

SCIENTIFIC AMERICAN

SEPTEMBER 1988

\$2.50

A new kind of cancer gene derails normal cell growth.

How the body makes insulin—new insights, new clinical promise.

Laser spectroscopy—powerful key to atomic discovery.



Shedding light on the solar system's birth: results from the Halley flyby, a vivid look at the comet's vaporizing surface.

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36

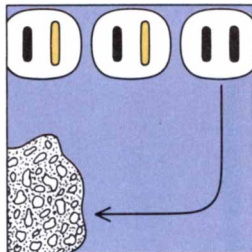


Civilian Casualties from Counterforce Attacks

Frank N. von Hippel, Barbara G. Levi, Theodore A. Postol and William H. Daugherty

From the standpoint of civilian casualties, the distinction between a nuclear attack on strategic targets and one on cities is largely academic. Computer simulations show that counterforce attacks by either side against the other side's missile sites, command-and-control centers and other strategic targets would produce very high civilian casualties.

44

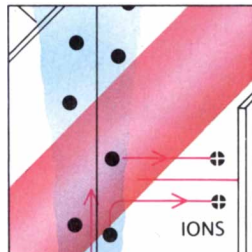


Finding the Anti-Oncogene

Robert A. Weinberg

Whereas oncogenes initiate cancer by actively promoting excessive cell growth, an anti-oncogene normally constrains growth; lacking it, a cell may proliferate out of control. The author and his colleagues have isolated the first anti-oncogene, whose inheritance in a mutated, inactive form confers an inborn susceptibility to retinoblastoma, an eye tumor.

54

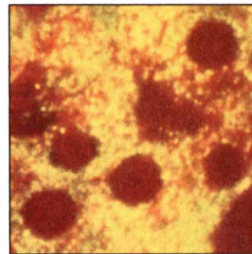


Detecting Individual Atoms and Molecules with Lasers

Vladilen S. Letokhov

The laser, tuned precisely to the frequency of the radiation emitted or absorbed by an atom or a molecule, becomes a highly sensitive probe. It can detect minute amounts of one substance in another (plucking a single platinum atom out of a trillion molecules of seawater, for example) or explore the energetic structure of an atomic nucleus.

85



The Insulin Factory

Lelio Orci, Jean-Dominique Vassalli and Alain Perrelet

Insulin is made in the beta cell of the pancreas—but how, and in what stages? Combining biochemistry with advanced electron microscopy, the authors and others have traced the subcellular assembly line, identifying successive workstations where a precursor molecule is synthesized and processed into insulin and the hormone is exported from the cell.

96



A Close Look at Halley's Comet

Hans Balsiger, Hugo Fechtig and Johannes Geiss

It has been two and a half years since an armada of spacecraft lifted off for a close encounter with Halley's comet. Intensive analysis of the data that were telemetered from European, Japanese and Soviet probes confirms the "dirty snowball" model of comet structure and provides clues to the nature of the materials that formed the solar system.

104



The Fossils of Montceau-les-Mines

Daniel Heyler and Cecile M. Poplin

Some 300 million years ago, when the continents were grouped near the Equator, France's Massif Central was tropical. Streams, lakes and estuaries teemed with amphibians, fish, arthropods and mollusks, and giant ferns covered the hills. A remarkable fossil cache has enabled paleontologists to reconstruct what life there was like in the Upper Carboniferous.

112



Plasma-sprayed Coatings

Herbert Herman

The plasma gun's high-temperature flame can convert almost any powdered material into a molten spray. Jet-engine components and other parts that will be subjected to fierce heat, mechanical stress or chemical attack can now be sheathed in an insulating ceramic almost as easily as a coat of latex paint can be laid down with a spray gun.

118



The Discovery of the Visual Cortex

Mitchell Glickstein

The foundations of today's knowledge of how the brain processes visual images were laid over a period of more than a century by a series of investigators, many of them now long forgotten. Ironically, knowledge of how the world is mapped onto the cortex owes much to the introduction of a new high-velocity rifle in the Russo-Japanese War of 1904-5.

DEPARTMENTS

8 Letters

132 The Amateur Scientist

10



50 and 100 Years Ago

1888: How gravity would impart high velocity to an urban railroad train.

136



Computer Recreations

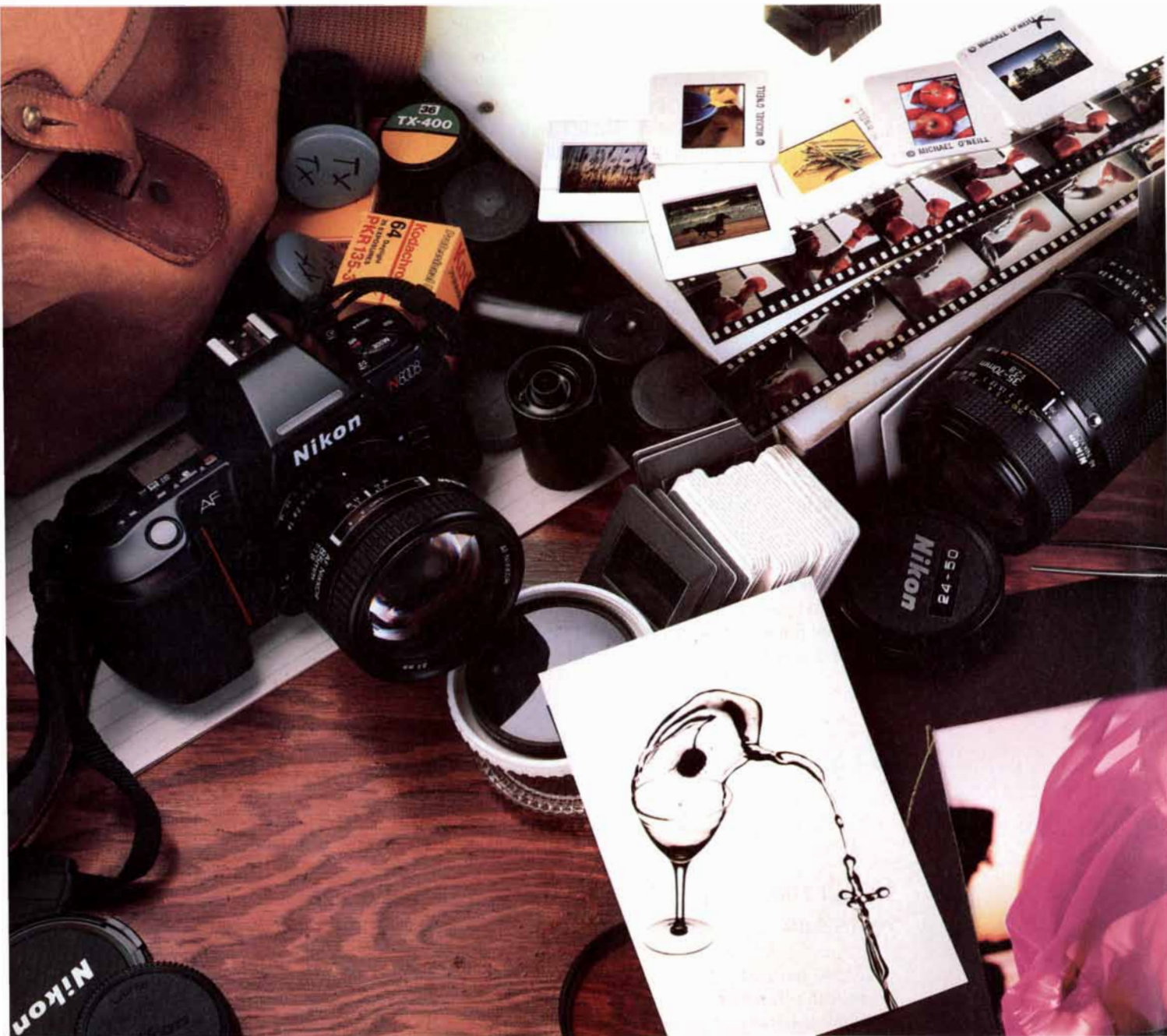
Could Theseus have got out of the labyrinth without having a thread to follow?

14 Science and the Citizen

140 Books

128 Science and Business

Introducing the Nikon photography is not



To some people, a 35mm camera is little more than an expensive toy.

To others, it's an instrument of self-expression that enriches their lives. A recorder of their personal vision and creativity.

It is for these people that the Nikon N8008 was created.

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designed to help the serious photographer take better, more inventive pictures.

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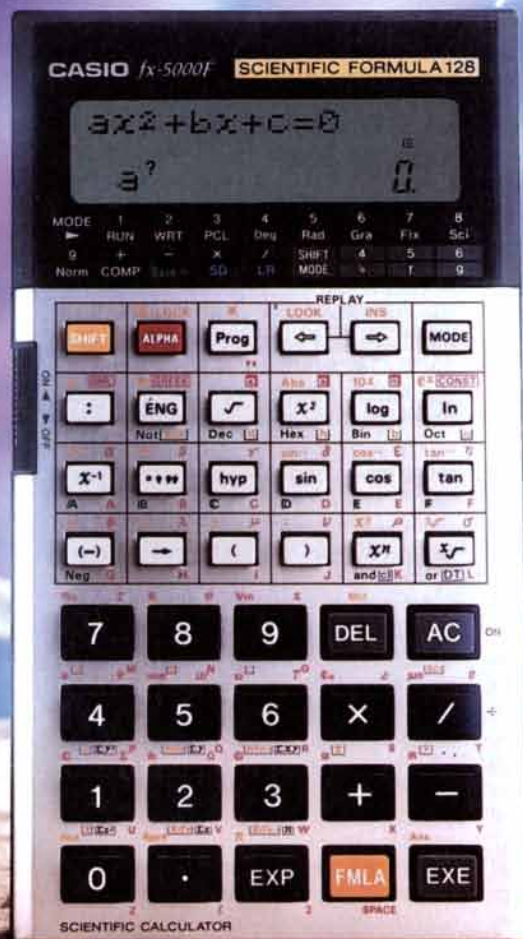
THE COVER painting, which is based on photographs taken by the European Space Agency's *Giotto* probe, depicts the nucleus of Halley's comet (see "A Close Look at Halley's Comet," by Hans Balsiger, Hugo Fechtig and Johannes Geiss, page 96). The nucleus measures about 16 by eight by eight kilometers. It is irregular in shape, and its rough, dark surface is marked by numerous pits and craterlike formations. Bright streams of gas and dust (*top*) jet from the comet's nucleus toward the sun.

THE ILLUSTRATIONS

Cover painting by Ian Worpole

Page	Source	Page	Source
37	Black Star	100	Murray Greenfield
38-42	Thomas C. Moore	101	Donald E. Brownlee
45	Jorge J. Yunis, University of Minnesota Medical School	102	H. Uwe Keller (<i>top</i>), <i>Spektrum der Wissenschaft</i> (<i>bottom</i>)
46	Jorge J. Yunis, Gabor Kiss	103	<i>Spektrum der Wissenschaft</i>
47-48	Gabor Kiss	105	Laurie Burnham (<i>left</i>), Daniel Heyler (<i>right</i>)
49	Thaddeus P. Dryja, Massachusetts Eye and Ear Infirmary	106	Laurie Burnham (<i>top and bottom right</i>), Daniel Heyler (<i>bottom left</i>)
50-51	Gabor Kiss	107	Daniel Heyler
55	B. P. Konstantinov Institute of Nuclear Physics	108-109	Patricia J. Wynne
56	Andrew Christie	110	Joe Lertola
57	Andrew Christie (<i>top left</i>), U.S.S.R. Academy of Sciences (<i>top right</i>), Andrew Christie (<i>bottom</i>)	113	Plasma-Technik Sulzers AG
58-59	Andrew Christie	114-115	George V. Kelvin
86	Dana Burns	116	Herbert Herman (<i>top and middle</i>), APS Materials, Inc. (<i>bottom</i>)
87-88	Institute of Histology and Embryology, University of Geneva	117	Plasma-Technik Sulzers AG
89	Dana Burns	119	Print courtesy of the New York Public Library, Astor, Lenox and Tilden Foundations. Gift of Donald Keene. Photograph by Robert D. Rubic
90-92	University of Geneva	122	Carol Donner
93	Dana Burns (<i>top</i>), University of Geneva (<i>bottom</i>)	123	Wellcome Institute Library, London
94	University of Geneva	124-125	Mitchell Glickstein
97	Astronomical Society of France	126	Andrew Christie
98	Hank Iken	132-135	Michael Goodman
99	Hannes Alfvén and Fritz M. Neubauer; bottom part reproduced with permission from <i>Comet Halley 1986: World-Wide Investigations, Results and Interpretations</i> , J. Mason, editor; to be published by Ellis Horwood, Ltd., Chichester, England, 1988	136-138	Hank Iken

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LETTERS

To the Editors:

"Solar Polar Bears" ["Science and the Citizen," March] is only the latest version of a story that has been in circulation now for almost 10 years. The fact that the story is largely fictional seems to go unnoticed.

The solar-polar-bear tale is a classic example of scientific folklore. Each time it is told, new elements are added, but the essential ingredients remain the same. Obviously the story has wide appeal, and most readers, including many scientists, it seems, are not aware of its problems. "It must be true," they say; "I saw it in the newspaper"—or in *Time* (December, 1978), *Natural History* (October, 1981) or *BBC Wildlife* magazine (February, 1988). Now that it has reached *Scientific American*, can textbooks be far away?

Space does not allow me to outline the entire history of this legend, but I should like to put your own story into perspective. It has been known since the late 1960's that the pelts of certain white animals are capable of trapping sunlight and converting some of it into warmth on sunny days in cold environments. The white hairs reflect and transmit much of the visible and near-infrared radiation (the major components of sunlight) down through the pelt, where it is absorbed by a dark skin. Skin temperatures well above the deep body temperature (37 degrees Celsius) have been recorded in such animals. The heat that is emitted from this warm skin then becomes trapped by the white hairs, warming the layer of insulating air in the pelt. Such a "greenhouse effect" is not unique to seals or polar bears; it was reported in certain arctic and subarctic plants and "woolly bear" caterpillars as early as 1955.

The seminal work that spawned the legend of "solar polar bears" was a more recent observation (but not as recent as suggested in your story). Working at the University of Guelph in the early 1970's, Nils Øritsland and I found that the pelts of several white animals, including whitecoated harp seal pups and polar bears, *absorb* much of the ultraviolet component in sunlight. (Short-wave UV rays make up less than 10 percent of sunlight; they contribute to the synthesis of vitamin D, cause sunburning and tanning and in highly reflective environments may cause damage to the human cornea, a

condition known as snow blindness.) Since ice and snow reflect UV, we found that UV photographs could reveal "black" seal pups and polar bears and also military equipment painted "white" for camouflage in the Arctic—but with UV-absorbent paint! (Other details of our work as they were outlined in the story are incorrect, but since these details are not essential elements of the legend, I shall not go into them here.)

With this brief overview we can now evaluate your version of the solar-polar-bear legend. Your piece states that polar-bear fur is a "natural collector that converts part of the solar-radiation spectrum into heat with an efficiency exceeding 95 percent." It does not say specifically which part of the solar spectrum might be involved, but I am not familiar with any such data. The information with which I am familiar suggests that polar-bear hair is not nearly as efficient as contended in utilizing visible and near-infrared components of sunlight, and not nearly as efficient as certain seal pelts. Even cow pelts appear to be more efficient in this regard than polar-bear fur.

Your piece also states that the polar bear is the "most efficient absorber" of the UV component in sunlight, but this is also not correct. Every white bird and mammal we have examined absorbs UV with wavelengths of between about 290 nanometers (the shortest wavelength found in sunlight) and 320 nm., and dark-colored birds and mammals are much more effective than any white animals, including polar bears, in absorbing the entire range of UV wavelengths in sunlight (between 290 and 400 nm.).

The observation that individual polar-bear hairs are "actually colorless, not white," attributed to Richard E. Grojean sometime within the past seven years, was actually published by Øritsland and Keith Ronald in 1978. Their observations pertained *only* to visible and near-infrared radiation, not to UV. And to compare a polar-bear hair to a "quartz fiber" is nonsense. Quartz transmits near-UV (that is why quartz lenses are used for UV photography), whereas, as the piece correctly notes, polar-bear hair absorbs UV.

It is for this reason that mechanisms proposed to explain how polar-bear hairs trap UV radiation to gain heat will not work. In early versions of the legend it was proposed that the UV somehow entered the hollow core of the polar-bear hair, which then functioned as a "light pipe" to direct the

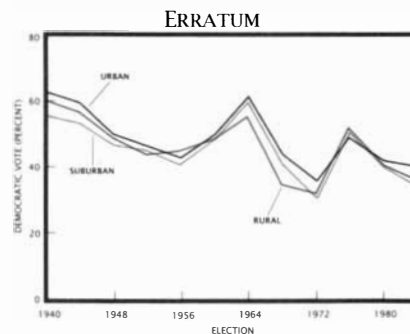
radiation to the skin. Of course, since the UV is absorbed by the protein in outer layers of the hair, little if any of it would actually reach the hollow core to be transmitted magically down the light pipe. Presumably in an attempt to overcome this problem, the legend has been modified, as is shown in the diagram for your piece. Now it is proposed that the UV is captured by the outer solid part of the hair (labeled "Transparent shaft") and aimed "toward the skin." Once again there is a serious problem: the "shaft" of the polar-bear hair is *not* transparent to UV; it absorbs it.

Yet if a UV-absorbent material could significantly improve the efficiency of solar collectors, then, as I have indicated above, researchers would choose a highly UV-absorbent dark pelt rather than a white polar-bear pelt for the purpose. Indeed, if one wants to fill solar collectors with hairlike fibers in order to *absorb* more of the solar spectrum, why not fill the collectors with black hairs?

This brings me to what is perhaps the most perplexing aspect of this bit of folklore: the tenuous connection between UV radiation and heat from the sun. No one to my knowledge has demonstrated that UV contributes anything to thermoregulation in polar bears and other mammals. And since UV is only a small part of incident solar radiation, it seems peculiar to concentrate on this part of the spectrum in order to improve solar collectors or, as in earlier versions of the legend, cold-weather clothing for the military.

D. M. LAVIGNE

Department of Zoology
University of Guelph
Guelph, Ontario



As a result of a mechanical error, a curve was omitted from the top illustration on page 50 in many copies of the July issue. The correct version of the graph is shown above.

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"The details of sun-spots and the like look sharp in the telescope. Yet there is nothing solid there, nothing liquid, nothing even as substantial as a thin summer cloud, with its tiny scat-

tered drops of water—only gas that is hotter in some places than in others. But since this gas is full of electron-haze, we cannot see deep into the sun—probably only a hundred miles or so into the haze. But the haze does not, and cannot, prevent a greater amount of radiation from escaping upward from deeper layers where they are hot than escapes where they are cooler—and so we have the spots."

