimmunity. Unfortunately, although islet cell transplants have been tried on humans since the 1970s, the engrafted cells have always been rejected by their new hosts.

Naji's unorthodox solution to this problem was to transplant islet cells directly into the thymus of laboratory animals in the hope of "teaching" the host to accept the graft as part of the self. After inserting the cells into the thymus, he administered a dose of *T* cell–killing antibodies to deplete existing lymphocyte reserves and to stimulate a new round of *T* cell production.

The islet cell grafts in the thymuses survived indefinitely. Apparently, they were protected from immunologic attack. Moreover, when similar islet cells were inserted elsewhere into the bodies of some of those rats, the new grafts were also tolerated.

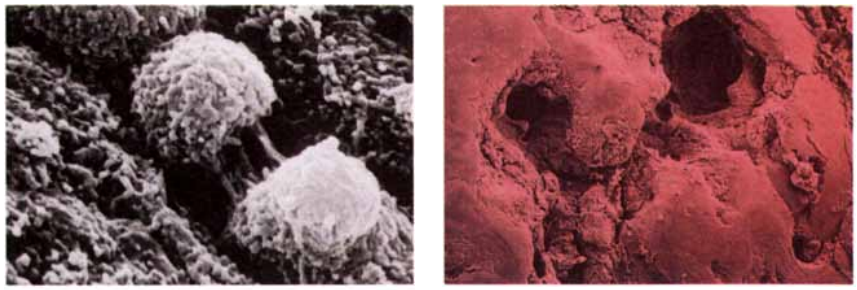
Naji believes the presence of the foreign cells in the thymus spurred the deletion or inactivation of *T* cells capable of recognizing the graft's antigens along with those recognizing the self-antigens. He and his colleagues are now continuing their studies to check whether such transplants can confer tolerance to tissues rejected because of autoimmunity. He reports that preliminary indications are encouraging.

Meanwhile Weiner and Hafler are investigating a very different system for overcoming autoimmunity that is based on a phenomenon called antigen-driven tolerance. Decades ago immunologists realized that the way in which a body is exposed to an antigen affects the immune system's reaction: animals injected with antigens often became sensitized and allergic to them, but animals fed antigens often became tolerant of them. "We don't generally become sensitized or allergic to proteins that we eat—it would be harmful," Weiner explains. Although no one understands precisely how tolerance arises in this way, he says that "we're using this natural mechanism to try to suppress autoimmune diseases."

In recent years Weiner and his colleagues have shown that by feeding myelin protein to rats, they can reduce the severity of EAE induced in the animals. They have had similar success in suppressing experimentally induced forms of arthritis and uveitis, an inflammation of the eye. Weiner was also able to induce antigen-specific suppression by transferring *T* cells from tolerant animals.

"We think this approach offers the possibility of becoming a nontoxic antigen-specific therapy," Weiner says. He is part of a research team at Brigham and Women's Hospital now conducting a small pilot study on MS patients who are receiving myelin antigens orally. The investigators are waiting to see whether they can generate antigen-specific suppression in these patients and whether the treatments can alter the progression of their MS. No results are yet available.

The effort to treat autoimmune diseases is advancing, therefore, notwithstanding the uncertainty of the guiding theories and the divisions among different camps of immunologists. It is ironic that the branch of immunology most concerned with tolerance has turned against a part of itself—treating suppression theories with not so benign neglect if not exactly rejecting them. The history of this fast-changing field shows, however, that one year's unfashionable concept can become the next year's dogma. Perhaps one day the entire elephant may come into view.



RHEUMATOID ARTHRITIS occurs when *T* lymphocytes infiltrate and attack the synovial fluid membrane lining the joints (*left*). A micrograph of the head of the femur from an arthritic hip (*right*), which should be smooth, shows deep pitting.

FURTHER READING

THE *T* CELL AND ITS RECEPTOR. Philippa Marrack and John Kappler in *Scientific American*, Vol. 254, No. 2, pages 36–45; February, 1986.

THE SELF, THE WORLD AND AUTOIMMUNITY. Irun R. Cohen in *Scientific American*, Vol. 258, No. 4, pages 52–60; April, 1988.

IMMUNOLOGICAL TOLERANCE: COLLABORATION BETWEEN ANTIGEN AND LYMPHOKINES. Gustav J. V. Nossal in *Science*, Vol. 245, No. 4914, pages 147–153; July 14, 1989.

FRONTIERS IN BIOTECHNOLOGY: TOLERANCE IN THE IMMUNE SYSTEM. *Science*, Vol. 248, No. 4961, pages 1335–1393; June 15, 1990.

Narrow Bandwidth

Broadcasters want more bits for the buck

Blanket alert, modeling muddle, healing energy

Cramming a big signal into a small-frequency hole has become a critical part of designing any new broadcast technology, from digital radio signals with the quality of compact discs to cellular telephones and automotive navigation systems. The reason is that room in most of the spectrum from 10 kilohertz to 300 gigahertz is as scarce as undeveloped real estate in midtown Manhattan. "It seems like we're in an era now in which everything we're regulating is demanding more spectrum," says Thomas P. Stanley, the chief engineer at the Federal Communications Commission. "It's the same kind of pressure population growth has put on urban development."

Nowhere will this prove more difficult than for the companies that are developing broadcast systems for high-definition television (HDTV). They must find a way to comply with the proposal by the FCC that HDTV—which doubles picture resolution and supplies compact disc–quality sound—fit within the narrow six-megahertz slot used for existing television. Yet those signals could consume anywhere from 10 to 100 times the amount of frequency the FCC currently allots each station.

The reason that anyone can even consider transmitting such a huge amount of data on existing channels is that current television transmissions make inefficient use of the six megahertz of frequency for each station. Frequencies set aside for transmitting the brightness and color portions of the signal are not fully used. In the very high frequency band, stations must be separated by one blank channel to prevent interference and in the ultrahigh frequency band up to five channels.

The major advance that makes compressed television and other spectrum-efficient technologies possible is affordable digital-signal processing and advanced modulation techniques. Both can be used to reduce the up to 1.2 billion bits a second in an uncompressed HDTV signal to fit within today's television channels.

The most recent entrant in the HDTV contest is General Instrument Corporation, which recently simulated the first all-digital HDTV system. The advantage of digital transmission is that despite the interference produced by buildings, police radios and other sources, a signal can be reconstructed to look as if it just came out of the studio camera.

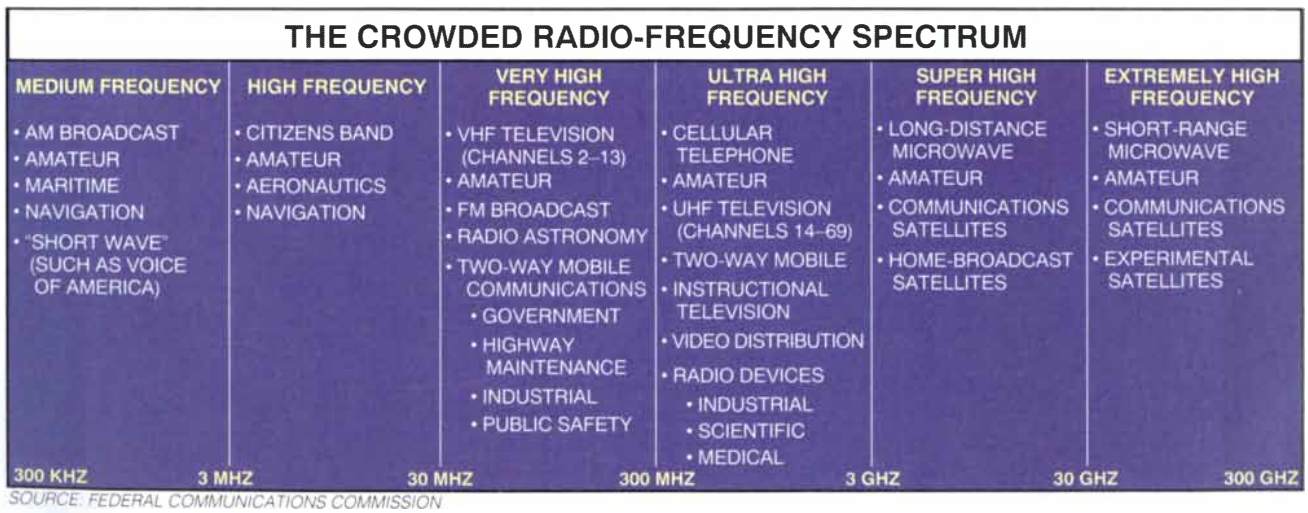
Although the systems of two other competitors, Zenith Electronics and the Massachusetts Institute of Technology, use a hybrid of digital and analog transmission methods, an all-digital system was thought to consume too big a frequency lump to be practicable for HDTV. "This digital proposal may cause other parties to rethink what they're doing," says Richard E. Wiley, chairman of an FCC advisory committee on HDTV and a former FCC chairman.

Despite having the newest approach, General Instrument uses the same menu of compression techniques as its competitors. Like its rivals, it begins the compression process by drastically reducing portions of the color signal. The high-frequency portions of the signal, corresponding to tiny picture areas, are not readily perceived, allowing them to be filtered out without penalizing picture quality.

Still more compression is gained by comparing information from one frame with another so that redundant data are not sent more than once: A cloudless blue sky may remain static from frame to frame. When a cloud passes over, only the difference between the old and new frame is sent.

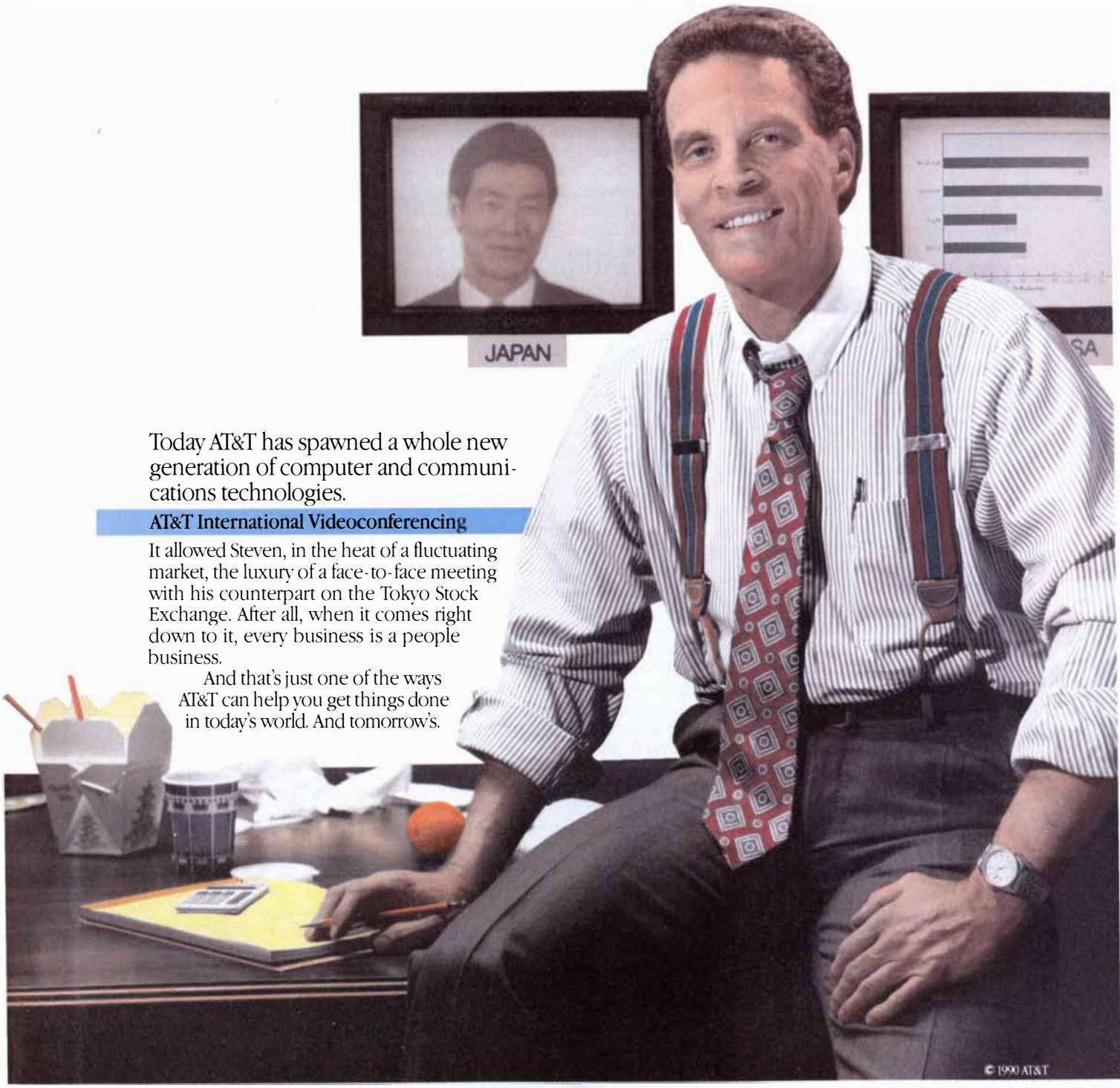
The compacting continues by only sending the frequencies in each picture that contain the most signal energy. In a busy scene, which requires that more information be sent to represent the changing picture, frequencies with negligible signal amplitudes are discarded. Although picture resolution may worsen, engineers are counting on the fact that the eye cannot distinguish detail when rapid changes occur. "Why send a letter when you can send a postcard?" asks Charles W. Rhodes, the chief scientist at the Advanced Television Test Center, Alexandria, Va., an independent testing laboratory for HDTV systems.

The compressed picture has been condensed 65 times. But it can be squeezed still further by carefully



SOURCE: FEDERAL COMMUNICATIONS COMMISSION

When Steven was just a kid, AT&T was just the phone company.