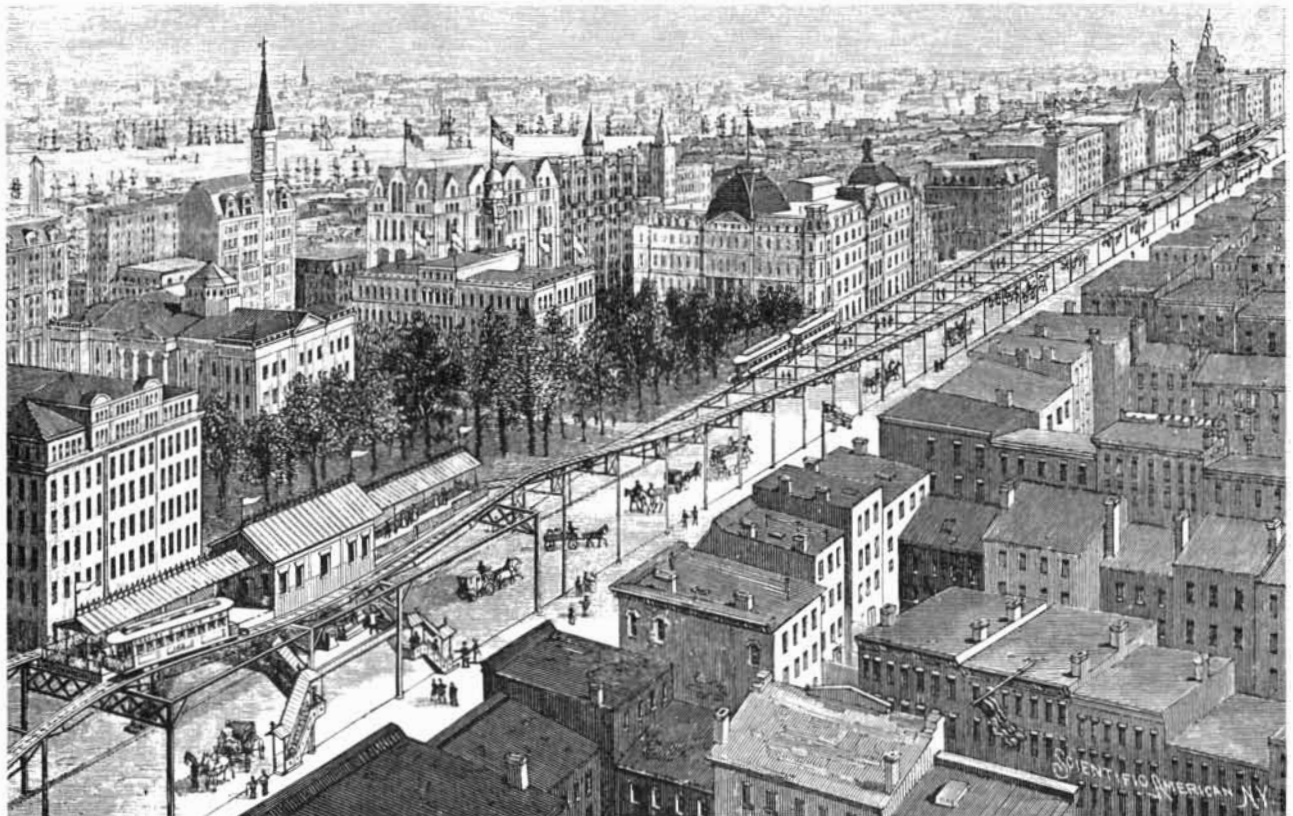
"If you examine a geology textbook of the late 19th century, you may find mention of the existence of valleys on the sea floor. In recent years, however, largely as a result of the work of the United States Coast and Geodetic Survey, information has become available that indicates these neglected submarine valleys include some of the deepest gashes in the face of the earth."

"There is real promise of a revival of interest in rotary-airfoil craft. The Army Air Corps, artillery experts, and other military authorities have become convinced that the Autogiro has a unique role to play in military operations, and a number of Autogiros are under construction by the Kellett Autogiro Company, *not* as experimental machines but as additions to the specialized equipment of the Army."

"Resins made from molasses may soon be used to bind road surfaces, if experiments now in progress in India are successful. The method consists of resinifying molasses with coal tar and asphalt in the presence of acids. A combination occurs between the sugars of the molasses and the phenols contained in the asphalt and tar to yield a product insoluble in water, which can be applied to the road as a liquid and which later solidifies. The new compound is expected to be cheaper than asphalt."

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SEPTEMBER, 1888: "A new system of operating passenger railroads in cities and towns is shown in our illustration. In this system, perfected by Mr. L. A. Thompson, of Philadelphia, the locomotive is dispensed with. Hence the railway structure may be very light and simple, offering but little obstruction to the streets. At the stations, it will be observed, there are two undulations in each track, a car approaching the station being carried up and over the slighter elevation of the first undulation, where it stops to discharge and receive passengers, after which



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it is carried up over the higher undulation beyond. It is then allowed to proceed on its way to the next station under the action of gravity alone, whereby a high velocity is imparted to the car. As the car arrives at the end of each long incline, and without at all checking its speed, its gripping mechanism comes in contact with a moving cable, driven at the station, by which the car is kept continuously on its journey."

"The perfection in the manufacture of gelatino-bromide sensitive compounds is now so complete that photographs are readily made instantaneously with far less trouble than was required in the days of the daguerreotype or of the more recent wet-plate process. One of the latest ideas based upon the dry process is the production of an extremely simple apparatus, so arranged that it cannot get out of order and adapted for use by the veriest 'greenhorn.' All that is required is to point the instrument at the object, press a button gently with a finger, and the picture is made. Another idea is that when a hundred exposures have been made, all one has to do is to send the apparatus to the manufacturers, who do all the work of finishing up the pictures. The 'Kodak,' for such is the name given this apparatus by the manufacturers, promises to make photography well-nigh universal."

"Why does the shell of the lobster become red on being boiled? The answer to this question in general terms is that the salts which make the color in the shell undergo a chemical change by being subjected to the action of hot water."

"There has been much said of late, in the newspapers and elsewhere, in regard to the parallel canals of Mars. It may be remarked that, of all the different methods of accounting for the appearances observed, perhaps the least probable is that they are water canals. A more plausible explanation is that they are due to differences in vegetation. Whether the stripes indicate vegetation, and the rest is a barren waste, or whether a large proportion of the vegetation of Mars is of a reddish color, and approaches in tint to our coleus and autumn leaves, is a matter of no consequence at present. If it can be shown that the stripes on Mars really change, this will be the hypothesis that we shall be forced to adopt, or, rather, we should say it is the only one presenting no serious improbabilities."

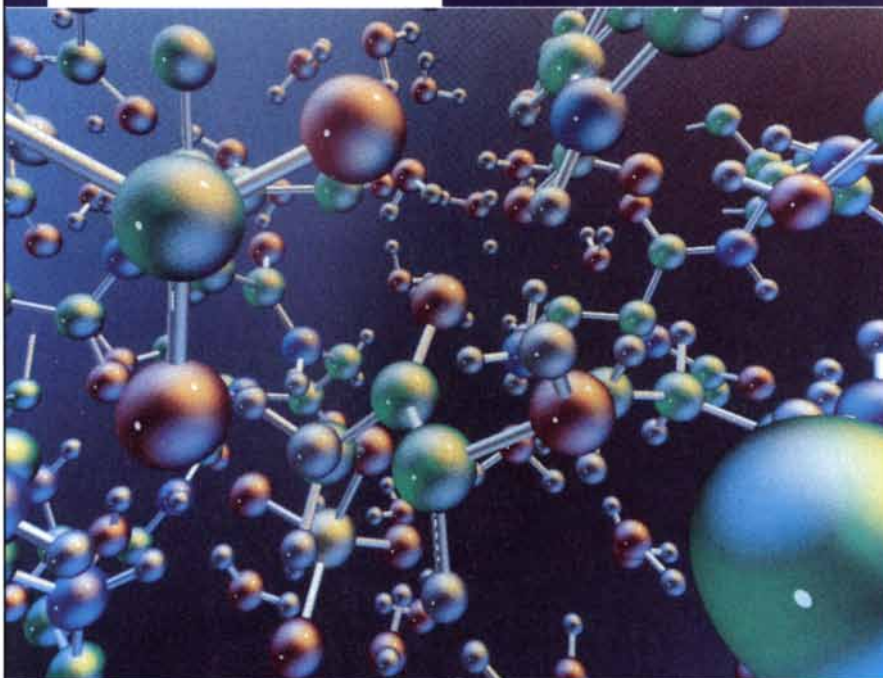
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SCIENCE AND THE CITIZEN

"Star Wars of the Seas"

Do the lessons of the Iranian Airbus tragedy apply to SDI?

The missile cruiser U.S.S. *Vincennes* is armed with a \$1.2 billion, state-of-the-art air-defense system called Aegis. The centerpiece of Aegis is a phased-array radar that, according to the Navy, can track hundreds of airborne objects over an area nearly the size of Texas. Aegis also performs battle management: computers analyze data and then recommend and even initiate courses of action. On July 3 the *Vincennes* made a terrible mistake. It destroyed a commercial airliner that it had erroneously identified as a hostile jet fighter.

Is Aegis comparable to the Strategic Defense Initiative, the shield against nuclear missiles envisioned by President Reagan? Pentagon officials apparently think so. They often call Aegis—admiringly—"Star Wars at sea." Major William J. O'Connell, an SDI spokesman, says Aegis proves that "the levels of sophistication [that the SDI's] battle management and command and control would require have already appeared." Richard L. Rumpf, a deputy assistant secretary of the Navy, points



22	PHYSICAL SCIENCES
26	BIOLOGICAL SCIENCES
29	TECHNOLOGY
32	OVERVIEW

out that Lt. General James A. Abrahamson, director of the SDI, is "very much impressed" by Aegis and has ordered SDI designers to "learn from what Aegis has."

To facilitate this technology transfer, the SDI Organization has enlisted Capt. John J. Donegan, a supervisor of the Aegis program for seven years, to manage its phase-1 program office. He notes that there is at least one fundamental parallel between Aegis and SDI. Although the Joint Chiefs of Staff have stipulated that a strategic defense should have a "man in the loop," it may share the capability of Aegis to fight independently of human control "when there's absolutely no question

about [the threat] and when it's hard for a man to react to the situation," Donegan says.

The *Vincennes*' Aegis had a man in the loop when it first detected an aircraft taking off from Iran and heading in its direction. Will C. Rogers 3rd, captain of the *Vincennes*, had about seven minutes to study the information supplied him by Aegis and act, or not act, on it. The data were confusing. The aircraft was apparently emitting both a civilian radio signal and a military IFF (identification friend or foe) code used by Iranian F-14 fighters. Unfortunately, all of the sensors and computers of the *Vincennes* could not inform Rogers that the putative F-14 was in fact an Airbus, a French-built plane more than three times larger than an F-14. To protect his ship he launched two surface-to-air missiles at the aircraft.

The accident illustrates "a classic military problem," remarks Thomas F. Curry, chief scientist at E-Systems, Inc., a defense contractor: "identifying the guy you're shooting at." Curry, who served as an electronic-combat specialist in the Navy for some 30 years, says neither radar nor any other technology now available can tell whether aircraft are friendly, hostile or neutral solely on the basis of an image. Lacking clear visual contact, combatants may rely on IFF, a "secret password" scheme utilizing coded radio signals instead of the human voice. But IFF can identify only "friends" who have the password. Even a correct IFF response cannot necessarily be taken at face value, since an enemy may have obtained the password (as the *Vincennes* apparently did in the case of the Iranian F-14 code). In spite of the seriousness of the identification problem, Curry notes, systems such as Aegis are usually tested only in "total war" situations, in which all unidentified objects are considered hostile.

A strategic defense based in space would be much more susceptible to identification errors than the *Vincennes*, according to Curry and other defense analysts. If the SDI does indeed include a man in the loop, he would be under much more pressure than Rogers; the entire U.S., not just one ship, would be in his charge. He would also probably have less time to react than Rogers had. Pentagon officials have acknowledged that a strategic defense would attempt to destroy

An SDI system might have even more ambiguous data and less time to act than the Vincennes



WIDE-SCREEN DISPLAYS of an Aegis-equipped missile cruiser (not the *Vincennes*) monitor the seas off the coast of Lebanon in 1984. Photograph from the U.S. Navy.

Photographs that show features one three-thousandth the width of a human hair have been obtained through the latest advances in miniaturization technology. The photographs were achieved with a microscope using a focused ion beam that scanned nickel crystals at 80,000 times their actual size. The images revealed features as small as 15 nanometers, equivalent to approximately 100 diameters of an atom. Used as a fabrication tool, the focused ion beam can produce the structures required for ultra-small microelectronics. The technique, developed by Hughes Aircraft Company, will be used in applications for ultra-small structures to produce improved microwave sources and amplifiers, faster integrated circuits, higher speed photodetectors, and new devices utilizing superconductive materials.

A Hughes-built probe descending through Jupiter's atmosphere will provide never-before-gathered data on its chemical composition, temperature, and density. The Galileo Mission, to be launched in 1989, will arrive in the Jovian system in 1995 for a two-year tour, after traveling a lengthy route including Earth and Venus fly-bys. The Galileo orbiter will release the onboard Hughes probe into Jupiter's atmosphere. It will descend by parachute, sending its scientific findings to the orbiter which will then relay them back to Earth. The orbiter will continue on its tour and pass within 600 miles of Io, the most volcanic body in the solar system, which pumps more than a ton of ash into space every second.

A new microwave modulated fiber optic link can modulate light from zero to 17 billion cycles per second, a world record. With this bandwidth, the link can accommodate the entire radio band, the TV band, and all the satellite communications bands. Developed by Hughes, this device has the capability to transmit the entire Encyclopedia Britannica in one-tenth of a second over a fiber approximately the size of a human hair. Intended for satellite terminal and radar applications, the device achieves a 20 decibel greater dynamic range than can be realized with conventional laser current modulation techniques.

A new radar system is used to measure the radar reflectivity of an object. The radar cross section (RCS) measurement system can reproduce a two-dimensional image of a target, such as an aircraft, and the information can be used to help redesign the aircraft to reduce its visibility to enemy radar, resulting in "low observable," or stealth-type vehicles. The Hughes RCS system is universal and programmable, and is designed to take measurements over a broad band of microwave frequencies, from 0.1 to 100 gigahertz. The system can thus tell the user how visible a target would be to the "eyes" of any radar in the world.

Hughes is seeking experienced engineers and scientists to further develop advanced spacecraft systems and components for communications satellites. Openings are in the fields of: software, computers, and data processing systems; electrical components; microwave/RF communication systems development; on-board spacecraft electronics and control systems; satellite design, integration, propulsion, and electrical power system development; spacecraft manufacturing, systems test and evaluation; GaAs applications R&D. Send your resume to Michael Martinez, Hughes Space & Communications Group, Dept. S2, S4/A300, P.O. Box 92919, Los Angeles, CA 90009. Equal opportunity employer. U.S. citizenship required.

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IBM The Bigger Picture

Soviet missiles in the boost stage, before they release their warheads together with obscurants and decoys. The boost stage would last perhaps five minutes, and less if the Soviets deploy fast-burning boosters.

The electronic "eyes" of an SDI system may be no sharper than those of the *Vincennes*, and would certainly face a much more difficult challenge. The proliferation of missiles on Soviet ships, submarines and mobile land-based platforms—and the possibility that other countries hostile to the U.S. might develop nuclear-armed missiles—would necessitate watching most of the globe. Satellite-based infrared sensors, which would probably be employed to detect launches, are notoriously prone to false alarms. Those that now provide the North American Aerospace Defense Command (NORAD) with early warning have mistaken forest fires and oil-well fires, among other phenomena, for missiles. The sensors must also distinguish threatening missiles from the 100 or so boosters that the Soviet Union now launches a year. Announcement prior to launches might mitigate this problem but would not eliminate it. The *Vincennes*, after all, had a schedule book that included Iran Air flight 655.

Unlike Aegis, which has undergone years of tests against live targets and in combat, a strategic defense could be tested only against those threats that SDI researchers can imagine and simulate, according to John E. Pike, a space specialist for the Federation of American Scientists. The Iranian-Airbus tragedy shows that "the world is stranger than we can imagine," Pike says. "Who would imagine that a civilian airliner would emit both a civilian and a military IFF?"

In one final sense, Aegis and the SDI are incomparable. The *Vincennes'* error in judgment cost 290 people their lives. A mistake by a strategic defense could be vastly more costly. Richard L. Garwin of the International Business Machines Corporation, a veteran critic of the SDI, points out that if both the Soviet Union and the U.S. deploy an SDI-type system, each side's space-based weapons would be the prime target of—and the prime threat to—the other's. In this hair-trigger situation, a meteorite, a piece of space debris or a satellite might be mistaken for an attack and thus precipitate a battle in space. Since strategic defenses are likely to be "closely linked" to offensive systems, Garwin says, the launching of missiles might soon follow. He adds: "Then the whole thing goes up in smoke." —*John Horgan*

Winds of Change

International talks address human effects on climate

Spurred by a scientific consensus that significant greenhouse-effect warming will occur in the early decades of the next century, delegates from 46 countries at a Conference on the Changing Atmosphere held in Toronto have called for an urgent action plan. The conferees, who included scientists and policymakers (but no senior U.S. Government official), recommended that governments initially reduce emissions of carbon dioxide—thought to play a major role in greenhouse warming—by 20 percent before the year 2005.

Some workers maintain that greenhouse warming, which results when trace gases prevent infrared radiation from the earth's surface from escaping to space, has already set in; indeed, a scientist at the National Aeronautics and Space Administration (NASA) is searching for a greenhouse "fingerprint" in existing data. The four warmest years in a century of instrumental records have all fallen within the 1980's, and the first five months of 1988 were the hottest five-month period ever recorded.

One climate analyst, James E. Hansen of NASA's Goddard Institute for Space Studies, told a Senate subcommittee in Washington just before the Toronto conference that the recent warming could be ascribed "with a high degree of confidence" to the greenhouse effect. At Toronto the delegates kept an open mind about whether the greenhouse effect has contributed to the warmth of the 1980's. They agreed, however, that past emissions of greenhouse gases make significant warming inevitable. Indeed, the most recent computer models predict that accumulating trace gases will warm the lower atmosphere sooner than expected.