Today AT&T has spawned a whole new generation of computer and communications technologies.

AT&T International Videoconferencing

It allowed Steven, in the heat of a fluctuating market, the luxury of a face-to-face meeting with his counterpart on the Tokyo Stock Exchange. After all, when it comes right down to it, every business is a people business.

And that's just one of the ways AT&T can help you get things done in today's world. And tomorrow's.

The way things get done.

AT&T
The right choice.

choosing the modulation scheme used in broadcasting. General Instrument and others use a technique called quadrature amplitude modulation, which shifts the signal's phase and amplitude to transmit four bits of information within each time slot, a quarter of the time that would otherwise be needed. The data rate of the signal—19.4 million bits a second—can then fit within six megahertz of bandwidth.

The drawback is the difficulty of transmitting a digital signal over long distances. Digital transmission provides perfect signal coverage within a given area and then abruptly falls off, whereas an analog signal degrades more gradually. Whether an HDTV signal of any kind can send a show to a television set 50 to 80 miles from a central-city transmitter, as can existing television technology, has yet to be proved.

The debate over the most spectrum-efficient technology extends to the cellular telephone industry. With the industry quintupling in size in three years, cellular services have decided to switch from analog to digital transmission, which allows a signal to be manipulated in various ways to expand the capacity of each cell. (In cellular telephone service, a service area is broken up into "cells," each with a base station that has its own transmitter and receiver to relay calls.)

An industry group, the Cellular Telecommunications Industry Association (CTIA), has endorsed a method called time division multiple access, which enables three voice conversations—and possibly as many as 12—to be sent within a single 30-kilohertz channel. Each channel is broken down into a number of time slots: a caller might use the third, sixth and ninth slots, for example, if three conversations are sharing the same channel.

Before the ink was dry on the CTIA agreement, a California company, Qualcomm, began to push an alternative proposal that it says could permit as many as 20 times the number of conversations normally reserved for a single cell. The technology, called spread spectrum, was used by Roosevelt and Churchill to send encoded messages during World War II. (One spread-spectrum technique, in fact, was patented by the actress Hedy Lamarr to prevent jamming of the control signals for torpedoes.)

Spread spectrum distributes the signal over a wide band of frequency and then recompresses it at a receiver that identifies the signal by a code. Because the power of a spread-spectrum signal is so diffuse, it provides little interference with other signals sharing the same bandwidth. "The advantage of spread spectrum is that the interference is benign," says Andrew J. Viterbi, Qualcomm's chief technical officer and vice chairman. "It allows many different kinds of users to coexist."

For this reason, another type of cellular service that will use spread spectrum has been targeted by the FCC for a series of trials beginning next year.

In the first trials in Houston and Orlando, so-called personal communications networks (PCNs)—tiny wireless telephones sometimes compared to Dick Tracy's wrist radio—will use the same frequencies already allocated for use by utility and other microwave transmitters. Because of the extremely low power signals, a PCN cell is needed every 1,000 feet or so as compared with the 10-mile range for a large cell in regular cellular telephone service.

Finding more electromagnetic real estate can also be accomplished by using a narrower signal. United Parcel Service (UPS) is planning to set up a network that will give each driver an "electronic clipboard" that can transmit delivery information to a dispatching depot. This network will be coupled with a geographic information system, a data base dispatchers can use to plot the most efficient routes. "Anything we can do to get a slight edge in travel time gives us a cost edge," says Paul Heller, program manager for UPS's vehicle communications network.

Trucks will communicate by using portions of the two megahertz of bandwidth set aside by the FCC for narrow-band transmission. Each narrow-band signal uses five kilohertz to transmit voice or data, a fifth of what is normally needed. When the FCC made its decision in 1988 to allocate these frequencies, it had to yank them away from amateur radio operators. Jealous of its turf rights, the American Radio Relay League—which speaks for hams—sued the FCC to get back a frequency slice it believed to be its own. (The case is scheduled to be heard in a federal court of appeals in November.) If these frequencies finally open up for traffic, UPS is considering several modulation and channel-sharing techniques for using the narrow bandwidth.

Despite the range of solutions, finding room for traffic growth in a crowded spectrum is a problem that is only likely to get worse. And like real estate, the price is likely to rise. In fact, the Bush administration wants to auction off or charge for using pieces of the radio-frequency spectrum. Ultimately, the few spare megahertz that do become available may go to the highest bidder. —*Gary Stix*

This Number Is You

Phone forwarding may put you permanently on call

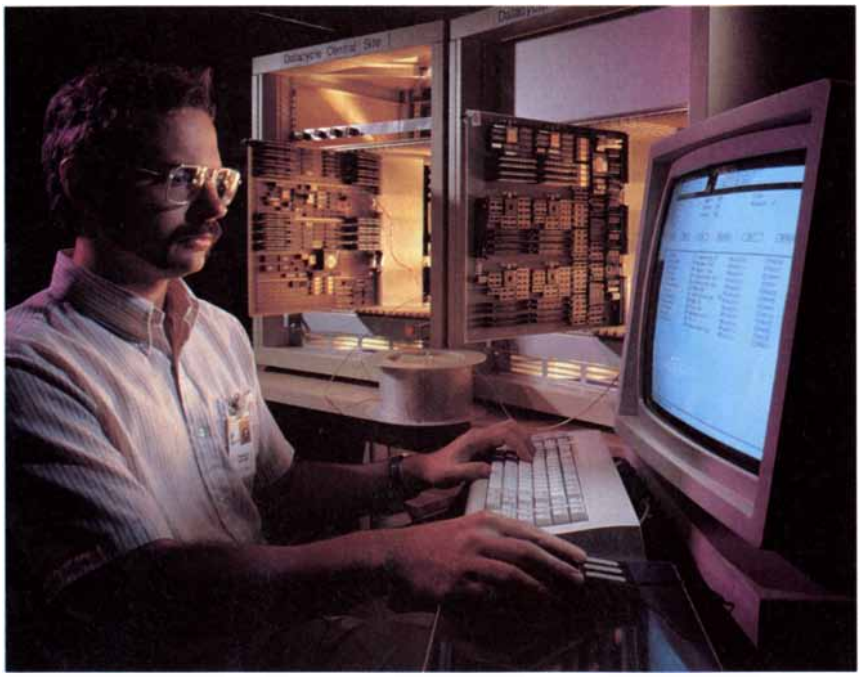
In addition to Guccis, country clubs and access to the corporate jet, where you stand in the corporate hierarchy may be represented by the number of telephone numbers attached to your name. An executive may sport two or three numbers both at office and at home and one for each facsimile, pager, modem and portable telephone kept in the car or briefcase.

In deference to the corporate elite—and to forestall the need for fanfold business cards—telephone companies are trying to do away with such number overload. The telephone network of the very near future may assign every subscriber a number that, when dialed, would hunt someone down by alerting the nearest telephone or beeper.

For those who find it a mental burden to keep track of even one number, not to worry. The combinatorial wizards at Bell Communications Research (Bellcore), the research arm of the local telephone companies, will let you choose a unique "name" in addition to a number—borrowing and enhancing on naming schemes already used for large computer networks. Besides what appears on a birth certificate, the newborn of the year 2000 might be christened Arthur of Nynex or Blanche of BellSouth.

This service—just one facet of a growing "intelligent" network for telecommunications—could respond to more than just a name or number. It could become, in effect, one large data base that lets a caller track you down by typing into a terminal or touch tone telephone any identifying trait: workplace, home or the fact that you live in the same block as a McDonald's. "We can resolve you using any piece of information," says Gary E. Herman, a division manager at Bellcore.

Much of the planning for this so-called personal number calling (PNC) is being cooked up in suburban New Jersey, where some 50 Bellcore employees and a small group of homes and businesses are already participating in "Anywhere Call Pickup," an experimental program in which a computer instructs a caller to wait while a paging system tracks down the person being called and routes the call to that location. Irwin Dorros, a Bellcore executive vice president who would like to consolidate his seven telephone numbers, is a strong backer. "This could be the largest change in the way telephone



PERSONAL NUMBER CALLING, a technology that takes advantage of high-speed access to computer data bases, is being developed at Bellcore. Photo: Dave Hoffman.

calls are made since the introduction of direct-dial calling," he glows.

The key to PNC is the severing of a universal identifier from its physical location. The telephone network already uses this principle for making toll-free calls. When an "800" number is dialed, a computer may route the call to one of several places, depending on time of day, volume of calls received or other programmed variables.

PNC would work the same way for a number or name, except that computers running telephone company networks will have to handle much more information than an "800" service does. PNC would let a user type into the network a daily itinerary using a device such as a touch tone telephone keypad. If plans change, the day's profile could be reprogrammed, perhaps by having a telephone identify a new location by "reading" information stored in a card equipped with a microprocessor. Scheduling a telephone might even become unnecessary since everyone would leave home with a pocket telephone that pinpoints location by transmitting a homing signal.

On a limited scale, PNC could be installed today. To make it work from coast to coast would consume immense amounts of computer processing time and network capacity. The network must be able to handle 100,000 inquiries a second, compared with just 1,000 a second for "800" service. Currently every computer processing "800" calls must keep mirror copies of subscriber routing information. Even if a network is more powerful, the bookkeeping tasks of making sure that each computer is regularly updated can eventually eat up much of its communications capacity.

So Bellcore researchers have designed a prototype system in which a central data base could take advantage of high-speed fiber-optic communications. The data base would contain a single copy of all the information needed for a PNC system. Contents of the data base—where you are on Thanksgiving, for example—may one day be pumped continuously over a nationwide fiber-optic network at several gigabytes a second, a task equivalent to transmitting all the nation's white-page listings every second. A computer near a caller would pluck from the stream of data the location and number of the person being contacted and then direct the call to the proper destination.

The potential intrusiveness of a hunt-and-locate service has not been lost on company officials. Bellcore employs a sociologist to examine the privacy issues involved in having government agencies or marketers use these data bases to follow an individual's every move. "People should be able to maintain their anonymity or not disclose their location if they so choose," asserts Bellcore sociologist James E. Katz.

In addition, PNC "could become a de facto national identification number," worries Rohan A. Samarajiva, an assistant professor in the department of communication at Ohio State University at Columbus. "In whichever country you are, in whichever state you are, this number is you." —*Gary Stix*

Sugar Fix?

A simple sugar may help hearts heal

Hearts are not fickle in matters of blood flow. Without blood to bring oxygen, the energy molecules in heart cells break down completely. Even after blood flow returns following a heart attack or cardiac surgery, healing is slow. It takes about 10 days for the heart to rebuild its energy stores and get fully back to the business of beating.

John E. Foker, a cardiovascular surgeon at the University of Minnesota Hospital and Clinic in Minneapolis, believes he has found out what causes the lag. When blood is withdrawn from the heart, the basic cellular energy molecules known as adenosine triphosphate (ATP) give up their high-energy bonds and crumble into ineffectual monophosphates. "You'd think they'd just sit there and wait to be recharged," Foker observes, "but they don't." These bits break down even further and wash out of the heart, leaving the organ to resynthesize ATP from scratch.

Foker decided to put back some of the pieces, to "prime the pump" for making ATP. When one of them, the simple sugar ribose, was given to dogs during and after cardiac surgery, ATP levels returned to normal in just 24 hours. The reason, Foker says, is that cells can utilize ribose directly, bypassing the normal, but slower, conversion of glucose into ribose. Ribose has to be given for a full five days, however. Foker won a U.S. patent in 1988 on this "method for stimulating recovery from ischemia," local anemia caused by stoppage of blood supply.

"The animals get better," declares Richard W. Bianco, director of the cardiovascular surgical research laboratories at the University of Minnesota. "In controlled studies, it's a clear fluid so the lab personnel don't know which dogs got ribose and which didn't. But they can always tell."

There is also anecdotal evidence that ribose works in humans. "I believe a lot of children made it out of the hospi-

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From Signals, *Guglielmo Marconi in 1896. Courtesy Marconi Company Ltd.*

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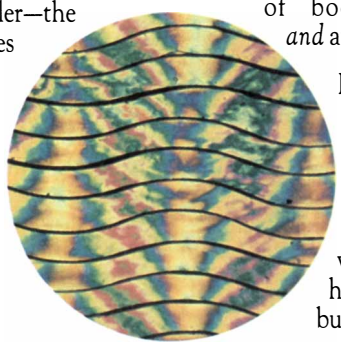

From The Science of Structures and Materials, *a polarized light view of a stressed graphite fiber-epoxy resin composite. Courtesy Tsu-Wei Chou.*

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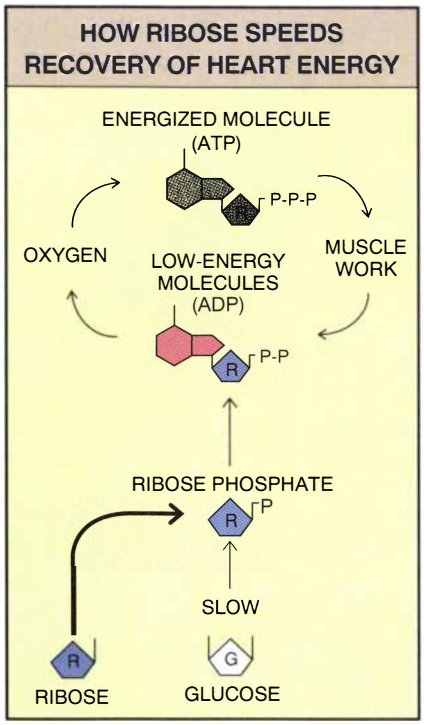


tal who otherwise would not have," says Stanley Einzig, head of pediatric cardiology at West Virginia University at Morgantown. He has given the sugar intravenously to children on maximum support systems to augment conventional drug therapy. "Ribose can be thought of as a nutritional supplement," he notes. The sugar was studied in the 1950s for possible use in diabetes and showed no toxic effects.