Carbon dioxide, which is increasing by .4 percent each year because of combustion of fossil fuels and the destruction of tropical forests, accounts for half of the predicted warming. Other greenhouse gases include methane, which is increasing at an even faster rate, and the synthetic refrigerants and solvents called chlorofluorocarbons (CFC's).

The consensus view was that a global warming of between three and nine degrees Fahrenheit is likely to occur by the middle of the next century if emissions are not curtailed. It is impossible to say what the climatic

consequences for particular regions would be—the current U.S. drought, for example, cannot necessarily be blamed on the greenhouse effect. Nevertheless, some studies suggest that continental interiors will become dryer as greenhouse warming occurs. The sea level is expected to rise by at least 30 centimeters over the next 50 to 100 years.

Delegates at Toronto stressed that the predicted rapid pace of change would have far-reaching consequences. For example, it could outstrip the ability of forests to respond. It would also affect agriculture and the lives of millions of people in low-lying deltas. The encroachment of seawater on the water supplies of coastal communities would be a major threat.

To delay the warming and give society and the ecosystem time to adjust, the Toronto conference urged development of energy policies that would reduce carbon dioxide emissions. The delegates also reiterated an earlier call for action on CFC's. In addition to their warming effect, CFC's appear to deplete the ozone layer, which intercepts ultraviolet rays in the stratosphere; in particular, CFC's produce the ozone "hole" that appears each September over Antarctica. As a first step toward coping with this problem the Toronto delegates urged immediate ratification of the Montreal Protocol on Substances That Deplete the Ozone Layer, which was signed by 31 countries last year and specifies targets for reducing CFC emissions. They also urged that the protocol be revised in 1990 to ensure near-complete elimination of the most destructive CFC's by the year 2000.

Those who support an international agreement on the atmosphere, such as F. Kenneth Hare, chairman of Canada's Climate Program Planning Board, pointed to the Montreal Protocol as a model for coping with the warming problem. Hare suggested that an agreement include an inventory of substances that should not be released into the atmosphere and a policy to restrict reliance on coal as a source of energy in order to reduce carbon dioxide emissions.

As many observers have pointed out, however, it is one thing to call for reductions in CFC's but another to ask countries—particularly developing countries—to reduce energy consumption. A senior official from Indonesia suggested that nations should contribute to the cost of protecting the atmosphere in proportion to their contribution to the problem.

The Reagan Administration maintains that more study is needed before any legal framework is considered. Nevertheless, the Environmental Protection Agency, under a Congressional mandate, has initiated studies of the regional effects of climate change and of policies for mitigating it.

Some uncertainty about the greenhouse effect may be reduced by the NASA search for evidence that the warming has already started. S. Ichtiague Rasool, NASA's chief scientist for global change, is organizing an inter-agency effort to examine archival data from meteorological satellites. In spite of more than a decade of discussion on the greenhouse effect, no one has systematically analyzed all the available data, according to Rasool. His low-budget exercise, which would search for specific changing atmospheric and oceanic temperature patterns around the globe, might begin as early as this fall. —Tim Beardsley

Now You See It...

An "unbelievable" experiment is found to be unbelievable

After an extraordinary on-site investigation of an experiment that reportedly yielded results inexplicable by conventional science, the influential journal *Nature* has charged that a French research group "fostered and then cherished a delusion about the interpretation of its data." A report describing the disputed experiment had been published in *Nature* in late June. It was written by a team of 13 scientists from four countries, headed by a well-known pharmacologist at the French National Institute of Health and Medical Research, Jacques Benveniste.

The team investigated an allergy-related phenomenon. When a particular kind of antibody encounters a human basophil, a type of white blood cell, it binds to a receptor on the basophil's surface and triggers "degranulation": histamine-containing granules within the basophil release their contents into the surrounding medium. Degranulation can be observed under a microscope with standard staining procedures.

The experiments were inspired by two of Benveniste's colleagues who practice homeopathy, a fringe medical philosophy that most scientists reject. Implicit in homeopathy is the idea that extremely dilute materials can have potent effects. The French workers sought to discover by how much an

antibody solution could be diluted and still evoke degranulation. The answer they arrived at—and still defend—was "surprising": a billion, billion, billion, billionfold, at least.

At such dilutions there is virtually no possibility that even a single antibody molecule is present. Nevertheless, Benveniste and his colleagues held that successive tenfold dilutions of apparently pure water produced a response in the basophils that, although it repeatedly tailed off, kept reappearing at greater dilutions. The intrigue was heightened by the fact that at each dilution, vigorous shaking—a practice favored in homeopathy—was necessary for the effect to emerge. Benveniste hypothesized that a strange self-perpetuating structure might be present in water and might somehow "remember" that antibodies have been present.

The experiment was successfully repeated in six laboratories in four countries by different personnel, according to Benveniste. His report stated that careful scientific controls were applied to rule out contamination and that "blind" procedures were followed so that the experimenters did not know, when they assessed the extent of degranulation by counting stained cells on microscope slides, whether antibody had been present in high or low dilution, or not at all.

Nature, uneasy about publishing such an extraordinary report even though reviewers had been unable to find fault with it, published alongside Benveniste's paper an "editorial reservation" pointing out that the results could have "no physical basis." As a condition for publishing the report, *Nature* asked that Benveniste allow a group of observers to watch the experiments as they were being performed in his laboratory, a condition Benveniste accepted.

Early in July the observers went to Paris. They were an unlikely group: James "The Amazing" Randi, a professional magician known for his successful debunking of fraudulent paranormal claims, and his assistant José Alvarez; Walter W. Stewart of the National Institutes of Health who in recent years has spent considerable time investigating errors and discrepancies in the scientific literature, and John Maddox, who is the editor of *Nature* and has a background as a physicist. The observers quickly established that the procedure does not work at all times of the year or with all blood samples. Benveniste also informed them that the first author of the *Nature* report, Elizabeth Davenas,

tended to produce better results than other workers.

According to *Nature's* investigation, errors in the experimental procedure cloud the statistical interpretation of the results previously obtained by the French workers. The *Nature* observers witnessed the experiment a total of seven times. The first three times were "open": everyone present knew which samples contained which solutions. In the fourth experiment, the workers did not know which slides they were counting. All of these first four experiments seemed to show evidence of some effect at extraordinary dilutions, although the results of the fourth one differed in detail from the earlier results. In the final three demonstrations a secret coding procedure, controlled by Randi, was introduced to prevent the experimenters from having any knowledge of which slides they were counting. Under these conditions, which the French workers had not employed previously, the high-dilution effect did not emerge at all; rather, the results were exactly as standard science would predict.

Nature concludes that "the phenomenon described is not reproducible in the ordinary meaning of that word." The observers suggest that self-deception, rather than fraud, probably produced biased results. If so, others seem to have been taken in beside the original team. Bruce Pomeranz of the University of Toronto, one of Benveniste's coauthors, says he has demonstrated Benveniste's dilution effect in Toronto but that his results are preliminary.

Benveniste is angry and dismayed by what he sees as unfair play by the investigators. He notes in particular that the fourth experiment of the seven witnessed by the *Nature* observers can be explained only by a genuine effect or by deliberate fraud by one of those involved, and he says he has completely excluded any possibility of fraud. He strongly disagrees with the *Nature* team's conclusion that data accumulated by the French workers contained less experimental error than is possible. He also maintains that science should not be conducted by having observers watch experiments. Instead, he says, other laboratories should repeat the experiments.

Nature published its critique of the experiments, along with a rebuttal by Benveniste, on July 28. Some scientists have criticized *Nature* for publishing Benveniste's study in the first place. "It's journalism of the worst kind," says Henry Metzger of the NIH, an expert on allergic responses. Others,

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however, say the exercise will have a chastening and therefore ultimately beneficial effect on science. Maddox says he has no regrets. "We all have learned a lot," he remarks, "although whether Benveniste will learn anything is another matter." —T.M.B.

PHYSICAL SCIENCES

The Solar Inconstant

More sunspots = more sunshine, but is the weather affected?

Astronomers noted more than 150 years ago that sunspots wax and wane in number in an 11-year cycle. Ever since, people have speculated that the solar cycle might exert some influence on the earth's weather. In this century, for example, workers have linked the solar cycle to droughts in the American Midwest. Until recent-

ly, however, none of these correlations has held up under close scrutiny.

One problem is that sunspots themselves are so poorly understood. Observations have revealed that the swirly smudges represent areas of intense magnetic activity where the sun's radiative energy has been blocked, and that they are considerably cooler than bright regions of the sun. Workers have not been able, however, to determine just how sunspots are created or what effect they have on the solar constant (a misnomer that refers to the sun's total radiance at any instant).

The latter question, at least, now seems to have been resolved by data from the *Solar Maximum Mission* satellite, which has monitored the solar constant since 1980, the peak of the last solar cycle. As the number of sunspots decreased through 1986, the satellite recorded a gradual dimming of the sun. Over the past year, as sunspots have proliferated, the sun has brightened. The data suggest that

the sun is .1 percent more luminous at the peak of the solar cycle, when the number of sunspots is greatest, than at its nadir, according to Richard C. Willson of the Jet Propulsion Laboratory and Hugh S. Hudson of the University of California at San Diego.

The data show that sunspots do not themselves make the sun shine brighter. Quite the contrary. When a sunspot appears, it initially causes the sun to dim slightly, but then—after a period of weeks or months—*islands of brilliance* called *faculas* usually emerge near the sunspot and more than compensate for its dimming effect. Willson says *faculas* may represent regions where energy that initially was blocked beneath a sunspot has finally breached the surface.

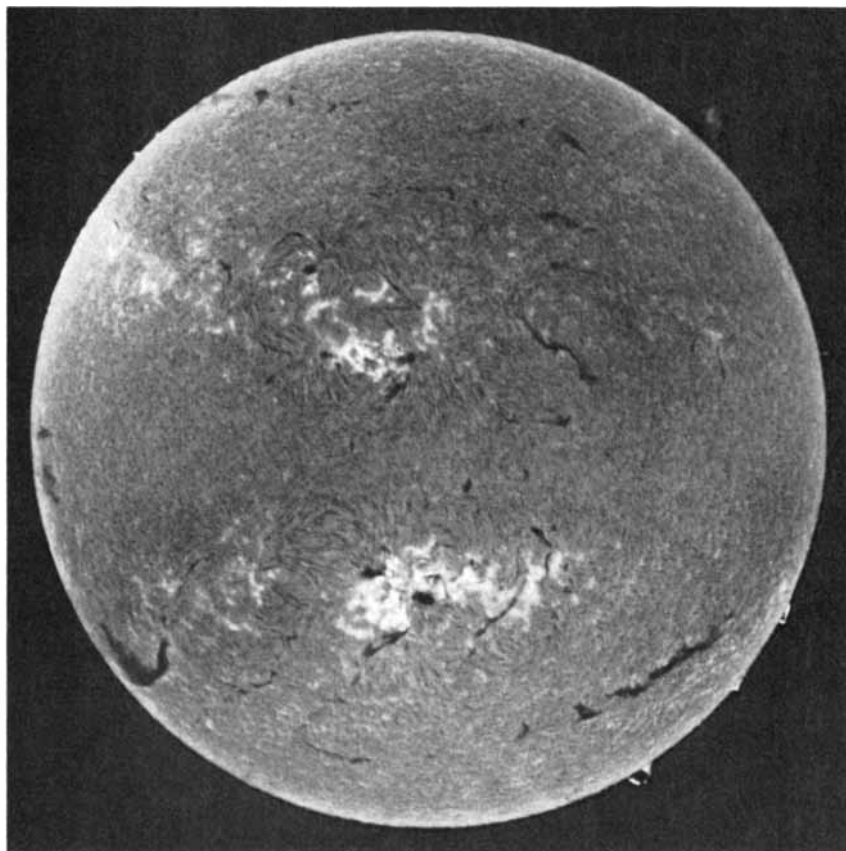
Does the subtle fluctuation in the solar constant manifest itself in the earth's weather? Some recent reports offer statistical evidence that it does, albeit rather indirectly. The link seems to be mediated by a phenomenon known as the quasi-biennial oscillation (QBO), a 180-degree shift in the direction of stratospheric winds above the Tropics that occurs about every two years.

Karin Labitzke of the Free University of Berlin and Harry van Loon of the National Center for Atmospheric Research in Boulder, Colo., were the first to uncover the QBO link. They gathered temperature and air-pressure readings from various latitudes and altitudes over the past three solar cycles. They found no correlation between the solar cycle and their data until they sorted the data into two categories: those gathered during the QBO's west phase (when the stratospheric winds blow west) and those gathered during its east phase. A remarkable correlation appeared: temperatures and pressures coincident with the QBO's west phase rose and fell in accordance with the solar cycle.

Building on this finding, Brian A. Tinsley of the National Science Foundation discovered a statistical correlation between the solar cycle and the position of storms in the North Atlantic. The latitude of storms during the west phase of the QBO, Tinsley found, varied with the solar cycle: storms occurring toward the peak of a solar cycle traveled at latitudes about six degrees nearer the Equator than storms during the cycle's nadir.

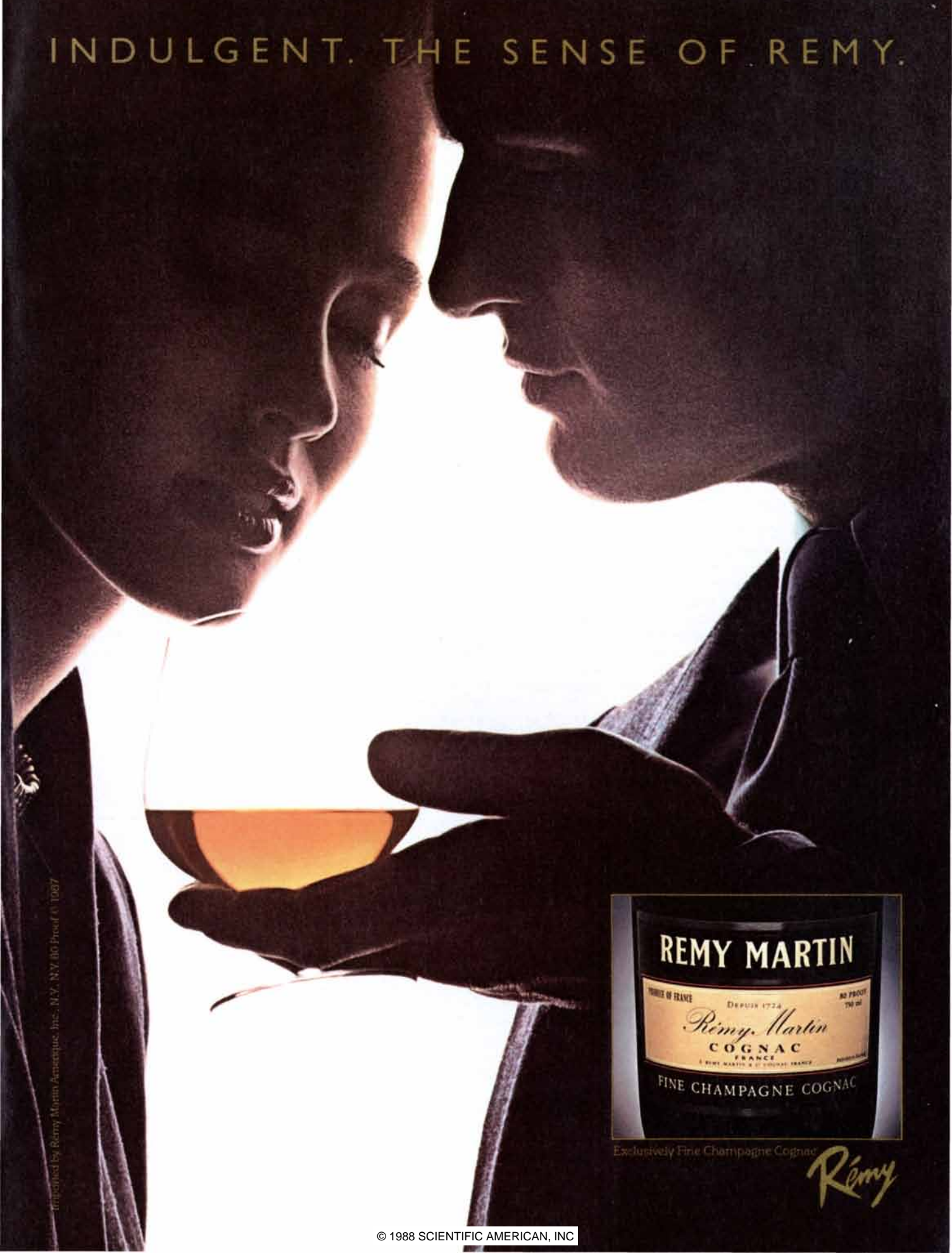
Labitzke, van Loon and Tinsley acknowledge that their findings are still rather mysterious. Why does the solar cycle seem to exert more of an influence during the west phase of the QBO than it does during the east phase?

Sol dims briefly as sunspots appear, then brightens as they yield to islands of brilliance called faculas



SUNSPOTS are encircled by faculas in a photograph, which was made on July 1, provided by the National Oceanic and Atmospheric Administration.

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How does the .1 percent variance in solar radiation trigger the much larger changes—up to six degrees Celsius in polar regions—observed by Labitzke and van Loon? Van Loon says simply, “We can’t explain it.”

John A. Eddy of the National Center for Atmospheric Research, nonetheless, thinks these QBO findings as well as the *Solar Maximum Mission* data “look like breakthroughs” in the search for a link between the solar cycle and weather. With further research, for example, into how the oceans damp the effects of solar flux, these findings may lead to models that have some predictive value. The next few years may be particularly rich in solar flux. Based on the rate at which sunspots have been appearing lately, some workers have predicted that the current solar cycle, due to peak in 1991, will produce a record-breaking number of sunspots. —J.H.

Microwave Mystery

A puzzling new probe of the cosmic background radiation

The faint microwave fuzz that pervades the heavens and is supposedly the afterglow of the big bang has perplexed cosmologists lately. For several years, as evidence has accumulated that the universe consists of clusters of galaxies surrounded by vast voids, investigators have searched in vain for corresponding unevenness within the microwave background. Now an entirely different puzzle has arisen. Measurements by a team of Japanese and American workers of previously unprobed wavelengths in the cosmic radiation suggest that it may have been distorted or amplified by some mysterious event soon after the big bang.