Yet winning Food and Drug Administration approval to treat the 300,000 patients who undergo open-heart operations in the U.S. or some of the 500,000 heart-attack survivors each year is not so simple. "It's not enough to just demonstrate a phenomenon like ATP going up," declares Raymond J. Lipicky, director of the FDA's division of cardiorenal drug products. "They've got to show that the drug improves either mortality or morbidity—that people die less or feel better."

Proving efficacy will take nothing less than a brand-new way of measuring human heart function, Foker reckons. So the tiny company he formed to commercialize ribose has spent the past two years designing specialized computer software to help substantiate its observations. The firm—called Bioenergy, Inc., for now—is developing a series of programs to interpret echocardiogram data in high detail. If the system works, it stands to find applications far beyond the evaluation of ribose.

Bioenergy's goal is to provide precise readings of diastole, the ability of the heart's chambers to relax and fill with blood. "Relaxation would be the most useful heart function to measure," comments David J. Skorton, a professor of internal medicine at the University of Iowa. He explains that lack of nutrient flow alters the heart's relaxation properties "even before it effects squeezing, or systole." Besides, systole is readily skewed by factors as changeable as blood pressure and circulating hormones, Skorton points out.

At the moment, sophisticated means of determining diastolic function are too complicated to be practical anywhere but in a laboratory. Tools that are straightforward enough for use in intensive care units or clinics tell little more than how fast the heart is filling. "We hope to straddle these extremes," to create a noninvasive but scientifically satisfying diagnostic method, explains David C. Homans, the University of Minnesota cardiologist developing Bioenergy's software. The company is now comparing its echocardiogram software with established ultrasound research devices. Homans plans to measure such characteristics as wall thickness and stiffness, the geometry of the chambers and total heart volume.

Knowing these attributes will help cardiologists make accurate comparisons of how a drug—ribose, for instance—works on a given individual and on people with dissimilar heart conditions or medications. Before the programs can be routinely applied to humans so that Bioenergy can collect the data it needs to satisfy the FDA, much work must be done in animals, Homans cautions.

By year's end Bioenergy expects to have decided which major pharmaceutical company will lead ribose through clinical trials. If the solution proves effective, the sugar might one day take the form of a pill. Not quite an ordinary sugar pill and certainly not a bitter one. —*Deborah Erickson*

Field Effects

A health worry for electric blanket makers

In 1945 a General Electric advertisement trumpeted one dividend U.S. consumers could expect at the end of World War II: an automatic blanket adapted from the "electrically warm" suits the company made for flyers on the "sky road to Tokyo." The ad's headline read: "How You'll Keep Warm in Bed—After the War."

Now, 45 years after peace broke out, two of the three major U.S. manufacturers of electric blankets—GE is no longer in the business—are quietly trying to stave off what could turn into a battle over the safety of their products. In response to controversy over the effects of electromagnetic fields on health, they have redesigned their blankets to minimize the magnetic field. The blankets are the first consumer product to undergo such a change. Unlike GE, the blanket makers did not flaunt their move in an advertisement.

The manufacturers may be just one step ahead of the government. A public meeting the Food and Drug Administration scheduled for mid-November may be a prelude to recommendations for reducing the magnetic and electric fields of blankets. The meeting was called after 18 Congressmen asked that blankets be labeled as hazardous for children and pregnant women.

Behind the congressional concern are studies suggesting that 60-hertz fields from power systems and electric blankets can be linked to cancer and other cellular changes ["Science and the Citizen," SCIENTIFIC AMERICAN, July]. Regular users of electric blankets may over a year's time be subjected to an average magnetic field of between .5 and one milligauss, comparable to the average field exposure from all other sources, says H. Keith Florig, a researcher who is studying the fields from blankets under a contract from the Electric Power Research Institute, the electric utilities' research arm.

So far the data on the effects of such fields are worrisome but inconclusive. A study by David A. Savitz and coworkers at the University of North Carolina at Chapel Hill, published in the May, 1990, issue of the *American Journal of Epidemiology,* indicated that children borne by women who used electric blankets when they were pregnant had two and a half times the expected incidence of brain tumors as well as a 70 percent greater likelihood of developing leukemia. The article pointed to a 30 percent increase in the rate of childhood cancers as a whole.

Yet the same issue of the journal reported results of research by René Verreault and co-workers at the Fred Hutchinson Cancer Research Center in Seattle that found little, if any, connection between testicular cancer and electric blanket use among adult white males. Other studies have shown similarly conflicting results.

Even though the jury is still out, consumers may be feeling less comfortable in their heated beds. *Consumer Reports,* noting the uncertainties surrounding the issue, recommended last year that children and pregnant wom-

en should avoid electric blankets and mattress pads in favor of comforters. And, after remaining stable for many years, sales of electric blankets did in fact drop by 11 percent to five million units in 1989, according to *Appliance Magazine*. But manufacturers say the decline may be caused by warm winter weather or financial woes of retailers.

Whether it is weather or fear that is affecting sales, some blanket makers are taking steps to reduce the magnetic fields their products generate. In initial FDA tests, a redesigned blanket made by Northern Electric Company in Chicago registered a maximum magnetic field of between five and 10 milligauss in direct-contact measurements. The manufacturer claims that is a 20-fold reduction in field strength from its earlier product.

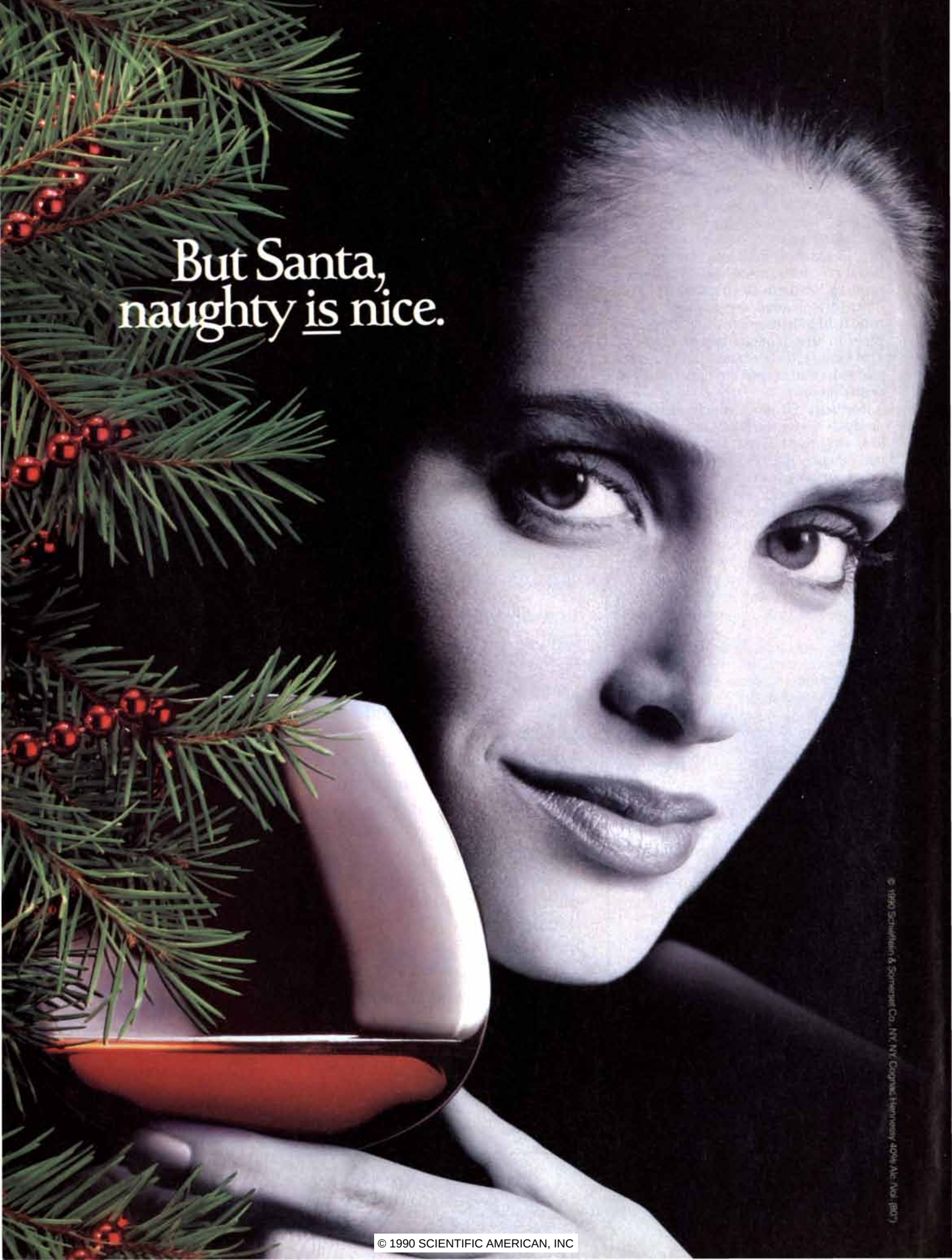
Northern Electric, which sells its products under the Sunbeam, Slumber Rest and private labels, says it canceled out most of the field by making current flow in opposite directions in two parallel wires. Another manfacturer—Casco-Belton Corporation in Grover, N.C.—also adopted the same principle. Preliminary FDA tests showed that the redesign also produced a maximum magnetic field between five and 10 milligauss, about five to 10 times less than the company claimed for its old blanket line.

These measures, however, do not eliminate electric fields, which have also been shown to cause biological changes in some studies. For these fields, the FDA says it may suggest that manufacturers encase wiring in grounded shielding—a more complex and expensive design change than those required for reducing the magnetic field.

The one major holdout against changing design is Fieldcrest Cannon in Greensboro, N.C., whose blankets were found in initial FDA tests to have a top magnetic field of 150 to 200 milligauss. "We continue to be concerned about all the research going on," says M. Kenneth Doss, a vice president there. "But it's difficult to take these tests and translate them into something meaningful."

When Northern Electric and Casco-Belton redesigned their products, they did not advertise that fact. "I think as an industry we don't want to draw too much attention to the issue," says David F. Brantley, sales manager for Casco-Belton.

If safety issues do persist, they may threaten an era when, as the GE ad noted, "'cold-blooded' Americans" could wear "gossamer nighties, keep windows wide open—and be perfectly comfortable." —*Gary Stix*



Food for Thought

Nutritionists earn the right to know

A food fight is taking shape in Washington over the Food and Drug Administration's plan to require nutritional labeling on most foods. Only some packaged foods now carry such information, and many of those are labeled voluntarily.

Under the FDA's proposals, the list of nutrients that must be disclosed on labels will be altered. Of the vitamins, only A and C would still have to be disclosed, but levels of saturated fatty acids, dietary fiber and cholesterol would be added. The agency also wants produce and seafood, as well as all packaged food, to be sold with nutritional labels—possibly on signs at the point of sale.

Food industry groups are already up in arms over an FDA plan to restrict the terms "low cholesterol" and "cholesterol free" to low-fat foods, which would prevent their use on vegetable cooking oils. And the National Academy of Sciences raised their ire further by rushing out a study that concludes the FDA's plans do not go far enough.

Among its recommendations, the academy says the FDA should also require fast-food restaurants to display information about the nutritional content of meals. "Imagine the amount of wall space that such information would need to cover," protests Michael E. Hurst, president of the National Restaurant Association. Hurst says three quarters of chain operators already offer nutritional information to patrons who request it. (An association spokesperson acknowledges, however, that the number who do request information is "very, very small.")

The academy report also calls for the FDA and the U.S. Department of Agriculture—which has jurisdiction over meat and poultry—to require calories per serving, total fat, saturated fat, unsaturated fat and cholesterol content to be listed on the new labels. It wants the FDA and the USDA to define descriptive terms that could be used on labels, such as "good source of protein."

Soon to be running the gauntlet between supporters of the academy and industry groups is David A. Kessler, a physician and lawyer at Albert Einstein College of Medicine. Kessler will soon be nominated to fill the post of FDA commissioner. If appointed, he is likely to support tight controls over health claims and greater disclosure of ingredients. "Sound public policy dictates that the information a label conveys should afford the greatest opportunity to affect health positively," he wrote last year in the *New England Journal of Medicine*.

Although the USDA is under pressure to follow the FDA's lead, so far it is keeping its cards close to the chest. "We're concerned that meat and poultry would appear to be bad foods" if they were labeled with saturated-fat content, says Sharin Sachs, director of the Information Office of the USDA's Food Safety and Inspection Service. Lester R. Crawford, administrator of the service, has suggested that the USDA might establish definitions within product categories—so that low-fat beef would be labeled low in fat in comparison with other kinds of meat.

The USDA is not the only organization with misgivings about the FDA's approach. "It might be counterproductive, as it will lead people to think that certain nutrients are bad and others good," says Agnes Heinz, a nutritionist at the American Council on Science and Health, an independent consortium of university scientists and physicians. "The most common nutritional problem in this country is too much food. By food labeling we single out certain fats and treat them as if they were pariahs," Heinz asserts.

Food labeling does have marketing power: a study conducted by Giant Food in Washington, D.C., in collaboration with the FDA concluded that giving products labels such as "low sodium" and "low cholesterol" stimulated shoppers to buy 4 to 8 percent more. Moreover, shoppers' ideas about nutrition have become more sophisticated, and buying habits have generally improved. As many as 20 percent of shoppers are now buying for someone on a restricted diet, says Timothy M. Hammonds, senior vice president of research at the Food Marketing Institute and a member of the academy panel. "If people want to know, they should be able to find what they need to know," adds Laura S. Sims, a University of Maryland nutritionist.

Still undecided is whether, as the academy urged, the FDA can prevent states from inventing their own regulations. Just before it retired in disarray, Congress passed legislation that would mandate FDA action on labeling and allow some state initiatives. In any event, the food wars are not yet over. The FDA is soon to define other food "descriptors"—seductive but officially meaningless terms such as "high fiber" and "lite." Food manufacturers may find themselves at odds with the agency again.

—Tim Beardsley

Garbage In, Garbage Out

Simple geometry brings supercomputers to their knees

Bigger, faster hardware is supposed to make computer models much more useful. Supercomputer-aided design, analysis and manufacturing could cut millions of dollars from product development costs. Airplanes could fly without wind-tunnel testing, and automobiles could enter production without first building costly prototypes. Even more prosaic tasks, such as injection molding plastic parts or precision machining, could be performed more cheaply and efficiently. Instead the results of computerized analysis all too often bear little resemblance to reality. "You can't trust any result obtained by interacting with solid modeling programs," says Joe Mundy, a computer scientist at General Electric.

The problem is not finding enough computer horsepower to crunch the reams of numbers; it's finding software that delivers the right answers. "There are some very beautiful theoretical algorithms" for doing so-called computational geometry, "but when you run them on real data, they don't work," says John E. Hopcroft, a professor of computer science at Cornell University. Hopcroft and others are working on new methods that are not nearly as beautiful but hold some promise of working correctly.

The elegant programs fail because of the approximate way that computers represent numbers. So-called floating-point representations use a limited number of bits—typically 23 or 54—to encode values and so are necessarily always slightly off. But they are not off consistently.

For example, three points define the equation of a plane that passes through them, but if a program plugs the positions of the points back into the equation, it may decide that one of the points is not in the plane after all. Further decisions based on this physically inconsistent result lead inevitably to disaster. "The screen goes blank, and you have to cold-start the machine," says Michael A. Wesley, manager of design automation research for manufacturing at IBM. When that happens, "it's good," he adds. Far worse is the case where a program continues to deliver answers with no indication that they may be meaningless.

To get around the problem, programmers first tried higher precision, but more bits just push the problem back a little. Instead of failing when two plane surfaces became aligned within one degree, for example, programs might fail at .1 degree.

The next tack for the programmers: special cases—extra snippets of algorithm designed to take care of situations in which the main program might go wrong. But that strategy defeats itself; soon "most of the code is special cases," says Tomas Lozano-Perez, a robotics researcher at the Massachusetts Institute of Technology. "You can't make it work by patching things up."

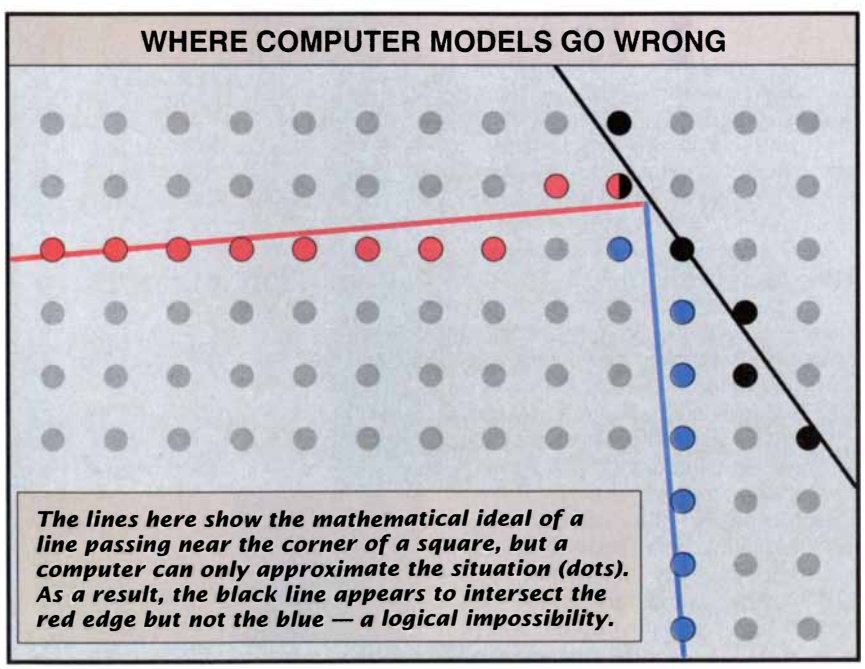
The problem is not a matter of precision or special cases, says GE's Mundy: it's simply mathematically intractable. Take two curved surfaces, each defined by a bicubic equation (of the form $ax^3y^3 + bx^3y^2 + cx^2y^3 \ldots$ typically used to model surfaces by computer). Determining the line where they meet requires an 81st-degree polynomial with several thousand terms. Any feasible program can only approximate the real solution, and the result is surfaces that contain tiny gaps or overlaps. Not only are the surfaces ugly to look at, Mundy says, using them as input to a structural analysis program or a numerically controlled milling machine is a recipe for certain disaster.

In practice, people work around the bugs. "Everybody's pretty blasé," Mundy says; programs crash so often that it becomes routine. Any particular geometric modeling program has its own largely unwritten list of things it can't do properly, and users do the best they can within those confines. "There's a tremendous amount of skill and cunning involved," he says. "A model is like a work of art."

Such artistry is considered beyond the call of duty by many people who want to use geometric modelers. More important, it is certainly beyond the capability of programs that might supply data to a modeling program or rely on a modeler for input. Some of Wesley's current work, for example, requires modeling the shapes of wires and semiconductor layers in integrated circuits. One set of programs determines how shapes change with each manufacturing step, and another set analyzes the operation of the resulting chip. Modeling software must become significantly more robust to be a trouble-free part of such a system.

Hopcroft and other computer science theorists are hoping to build more usable software by discarding the elegant, simple algorithms and starting from a completely different base. Their new programs reduce each geometric problem to a set of logically independent questions, calculate the answers once and use the results in all subsequent processing. Inconsistencies are impossible.

Reducing problems to sets of logically independent questions is not easy, however. Some problems, Hopcroft says, don't lend themselves to analysis. Furthermore, the issue extends beyond pure geometric modeling. Any application that involves calculating values on a grid of points—such as finite element analysis or simulations of fluid flow—can fall prey to the inconsistency bug. Researchers have their hopes, but meanwhile engineers avoid software models when they can, and the supercomputers still crash. —*Paul Wallich*



The lines here show the mathematical ideal of a line passing near the corner of a square, but a computer can only approximate the situation (dots). As a result, the black line appears to intersect the red edge but not the blue — a logical impossibility.

THE ANALYTICAL ECONOMIST

Downturns that echo

"...these decennial [business] *crises do depend upon meteorological variations of like period, which again depend, in all probability, upon cosmical variations of which we have evidence in the frequency of sun-spots, auroras, and magnetic perturbations."*

—WILLIAM S. JEVONS, 1879

Economists no longer resort to a telescope to determine whether a nation is sliding into a recession. Increasingly, however, U.S. observers may need to look overseas to fathom economic shifts. While every nation still is responsible for broad, up-and-down swings of its economy, the precise course can be significantly affected by business trends elsewhere.

For decades, economists have built elaborate models in the hope of determining what drives business cycles, (shorthand for the expansions and contractions of an economy). Linkages between gross national product, employment, the money supply and dozens of other variables have been explored.

During the U.S.'s long period of postwar economic dominance, other industrialized economies played only a cameo role in influencing American business cycles. Openly orchestrated policies, such as efforts to manage exchange rates, brought the U.S. into closer synch with economic cycles in other nations. Global economic shocks (foremost the ballooning oil prices of the 1970s) strained many economies simultaneously.

Traditionally the American economy has served as a leading indicator, or early warning signal, of economic waves, observes Geoffrey H. Moore, who directs the Center for International Business Cycle Research at the Business School of Columbia University. The onset of a recession in the U.S. was typically followed by downturns months later in Europe and Asia. For instance, Moore and his colleagues say U.S. growth began to slow in February, 1989; nine other industrial countries showed signs of weakening this past summer. (West Germany was the principal exception, Moore adds.)

Over the past decade the economies and financial markets of Japan, West Germany and other major trading partners have become much more closely tied with their U.S. counterparts, diluting the nation's leadership. Imports amounted to almost 9 percent of the U.S. gross national product in 1988, for example, up from less than 4 percent in 1970. (Exports in 1988 were another 6.6 percent of GNP.)

In addition, foreign investment in the U.S., at more than $72 billion last year, amounts to more than one sixth of all investment at home. Before 1979, excess U.S. savings funded capital investments abroad; cash from abroad is now seen as playing a vital role in U.S. growth. As the *1990 Economic Report of the President* points out: "Interfering with the free flow of foreign direct investment into the United States would harm the U.S. economy."

As a result, trouble abroad—regardless of what causes it—can pummel an already teetering U.S. economy. No growth here means that the value of the dollar will decline against other currencies, thus making goods from Cleveland cheap in Calais. Yet if foreign economies stall as well, U.S. producers will still not find many customers.

If the trade picture is dim, that of the financial markets is worse. A tumultuous decline in the Tokyo stock market, which lost about 40 percent of its value during the first 10 months of 1990, has discouraged Japanese investment in the U.S. In the last six months of 1989, Japanese institutions bought $17.5 billion in U.S. securities. In contrast, those institutions turned into net sellers of such securities in the first half of 1990, to the tune to $8.9 billion.

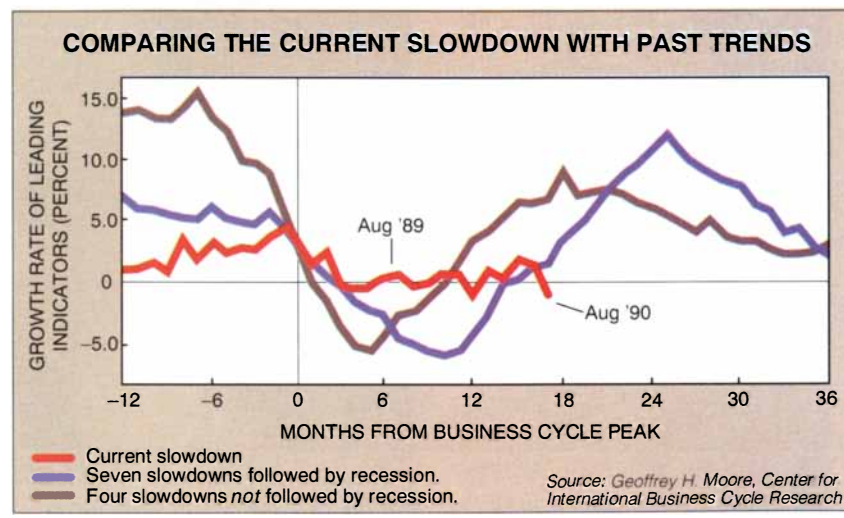
Closer ties to other economies also mean the U.S. has sacrificed some control over its own economic destiny, says Paul R. Krugman, an economist at the Massachusetts Institute of Technology. Traditionally the Federal Reserve has wielded enormous power to spur a recession—or stall one—by shifting interest rates. For instance, the Federal Reserve could rein in a recession by lowering interest rates (thus boosting demand). Now, however, such a move could further weaken an anemic dollar, making imports more expensive, significantly exacerbating inflation and possibly hastening the flight of foreign capital. "So what's really happened is that the Federal Reserve has less room to maneuver, less opportunity for independent action," Krugman says.

A U.S. recession, in turn, would also crimp some economies, notably in developing countries. "As U.S. purchasing power weakens in durable and nondurable goods—such as raw materials from Latin America and Asia—then the vitality of our trading partners will also be eroded," says Philip Braverman, chief economist with DKB Securities in New York City, a division of Dai Ichi Kangyo Bank.

Others might feel less of a pinch. U.S. appetites for Japanese goods such as compact disc players and televisions will doubtless diminish in a recession. But since the Japanese government began coaxing consumers three years ago to spend rather than save, Japanese manufacturers have found ravenous buyers at home, Braverman says.

Regardless of complex links to other economies, final responsibility for U.S. economic spasms lies nowhere else but here. Rudiger Dornbusch, an economist at M.I.T., comments, "We have too high interest rates, too large a budget deficit, industry that is too lazy, research that is too slow, declining literacy, unbounded mediocrity in our politicians—all that makes for a slow economy. The only growth industry has been the financial services, and that's done nothing but got us into trouble. We'll spend the 1990s paying these bills."

—Elizabeth Corcoran and Paul Wallich



MATHEMATICAL RECREATIONS

Fermat's Christmas Theorem is explained in one dickens of a tale

by Ian Stewart

'Twas Christmath Eve. In a chilly, cramped office, a grandfather clock moved its hands inexorably toward the vertical and chimed a perfect number of bongs. Bob Scratchit blotted his ledger with Möbius paper, which had only one side so the ink didn't soak through. He closed the ledger and replaced it on its shelf. Tomorrow was his annual holiday. No work to do for the next factorial-four hours. He put on his coat and a scarf so threadbare that its fractal dimension was less than two. On the way out, he passed his employer. "Merry Christmath, Mr. Stooge," he said cheerfully.

"Bah! Humbug!" exclaimed the old man grumpily. "Shop's closed on Christmath Day, Scratchit. You know what that means?"

"It means we get a whole day off, Mr. Stooge."

"It means, Scratchit, that there are no customers tomorrow. A day without income. A day when the tills of Ye Olde Mathematickal Curiositye Shoppe will not admit a single coin!"

It was hardly a propitious moment, but Scratchit had promised his wife he would ask. "Er—Sir?"

"What now?"

"I was promised a Christmath bonus, sir. It's for Whiny Jim, you see, sir. My youngest, the one who's a chronic complainer, sir. Just a small—"

"Bonus? Bonus! Another word, Scratchit, and you're fired!"