Cosmologists had assumed that the flash from the big bang has come down through the ages essentially unaltered, except for a large red shift corresponding to the expansion of the universe. The assumption was based on measurements indicating that the microwave background has the distinctive spectrum of so-called black-body radiation. If undistorted by radiation from other sources or by an intervening medium, the thermal emission from a hot object—a toaster, a star or the big bang’s primordial fireball—often resembles black-body radiation. The spectrum of such radiation always peaks in power at a wavelength dependent on the temperature of the object. The peak wavelength is

shorter, or bluer, for hotter objects and longer, or redder, for cooler ones. The black-body spectrum then drops off at shorter and longer wavelengths at a characteristic rate.

Previous observations had shown that the microwave background peaks at wavelengths slightly longer than one millimeter and drops off at longer wavelengths—just as black-body radiation from an object having a temperature of 2.7 degrees Kelvin would. However, workers have never successfully gauged the spectrum at shorter wavelengths, in the so-called submillimeter band beyond the peak. Extraneous thermal emissions, usually from the atmosphere or from the experimental apparatus itself, have always contaminated the measurements.

The submillimeter band may have finally yielded its secrets to a team from Nagoya University in Japan and from the University of California at Berkeley. Early last year the group launched a helium-cooled radiometer some 200 miles above the earth, far outside the atmosphere. Data transmitted from the instrument showed no signs of contamination. What the data did show was that the intensity of the submillimeter radiation greatly exceeds that expected from a 2.7-degree black body. The excess radiation corresponds to about 10 percent of the total microwave background. “It’s an enormous effect,” according to team member Paul L. Richards of Berkeley.

Although the group published its findings in the *Astrophysical Journal* only in June, theorists have been speculating about their meaning for more than a year. Indeed, just two weeks after publishing the Nagoya/Berkeley report, the *Astrophysical Journal* published a critique by Cedric G. Lacey and George B. Field of the Harvard-Smithsonian Center for Astrophysics of two of the first theories to be put forth. One theory holds that during the very early stages of the universe the void between galaxies was filled with ionized gas; hot electrons in this plasma imparted some of their energy to photons from the big bang, distorting their black-body spectrum. The second theory posits that supernova explosions of the very first generation of stars filled the universe with dust; as radiation from other stars heated the dust, its glow added to the big bang’s residual radiation.

Lacey and Field maintain that neither scenario would produce the excess radiation observed by the Nagoya/Berkeley group. According to their calculations, the first would fall short by a factor of at least 700 and

the second by a factor of at least 2. The investigators mention but do not analyze certain other exotic mechanisms that might have supplied the energy needed to produce the excess submillimeter radiation. These hypothetical phenomena include superconducting cosmic strings, particles that decayed soon after the big bang and supermassive black holes.

To be sure, there is another, less exciting explanation for the submillimeter measurements. David T. Wilkinson of Princeton University points out that the observations may have been contaminated by exhaust from the rocket, by ice that gathered on the instrument while it passed through the atmosphere or by some other, unknown effect. “The history of rocket experiments near the infrared spectrum,” he notes, “is filled with errors.” He adds, however, that the Nagoya/Berkeley team “is very expert. You couldn’t find a better collaboration.”

Richards says he and his co-workers are well aware of the need to corroborate their data. They hope to do that with a follow-up experiment next year. If the experiment does not eliminate doubts about the data’s validity, the *Cosmic Background Explorer* satellite, also scheduled for launch in 1989, may provide an independent cross-check. The satellite’s primary mission, however, is to search for the regional “lumps and bumps” that so many cosmologists now think must be in the microwave background. —J.H.

Woody Witnesses

Tree rings provide evidence of an 1812 San Andreas quake

What can trees reveal about earthquakes? Quite a bit, as it turns out. When an earthquake takes place along the San Andreas Fault, crust lying to the west of the fault moves rapidly to the northwest with respect to crust lying east of the fault. The shifting and shaking can severely traumatize any trees growing on or near the fault: roots growing across the fault may be severed and the vibration may shake off the tree’s crown, which includes most of its photosynthetic surface area. If the tree survives, its growth may be stunted for years, leaving a permanent record in the pattern of the tree’s annual growth rings. An analysis of such tree-ring patterns published in *Science* shows that the intervals between major earthquakes along the San Andreas are surprisingly irregular, so that pre-

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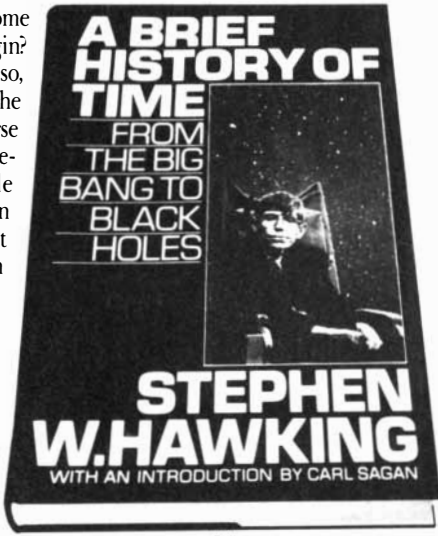
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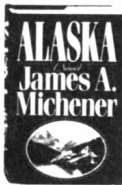
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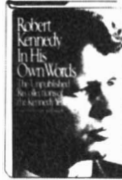
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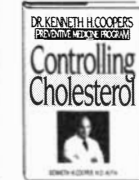
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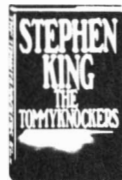
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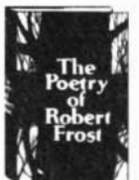
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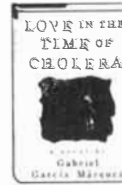
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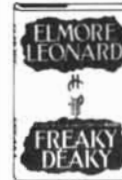
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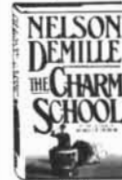
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dicting when the next great earthquake will occur there may be much more difficult than has been thought.

The authors of the study, Gordon C. Jacoby, Jr., and Paul R. Sheppard of Columbia University's Lamont-Doherty Geological Observatory along with Kerry E. Sieh of the California Institute of Technology, drilled core samples from a number of trees near the fault and measured the width of each ring to within the nearest .01 millimeter. The rings in each core were dated by finding the narrow rings representing known drought years.

The investigators found that nine trees growing along a 12-kilometer section of the fault near Los Angeles had experienced severe trauma some time between the growing seasons of 1812 and 1813 that led to several years of poor growth, as evidenced by a series of thin or missing rings. It took four of the trees more than 50 years to return to normal growth. In

addition to evidence from ring patterns, the shapes of the growing trees show that at least three lost some or all of their crown at some time in their life, presumably in the course of the trauma that stunted their growth.

The thin and missing rings cannot be attributed to drought, since a drought results in only a single year of poor growth. Fires, insect infestations, windstorms and other nonearthquake causes can be ruled out by similar reasoning; shaking that was due to an earthquake on another fault would not have damaged only trees growing near the San Andreas.

The workers suggest that the cause of the damage was an earthquake that struck California on December 8, 1812, which was reported in places as far apart as San Diego and Santa Barbara. That earthquake had been thought to have occurred at a different, coastal fault, because it resulted in extensive damage at settlements

along the California coast, but the tree-ring evidence seems to point to the San Andreas, Jacoby and his co-workers say.

If they are correct, then the section of the San Andreas Fault near Los Angeles experienced two great earthquakes within a mere 44 years: the 1812 event and a famous rupture in January, 1857. Before the supposed 1812 event, that section of the fault had lain dormant for about 330 years. The implication is that the actual time between major earthquakes can vary considerably from the average interval, which is about 130 years.

The study comes at an appropriate time. The U.S. Geological Survey has just released a revised set of calculations estimating a 60 percent probability that a major earthquake will strike southern California in the next 30 years. The work reported in *Science* suggests that the techniques and theories employed in arriving at such predictions may themselves need to be reconsidered.

—Ari W. Epstein

The color of seashells on the seashore may be an evolutionary response to physiological stress



BROWN-SHELLED SNAILS abound on a shore with constant wave action and mussel beds (top); **white-shelled snails** predominate on a protected beach (bottom).

BIOLOGICAL SCIENCES

The Hard Shell

Heat stress, not camouflage, controls color in an adult snail

As any beachcomber knows, snail shells come in different shapes, sizes and colors. Even within a single species it is not uncommon to find considerable polymorphism, or variation, in a single trait. Variation is the raw material on which natural selection operates, and for many years it has been thought that variation in shell color evolved as protective camouflage in response to birds and other visual predators. Brown shells seem to be more frequent when the substrate is dark, white shells when it is light.

Now a report in *Evolution* suggests that, in one snail species at least, the color of adult snails is related more to physiological stress than it is to camouflage. In a series of experiments conducted along a stretch of the north shore of Massachusetts, Ron J. Etter of Harvard University found that in the intertidal snail *Nucella lapillus*, color varies according to the nature of the coastline the snail inhabits. Along exposed areas of the shore where wave action is great, the snails are mostly brown; in the more sheltered bays and inlets the snails are predominately white.

Etter measured the internal temper-

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ature of both brown and white forms under natural conditions at exposed and protected sites along the shore and found that the extent to which the snail absorbs heat is strongly influenced by shell color. In direct sunlight brown snails had faster rates of temperature increase, reached a higher maximum temperature and desiccated more quickly than white snails. After one hour in direct sunlight at an air temperature of 21 degrees Celsius and a relative humidity of 64 percent, brown snails begin to die; white snails show no sign of stress.

Such differential susceptibility to physiological stress, rather than camouflage, may explain the geographical distribution of *N. lapillus*, Etter thinks. On exposed shores, where wave action is heavy and mussel beds retain water when the tide recedes, the more vulnerable brown snails predominate. On protected shores, where wave action is limited and receding tides create a substrate that is relatively hot and dry, white forms are dominant.

Although brown snails can avoid exposure to the sun by moving to more shaded and moist microhabitats, Etter thinks their greater susceptibility to stress nonetheless puts them at a disadvantage by limiting their foraging area and increasing the amount of time they must spend in hiding. This in turn could lead to slower growth rates and reduced levels of fecundity.

Does the physiological-stress hypothesis suggest that these snails have no predators? "Absolutely not," Etter says. Juvenile snails, which are thin-shelled and may measure no more than a millimeter in length, are abundant in the stomachs and fecal pellets of both fish and shorebirds. For that reason Etter thinks camouflage probably does affect survivorship among juveniles. But he hastens to add that by the time the snails are mature, physiological stress and not camouflage is the important determinant of shell color. —*Laurie Burnham*

purified these cells from the marrow and could point them out under a microscope. In fact, stem cells have eluded biologists for decades; evidence of their existence has been entirely indirect. Now stem cells have been found at last, and the advance holds promise for victims of cancer, radiation sickness, hemophilia and anemia.

Gerald J. Spangrude, Shelly Heimfeld and Irving L. Weissman at the Stanford University School of Medicine report the first unequivocal identification of stem cells in a recent issue of *Science*. When they began their investigation the workers knew that stem cells do not carry the same surface markers as mature blood-cell lineages such as red cells and lymphocytes; therefore, they screened out the cells in mouse bone marrow that bound antibodies to various lineage markers. They then measured the stem-cell activity of the remaining cells to see whether they had obtained a homogeneous stem-cell population or a population diluted with more mature marrow cells. The most spectacular demonstration of their success came in an experiment with mice that had been irradiated to inactivate the marrow. When the mice were injected with just 30 of the presumptive stem cells, half of the animals regained their ability to make all varieties of blood cells.

Heimfeld says stem cells have been hard to identify because they are rare, comprising only .05 percent of bone-marrow cells, and because they are, for the most part, negatively defined. That is, a stem cell is the cell in the marrow to which most blood-cell antibodies will not bind. Finding the proper combination of antibody screens took the Stanford team six years; the antibody that finally clinched the selection came from a laboratory in West Germany that was studying *T* lymphocytes. Now that they have a pure population of stem cells to work with, Heimfeld says, they can try to raise an antibody specific for stem cells that would expedite the isolation process.

The development of several potent therapies has been stalled by the inability to isolate stem cells. The Stanford irradiation experiment demonstrates the potential of stem-cell injections in treating radiation sickness. It is possible that leukemia could one day be treated by removing a patient's healthy stem cells, killing the cancerous cells with radiation and then re-injecting the stem cells to reconstitute the blood. Congenital immunodeficiencies, anemia and hemophilia might be corrected by genetically en-

Thrilled to the Marrow

Biologists finally corner the rare forebear of all blood cells

In almost any introductory biology course given during the past 30 years the instructor probably held forth on the subject of stem cells, immature cells in the bone marrow from which all blood cells—red and white alike—are derived. From the tone of the lecture, it would be easy to assume that someone had actually

gineering and then reintroducing part of a person's stem-cell population.

Before research on such therapies can get under way, workers have to find out what particular cohort of antibodies identifies human, rather than mouse, stem cells. Heimfeld thinks the markers may not vary much among mammalian species, so that the same antibody types that zero in on mouse stem cells could define the human cells as well. A group at the Fred Hutchinson Cancer Research Center in Seattle has already managed to narrow the field considerably: their antibodies culled cells from human marrow that have kept irradiated baboons alive. And the Stanford group has bred a mouse strain that can be used to test human stem-cell activity. With these projects begun, Heimfeld thinks isolation of the human cells may be only a few years away. —Karen Wright

TECHNOLOGY

Safer Skies?

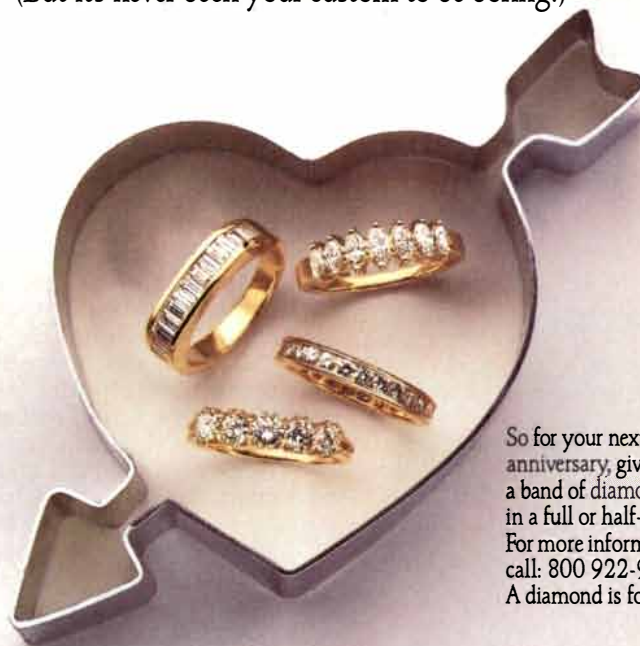
The FAA is trying to reduce the midair-collision threat

Flying the friendly skies has become a nerve-wracking business for airline pilots: the number of midair near-collisions reported to the Federal Aviation Administration (FAA) rose from 311 in 1982 to 1,063 last year. More than three-quarters of the near-collisions included at least one private or other noncommercial aircraft flying not under the direction of air-traffic controllers but on "visual flight rules." Pressure on the FAA to do something has been intense.

In June the FAA issued a long awaited regulation that significantly expands the areas within which all aircraft must carry a Mode-C transponder: a device that reports altitude automatically when it is interrogated by ground radar. Controllers can immediately see on their radar screens whether an aircraft equipped with a Mode-C transponder is a threat to other aircraft under their control.

The new FAA rule means Mode-C transponders will have to be used by all aircraft within 30 miles of the 27 busiest airports in the country and in smaller control zones around 111 medium-activity airports. At present they are required only within control zones close to the busiest airports. The new rule also requires aircraft to use Mode-C transponders at altitudes above 10,000 feet. Pressure from Con-

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gress and strong lobbying by the Aircraft Owners and Pilots Association and other groups forced the FAA to back off from an earlier proposal. It would have required use of the transponders on all planes flying within a 40-mile radius of both large and medium-size airports and anywhere above 6,000 feet; currently fewer than half of all nonairline planes are so equipped.

Besides providing better information to ground controllers, the transponders improve the effectiveness of a radar alert system called TCAS (Traffic Alert and Collision Avoidance System). TCAS, which is carried on airliners, suggests avoidance maneuvers to pilots if another plane is approaching too closely. A TCAS that gives instructions for vertical maneuvers has already been tried out on several commercial airliners. A more sophisticated version called TCAS III should eventually suggest lateral as well as vertical maneuvers, but its development has been delayed.

The Air Line Pilots Association argues that the FAA's proposed 6,000-foot ceiling for aircraft lacking transponders should have been retained, because a growing number of commuter planes fly between 6,000 and 10,000 feet and will be equipped with TCAS. It also believes the control zones around medium-activity airports are inadequate. But the association plans to join private pilots in asking the FAA to relax the requirement that the transponders be used even at low altitudes within a 30-mile radius around busy airports. Both groups agree that requirement could cause confusion for controllers.

Whatever minor revisions may be proposed, the FAA—with urging from the National Transportation Safety Board—has decided to accelerate its plan to install systems to alert controllers when an uncontrolled plane equipped with a Mode-C transponder comes too close to a controlled one. Rather than wait for the new air-traffic computer system scheduled to be installed late in the next decade, the FAA has ordered that existing systems be modified to achieve the alerting capability by 1991.

—T.M.B.

Phase Transition

Electrorheological fluids flourish in drought

Phase changes are a fact of daily life: cooling water sufficiently changes it to ice; heating water changes it to steam. Heat is not the

only agent that can cause phase transitions. Since the 1940's it has been known that electric fields can induce certain materials in a fluid state to become increasingly viscous and then solid. Such materials are called electrorheological fluids, or ERF's. Recent progress in the field has propelled ERF's from a laboratory curiosity to a promising technology.

A typical ERF consists of fine particles of glass, limestone or even starch suspended in a nonconducting fluid, for example, transformer oil. When several thousand volts are put across a cell containing this kind of mixture, the suspension can become as solid as Jell-O within a fraction of a second. Although no one understands quite how ERF's work, many applications immediately suggest themselves, in particular a number relevant to the automobile industry: electrically adjustable brakes, valves, suspension and transmission systems, solenoids and clutches.

The trouble with traditional ERF's is that they all contain water, which indeed was assumed to be an essential element: without it an ERF would not be able to change from liquid to solid form. Water tends, however, to corrode any parts of the device exposed to it and restricts the temperature range of operation as well. Below zero degrees Celsius the water freezes and above 70 degrees it evaporates. When water evaporates, increased electric currents heat the ERF, making it weaker; a greater electric field must then be applied to strengthen it, which makes the ERF hotter yet. The water boils off and thermal runaway results.

Now the water problem may have been solved. Last year Hermann Block and Jeffrey P. Kelly of the Cranfield Institute of Technology in England received a patent for a "substantially anhydrous" ERF: an ERF that functions without substantial amounts of water. Their fluid consists of a semiconducting organic polymer suspended in oil that can operate between -30 and 200 degrees C.