Scratchit left in disappointment. But by the time he reached home, the spirit of Christmath had negated his despair, endowing him with a more positive outlook on life.

"You mean no presents?" screamed Whiny Jim.

"We'll just have to make do, son," Scratchit said, his cheerfulness decaying exponentially.

"I want a present! I want a new theorem! Or at least a secondhand lemma! Charlie Pickens has a super one! Crumbs, Dad, even a conjecture would be better than nothing!"

"I'm sorry, Whiny Jim, but Mr. Stooge keeps his conjectures to himself. I can't even manage a straightforward fallacy, I'm afraid. I'm flat broke."

"Your problem, Dad, is you've got no ambition. You ought to apply for that job at Pithy Pythagoras's Pawn Shop!"

"Whiny Jim, I am not a proud man, but I will never stoop so low as to sell worn-out right triangles with the hypotenuse turned back!" Scratchit forced himself to calm down. "It will be the traditional soggy pudding left over from Easter, and you'll enjoy it like every other Christmath! If you're really lucky, I might just be able to dig out an old paradox that your mother gave me. A fresh coat of logic and it'll be just like new!"

"Intuitionist logic?" Whiny Jim asked hopefully. "Not just the ordinary true-and-false stuff?"

"A brilliant idea, my boy!" agreed Scratchit. Whiny Jim went off, temporarily mollified, leaving Scratchit frantically trying to find a statement whose truth or falsity cannot be determined. He decided to call Mr. Stooge to ask for an indeterminate truth value, but the telephone operator told him the number had been disconnected because of underuse.

In a dusty apartment on the other side of town, Ebeneezer Stooge settled himself snugly in his bed, thoughts of money and taxes dancing in his head.

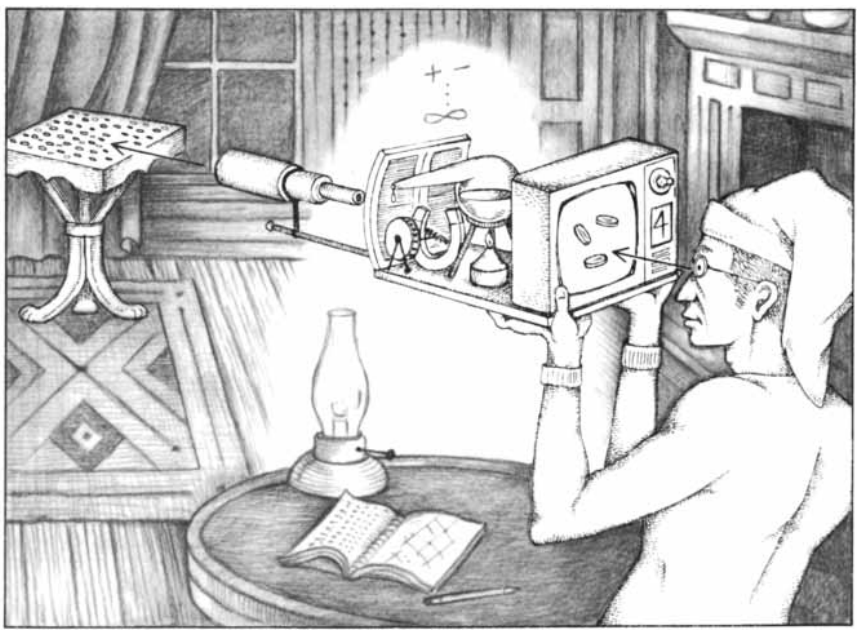
He awoke when a cold wind tangled the curtains and rattled the windowpanes. He leaped from the bed to close the window but found it was already shut. From where could the wind be—?

"Ebeneeeeeezerrrrr," came a dismal voice. Stooge flung himself back into the bed and cowered beneath the blankets. "Who ... who are you?"

"I," bellowed the voice, "am the Ghost of Theorems Past. I have come to take you with me, Stooge!" The ghost stretched out his ethereal hand, which Stooge reluctantly grasped.

Stooge suddenly found himself in a wood-paneled room. A man dressed in a black robe was writing with a quill pen. "Where are we?" Stooge asked.

"France. It is Christmas Day, exactly 350 years ago."



"Stooge glanced through the moduloscope at the 147 coins on his night table."

"Who's the mug in the rug?"

"The gentleman with the wig, Stooge, is the great mathematician Pierre de Fermat, best remembered for his unproved 'Last Theorem' and one of the founders of number theory. He is signing a letter to his friend Marin Mersenne. If we traveled back to the present, we could read the original letter, which is dated December 25, 1640. The letter tells Mersenne of a wonderful discovery."

"And what is that revelation?"

"It's known as Fermat's Christmas Theorem. Some prime numbers can be expressed as the sum of two perfect square numbers: for example,

$$5 = 1 + 4 = 1^2 + 2^2 \text{ or } 13 = 4 + 9 = 2^2 + 3^2.$$

Other primes cannot be so expressed: for instance, 3 or 11. Fermat discovered which primes are which."

Stooge got out a scruffy notebook and began calculating. Soon he had solved the problem for all primes up to 100 [*see table at right*].

"Do you see the pattern?" asked the Ghost of Theorems Past. Stooge shook his head. "Seeing as it's Christmath, I'll give you two clues. The first is to ignore the prime number 2, which is exceptional. [As the sole even prime, it usually is!] The second is to look at the remainder on division by 4. Every odd prime is either greater by 1 than a multiple of 4 or greater by 3: that is, it is of the form $4k+1$ or $4k+3$. For example, $5 = 4 \times 1 + 1$ is of the form $4k+1$."

Stooge added a new column to his table to show whether a prime was of the form $4k+1$ or $4k+3$; the pattern of primes emerged. "Primes that can be expressed as the sum of squares seem to be of the form $4k+1$," said Stooge in surprise. "Apart from 2, which you tell me is exceptional."

"Excellent. Now Fermat didn't just guess this: he proved it. At least he outlined a method to prove it." As the Ghost of Theorems Past faded away, Stooge could still hear it muttering: "Leonhard Euler definitely did prove it, in 1754 or thereabout…."

Stooge found himself back in his chilly bedroom. He tried to sleep, but Fermat's strange theorem kept churning in his mind. Primes. Sums of two squares. Remainders on division by 4. Madness! He tossed, he turned, he raided the refrigerator, but he could not sleep.

Tossing and turning in a far less comfortable bed was Bob Scratchit, who wondered where he could lay his hands on an indeterminate truth value in time to slip it into Whiny Jim's Christmath stocking.

Stooge had been asleep for less than $29 = 4 + 25$ seconds when he heard a terrible yowling sound and a thunderous crash. Had Parson Snows thrown his chamber pot at Widow Kleene's cat again? No, the noise had been within Ebeneezer's bedroom. He began to quiver with fear. A luminous shape was materializing before him.

"I," boomed the shape, "am the Ghost of Insights Yet to Come."

"Foul fiend, do what you will, for I am too tired to protest."

The Ghost of Insights Yet to Come placed a box on the table and commanded, "Open it."

Inside Stooge saw what looked like a television screen with a dial. He held it up in his hands. "What is it?"

"A moduloscope. It lets you ignore those things that you don't really want to see."

"You mean, like poor people? I always do that anyway."

"Ah, but with a moduloscope you can avoid seeing things in a perfectly consistent fashion. In particular, if you tune the dial to a number and look through the device, you won't see any multiples of that number. Set it to 'channel 4' and look at my two hands. How many fingers do you see?"

"Two. Where did the other eight go?"

"The moduloscope first subtracts eight fingers because 8 is the greatest multiple of 4 that is less than 10; it then displays the remaining two fingers. Mathematicians describe the operation of the instrument more succinctly: '10 modulo 4 equals 2.'" Stooge glanced through the moduloscope at the 147 coins on his night table. Only seeing three, he shrieked. He jerked the moduloscope away from his eyes and found to his relief that all the coins were still there.

"Stop fooling around," snapped the ghost. "Leave the dial on channel 4, get out that notebook of yours and look at your table of primes. What do you see?"

"Nothing but 1's and 3's—apart from 2, which is exceptional. Every prime that is a sum of two squares looks like a 1; all the primes that are not sums of two squares look like a 3! But of course, that's just the $4k+1$ or $4k+3$ condition; either 1 or 3 modulo 4."

He paused. "But I still do not understand why the value of the prime modulo 4 is important."

"Instead of the primes, look at the squares."

Stooge peered at the table through the moduloscope. There was a lengthy silence. "All I see," he said at last, " is the equation $1 = 0 + 1$, repeated over and over again."

PRIME NUMBER	SUM OF SQUARES?	$4k+1$ OR $4k+3$?
2	$1^2 + 1^2$	exception
3	no	(4 x 0) + 3
5	$1^2 + 2^2$	(4 x 1) + 1
7	no	(4 x 1) + 3
11	no	(4 x 2) + 3
13	$2^2 + 3^2$	(4 x 3) + 1
17	$1^2 + 4^2$	(4 x 4) + 1
19	no	(4 x 4) + 3
23	no	(4 x 5) + 3
29	$2^2 + 5^2$	(4 x 7) + 1
31	no	(4 x 7) + 3
37	$1^2 + 6^2$	(4 x 9) + 1
41	$4^2 + 5^2$	(4 x 10) + 1
43	no	(4 x 10) + 3
47	no	(4 x 11) + 3
53	$2^2 + 7^2$	(4 x 13) + 1
59	no	(4 x 14) + 3
61	$5^2 + 6^2$	(4 x 15) + 1
67	no	(4 x 16) + 3
71	no	(4 x 17) + 3
73	$3^2 + 8^2$	(4 x 18) + 1
79	no	(4 x 19) + 3
83	no	(4 x 20) + 3
89	$5^2 + 8^2$	(4 x 22) + 1
97	$4^2 + 9^2$	(4 x 24) + 1

What primes are sums of squares?

"Yes. And do you see why?"

"Because the only squares modulo 4 are 0 and 1?"

"Exactly. If you square an even number, you get a multiple of 4, which looks like 0 through the moduloscope. If you square an odd number, you get 1, 9, 25, 49—all one more than a multiple of 4. So sums of squares of modulo 4 are either $0+0=0$, $0+1=1$ or $1+1=2$. What's missing?"

"3," said Stooge.

"Correct. A sum of two squares can be 0, 1 or 2 modulo 4, but never 3. So primes—indeed any number at all—of the form $4k+3$ cannot possibly be a sum of two squares. And now you see why modulo 4 is important, yes?" The ghost began to disappear.

"Don't go!" cried Stooge in despair. "That's all very well, but it doesn't prove that all primes of the form $4k+1$ are sums of two squares, does it? Just that the others definitely aren't."

Faintly came the reply: "You are right. But salvation is at hand. Keep hold of the moduloscope, and waaaait."

Drat, thought Stooge, it must be another ghost. Trouble always comes in threes. He shouted toward the ceiling, "Come on then, materialize, we haven't got all night!"

"I am the Gh—atchoo!"

"What?"

"The Ghost of Proofs Present. It's freezing in here! Don't you ever light a fire?" The ghost blew its nose loudly on a wisp of ectoplasm.

"You've come to show me how to prove that every prime of the form $4k+1$ is a sum of two squares?"

"Right on, bro! We ghosts get some real weird jobs! But time's a-wasting, Ebeneezy Stooge. Tune your dial to channel 17, and all will be cool!" With a flourish, the Ghost of Proofs Present produced a sheet of plastic, divided into squares, and laid it on the table. "I'll show you the proof for the prime 17, but the same method works in general. The idea, Ebeneezy my friend, is to stop thinking about the primes and start with sums of squares. This special sheet has all possible sums of two squares on it, with x^2+y^2 written in column x and row y. Look at it through your moduloscope. What do you see?"

"Lots of numbers between 0 and 16, all over the place."

"Oh, yeah, I forgot. Take this felt-tipped pen and draw a circle around every 0 you see, okay?" Stooge created a curious periodic pattern of circles [*see illustration below*], stared at it and then shook his head dubiously.

"There's a hidden pattern," said the ghost. "Let me color some of the circles red, the rest green.... Do you see anything?"

"My word! It's just two regular grids, laid on top of each other."

"Correct! The proper name for such a grid is a lattice. The colored dots that we have made are all the points (x,y) in column x and row y such that x^2+y^2 is a multiple of 17. Now, look at the red lattice, and tell me which dot is nearest to the origin (column 0, row 0)."

"That's easy. It's in column 1, row 4."

"And the corresponding sum of squares is which multiple of 17?"

"$1^2+4^2=17$ itself! I see! You're telling me that the point in the red lattice nearest to the origin solves the problem of representing 17 as a sum of two squares!"

"Right you are. The green lattice works, too, but it just gives the solution 4^2+1^2, in the opposite order. Try another one: tune your dial to channel 41 this time. Does the same sort of thing happen?"

"Yes. Look, we get two superposed lattices again!" said Stooge. "And the nearest point to the origin in the red grid is in column 4, row 5, and 4^2+5^2 is equal to 41!"

"Great! You can have a lot fun trying other channels on the moduloscope. Choose your prime p and mark all positions (x,y) where x^2+y^2 is a multiple of p. You always get a pattern that is formed from two lattices, although you probably wouldn't have noticed that if you weren't told to look for it.

"But I am the Ghost of Proofs Present, not just Examples! I must explain why there are two lattices and why the lattice point nearest the origin always solves the problem! First, the existence of the two lattices. That depends on the square root of –1."

"Didn't know –1 had a square root," interrupted Stooge.