U.S. researchers have not been idle. In May Frank E. Filisko and William E. Armstrong of the University of Michigan at Ann Arbor also received a patent for a class of ERF's "substantially free of adsorbed water." The Michigan ERF's are made from aluminosilicate ceramic particles immersed in oil and have been tested at temperatures of up to 300 degrees.

Neither patent quantifies the phrases "substantially anhydrous" or "substantially free of adsorbed water." The Cranfield group has publicly claimed

that their ERF has less than 5 percent water, whereas Filisko says his ERF operates "down to any detectable level of water," meaning less than one part per million. Will conflicting patents generate legal problems? The English and American ERF's differ substantially in composition but, Filisko says, "anytime more than a dollar is involved, there are legal problems."

More than a dollar is clearly involved. Since receiving his patent Filisko has been approached by Chrysler, Ford, GM, TRW, Exxon, Toyota, Mitsubishi—"you name it"—and has talked to more than 100 companies about potential applications. The scientific task, meanwhile, is to find a physical explanation for the behavior of ERF's. "The explanations people give now are wrong," Filisko maintains. He hopes to have a correct model in about a year, but for now he refuses to speculate on the mechanism behind the ERF phase change.

—Tony Rothman

Pitching Electrons





Momentum spectrometers expose the shape of orbitals

Pitching a quadrillion baseballs to throw one strike may not be the best way to play baseball, but shooting a quadrillion electrons at an atom seems to be an excellent way to observe electrons swarming around the nucleus. This lavish strategy underlies a device called the electron-momentum spectrometer (EMS). The EMS, after a decade of development and analysis, has provided the first direct observations of specific electron orbitals (the paths traced by electrons around the nucleus), thus revealing molecular structure and bonds in unprecedented detail.

For physicists, electron-momentum spectroscopy should provide a way to understand the complex interactions of the many nuclei and electrons that make up a molecule. For chemists, the EMS should unfold a molecular map showing how particular molecules will interact to produce compounds and chemical reactions.

The realm the electron-momentum spectrometer explores is inherently imprecise. Unlike the path of the moon around the earth, the exact path of electrons around atoms cannot be determined. This follows from Heisenberg's uncertainty principle, which holds that if position is determined, momentum information is lost, and vice versa. Electron orbitals describe instead the probability that an elec-

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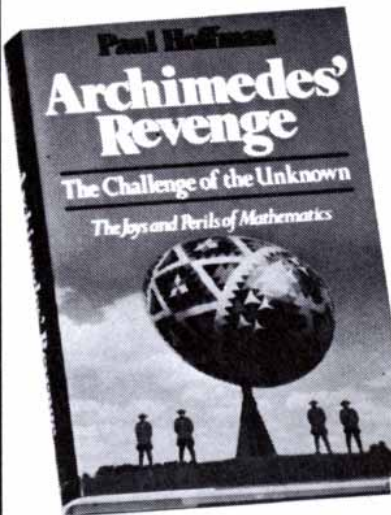
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STAIR-WALKER at the Georgia Institute of Technology, outfitted with a harness and reflectors, breaks an electric-eye beam, causing the staircase to collapse and a strobe-lit camera to switch on.

for the momentum. Since typically only one electron will hit the detector for every quadrillion fired into the gas per minute, a single experiment can last for weeks. Once the data are collected, the position probability and orbital shape can be assessed with a complex mathematical calculation.

Although the new spectroscopy was first tested in Italy and Australia in 1973, acceptance of the technique was delayed by the emergence of discrepancies between predictions from molecular quantum theory and measurements by the EMS. At first some investigators suspected that the fault lay with the EMS. Then in April, 1987, in an analysis of water molecules, Alexis O. Bawagan and Christopher E. Brion of the University of British Columbia and Ernest R. Davidson and David Feller of Indiana University determined that the theoretical predictions, and not the measurements by the EMS, were in error.

—Russell Ruthen

All Fall Down *Researchers stumble to make stairs safer*

As many as 2.6 million people are injured in the U.S. every year while climbing or descending stairs, according to Government statistics. Only automobiles cause more injuries. That is why for the past two years the National Science Foundation has been paying workers at the Georgia Institute of Technology to fall down stairs. The goal is to learn how people hurt themselves on stairs and so to make stairs safer, according to Deborah Hyde, who with John Timpler, also of Georgia Tech, supervises the project.

Subjects of the experiment, wearing a padded suit and crash helmet and suspended in a parachute harness, walk up or down a 12-step, pneumatically controlled staircase. When a subject breaks an electric-eye beam preceding one of the steps, the step collapses. A camera equipped with a strobe light films the resulting tumble. "The object is to generate a set of data points and make a computer simulation," Hyde notes. "Then we can find out how and where people land and with what force." This information in turn should suggest how stairs can be made more forgiving.

Hyde and her co-workers are already searching for materials that can absorb the shock of a falling body and yet are not so "springy" as to throw someone off-balance. The investiga-

tors have considered materials used in automobile dashboards, bulletproof vests and gym mats, as well as novel foams developed at Georgia Tech. "But it could be something as simple as carpeting with a soft underlayer," Hyde says.

—J.H.

OVERVIEW

Clouded Crystal Ball

Predictive medical tests raise legal and ethical questions

Few people doubt that the past few years' progress in understanding the molecular biology of many diseases will ultimately lead to new therapies. Usually, however, such new understanding suggests ways to predict, diagnose and monitor disease before it leads to cures. Diagnostic and predictive tests are now becoming available for far more diseases than was the case in the past. Tests that assess the likelihood of cardiovascular disease by looking at the composition of blood lipids have become standard; screening of neonates for phenylketonuria, which can cause brain damage if untreated, is almost universal. Many more tests now being developed will be able to peer farther into a patient's future. They will raise hosts of questions—questions that lawyers and ethicists are only beginning to consider.

For example, probes are already available that detect characteristic antigens in the blood from metastatic tumor cells "months if not years" before metastasis becomes clinically evident, according to Morton K. Schwartz of the Memorial Sloan-Kettering Cancer Center. Helping patients to cope with such disturbing news is becoming increasingly difficult, he says, particularly if a cancer had been pronounced cured and if the impending spread seems likely to be untreatable.

Often a test helps a physician to clarify a prognosis, thereby suggesting how aggressive treatment should be. For example, the Food and Drug Administration is considering approval of a diagnostic test that improves detection of a particular chromosomal rearrangement often seen in patients with chronic myelogenous leukemia. Tests that detect the presence in unusual numbers of particular oncogenes—genes implicated in the causation of cancers—or the absence of growth-suppressing anti-oncogenes are likely to be even more significant,

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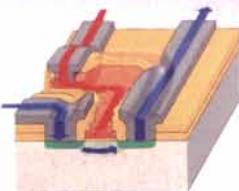
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Schwartz says; some may predict malignancy before any disease is apparent clinically.

Diagnostic information can have damaging consequences if it gets into the wrong hands. The test for antibodies to the AIDS virus is a notable example. In spite of all the evidence that AIDS cannot be transmitted by casual contact, a positive result has frequently led to discrimination and, in some cases, to violence against the person tested. "Confidentiality is critically important," says Alan P. Brownstein of the National Hemophilia Foundation. Many of the foundation's members have been infected with the AIDS virus by contaminated blood products. The degree of confidentiality normally given to medical records is insufficient, Brownstein argues: he points out that such records are often displayed in semipublic places such as nurses' workstations and are discussed casually by health professionals.

Some jurisdictions already have legislation prohibiting discrimination against people infected with the AIDS virus. Admiral James D. Watkins, the chairman of the President's Commission on AIDS, made a strong plea in his recent report for Federal laws to prohibit discrimination against infected individuals. Watkins' plea may be go-

ing unheard: a bill currently working its way through Congress that would provide funds for AIDS-antibody testing has been stripped of its confidentiality provisions by a committee of the House of Representatives.

If legislation to protect people infected with the AIDS virus is passed, it could pave the way for laws to protect those diagnosed with other conditions. The danger that a test will be misused seems to be greatest when it predicts a condition or a predisposition a long time before any illness shows itself naturally, according to Kenneth L. Vaux, a medical ethicist at the University of Illinois at Chicago.

Tests that indicate a predisposition to a given disease are also particularly valuable, since they can suggest strategies for prevention. A company called Focus Technologies, Inc., in Washington, D.C., has experimentally offered a battery of diagnostic tests in combination with counseling to more than 600 employees of a local telephone company. The company plans to offer the package more widely but intends to include only those tests that suggest preventive or mitigating measures, such as tests for a predisposition to diabetes, cardiovascular disease or gum disease.

Tests based on analyzing DNA raise

the most difficult questions because they often bear on reproductive decisions. At present they are being done only on a small scale in a few medical centers, usually for rare conditions such as cystic fibrosis, muscular dystrophy or polycystic kidney disease. The results are now generally used to help potential parents decide whether to conceive or to determine whether a fetus has inherited a genetic disease. The applications may become broader: the approximate locations of genes that play a role in more common diseases, such as Alzheimer's disease, cardiovascular disease and even some mental illnesses, have all been identified. Genetic testing for susceptibility to such conditions is probably only a matter of time.

No disease illustrates the difficulties of knowledge without a cure more starkly than Huntington's disease, a devastating and fatal late-onset neurological disease that develops inevitably in people who inherit a particular defective gene from an affected parent. Diagnosis is accomplished through analysis of restriction-fragment length polymorphisms, or RFLP's (see "Chromosome Mapping with DNA Markers," by Ray White and Jean-Marc Lalouel; SCIENTIFIC AMERICAN, February). Several medical centers have re-



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cently begun to offer tests for Huntington's disease.

At the Boston University Medical Center, 45 patients at risk of developing the disease because they have an affected parent have elected to take the test and receive counseling. Although some counselors feared that a positive test result could make patients suicidal, there have been no such tragic consequences. Test results have, however, led to broken marriages, according to Nancy S. Wexler, president of the Hereditary Disease Foundation, who runs a similar program at Columbia University. They also raise agonizing dilemmas about the limits of confidentiality when someone wants to conceal a positive result from a spouse.

"The rule of thumb is that test results should be kept confidential," Wexler says, but testing and counseling for Huntington's disease can cost as much as \$4,000, and insurance companies are likely to see the results of a test if an insurance claim is filed. Moreover, Wexler says she has come across cases in which insurance companies have charged higher premiums on the mere suspicion that someone might have a genetic disease—if they learn, for example, that a client has an affected parent. Insurance is

"the major problem," she remarks.

Insurance companies, for their part, argue that they need access to any diagnostic-test results to which their clients have access. Otherwise, Robert J. Pokorski of the Lincoln National Life Insurance Co. points out, clients with an unfavorable prognosis could over-insure themselves, thus in effect exploiting the healthy. Vaux disagrees, saying that most medical information should remain part of the "mystery of one's being." At present only blood-lipid tests are routinely required by insurers. New tests will probably lead eventually to a reconsideration of the concept of health insurance, according to Lori B. Andrews of the American Bar Foundation, who is studying legal aspects of medical genetics.

Mark A. Rothstein of the Health Law Institute at the University of Houston foresees another area of difficulty. He points out that the large-scale genetic testing some employers did in the early 1980's was intended to screen out workers who might be peculiarly susceptible to injury by their working conditions—for example, by exposure to chemicals. In the future, he believes, companies may seek to administer long-range predictive tests that would instead provide information about a worker's probable medical expenses

and absenteeism. Rothstein sees potential for injustice in that area, since most medical tests have significant error rates.

Vaux concedes that in some situations the presumption of confidentiality should be waived. Few people would want to see someone who is known to be at high risk of an early heart attack employed as an airline pilot, for example. Such instances should be the exception rather than the rule, Wexler believes.

Congress has not yet addressed these issues. It will be important to ensure that lawmakers are thoroughly briefed, Andrews says. She argues that poorly conceived laws that were passed in the early 1970's, which mandated the screening of newborns and children for sickle-cell disease, did much to bring screening programs into disrepute: legislators failed to distinguish between someone with the sickle-cell trait (who has only one sickle-cell gene) and someone actually affected by the disease. The distrust engendered by that mistake is now impeding attempts to introduce sickle-cell screening programs for newborns. According to a review done recently by the National Institutes of Health, such programs could now be saving lives.

—Tim Beardsley

Civilian Casualties from Counterforce Attacks

New estimates of the number of civilian deaths resulting from nuclear attacks by one superpower on the strategic forces of the other further undermine the rationale for such attacks

by Frank N. von Hippel, Barbara G. Levi, Theodore A. Postol and William H. Daugherty

The ratification of the agreement between the U.S. and the Soviet Union to ban all intermediate-range nuclear missiles and the apparent progress in the so-called Strategic Arms Reduction Talks (START), which have as their primary aim a 50 percent cut in the number of long-range ballis-

tic-missile warheads, have given many observers reason to be optimistic about the prospect for further reductions in nuclear arms. Further reductions, however, will require the U.S. and the Soviet Union to reassess many of the military missions they have planned for their nuclear forces in the event of war.

The missions that would be most affected by further nuclear-arms reductions are generally known as counterforce missions. Their purpose is to destroy the military capabilities of the opponent, including nuclear and non-nuclear forces as well as the industrial base on which the forces depend. Since an opponent's strategic forces represent the greatest threat, they are considered to be the highest-priority targets for counterforce missions. Because there are thousands of potential targets for a strategic counterforce mission, it requires a nuclear arsenal of vast size.

Many defense analysts argue that threatening to destroy a variety of military targets deters limited aggression more effectively than threatening to attack cities, because such threats are less likely to elicit a devastating counterstrike against the cities of the attacker and can therefore be made more credibly. In addition the country that first executes such missions might hope to destroy many more of the other side's warheads than it

employs in carrying out the attack. Such a lopsided exchange is made possible by modern nuclear missiles that carry multiple warheads, each of which is capable of destroying a different target. Unfortunately the perception that one might gain by striking first leads to crisis instability: each side is tempted to preempt the other side's attack if nuclear war appears inevitable.

That dangerous situation can be prevented if nuclear forces are structured in such a way that neither side would gain an advantage by striking first. A START agreement as outlined in the current negotiations would not achieve this, since it would allow each side to retain its most modern multiple-warhead missiles. Crisis stability can be achieved by ensuring that reduced nuclear forces incorporate single-warhead intercontinental ballistic missiles (ICBM's) and survivable basing modes for all weapon launchers. Such a nuclear-force structure, however, is incompatible with the strategic counterforce mission.

But does the U.S. or the U.S.S.R. need to rely on a strategic counterforce mission to prevent nuclear aggression? Does it really provide a more credible deterrent by threatening military targets and not civilian ones? Our calculations suggest the answer is no: they show that a large-scale attack on strategic forces would cause so many

FRANK N. VON HIPPEL, BARBARA G. LEVI, THEODORE A. POSTOL AND WILLIAM H. DAUGHERTY have studied—separately and together—various issues in nuclear-arms control. Von Hippel is professor of public and international affairs at Princeton University; he is also associated with the university's Center for Energy and Environmental Studies (CEES) and Center of International Studies. He obtained his B.S. from the Massachusetts Institute of Technology and his D.Phil. from the University of Oxford. Levi, who has a B.A. from Carleton College and an M.S. and a Ph.D. from Stanford University, is visiting professor of physics at Rutgers University. She was on the research staff of the CEES from 1981 to 1987. Postol is a science fellow at Stanford's Center for International Security and Arms Control. He earned a B.S., an M.S. and a Ph.D.—all in nuclear engineering—from M.I.T. Before going to Stanford, he worked for the Congressional Office of Technology Assessment and for the Office of the U.S. Chief of Naval Operations. Daugherty, who has an undergraduate degree from Princeton, is a candidate for a Ph.D. in political science at Columbia University.

civilian casualties that it would be difficult to distinguish from a deliberate attack on the population.

Curiously enough, the number of civilian deaths that counterforce attacks would cause remains largely a neglected topic in the nuclear-weapons policy debate. Even during the 1980 presidential campaign, when the vulnerability of U.S. ICBM's became a political issue, the civilian casualties that would result from an attack on the ICBM's was not even mentioned. Indeed, we know of only one public discussion of the subject by the U.S. Department of Defense—and that took place in 1975 [see "Limited Nuclear War," by Sidney D. Drell and Frank von Hippel; *SCIENTIFIC AMERICAN*, November, 1976]. We reexamine the subject here in order to present estimates of the civilian casualties from a U.S. attack on Soviet strategic forces as well as the reverse. In doing so we gauge the impact of changing some of the assumptions made by the Defense Department in estimating U.S. casualties.

In our calculations we considered the consequences of attacking with nuclear weapons 1,215 military facilities in the U.S. and 1,740 military facilities in the U.S.S.R. All but approximately 100 of the targets on each side are either missile silos or their associated

launch-control centers. The disparity between the numbers of targets is due to the fact that the Soviet Union has more missile silos than the U.S. Other targets on the lists are bases for long-range bombers, ballistic-missile submarines, aircraft carriers and ships carrying long-range, nuclear-armed cruise missiles. Furthermore, we assumed that early-warning radar installations and key command-and-communication facilities would also be struck by nuclear weapons in order to effect the maximum surprise and blunt the effectiveness of any retaliatory attack. (It should perhaps be pointed out that some defense planners argue against attacking command-and-communication facilities, since it could preclude a negotiated end to the conflict.)

The list of targets in the U.S. includes major nuclear-weapon depots and bases for the tanker aircraft that would refuel U.S. bombers on the way to and from their targets in the Soviet Union. The list of targets in the U.S.S.R. includes anti-ballistic-missile launchers around Moscow and bases for mobile intermediate-range missiles and nuclear-armed bombers, which could be employed to attack facilities of the North Atlantic Treaty Organization in Europe.

A review of the listed targets indicates that many of them lie in or near

major urban areas. (Their approximate locations are known from the enormous amount of information that is made public by the U.S. Defense Department.) In the U.S., for example, tanker aircraft are based at airports near Chicago, Milwaukee, Phoenix and Salt Lake City; Navy bases for nuclear-armed vessels are situated in San Francisco Bay and at Long Beach near Los Angeles (and one is planned for Staten Island in New York Harbor); key command posts are in the vicinity of Washington, D.C., and Navy radio transmitters are located in or near Jacksonville, Sacramento and San Diego. In the U.S.S.R. there is a similar collocation of strategic-weapon facilities and urban areas: Moscow is ringed with underground command bunkers; Leningrad is the headquarters of the Baltic fleet; Vladivostok is a home port for ballistic-missile submarines, and many ICBM fields are found in the densely populated western region of the country.