"Ah. No real number can have square –1, so a new number i was invented for which $i^2=-1$, and the complex number system was born. But with a moduloscope you don't need complex numbers." He wrote something on the plastic sheet. "Take a look at this through your moduloscope, still on channel 17." Stooge looked. The sheet read:

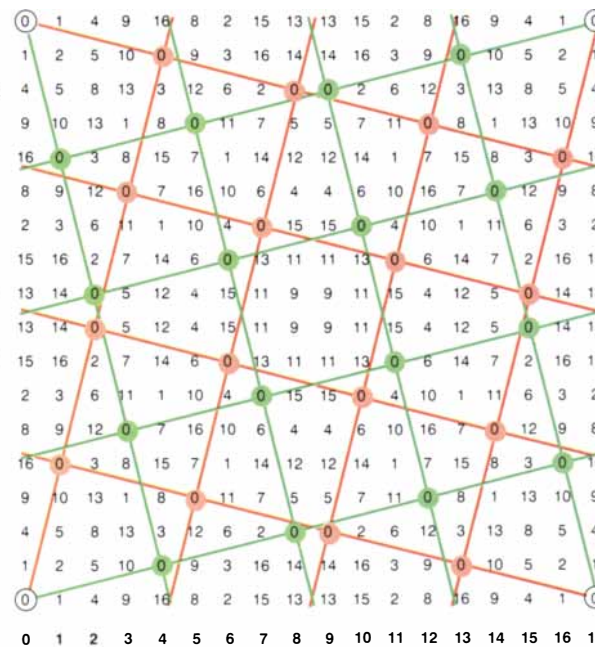
$$x^2+y^2=(x+4y)(x-4y)$$

"Seems crazy, huh? But most things are crazy, seen through the moduloscope—until you interpret them correctly. From basic algebra we know that $(x+4y)(x-4y)=x^2-16y^2$. But through the moduloscope, –16 is the same as 17 – 16 (because multiples of 17 are invisible), and that's just 1. So, through the moduloscope, $x^2-16y^2=x^2+y^2$.

"The dots that you marked," the ghost pointed out, "are those that—seen through the moduloscope—satisfy the equation $x^2+y^2=0$, but the equation modulo 17 factors as $(x+4y)(x-4y)=0$; that is, $x=-4y$ or $x=4y$. Each factor corresponds to one of the lattices. The red lattice is given by the equation $x=-4y$ and the green one by $x=4y$. All modulo 17, of course! Look at the lattices and check. For example, in the green lattice, you'll find all the points—(4,1), (8,2), (12,3), (16,4) and so on—satisfying the equation $x=4y$.

"That's the first important idea. When viewed through the moduloscope, tuned to channel 17, the number –1 has a square root, namely, 4!

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
17	289	290	293	298	305	314	325	338	353	370	389	410	433	458	485	514	545	578
16	256	257	260	265	272	281	292	305	320	337	356	377	400	425	452	481	512	545
15	225	226	229	234	241	250	261	274	289	306	325	346	369	394	421	450	481	514
14	196	197	200	205	212	221	232	245	260	277	296	317	340	365	392	421	452	485
13	169	170	173	178	185	194	205	218	233	250	269	290	313	338	365	394	425	458
12	144	145	148	153	160	169	180	193	208	225	244	265	288	313	340	369	400	433
11	121	122	125	130	137	146	157	170	185	202	221	242	265	290	317	346	377	410
10	100	101	104	109	116	125	136	149	164	181	200	221	244	269	296	325	356	389
9	81	82	85	90	97	106	117	130	145	162	181	202	225	250	277	306	337	370
8	64	65	68	73	80	89	100	113	128	145	164	185	208	233	260	289	320	353
7	49	50	53	58	65	74	85	98	113	130	149	170	193	218	245	274	305	338
6	36	37	40	45	52	61	72	85	100	117	136	157	180	205	232	261	292	325
5	25	26	29	34	41	50	61	74	89	106	125	146	169	194	221	250	281	314
4	16	17	20	25	32	41	52	65	80	97	116	137	160	185	212	241	272	305
3	9	10	13	18	25	34	45	58	73	90	109	130	153	178	205	234	265	298
2	4	5	8	13	20	29	40	53	68	85	104	125	148	173	200	229	260	293
1	1	2	5	10	17	26	37	50	65	82	101	122	145	170	197	226	257	290
0	0	1	4	9	16	25	36	49	64	81	100	121	144	169	196	225	256	289



***The sums of squares* (left) *and the same table as seen through channel 17 of the moduloscope* (right)**

In fact, $4^2 + 1 = 17 = 0$. And that leads directly to the existence of the two lattices. Exactly the same thing happens for any prime of the form $4k+1$. Those primes, it turns out, are precisely the primes modulo for which –1 has a square root. Are you ready for the second important idea?"

"As ready as I'll ever be," replied Stooge.

"Every lattice is made up of identical parallelograms. [Here the parallelograms are actually tilted squares, but for many lattices they aren't, so we'll keep calling them parallelograms.] What area does such a parallelogram have? Try some examples."

Ebeneezer scribbled in his notebook and said, "When $p=17$, the parallelogram has area 17 square units. And when $p=41$, it has area 41 square units. I suppose that for a general prime p the parallelogram has area p square units."

"It does, though I won't stop to prove it. But you're probably wondering why I'm interested in the area of the parallelogram."

"It did cross my mind."

"It's because of a theorem proved by Hermann Minkowski, a Russian mathematician who taught in Germany. He invented Minkowski space, which was used by Einstein in his theory of relativity. Minkowski had a bright idea about lattices. It's deceptively simple: if the area of the parallelogram is fairly small, then the lattice points must be fairly close together! So some of them must be quite near the origin.

"Minkowski proved a theorem making this idea precise. Suppose you have a lattice formed by parallelograms, and suppose you have a circle centered on the origin. Minkowski's Theorem says that provided the area of the circle is at least four times as big as the area of the parallelogram, then some lattice point other than the origin lies inside the circle.

"We can use Minkowski's Theorem to show that the nearest lattice point to the origin solves the problem of representing p as a sum of two squares. Let's take the example $p=17$. The area of the parallelogram is also 17. Take a circle of radius slightly bigger than radical 17, say radius 5. Its area is $5^2\pi = 25\pi = 78.54$, and this is greater than $4 \times 17 = 68$, so Minkowski's Theorem applies. Okay so far?"

"Hanging on your every word."

"According to Minkowski's Theorem, a lattice point other than the origin lies inside this circle. Call it (x,y). Then x^2+y^2 is less than or equal to the square of the radius of the circle. That is, x^2+y^2 is less than or equal to 25. But for lattice points, x^2+y^2 is a multiple of 17. That multiple is nonzero since the lattice point is not the origin. Which nonzero multiples of 17 are less than or equal to 25?"

"17 itself," said Stooge. "That's all."

"You got it! So x^2+y^2 must be exactly 17, solving the problem! The same method works in general," boasted the ghost [*see box above*]. "Minkowski's far-out idea started a new branch of mathematics, named the geometry of numbers after his 1896 book of that title. It uses geometry to study number theory. Not two subjects you'd normally think of as being connected! Another application of the geometry of numbers is the four-squares theorem: every positive whole number (prime or not) is the sum of four perfect squares. But we'll let that problem haunt you till next Christmath, Ebeneezy."

Stooge could relax at last, his mental turmoil finally laid to rest. As he dozed off, he recalled Bob Scratchit. In an unusually mellow mood, he vowed to be kinder to his employee in the future.

Just how far into the future, he hadn't decided.

Whiny Jim woke in good spirits on Christmath morning. "Dad, Dad! Did'ja get me mom's old paradox with a fresh coat of intuitionist logic, huh, did'ja, did'ja? The one with an indeterminate truth value?"

"Well," said Scratchit. "That's kind of hard to say, son." He handed over a battered cardboard box, hunting for the words that would suppress Whiny Jim's earsplitting shrieks. "*I'm not sure whether I did or not!*"

It was a stroke of genius. Or perhaps the Ghost of Insights Yet to Come was sitting on his shoulder, whispering in his ear. For Whiny Jim's face lit up like a Christmath tree. "Oh, Dad! You did!"

Let's face it: you could hardly find a truth value more indeterminate than Scratchit's answer.

Minkowski's proof of the two-squares theorem

Prove that if p is a prime number of the form $4k+1$, then p can be represented as the sum of squares.

Suppose that p is a prime number of the form $4k+1$.

Find all points (x,y) where $x^2 + y^2$ is a multiple of p.

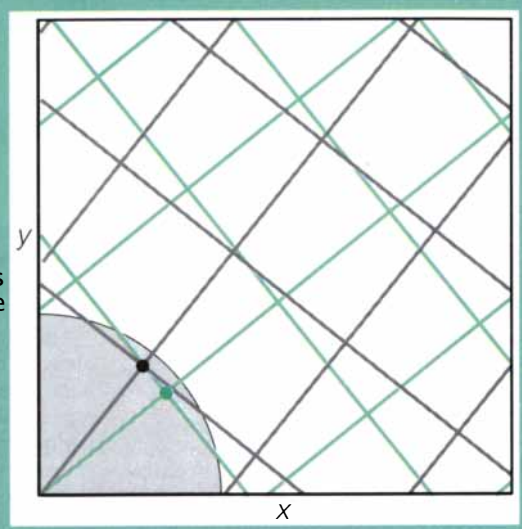
Choose one of the two lattices formed by points (x,y).

The area of the parallelograms in each lattice is p square units.

Draw a circle, centered at the origin, whose radius is sufficiently larger than the $\sqrt{p}$, say, $1.2\sqrt{p}$.

The area of the circle is $1.44\pi p \approx 4.52p$, which is larger than $4p$.

By Minkowski's Theorem, the circle contains a nonzero point (x,y) of the lattice.



By definition, $x^2 + y^2$ is a multiple of p, but because (x,y) is inside the circle, $x^2 + y^2 \leq 1.44p$.

The only nonzero multiple of p that is less than or equal to $1.44p$ is p itself because the next smallest multiple is $2p$, which is too large. So $x^2 + y^2 = p$ exactly, and we have proved the theorem.

FURTHER READING

THE THEORY OF ALGEBRAIC NUMBERS. Harry Pollard. Mathematical Association of America, 1950.

MATHEMATICAL THOUGHT FROM ANCIENT TO MODERN TIMES. Morris Kline. Oxford University Press, 1972.

ALGEBRAIC NUMBER THEORY. Ian N. Stewart and David O. Tall. Chapman and Hall, 1987.

BOOKS

'Tis the season for science books for young readers

by Philip and Phylis Morrison

Creating

BERTA BENZ AND THE MOTORWAGEN: THE STORY OF THE FIRST AUTOMOBILE JOURNEY, by Mindy Bingham. Illustrated by Itoko Maeno. Advocacy Press, 1989 (P.O. Box 236, Santa Barbara, CA 93102) ($14.95).

Early one August morning in 1888 Frau Berta Benz and her two teenaged sons pushed Model 3 out of the shed and down the block so as not to waken Father once the flywheel was spun and the noisy little engine started. They were off to Grandmother's house, 60 miles away in the hills beyond Heidelberg. The car they had quietly borrowed was one of Karl Benz's tricycle Motorwagens, then, along with Gustav Daimler's, the only working automobiles in the world. Off in gentle conspiracy they sped at 15 miles an hour—their overloaded vehicle traveling along a road utterly innocent of engines and hostile to them by local law.

The three had little driving experience. Although the Motorwagens had been mobile for two years, Karl had never taken one beyond a few prescribed streets and to the Mannheim railroad station, a half mile away from their house. Intrepid, independent Berta alone in the Benz household realized that the future they foresaw for the little cars would not come until the public imagination was caught; this was her day to break the leash of timid use.

The car needed water every hour or so: no radiator, but plenty of horse troughs. Its fuel was a popular dry-cleaning fluid and could be eked out by stopping at every pharmacy en route to buy a few bottles. Tires were solid: no punctures. By afternoon a shoemaker was cajoled into replacing the leather brake lining that had burnt out down the steep grades. Later, resourceful Berta replaced a broken spring control cable by the elastic she discreetly removed from her garter belt.

They made it! News of their journey had preceded them, and a lively torchlight parade came out from town to lead their roofless, lightless, horseless contraption down the final dark mile.

The text is lively, the events carefully authenticated and illustrated by page after page of color wash paintings of dazzling detail and evocative power: places, period costumes, a wonderful telegraph counter and plenty of cars past and present. This deliciously tendentious book has a timely moral in mind: "Encourage your daughters to get dirty, take things apart…and challenge the question as well as the answer." (If you haven't any daughters, tell it to your sons.)

IN FIRST LONG-DISTANCE JOURNEY by motor vehicle, Berta Benz and her two sons stop at a shoemaker's to replace the leather brake lining.

LEONARDO DA VINCI: THE ARTIST-INVENTOR-SCIENTIST IN THREE-DIMENSIONAL, MOVABLE PICTURES, by Alice and Martin Provenson. Paper engineering by John Strejan. Viking Press, 1984 ($16.95).

Six spreads form this striking book. They should fascinate all ages, not only for the excellence of their pop-ups and spinners but even more for their richness and wit in text and image. The towers of Florence pop up grandly, and the ur-helicopter has blades that turn briskly, but it rises out of the square no better than the original, one of the Master's ambitious fiascos. As you turn the tab, a disk unfolds out of his big notebook; on it eight small drawings from the 5,000 pages of his notebooks are reproduced: human bones, a stirring horse's head, a strong derrick, gears, delicate flowers. Other pages show a big armillary sphere, a vanishing fresco, a grand monster in paint and more.

The last spread shows a big, sunny room of a palazzo, a lute set aside on the marbled floor as the lutenist retires and three other musicians play; two bowls of peaches, pears and grapes lie ripe on the side table. Madonna Lisa is posing in her chair, her face turned from you but seen by majestically bearded Leonardo, who represents it so subtly in the celebrated portrait shown here on its easel at about the size of a calling card. Even the empty hall outside the room is visible on the other side of the pop-up backdrop.