We assigned nuclear weapons to each target and specified their mode of employment according to target type. If the target was an ICBM silo or its associated launch-control center, the most accurate ballistic-missile warheads were assigned to it, because such "hard" targets can be destroyed only by powerful nuclear weapons detonated no more than a



DEVASTATION wrought by the Allied incendiary attack on Hamburg in July of 1943 approaches what would result from huge conflagrations ignited by nuclear explosions over modern urban centers. The fire damage would extend beyond the

areas affected by the blast of the explosions. The authors have taken the possibility of such "superfires" into account in estimating the number of civilian deaths associated with nuclear attacks on the strategic forces of the U.S. and the U.S.S.R.

few hundred meters away. The fireballs of such explosions would inevitably come in contact with the ground, and as a result they would produce large amounts of radioactive fallout. In keeping with standard military planning, such facilities were targeted

with two nuclear warheads to ensure against the failure of one of them.

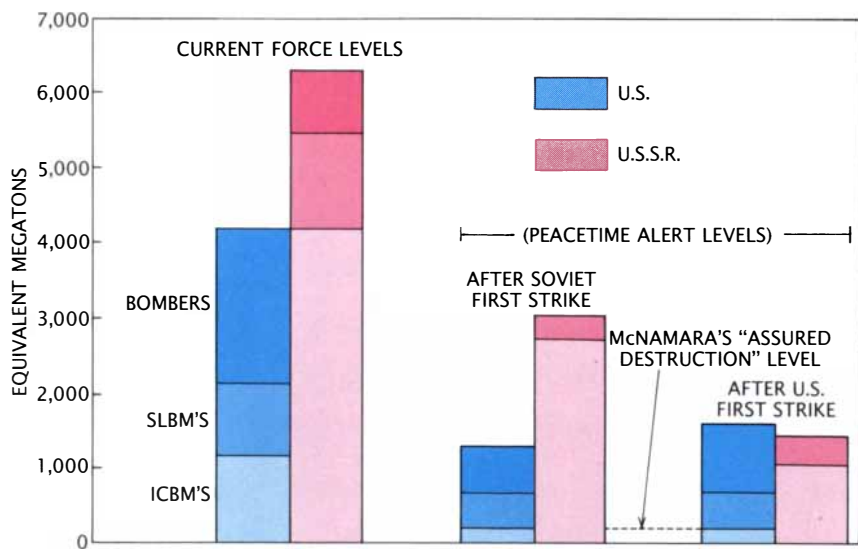
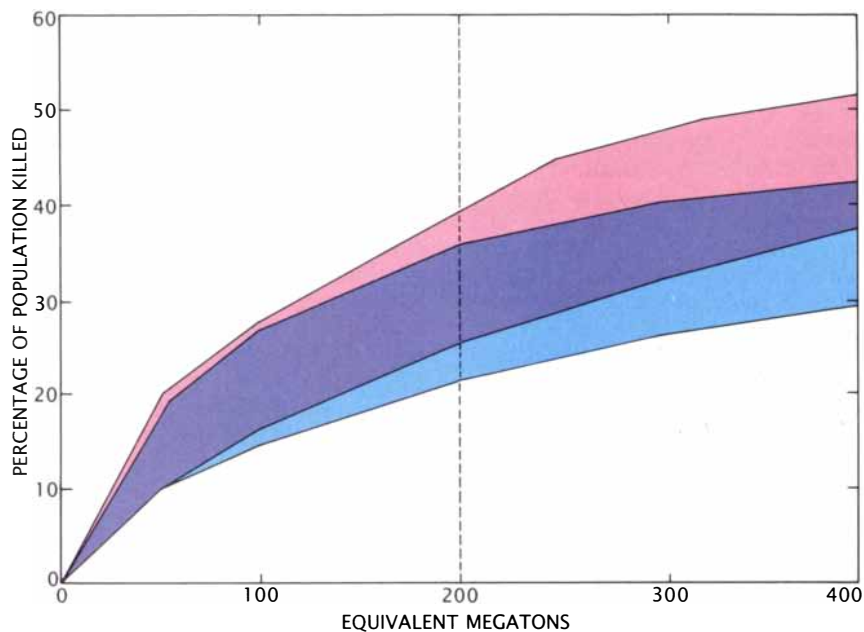
If the target in question was an airbase, we assumed it would be attacked not only with one large warhead detonated at or near ground level but also with some 15 warheads detonat-

ed in the air, which could be delivered by two multiple-warhead submarine-launched ballistic missiles (SLBM's). The reason is that a significant fraction of U.S. long-range bombers and their associated tanker aircraft are kept on alert, ready to take off on warning of an attack. A groundburst and several airbursts would be intended to destroy the aircraft still on the ground and those already airborne but not yet out of the area. We have assumed in our calculations that Soviet mobile-missile bases would be attacked in a similar way.

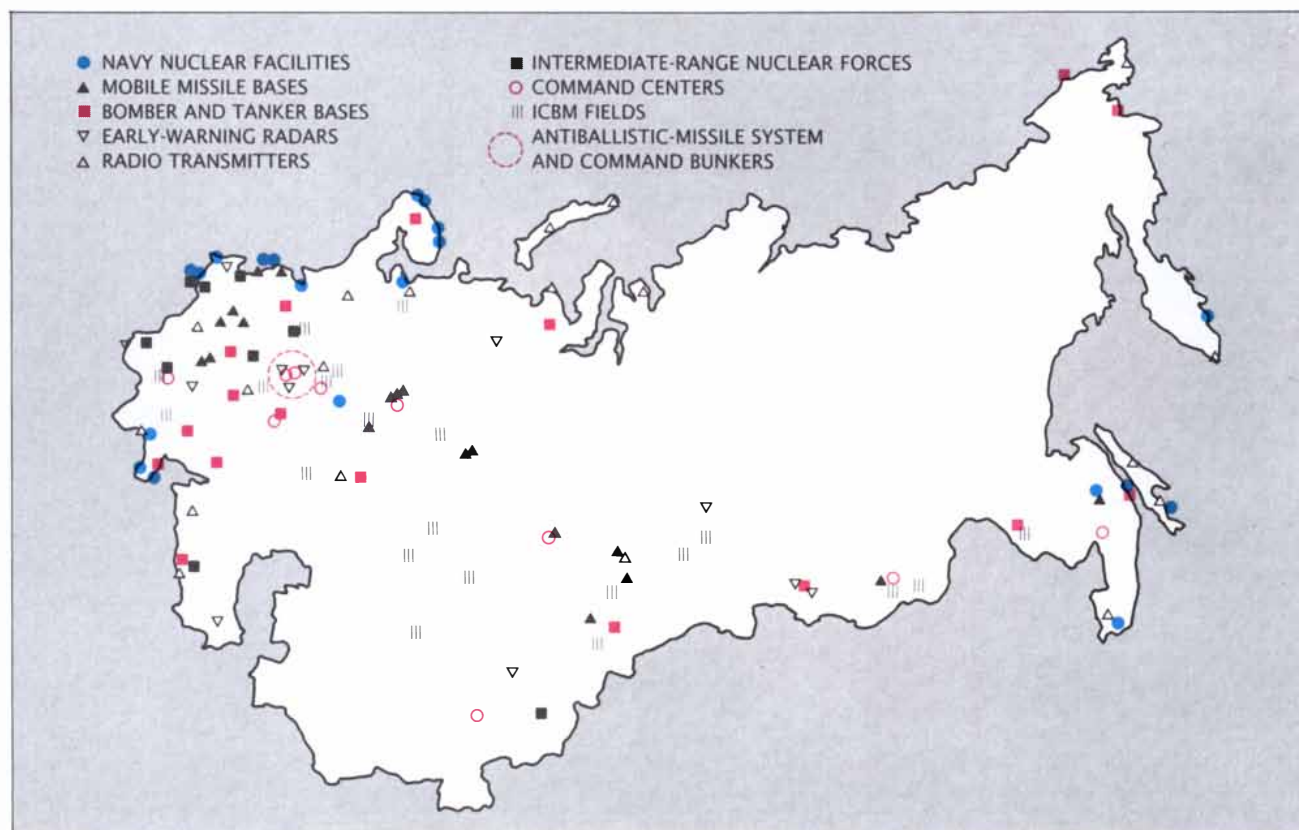
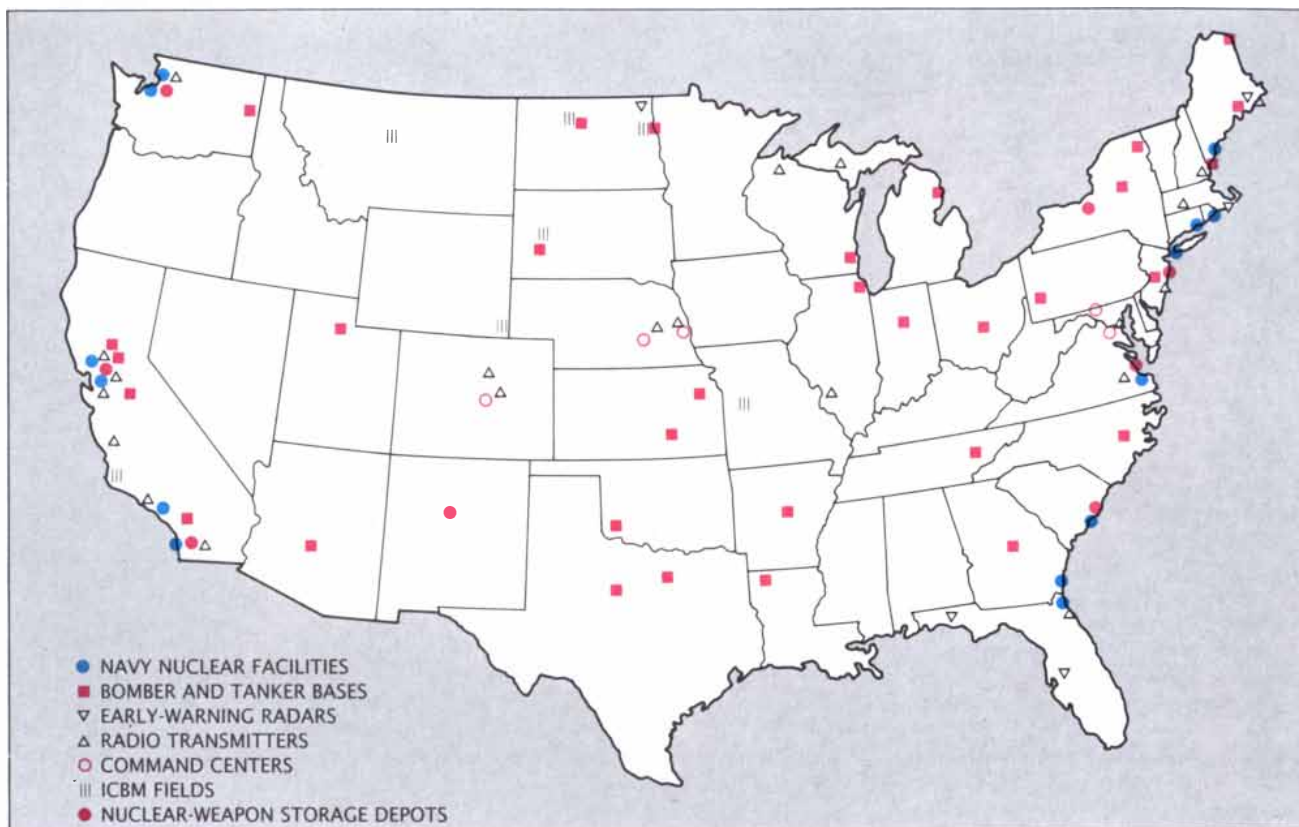
Overall, the hypothetical Soviet strategic counterforce attack on the U.S. involved about 3,000 warheads with a total yield of about 1,300 megatons, whereas the U.S. attack on the Soviet Union involved slightly more than 4,000 warheads with a total yield of about 800 megatons. (A megaton is defined as the energy released by the detonation of a million tons of TNT.) Such attacks are well within the capabilities of each nation, even after the reductions envisioned in the START negotiations. The greater number of warheads and lower total megatonnage of the U.S. attack on the Soviet Union result from respectively the greater number of Soviet missile silos and the smaller average yield of U.S. strategic warheads.

In calculating the number of civilians who might die or sustain injury as a result of a large-scale strategic counterforce attack, we considered only the direct effects of nuclear explosions: blast, fire and radioactive fallout. The standard method applied by the U.S. Defense Department and the Federal Emergency Management Agency (FEMA) for estimating the casualties arising from the first two nuclear-weapon effects relies on extrapolating the consequences of the relatively small-yield (.015 megaton) explosion over Hiroshima to the much more powerful nuclear explosives in modern strategic arsenals. To be specific, the model applied in the Government's extrapolation, which we call the overpressure model, assumes that the casualty rate would be the same as the rate observed in Hiroshima for a given value of the peak blast overpressure: the maximum air pressure (above the ambient level) produced by the explosion's blast.

Yet some of the casualties at Hiroshima were a consequence of a huge fire that developed approximately 20 minutes after the explosion and covered a roughly circular area having a radius of about two kilometers. The

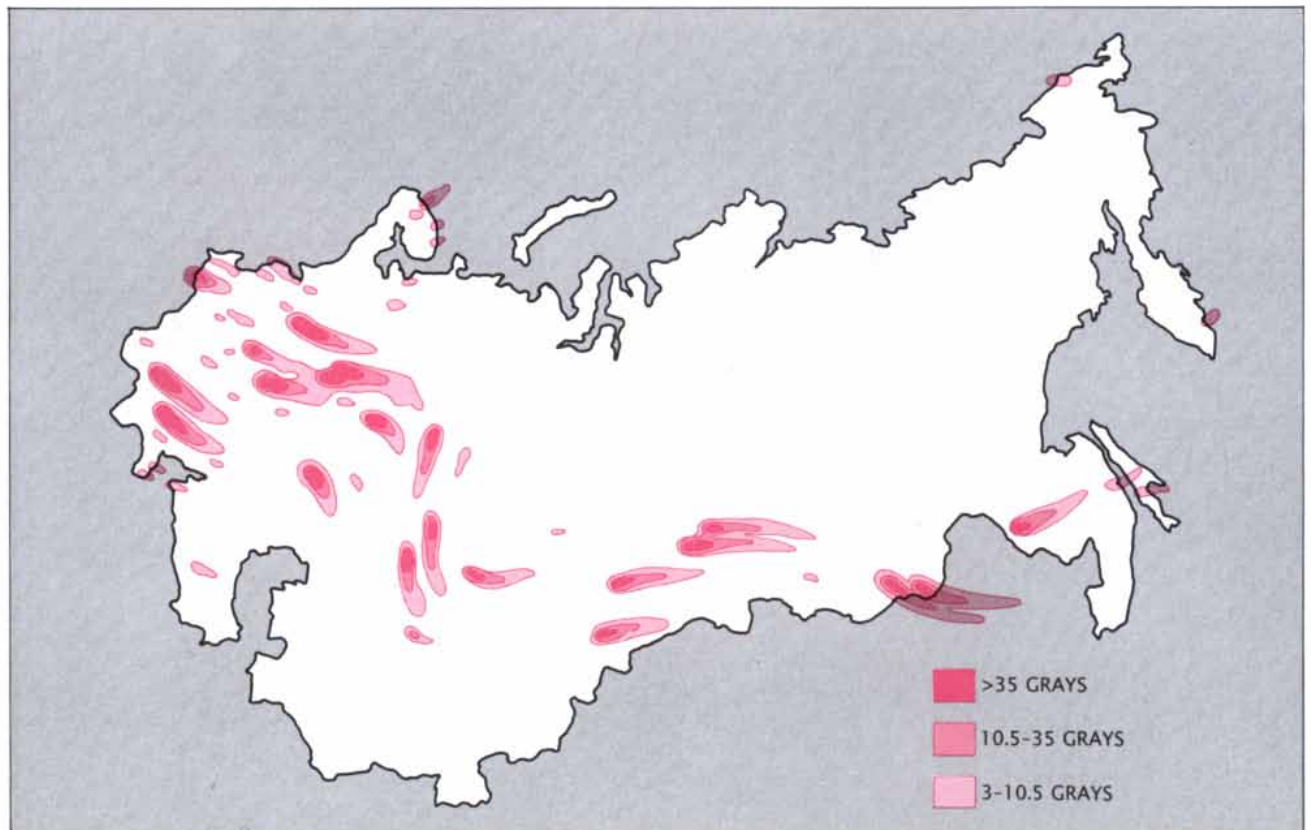
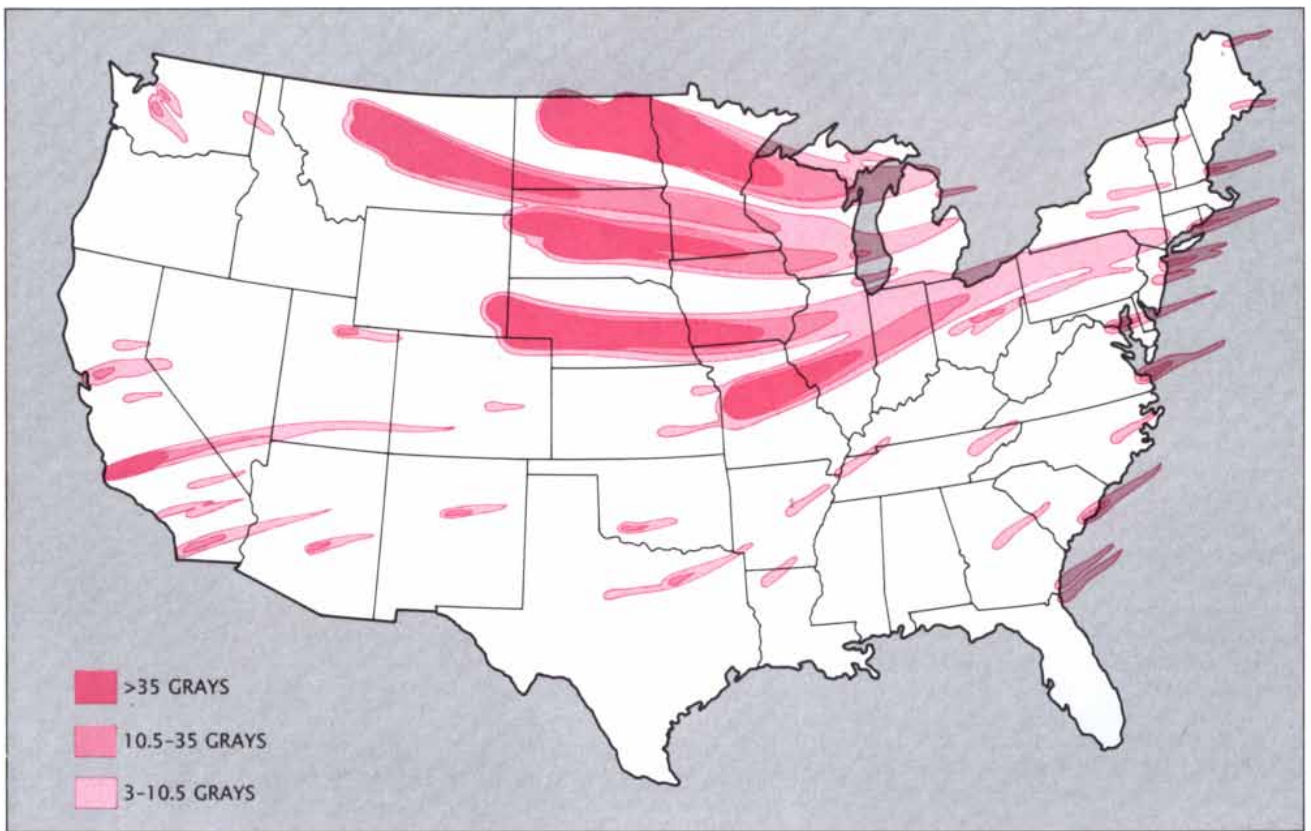


HOW MANY NUCLEAR WEAPONS does it take to deter a nuclear attack? According to the "assured destruction" criterion first laid out in the late 1960's by Secretary of Defense Robert S. McNamara, the capability of detonating—in a retaliatory attack—200 equivalent megatons over Soviet cities would effectively deter the U.S.S.R. (An equivalent megaton represents a combination of nuclear weapons whose blast damage equals that of a one-megaton explosion.) The authors' calculations (top) show that such an attack on the U.S. (blue) or on the Soviet Union (red) would result in prompt fatalities amounting to as much as 40 percent of the population (about 100 million people) if the lethal effects of superfires are taken into account. As can be seen (bottom), both the U.S. and the U.S.S.R. have substantially more equivalent megatons in their respective strategic arsenals than are necessary to meet McNamara's assured-destruction criterion—even after their strategic forces have suffered a "worst case" nuclear attack. The excess weapons are justified largely on the grounds that they are required to execute "counterforce" attacks on military facilities, in particular those associated with the nuclear forces of the other side.