This happy excursion to the Renaissance opens with the remark that "1492 was a very good year," when

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of ants into slaves. Who are they? They're

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THE POWER IS ON

Leonardo was teaching his apprentices to play and sing and reckon and mix paint and "create masterpieces."

SIGNALS: THE SCIENCE OF TELECOMMUNICATIONS, by John R. Pierce and A. Michael Noll. Scientific American Library, 1990. Distributed by W. H. Freeman and Company ($32.95).

"Television is *theirs*…yet the complex international telephone network is *ours,* to use as we will." On so plain a declaration of affection, the two adroit authors, veteran engineers of glorious days in the Bell Telephone Laboratories, open an insightful and humane summary of telecommunications and its roots in "the laws of God…and man." The phone system serves its individual users; in contrast, mass communications attract an audience. So it is engineers who run telephony but marketers, programmers and civil servants who direct broadcasting organizations. A shadow of change is falling on this long-standing distinction and adds an undertone of concern to this personal exposition of a changing world.

Eleven chapters offer a distillation of the history, mathematical foundations, physics and present techniques of the world web. Fourier analysis and information theory, modulation and encoding, multiplexing, massive switching and the electromagnetic medium within which it all occurs are what is here in text, diagram and example.

A few of the telling instances that turn generalities credible and concrete are all we can hope to cite. The bandwidth of a good compact disc stereo recording is about 1.4 million bits per second. But a modern Yamaha digital player piano system can now drive the keys and pedals of a real piano to reproduce just what the artist did. It sounds even better than on CD; after all, it is the piano direct you are hearing, not a loudspeaker. But the bandwidth on the floppy disc that is in full control is only 1,066 bits per second. Of course, the same CD system would let you hear instead a flute concerto or a stampede of elephants; the price of its universality is its wasted bandwidth.

Already the most used long-distance channels are not cable or microwave or satellite link but composite threads of glass that carry a myriad of 10-picosecond laser pulses of near infrared light. Optical fibers dominate even the up-to-date digital switching exchanges. The remarkable potential of optical fiber was first discussed in 1968. The transparency of the best fiber is now about 96 percent per kilometer; in 1968 it was lower by 100 powers of 10!

It is the purposeful context and the engineer's air of tempered optimism and cheerful goodwill that make the technical discussion so readable. High school readers—as well as those with less youthful intellectual energy—can follow the uncertain challenges of tomorrow's wide networks, sure to come, still dimly seen, but bound to open new careers for young men and women. Expect to see a little videotext, less teleconferencing and no picturephone at all: "Many consumers…would pay extra not to have it!"

MAKING AND PLAYING MUSICAL INSTRUMENTS, by Jack Botermans, Herman Dewit and Hans Goddefroy. Text by Afke den Boer and Margot de Zeeuw. Translation by Anthony Burrett. Working drawings by Piet Hohmann. University of Washington Press, 1989 ($19.95).

Strong currents of image and idea flow in this work by an expert team mostly from Belgium and the Netherlands. They have joined high art, dedicated craftsmanship and folk musicians worldwide into a single stream. Engravings and paintings, old costumes, tools and materials, and careful working drawings fill the colorful pages. Here a young Tanzanian happily beats his own double-skinned drum, two boys pose with hurdy-gurdies in Edwardian London, and the Goddefroys in street musicians' costume play old tunes, while their small waif of a puppet held on strings from their legs dances in time between them.

The book entices readers to set out down the same fresh stream by learning to make and play some folk instrument. About 40 of them are listed and detailed in increasing order of ambition. An ocarina can be made of hobby clay, which needs no firing, and may be delightfully decorated. A set of musical bottles is even easier. A pair of clap sticks is a little harder to play. There is a clever set of tuned drums made of cardboard tubes, all the same diameter but of differing heights; their drumheads consist of stiff paper tensioned with model airplane lacquer.

The parade of skill continues far longer; only expert craftsmen will march very far. The complex hurdy-gurdy with its wheel-driven strings is at the head of the procession, a challenge for the pros: "Highly exacting and painstaking work…be warned!… An experienced…maker requires a minimum of 160 hours to construct the instrument," not to mention the example shown decorated with miniature paintings. It is wonderful how these bookmakers have linked so seamlessly something most people could build with what only a consummate artist can fashion.

Digging

DIGGING DINOSAURS, by John R. Horner and James Gorman. Harper & Row, Publishers, 1990 (paperbound, $8.95). **DINOSAUR DIG,** by Kathryn Lasky. Photographs by Christopher G. Knight. Morrow Junior Books, 1990 ($13.95). **THE DINOSAUR DATA BOOK (FACTS AND FICTIONS ABOUT THE WORLD'S LARGEST CREATURES),** by David Lambert and The Diagram Group. Avon Books, 1990 (paperbound, $12.95).

Dinosaurs always bulk large on the ridgeline of children's books. This year it was simply impossible to look the other way, so three of the best are celebrated here instead.

John Horner of Montana State University and his expert co-author tell the best firsthand paleontological story of a decade. It turns on Horner's dinosaur finds buried well below the boundary of the Cretaceous period, some 65 million years ago. The swift narrative is sure to enthrall any bone-conscious reader of 12 and up, way up. "Paleontology is always divided into two seasons.… First is the field…you carry your tents with you and search.… Then…is the laboratory season, a time for reflection and study.… The second…has different demands, subtler pleasures. You might say that the difference…is like the difference…between Choteau, Montana, and Paris, France." Choteau is a county seat of about 2,000 souls out under the Big Sky, 10 or so rough, gravelly miles from the camp among the duckbill nests. Paris is "the city where paleontology began" and where still it is most sagaciously practiced.

The book treats both kinds of seasons well, but the inferences from the lucky find of 15 little duckbill skeletons in the mudstone lump are so convincingly drawn that it is Parisian insights we best recall. The first bones of the nestlings evoked a whole noisy coastal rookery of big, gregarious, parental, fast-growing and warm-blooded duckbills. Plenty more bones were later found in support; it is that confirming experience and not logic alone that lies at the heart of scientific reasoning. Sure, it was good luck, but as Branch Rickey said of baseball: "Luck is the residue of design."

Kathryn Lasky's book instead is a

season à la Choteau but equally delightful. It also takes place in Montana, well to the east, next to the Fort Peck reservoir and in rock formations close to the end of the Cretaceous. The story tells of a camping summer for two city families who shared the cares and triumphs of two paleontologists. It ends in high Choteau style once they lug the big plaster-encased bones of *Triceratops* to where the trucks waited. Genuine hard work ended in deserved success—what a rib they found! Scary and tedious by turns, the weeks saw the pickup in real peril of capsizing on the rolling hills and Lasky and her young daughter, Meribah, daring the high face of one butte in the inchworm mode, "a full three minutes to go one foot." The warmth of the photographs and text, the awful mud and the awesome stars make this book prime reading for middle graders.

The Data Book is a storehouse of concise richness, a little like the famous libraries and museums of Paris. Seventy pages are crammed with dinosaurs from A to Z, the outline drawings in the margin recalling identification profiles of planes and ships. Illustrated chapters recount dino classification and dino biology, summarize museums and finds worldwide, and present a long list of dinosaurologists by name and accomplishment, from Luis Alvarez to Zhou Shiwu. The volume ends with an account of dinosaurs revived, some as statues in concrete, some as mobile robotic replicas, buttressed by a list of about 50 films featuring the old saurians. (This reviewer confesses that in 1925–1926 he sat through the original *Lost World* for nine thrilling times; don't miss it. The 1960 version is smoother but not as good.)

Viewing

SEEING EARTH FROM SPACE, by Patricia Lauber. Orchard Books, 1990 ($19.95). **UNDER THE MICROSCOPE: A HIDDEN WORLD REVEALED,** by Jeremy Burgess, Michael Marten and Rosemary Taylor. Cambridge University Press, 1990 (paperbound, $19.95).

The fog has billowed through a not-so-Golden Gate to hide a third of the gleaming city. We see it compellingly—we all but feel the chill—in a weather satellite image that discloses the entire Bay, still as sunny as that cold Pacific shoreline is socked in. Almost 50 such images, immediate and colorful (most of them are falsely but meaningfully color coded), show us the earth from far above. Circles of green crops under pivot irrigation pave an oasis in the Arabian desert just as they dot Kansas; we see named atolls and volcanoes, cities, canyons and deltas, hurricane clouds and polar ice caps, and long plumes of smoke drifting far downwind from the Yellowstone forests ablaze. Here are half a dozen views of the entire earth, several in sharp contrast against a foreground moon. One map shows, almost magically, mid-ocean ridges and seafloor trenches as disclosed by a radar altimeter, able to pick up the subtle dips and rises in the sea surface that the big sunken features induce by gravity.

Would you peer instead into the small? The second book presents a treasury of a couple of hundred images of the microcosm, up from sixfold ring molecules past threads of DNA to chloroplasts, human eggs and sperm to the gemlike eye of a dragonfly. Artifacts are here, too, alloy grains, microchips, Velcro and 1,000 tiny bumps of evaporated aluminum that on a compact disc so elegantly code a millisecond of Mozart.

The space images are a large catch at a good price for all young readers, with a simple and helpful text (once or twice a clue to the size on the ground is lacking). The microscopy compilation—views through the chief kinds of microscopes, all of them well explained—is a paperbound bargain reissue of a book for adults. That book was praised here years back under another title for its width of interest and attractive images. Of the two worlds, the realm of the minute seems the more distant, even though we enter it through the inviting gateway of what is directly visible.

THE BIG DIPPER AND YOU, by E. C. Krupp. Illustrated by Robin Rector Krupp. Morrow Junior Books, 1989 ($13.95). **THE GREENWICH GUIDE TO STARGAZING,** by Carole Stott. Cambridge University Press, 1989 (paperbound, $9.95).

Fifty vivid pages of white-on-black paintings invite a romp among large ideas, as we chart Earth moving among the stars. The seven Dipper stars are embossed on the cover, and in the final pictures of the book they shine again as the viewer looks through an open cabin door out onto the snow. In between, we encounter a real water-filled tin dipper—how many kids have seen one in these faucet-served days?—among a parade of compasses, ice bears, mummies, a spread of costumes, buildings and script from Vikings to the Taj Mahal, a spinning umbrella model for the moving sky, and a long

pleasing effort to explain the motions of that sky, by day, by year and under the slow axial precession.

This couple, astronomer and painter, have actively joined talents to engage readers in the middle grades; the humor of the pictures goes with a good helping of basic geometry, even to the trillion-mile distances of the Dipper stars, a lot here to think about amid all the fun.

Stargazers can be at home under city skies with *The Greenwich Guide*. Its freshest material is a set of 10 or more color photographs of large patches of night sky, exposed to show a bright constellation or two much as the eye sees it. The green-gold glow that is the Thameside night sky seen from what once was velvet-dark and rustic Greenwich Hill makes the key point. "A light-polluted sky will only be dark enough to show up the brightest stars.... Once you are familiar with these patterns you can graduate to darker skies."

Here you can begin with Scorpio and Orion, Taurus and Ursa Major, a time exposure of stars that encircle the pole and others that glide along the equator, all colors clear. Around that naked-eye core the author, who is curator at the Old Royal Observatory, wraps a concise astronomical primer, complete with Greek letters, lists of bright stars, variable stars, double stars, maps of naked-eye and telescopic skies, even to a few rarities like the Crab Nebula and the supernova of February, 1987, before and after. This book is as crisp and pointed as the Dipper book is playful; differentiated from many guides by its concern with naked-eye observing from first to last, it should help initiate an eager audience among teenagers on up.

Living

THE CLOVER & THE BEE: A BOOK OF POLLINATION, by Anne Ophelia Dowden. Illustrated by the author. Thomas Y. Crowell, 1990 ($17.95).

A botany book usually has a few line diagrams to help make all those Greek-named structures plain. Anne Dowden has tackled the same task brilliantly with palette and fine brush, to make a garden of little paintings sure to attract to her brief text any reader fond of flowers. She treats many flowering species, the better to make clear their strategems, from enticing scent and showy blossom to nectar candy and nutritious pollen.

The opening two chapters are written from the viewpoint of the plant, with a fascinating account of the devices that guard against self-pollination. Flowers often provide even for that long-term dead end as a prudent backup, for instance, in the tiny, hidden, closed flowers that snuggle at the base of the showiest violets. The third chapter musters the varied animal pollinators, who complete the ancient coevolutionary partnership, the reciprocal engineering of animal structure and behavior to match the form of flowers, from open platters to cunning traps.

A fine chapter—the most inviting—tells of broken rules. The inch-size yucca moth, sole pollinator of the big spiky plant, collects pollen widely but does not eat it. Instead she rubs the whole mass right into the stigma, to fertilize for certain the ovules below. She has already deposited a few eggs down there; one day her larvae will feed on the ripened seeds. Yucca nectar exists, others take it, but most yucca species depend on one of the little moth horticulturists. No other case of insect pollination is so "foresighted."

There are exotics, but most of the colorful blossoms painted here abound in parks and fields. From fourth graders to teachers of biology, all who read this classic evolutionary evidence of adaptation will enjoy it. The complementary genetic side of the story is not present at all; that is a tale still more deeply hidden.

TOMATO, by Barrie Watts. Silver Burdett Press, 1989 ($6.95). **LARGE AS LIFE ANIMALS (IN BEAUTIFUL LIFE-SIZE PAINTINGS).** Paintings by Kenneth Lilly. Text by Joanna Cole. Alfred A. Knopf, 1985 ($14.95).

These two books each have simple text and bright images to open access by readers in the early grades. The quality of the images is so striking and the texts so clear and natural, if brief, that the books may well delight much more experienced readers.