MILITARY FACILITIES associated with the strategic forces of the U.S. (top) and the strategic and intermediate-range forces of the U.S.S.R. (bottom) are numerous. Many are also found near

urban centers. As a result there are likely to be tens of millions of civilian deaths from a counterforce attack, even though only military facilities (and not cities per se) are the targets.



FALLOUT from a nuclear attack on the military facilities shown on the preceding page would expose millions of people to lethal doses of gamma radiation. (Typical February wind patterns are assumed here.) If the median lethal dose is taken to

be 3.5 of the units called grays, most people who were not in shelters within the outermost radiation-level contours would suffer severe radiation sickness. Even people sheltered in windowless cellars would die within the innermost contours.

area was small enough so that most of the people who had not been trapped under collapsed buildings or otherwise incapacitated were able to escape before the environment in the fire area became lethal. Recent studies done for the Defense Nuclear Agency by Harold L. Brode and Richard D. Small of the Pacific-Sierra Research Corporation suggest that detonation of nuclear warheads over U.S. and Soviet cities and suburbs could result in much larger superfires: huge conflagrations fanned by hurricane-force winds. Given the typical yield of today's strategic nuclear weapons (at least 10 times greater than the Hiroshima weapon), the conflagration area would be so large that people would not be able to escape before they succumbed to the combined effects of heat, smoke and toxic gases. On these grounds one of us (Postol) suggested in 1985 that the Defense Department and FEMA might be seriously underestimating the potential fatalities from the direct effects of nuclear explosions.

The conditions that would prevail in a superfire caused by a nuclear explosion resemble the conditions during the fire storm that developed in Hamburg after an intense Allied incendiary attack in July, 1943. In that case basement shelters provided little protection from the lethal effects of carbon monoxide and the extreme temperatures generated by the overlying smoldering debris. In spite of the fact that Hamburg was not subjected to blast or radiation effects during the attack, the area destroyed was about 12 square kilometers (about the same as the area of conflagration at Hiroshima) and the death toll was estimated at between 50,000 and 60,000 (also comparable to that at Hiroshima).

Although any prediction about the extent of urban fires caused by nuclear explosions is uncertain, we believe the probability of lethal superfires is great enough so that casualty estimates should take them into account. We have done so by making casualty estimates with both the traditional overpressure model and our own superfire model. The respective results define the lower and upper end of a range of uncertainty.

The other cause of death associated with nuclear explosions is fallout: soil and debris sucked up into the fireball of a low-altitude nuclear explosion that eventually falls back to the ground heavily contaminated by fission products. The fallout that settles downwind of a nuclear explosion can create a zone of gamma

radiation so intense that people without adequate shielding in the zone would die of severe radiation sickness. In estimating the casualties caused by radioactive fallout, we adapted a Government computer model designed to predict the way fallout would be dispersed and drew on Government data bases for wind patterns and population distributions.

We also considered the possibility that the resistance of human beings to ionizing radiation under wartime conditions might be much less than has been traditionally assumed. This possibility was suggested by a recent reanalysis of the data on the casualties at Hiroshima.

Since World War II the standard assumption made in Government analyses has been that an exposure to 4.5 grays of gamma radiation within a period of less than two weeks constitutes the so-called LD-50 dose: the dose that causes lethal radiation sickness in 50 percent of an exposed population within about 60 days. (A gray is the metric unit for measuring doses of ionizing radiation. A rad, which may be more familiar in the U.S., is one-hundredth of a gray.) That assumption was based primarily on experimental data from animals, but it seemed to be consistent with the human data from Hiroshima.

A few years ago, however, investigators at the Lawrence Livermore National Laboratory discovered that the estimated radiation exposures for those unfortunate enough to be in Hiroshima at the time the atom bomb was dropped were too high. This led a group of Japanese investigators to re-examine the fates of more than 3,000 Hiroshima inhabitants who had not suffered severe blast or burn injuries from the bomb's explosion but were near enough to ground zero to be exposed to direct gamma radiation. When the new Lawrence Livermore results were applied to determine the radiation doses for each individual in the Hiroshima group, a surprisingly low estimate for the LD-50 was obtained: just 2.5 grays.

The Hiroshima victims, of course, did not benefit from the modern treatment for radiation sickness, which involves placing the victim in a sterile environment and administering heavy doses of antibiotics. Yet modern medicines and hospital care would probably be as unavailable to the survivors of a large-scale nuclear attack today as it was to the survivors of Hiroshima. We therefore varied the values of the LD-50 in our calculations from 2.5 to 4.5 grays.

The number of casualties estimated for the attacks also depends on the strength and direction of the winds at the time of the attack, because it is the wind that disperses radioactive fallout. Of the four seasonal wind patterns we considered, we found that the strong winds typical of February produced the highest number of deaths in both the U.S. and the U.S.S.R. The doses from fallout radiation could be reduced to a certain extent by taking refuge in shelters.

Every shelter can be assigned a protection factor: the number by which the open-air fallout-radiation exposures would have to be divided in order to give the actual radiation dose in the shelter. We assumed that the population of both the U.S. and the U.S.S.R. would be equally divided between a group that did not spend much time in underground shelters (and therefore had an average effective protection factor of about three) and a group that did spend most of its time in shelters (and therefore had an average effective protection factor of about 10).

Fallout shelters with higher protection factors do exist, but it would be difficult for people in them to reduce their average radiation dose to levels substantially lower than what we assumed. The reason is that most of the sheltered population would have to emerge within a few days to replenish supplies or seek help, and even a short period spent outside the shelters would greatly increase the radiation dose. Average radiation doses would be increased anyway within a relatively short time as people began to consume water and food contaminated by radioactivity.

Our calculations indicate that the direct effects of the blast, fire and radioactive fallout of a Soviet attack on U.S. strategic nuclear facilities could kill between 12 and 27 million people. The corresponding U.S. attack on Soviet strategic nuclear facilities could kill a comparable number: between 15 and 32 million people. (We also estimate that the survivors of the attacks would suffer between one and eight million additional deaths from cancer over their remaining lifetimes as a result of their exposure to fallout radiation.)

The numbers at the low end of our ranges, which were derived by applying the overpressure model and assuming an LD-50 of 4.5 grays, are consistent with the estimates presented by the Defense Department in 1975. The numbers at the upper end of our

ranges were obtained from the superfire model and an LD-50 of 2.5 grays.

In our results the deaths from blast and fire are roughly comparable in number to those from fallout. Although the percentage of the area of the U.S. subjected to lethal levels of fallout radiation was found to be larger than that for the U.S.S.R., there would nonetheless be comparable numbers of casualties from the radiation in both countries, since much of the fallout over the Soviet Union would descend on the heavily populated European region of the country.

Limiting the attack to any subset of counterforce targets, such as missile silos, bomber bases, naval bases, weapon storage depots, command-and-communication facilities or intermediate-range forces (in the case of the U.S.S.R.) would cause at least a million deaths in all cases but one [see illustration below]. Hence one could not hope to reduce the casualties below many millions by eliminating one or two classes of targets. Our casualty estimates for the U.S.S.R., for example, would be only about 10 percent lower if we had not included as targets the intermediate-range missiles, which are to be eliminated over the next few years. (Actually the effect of the elimination of the Soviet intermediate-range missile will be approximately offset by the replacement of Trident

I warheads with more powerful Trident II warheads on U.S. ballistic-missile submarines.) On the other hand, our casualty estimates for both sides would have been considerably higher if we had included other classes of plausible military-related targets.

For example, we estimated separately the civilian casualties that would result from an attack with one-megaton airburst warheads on a group of 101 factories identified as being among the highest-priority targets in an attack on U.S. military-industrial capability. These factories manufacture such items as missile-guidance systems, automatic guns for aircraft, antitank missiles, radars and command-and-control systems. We found that the attack would kill between 11 and 29 million people. The toll is that high because most of the military-industrial targets are in major urban areas, such as those surrounding Boston, Detroit and Los Angeles.

Finally, it should also be kept in mind that we have considered only the casualties that would be caused by the direct effects of nuclear explosions. Tens of millions of additional deaths might result from exposure, famine and disease if—as seems likely—the U.S. or the Soviet Union suffered economic and social collapse after a nuclear attack. The populations of other nations around the world would also

suffer indirectly from the manifold economic and environmental effects of such an attack.

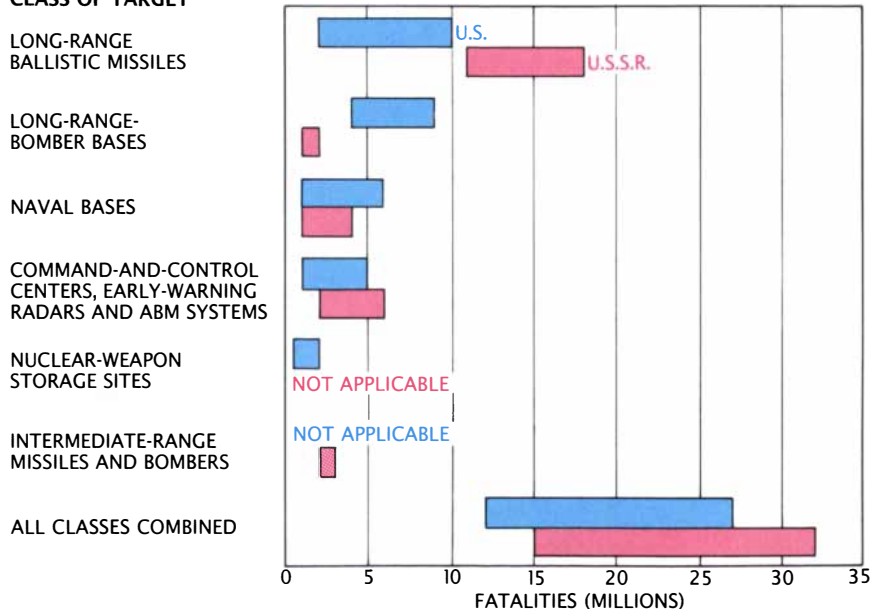
Our results reaffirm an assertion made more than 25 years ago by the chairman of the Joint Chiefs of Staff, Gen. Lyman L. Lemnitzer, when he briefed President John F. Kennedy on the U.S. nuclear war plans:

“There is considerable question that the Soviets would be able to distinguish between a total attack and an attack on military targets only. . . . Because of fallout from attack of military targets and colocation of many military targets with [cities], the casualties would be many million in number. Thus, limiting attack to military targets has little practical meaning as a humanitarian measure.”

Yet for the past two decades the U.S. and the U.S.S.R. have continued to develop increasingly elaborate counterforce targeting strategies, ignoring the fact that the large-scale application of nuclear weapons against military targets is not qualitatively different from their application against civilians. In view of the massive civilian casualties counterforce attacks would entail, threatening to execute such attacks can be no more credible than threatening to destroy cities.

It is clear that eliminating counterforce weaponry by treaty would be preferable to eliminating them by use on one another. Yet it is the very reliance on counterforce strategies that blocks stabilizing nuclear-force reductions beyond those currently being considered in the START negotiations.

CLASS OF TARGET



RANGES OF CIVILIAN FATALITIES that can be expected as a direct consequence of counterforce attacks on various classes of military targets have been calculated by the authors. The fatalities associated with a counterforce attack on all targets do not equal the sum of the fatalities for attacks on individual classes of targets, because there is some overlap in the areas affected and because the lower and upper values of the fatality ranges apply to different months in different attacks.

FURTHER READING

ANALYSES OF EFFECTS OF LIMITED NUCLEAR WARFARE. Subcommittee on Arms Control, International Organizations and Security Agreements of the U.S. Senate Committee on Foreign Relations. U.S. Government Printing Office, 1975.

POSSIBLE FATALITIES FROM SUPERFIRES FOLLOWING NUCLEAR ATTACKS IN OR NEAR URBAN AREAS. Theodore A. Postol in *The Medical Implications of Nuclear War*, compiled for the Institute of Medicine, National Academy of Sciences. National Academy Press, 1986.

THE CONSEQUENCES OF "LIMITED" NUCLEAR ATTACKS ON THE UNITED STATES. William Daugherty, Barbara Levi and Frank von Hippel in *International Security*, Vol. 10, No. 4, pages 3-45; Spring, 1986.

CIVILIAN CASUALTIES FROM "LIMITED" NUCLEAR ATTACKS ON THE USSR. Barbara G. Levi, Frank N. von Hippel and William H. Daugherty in *International Security*, Vol. 12, No. 3, pages 168-189; Winter, 1987/88.

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Finding the Anti-Oncogene

Inheritance of certain growth-suppressing genes in a mutated form confers susceptibility to cancer. The first such gene to be isolated gives rise to a predisposition to retinoblastoma, an eye tumor

by Robert A. Weinberg

The roots of cancer lie in our genes. Cancer often begins when a carcinogenic agent—radiation or a chemical—damages the DNA of a critical target gene in a particular cell. The mutant cell then multiplies, and its descendants ultimately form the large aggregate of cells called a tumor.

This generalized scheme has been given focus and precision in the past decade with the identification of some of the genetic targets of carcinogens: the oncogenes. Once activated by a mutation, an oncogene promotes excessive or inappropriate cell proliferation; its activation represents one critical step in the creation of many types of cancerous growths.

Within the past few years a quite different class of cancer genes has been discovered. They act in normal cells not to promote proliferation but to suppress it. The loss of growth-suppressor genes from a cell removes a normal constraint on its growth. Such a genetically depleted cell may proliferate uncontrollably, and this too may lead to cancer. The discovery of growth-suppressor genes enriches understanding of the genetics of cancer and in time will lead to the reformulation of ideas about how the growth of normal cells is regulated.

An understanding of growth-suppressor genes must begin with an understanding of their mirror images, the growth-promoting oncogenes. When oncogenes isolated

from tumors are inserted into normal cells, the latter take on many traits of cancer cells [see "A Molecular Basis of Cancer," by Robert A. Weinberg; SCIENTIFIC AMERICAN, November, 1983]. Such gene-transfer experiments have shown that oncogenes act to deregulate the growth of the cells into which they are introduced and so must (by implication) be responsible at least in part for the aberrant behavior of the tumor cells from which they are extracted. Several lines of investigation have made it clear that such oncogenes are altered versions of normal genes, called proto-oncogenes, that act as central regulators of growth in normal cells. In the course of a lifetime any of a variety of mutations can convert one of these normal genes into a malignant oncogene.

The creation of a single oncogene may be necessary for the genesis of a tumor, but it is far from being sufficient. Tumorigenesis is a multistep process. The evolution of a line of tumor cells seems to depend, at the very least, on the accumulation of mutations altering a number of genes, among them oncogenes. The altered genes then function in concert to create full-fledged malignant growth.

To date, however, oncogenes have been detected in only 15 or 20 percent of human tumors. Human tumor cells may well carry other growth-promoting activated oncogenes, which remain elusive simply because current methods for detecting such genes are rather insensitive. It has seemed likely, however, that yet other cancer genes could not be identified because they operate on totally different principles. For example, if some tumors arise through the loss of growth-suppressor genes, the genes' influence would be felt only when they were absent.

Another basic principle distinguishes oncogenes from growth-suppressor genes. The oncogenes studied to date are invariably activated through somatic mutations: genetic changes

occurring in one or another target organ and not in the germ cells. Mutant, activated oncogenes are therefore not transmitted from parent to offspring. In strong contrast, mutant forms of the growth-suppressor genes might indeed be found in germ cells—sperm or eggs—and be passed from one generation to the next. A child acquiring a mutant growth-suppressor gene at conception would have a greater lifetime risk of the onset of cancer.

A window on the operation of such growth-suppressor genes has been opened by studies of retinoblastoma, a tumor of the eye. The tumor is fairly rare, afflicting about one in 20,000 infants and young children, but it serves as a model for many other, ostensibly unrelated types of cancer. What has been learned about the gene that causes it has already put in place several large pieces of the genetic puzzle of cancer causation.

Retinoblasts are the precursors of cells in the retina, the light-sensitive screen at the back of the eye; the particular cells that form a retinoblastoma seem to be ones ordinarily destined to become the photoreceptor cells called cones. Once a retinoblast differentiates to form a specialized retinal cell, it stops dividing and can no longer serve as a target for tumorigenesis. This would seem to underlie the age distribution of retinoblastomas, which are never seen in older children or adults.