In the first book the curtain rises on a batch of ripe tomatoes of all sizes lying on a plate and falls on a single, flawless, ripe, ruddy sphere. Ten color photographs trace the life history of a tomato, from a hairy little seed shown much magnified (with a pinhead for scale) to the first tiny shoot, the two-leaved plant an inch high, and on through bud, yellow blossoms and green fruit to final ripeness. The next step is not here but is hard to resist, plainly a live tomato plant in window box or garden. This story is fit reading for consolation on cold winter evenings, and even the most tentative beginners at reading can happily puzzle out the simple narrative headings.

The much larger second book presents what we rarely see in this world of screens and small cameras, the perceptual surprise and pleasure of images of animals at full life size. Both exotic and more familiar forms are shown very naturally by meticulous habitat paintings in engaging color. Some are seen by day, others by night. A thumb-size green tree frog sits amid the tiny leaves of spring. A squirrel monkey infant, sucking its left thumb, looks at you from its mother's back. The mother, perched on an upright yellow banana, "would fit inside your school bag. And her baby could go in your pocket." An elf owlet peers out at her mate from their nest hole in a giant saguaro. The fennec fox tests these big double spreads of almost 12×20 inches; its huge ears push the margins. A paragraph of primer goes with each painting; fuller information appears in notes at the end. One would have welcomed a little more about the plants that are so invitingly painted along with the animals.

THE GREAT MIGRATION, by Jonathan Scott. Rodale Press, 1989 ($35).

The Serengeti grasslands, mainly the Park and its extension across the border into Kenya's Masai Mara Reserve, spread flat and as wide as four or five Yellowstones. It is "as if God had steam-rolled this...enormous plain" and sown its fertile, wind-blown volcanic soils with short, drought-resistant green grass. Nowadays two million hoofed beasts and the predators, scavengers, camp followers and onlookers they irresistibly draw to them tread these lands. More than two thirds of the animals are the odd-shaped wildebeest, antelope kin recalling smallish, ungainly, horned cattle. (Once they were called gnus.) They are nomads, opportunists, obliged to follow the grasses from woodlands to breeding grounds on the short-grass plain and back again by shifting, uncertain routes in seasonal migration.

These migrations are bone-old, as witnessed by the fossils of the Olduvai not far away. For the past seven or so of those million years, Jonathan Scott, zoologist, photographer and artist, has followed the herd. He dwells alone for a month or so at a time out on the range in his diesel vehicle, usually shooting pictures from a table fixed to the inside of the car door. In Kodacolor, with long lens and short, and with pen and paper, he takes us with him in this intimate book of animals and events, the reflections of an awed and knowing zoologist reporting

from the Pleistocene. The lions who wait along with him he knows and names, from the blonde young lionesses with their cubs to the lord of the pride, their old father. We see elephants and zebra and wary impala, the rare wild dogs, the few rhinos, even a little malachite kingfisher.

But first of all this is the place of wildebeest, by ones and twos, in long strings and unending herds, or even one single hide pressed into the mud in striking silhouette, emptied by many scavengers. They canter by or crash to death over unexpected cliffs or cross the river peacefully to graze indifferently as cause and chance enforce. Downstream from each favored crossing, the drowned float in hundreds, a minute fraction of the herd.

Light aircraft can carefully count them. When 30 years ago we first heard of the Serengeti's wonders in books and films by the Grzimeks, aerial census found fewer than 100,000 wildebeest, well less than a tenth of the present population. (Data from 1988 are not yet in.) That was probably the consequence of a plague of rinderpest, a kind of bovine measles. The virus might return any time, although now the domestic cattle are vaccinated. The final limit to wildebeest numbers is the amount of dry-season woodland forage. All this we see and learn in this big glowing book, good for any who can read its clear, explicit prose and pore over the vivid images.

THE FLYING ARK, by Carolyn Jackson. Illustrated by Graham Bardell. Oxford University Press, 1990 ($14.95).

A whole class of real arks are flying today; lucky kids may even have ridden in one of them. Any day in the belly of a big, long-haul jet all kinds of creatures may be flying along with the passengers seated above, each in a special container, each given the surroundings and "the right care to keep it healthy and happy."

From the anxious gorilla munching on jam and honey sandwiches in his strong but boring cage, on to the octopus in a plastic bag of seawater topped off with oxygen that is replenished during long flights, we read of the provisions made for animal travelers. We see bees and hummingbirds, ostriches, camels, giraffes, the quietly hanging moss-bellied sloth, horses, penguins and more in their flight gear. The paintings are big, droll and detailed.

Everyone would concede that passenger aircraft are not designed for elephants. They are thoughtful, steady-nerved travelers in their big crates, but

they have one embarrassing problem. They need about 100 quarts of water a day, so they always drink heavily before boarding. It is easy to guess what happens later. The tiny washrooms aloft are useless to them, so their crates are filled knee high with absorbent peat moss and wood shavings.

The many questions this original book so artlessly raises are sure to open instructive paths of thought for grade school readers and others. Each animal does earn a few lines about its particular nature outside of air travel; a more generalizing page or two on animal needs would have been natural enough. All the same, "Wouldn't Noah be pleased?"

Reasoning

THE KIDS' BOOK OF SECRET CODES, SIGNALS, AND CIPHERS, by E. A. Grant. With cipher wheel. Running Press, 1989 (paperbound, $6.95).

"Don't let this book fall into enemy hands." It seems unlikely that there are any true enemies for so winning and simple a primer of symbol systems. The right stuff is all here, in a brief and easy text illustrated with cheery, cartoonlike drawings at a bargain price, including a single-alphabet cipher disk in pasteboard. Of course, you will read a little history and see Braille, Morse, a few hieroglyphics, a semaphore flag alphabet, a touch of binary computer ASCII, the Rosetta Stone and even how to make one authentic sign of the American Sign Language, "my name," along with the manual alphabet to spell it out. Here you learn the use of key words and the pigpen cipher, among other substitution schemes, all sharply aimed at young grade school readers. Along her path the expert author has even picked up an easy scheme, quite new to the reviewer, to encode a message as a bumpy line graph on squared paper.

BEYOND THE THIRD DIMENSION: GEOMETRY, COMPUTER GRAPHICS, AND HIGHER DIMENSIONS, by Thomas F. Banchoff. Scientific American Library, 1990. Distributed by W. H. Freeman and Company ($32.95).

That imaginative classic of geometry, *Flatland,* appeared in 1884. During that decade the Euclidean geometry of higher dimensions was a hot field for amateur and professional alike; the pros wrangled over priority in enumerating all the regular higher-dimensional figures, only to learn that Ludwig Schläfli had anticipated them in his monograph, then a generation old, a book without a single diagram! The tension between geometric figure and its logical equivalent in algebra is a kind of continuo throughout this very visual book, with few formulas but many figures and lots of appealing (hyper)solid argument. Anyone able to enjoy Euclid's enumeration of the five regular solids in three dimensions will like this book and can follow most of its chapters in all detail.

An introduction through *Flatland* establishes what has revived interest in the topic, not only in recreational mathematics but in research: it is the graphics of the digital computer that enable quick and flexible visual realization of geometric intricacies once daunting to all. Working from scaling to slices and contours (a dunked doughnut and a conventionally cut bagel show us the slicing sequences of the torus) and beyond them to shadows and projections allows the grasp of all the arguments behind one neat table that counts the parts of four-dimensional hypercubes—their corners, edges, faces and solid boundaries—even to *n*-dimensional cubes generally. You come to be almost at home in hyperspace. After all, without any advanced mathematical training, Mrs. Alicia Boole Stott, a Victorian amateur of genius, was the first to describe the slicing sequences of many four-dimensional figures.

The artists have followed. Salvador Dali was much taken by the foldout of the 4-cube into eight solid 3-cubes (as a 3-cube unfolds into six flat 2-squares). Contemporary artists have gone well beyond him in wire models of elaborate projections of hyperspace figures. Advanced visual representations and many-dimensional hyperspace colorfully computer-mapped into three-dimensional perspective are a powerful tool for many applications with a lot of variables, shown with examples from archaeology, dynamics, wave propagation, even stage lighting and dance. In that way, complex problems are rendered visualizable, a big gain for most of us over long tables of values or even lengthy formulas.

The last chapter or two on coordinate and non-Euclidean geometry are more difficult and less explicit. But they are exciting, too; one begins to see how a world of many dimensions might help describe particles that differ only in simple modular properties. This fine book is a real winner for small groups of high school students and their teachers and equally for the mathematical armchair reader—one of the best works of its kind in years.

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ESSAY

Should we implant life on Mars?

by Christopher P. McKay and Robert H. Haynes

The question of whether or not we should implant life on Mars has at its core another question. Could we implant life on Mars? As interesting as the ethical considerations of the proposition are—and we shall look at these—they are moot unless the concept itself is feasible.

Mars might be brought to life through a strategy we have termed ecopoiesis—the fabrication of a self-sustaining ecosystem on a lifeless planet. The word's Greek roots mean "the making of home," a new abode for life. Establishing an ecosystem would create an arena in which evolution could proceed, perhaps independently of further human intervention. The idea of propagating life on other planets is no longer confined to science fiction. Indeed, a small group of scientists met in 1988 at the NASA Ames Research Center to assess the merits of ecopoiesis as a long-range international objective for space exploration.

Missions to Mars have revealed that the planet's surface is cold (temperate latitudes in summer average –60 degrees Celsius, or about –140 degrees Fahrenheit), dry and almost certainly lifeless. Other than Earth, it is the least hostile planet in the solar system, even though any unprotected organisms that might arrive there would be freeze-dried, oxidized and soon reduced to dust. Substantial quantities of water (in the form of permafrost) and other materials essential for the development of biogeochemical cycles may exist in the Martian crust. It has a thin atmosphere (eight millibars of pressure), consisting mainly of carbon dioxide. Its orbit, gravity, likely volatile inventory and other unalterable planetary parameters could support, in principle, a thicker carbon dioxide atmosphere (two bars), whose climate might be suitable for anaerobic microorganisms.

Ecopoiesis on Mars would proceed through two main phases. The first would consist of planetary engineering to warm the climate sufficiently to allow the presence of liquid water and to increase the thickness of the atmosphere by the release of frozen gases. The second would involve biological engineering to create communities of microorganisms selected (or genetically engineered) for growth in the newly salubrious Martian environment. Rough calculations indicate that a microbial ecosystem could be implanted in about 200 years. The lifetime of the new habitable conditions is difficult to predict, although it could be substantial, perhaps on the order of 100 million years.

It is likely that Mars once possessed a much thicker atmosphere and abundant surface water. According to current estimates, these clement conditions lasted for at least 500 million years but came to an end because Mars lacks a long-term geologic cycle. Biological evolution might have started during this period, and remnants of earlier life may be discovered during future missions to the planet. If and only if no potentially viable forms of life are found should we attempt to introduce emigrant species from Earth.

Although the success of ecopoiesis on Mars cannot be assessed on the basis of present knowledge, current and proposed research opens the door to many answers. And much of the scientific harvest from that research would be relevant to environmental concerns on Earth whether or not ecopoiesis were found to be practicable.

A feasibility study would require investigating in detail the climatology of Earth and Mars, past and present ecologies of Earth and technologies for planetary engineering. Earthbound research would have to include studies of the interrelations of biogeochemical cycles and their relation to geologic activity and the factors that promote stability in ecosystems, as well as the mechanisms of biochemical adaption, particularly those used by exotic organisms living in extreme environments. Planetary engineering would focus on developing techniques for warming the Martian atmosphere and surface. Warming might be achieved by reducing the reflectivity of the polar ice caps coupled with injecting trace amounts of greenhouse gases into the atmosphere.

Ecopoiesis raises some novel ethical issues. Traditional theories of value are based on two ingrained habits of human thought: anthropocentrism and geocentrism. Principles of ethics have been formulated primarily to guide and govern the relations among people here on Earth. The scope of ethical theory has recently been expanded, however, to encompass all forms of nonhuman life, ecosystems and even inanimate structures, such as rocks, landforms and barren planets. This radical environmental ethic includes the idea that Earth's rich and diverse biota is inherently good. Thus, the biosphere as we know it is by definition what these theories assert ought to be. This conclusion clearly violates Hume's law: "No ought deducible from is." This gaffe in logic is easy to overlook, however, in light of the serious problems of environmental degradation we must solve. In such circumstances, what is (or perhaps was, a few generations ago) accords well with popular notions of what ought to be.

Ecopoiesis presents us with a choice between a dead and a living planet: What would be the greater good, Mars barren or Mars endowed with life? It is illogical to argue that a dead planet ought to remain as it is, simply because it is. On the other hand, arguments in favor of ecopoiesis conflict with latterday claims of environmental ethics regarding the "moral standing" of planets. If a viable ecosystem can be established on Mars, another question arises: Does this newly indigenous biota have a right to its own natural, but unpredictable, evolutionary trajectory, as currently exists for organisms on Earth? Or should the Martian biosphere be tended to ensure at least early development in a manner agreeable to *Homo sapiens*? Clearly, ecopoiesis raises philosophical issues that can be resolved only by adopting a cosmocentric theory of intrinsic values.

Suppose that a feasibility study does indicate that ecopoiesis is achievable. Suppose further that a living planet is viewed generally as having greater cosmic value than a dead one. Why, then, would humans decide to undertake such a historic task, inasmuch as scientific feasibility and moral acceptability do not entail any obligation to proceed? Possible motives range from the sublime to the mundane. Perhaps the deepest reason would be the consistency of this project with the Promethean myths of many human cultures and the reproductive and proliferative imperatives that characterize life itself. The complementary challenges to preserve, and perhaps to propagate, life in the solar system bode well to sustain and inspire the global villagers of the 21st century.

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