Until the middle of the 19th century the onset of retinoblastoma signaled a uniformly fatal disease course. Tumors rapidly invaded the brain and led to the death of an afflicted child. With the invention of the ophthalmoscope by Hermann von Helmholtz in 1850, it became possible to look into the globe of the eye and detect the tumor long before it expanded to invade adjacent tissues. With early diagnosis came the possibility of cure (through surgical removal of the af-

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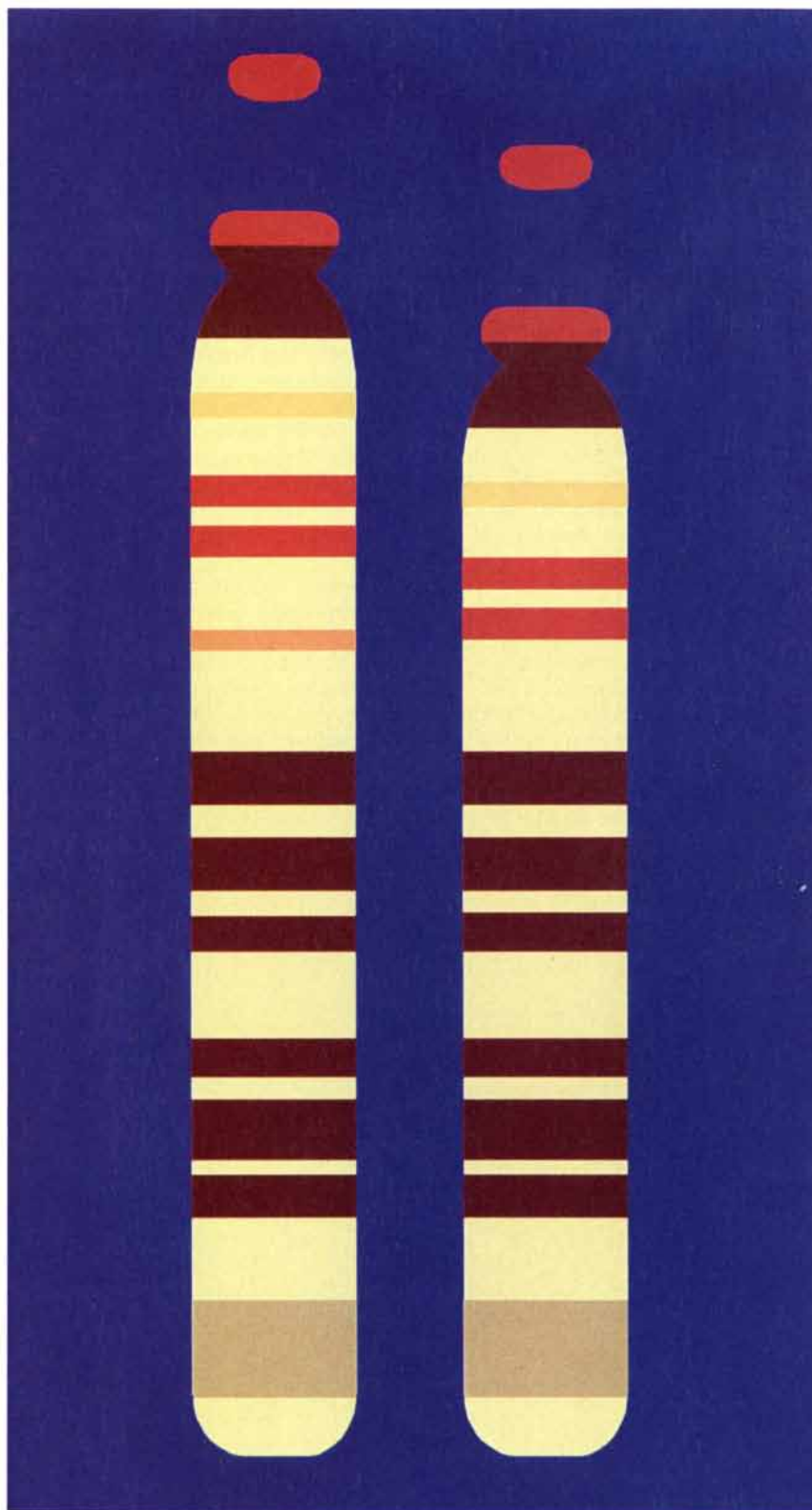
flicted eyeball), and this led in turn to the first cases of "familial" retinoblastoma: many patients survived to reach adulthood and have children, about half of whom contracted this otherwise very rare tumor. Retinoblastoma also continued to strike in its historic "sporadic" form, which is seen in children whose families have no history of the disease.

By the middle of this century the two types of retinoblastoma were recognized as being distinct manifestations of a single disease. For the geneticist they represented a bewildering. The familial form of the disease clearly depended on the transmission of a gene from parent to offspring. Just how genes could be involved in triggering the sporadic disease was not clear, however. If genes were indeed involved, were they the same ones responsible for triggering the familial disease, or were different genes implicated in each form?

In 1971 Alfred G. Knudson, Jr., of the Institute for Cancer Research in Philadelphia proposed a simple genetic explanation for these apparently complex phenomena. His hypothesis recognized that mutated genes can come to a person through the two routes I have alluded to: as an inheritance from a parent or through the somatic mutations that occur accidentally in tissues during one's lifetime. He theorized that the origins of both types of retinoblastoma could be traced to changes in the same set of genes.

After studying the rate at which the disease appeared in young children, Knudson concluded that all tumor cells actually carry not one mutant gene but rather two such genes. In familial retinoblastoma, he argued, the first of the two required mutations is present in a critical gene from the moment of conception and so becomes disseminated to all the cells in a child's body, including all the cells of the retina. Such a mutated gene, which confers susceptibility to the tumor, might have been acquired from a genetically afflicted parent or from a genetic accident during the formation of a parent's egg or sperm. The second required mutation could then occur somatically, and thus locally in one of the many retinal cells that already carried a congenitally acquired mutation. In the contrasting nonfamilial, sporadic retinoblastoma, Knudson proposed, both of the required mutations occur somatically and locally within a single retinal cell, whose descendants then expand to form a tumor.

It is clear now that Knudson's formulation was essentially correct. At



SITE ON CHROMOSOME 13 was first implicated in retinoblastoma by Jorge J. Yunis of the University of Minnesota Medical School. When he stained chromosomes from retinoblastomas to highlight their banding, he noted that a segment of the long arm of one chromosome 13 was often missing. The computer image, made by Yunis, compares a normal chromosome 13 (*left*) with the abnormal one he first reported (*see illustration on next page*). Part of a large light band near the top of the normal chromosome, including the orange subband, is deleted in the abnormal version. (The oval shapes at the top represent the telomeres, the ends of the chromosomes, which in micrographs seem not to be connected to the rest of the chromosome.)

the time, it crystallized thinking about retinoblastoma, but it did leave two major questions unresolved. First, what is the nature of the gene or genes that are acquired in mutant form from a parent or are altered by somatic mutations? Is one gene involved or several distinct genes? Second, what kinds of mutation intervene to create the cancer-causing alleles (specific versions of a gene)? Are they mutations of the kind that hyperactivate a proto-oncogene and thereby create an oncogene? Or do these mutations serve on the contrary to inactivate a gene and thereby wipe out its functioning?

The essential clues to solving these puzzles came from microscopic examination of the chromosomes present in normal cells and in retinoblastoma cells. When an experimenter traps cells in an early stage of cell division, their chromosomes can be viewed with special clarity. A good microscopist can even discern the detailed structure of a chromosome through the presence of individual bands arrayed in characteristic positions along its length.

The chromosomes of a tumor cell often look different from those of

a normal human cell. The deviations may simply reflect the genetic chaos that accumulates in tumor cells during their tortuous evolution from the normal to the malignant state. On occasion, however, microscopists can identify specific chromosomal changes that occur reproducibly in many tumors of a given type.

This was the case when Jorge J. Yunis of the University of Minnesota Medical School studied cells from a number of different retinoblastomas. The longer of the two arms (the q arm) of one chromosome, No. 13, was often found to have a deletion: one or another of the bands ordinarily seen on the chromosome was often missing. Most often it was some part of band 14. The association of 13q14 alterations with retinoblastoma was much too frequent to be attributed simply to random genetic accidents; instead it seemed the deletion must confer a growth advantage of some kind on the cells that spawn the tumor.

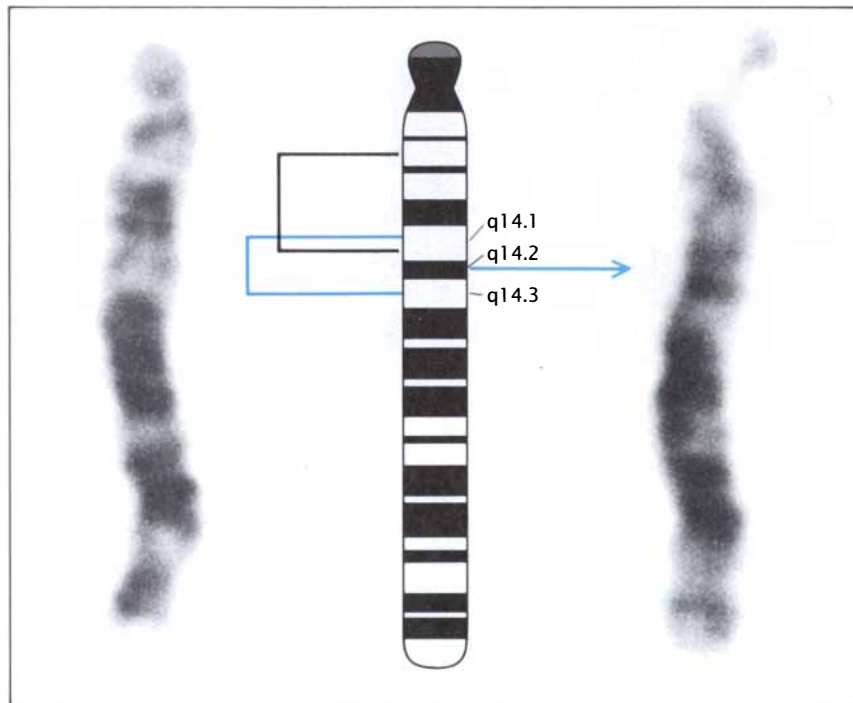
These data provided the beginnings of an answer to Knudson's puzzles: they showed that one of the mutational events associated with retinoblastoma is a deletion that could well lead to the total loss of a gene and thus to the

loss of some critical function. Further chromosomal analysis showed that in certain children afflicted with familial retinoblastoma, the chromosome-13 deletions could be found not only in the tumor cells but also in normal cells throughout the child's body and in the body cells of one parent. When the deletions were found in sporadic cases, on the other hand, they were invariably confined to the tumor cells. The damaged chromosomes could be found, in other words, in precisely the cells Knudson had predicted would carry the mutant genes responsible for the two forms of retinoblastoma.

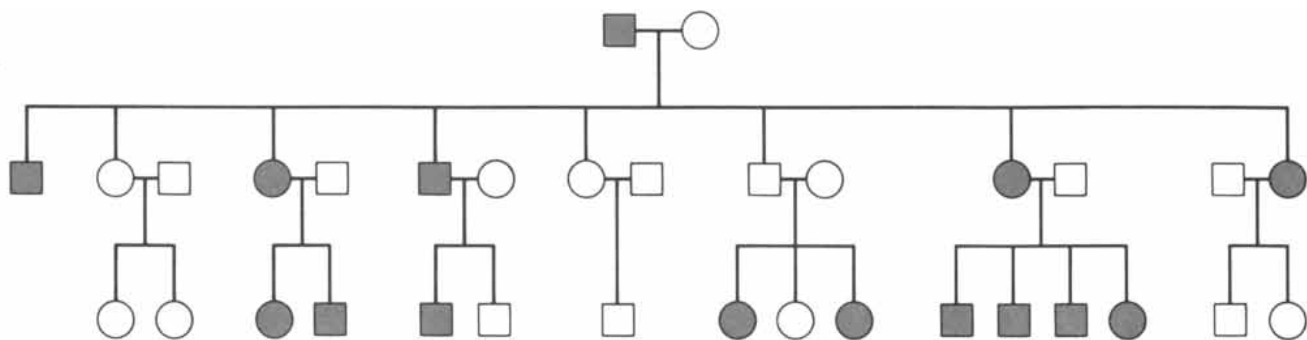
The chromosome-13 gene ostensibly involved in triggering these tumors was given the name *Rb*. It had been identified by the presence of a microscopically visible deletion, which at the molecular level involves the loss of a segment of DNA encompassing hundreds of thousands of the bases that constitute a strand of the genetic material. Yet such a large chromosomal lesion is only one of a number of mutational mechanisms by means of which the *Rb* gene might be inactivated. Much smaller deletions that have no effect on the microscopically visible structure of the chromosome can be just as effective in knocking out gene function. Indeed, recent work has shown that changes affecting single DNA bases ("point mutations") may suffice.

At this stage one of Knudson's two critical target genes had been associated with a specific site on chromosome 13, but the identity of the second target was still elusive. It might be a different gene on one or another of the 23 chromosomes of the cell, all but two of which are present in two copies. Alternatively, the second target for mutation might be the second copy of the initially affected chromosome-13 gene, which still survived on the intact, paired chromosome 13.

Through a clever genetic trick, data were in hand by 1983 suggesting that the second genetic target for mutation was indeed to be found on the second chromosome 13. The evidence came from an indirect genetic analysis that traced the fate of another gene—one that is conveniently situated very near the *Rb* gene on chromosome 13. By staking such a "marker" gene one can often predict the fate of a closely linked but invisible neighbor. Robert S. Sparkes of the University of California School of Medicine at Los Angeles found such a marker: the gene encoding an enzyme called esterase *D*. Rosalind Godbout, Brenda Gallie and Rob-



PHOTOMICROGRAPHS of the normal and abnormal chromosome 13's are shown here, flanking a diagram of the normal chromosome. The deletion undergone by the abnormal chromosome (right) is indicated on the diagram by the blue bracket. A different deletion, observed in a chromosome from a different retinoblastoma, is bracketed in black. The two deletions overlapped somewhat, pinpointing the site of a putative retinoblastoma gene in a small region of subband 13q14.1, close to subband 13q14.2; *q* designates the long arm of a chromosome. (Chromosome 13 has a minute short arm: the segment above the constriction near the top of the chromosome.)



PEDIGREE of a family with familial retinoblastoma was published by Thaddeus P. Dryja and his collaborators. Affected members are indicated by solid circles (females) or squares (males). Five children in the second generation developed the tumor. One son who was unaffected had nonetheless inherited a mutated chromosome 13: two of his daughters were affected.

ert A. Phillips of Toronto's Hospital for Sick Children found that in some retinoblastoma patients the esterase *D* gene was present in normal cells in two different versions, one on each of the paired chromosome 13's. In the patients' tumor cells, however, the esterase *D* marker gene was often found in two identical copies. One of the two alleles (versions) had been lost and had been replaced by a duplicate of the other allele.

The esterase *D* gene itself has no functional role in retinoblastoma, but it served as an easily traced proxy for the neighboring *Rb* gene. If one of the two versions of the enzyme gene was lost and replaced by the survivor, the same fate was imputed to the neighboring *Rb* gene. It appeared, then, that if a retinal cell began with one normal and one mutated version of its *Rb* gene, it might sometimes end up with two mutated copies of the gene. More detailed analysis confirmed that possibility: tumor cells were often seen to carry two copies of the defective allele of the *Rb* gene. This finding provided the critical clue to the second step in tumor formation. It was the loss of the surviving, intact copy of the *Rb* gene.

Knudson's theory could now be reformulated. The two hits required to trigger cancer involve the two copies of the *Rb* gene. Each hit inactivates one copy of the gene, creating an inactive, or "null," allele. Children born with one intact and one defective copy of the *Rb* gene might lose the intact copy through somatic mutation in one of their retinal cells, triggering cancer. Others, although born with two good copies, might through rare misfortune happen to lose both copies of the gene in a retinal cell early in life, leading to the same end result.

The children carrying a congenitally acquired, mutant *Rb* gene are fully normal save for their greatly increased

risk of cancer. Although they have only one normal copy of the gene in virtually every cell of their body, their fetal development is unremarkable. The single normal *Rb* allele is clearly sufficient to fulfill the gene's function in programming normal development; the defective *Rb* allele in every cell does not actively perturb this development. In other words, the mutation is "recessive" and is manifested only when the surviving, intact copy of the gene (which is "dominant" at the cellular level) is lost in one or another retinal cell.

Now, if the inactivation of a gene such as *Rb* serves to trigger the runaway growth of cancer, it follows that the gene in its normal incarnation must act to restrain cell growth. This implies the existence of a class of genes dedicated to the negative regulation of normal growth, which I prefer to call growth-suppressor genes. Because loss of these genes can lead to malignant growth and because many oncogenes act in a diametrically opposite way—by promoting aberrant growth—such genes as *Rb* have come to be called anti-oncogenes or tumor-suppressing genes. These terms are likely to survive, but they are imprecise. The normal function of the *Rb* gene is surely to suppress growth in general; any involvement in cancer is rare and unintended.

Imprecise or not, the term anti-oncogene has some logical basis. A gene such as *Rb*, when it is intact, may well function to oppose the action of an oncogene. By the same token, a cancer cell, which gains a growth advantage by developing oncogenes that actively promote cell growth, might further help itself to proliferate by getting rid of genes that have hitherto constrained its growth. Indeed, this may be a particularly frequent mechanism of cancer causation, since it is much

easier to knock out a gene by crude genetic blows than to hyperactivate a gene by subtle mutational tinkering.

The loss of anti-oncogenes may be a quite common occurrence in the development of cancer. Examination of the chromosomes of various tumor types often reveals characteristic chromosomal aberrations. On occasion there is a loss of specific chromosomal segments, but in other instances more subtle genetic analyses have been required to pinpoint the loss of specific genes.

These genetic analyses, pioneered by Webster K. Cavenee (who is now at the Ludwig Institute for Cancer Research in Montreal), follow in outline the same strategy whereby the fate of the *Rb* gene was traced by examining the fate of its closely linked neighbor, the esterase *D* gene. In Cavenee's analyses the closely linked neighbors are specific DNA sequences that may be present in dissimilar (heterozygous) versions in normal tissue and in identical (homozygous) versions in tumor tissue. The progression from heterozygosity to homozygosity of these DNA segments provides a good indication of the fate of closely linked anti-oncogenes.

By now there is a substantial list of genes that appear to lose both functional copies during the creation of one or another type of tumor. Ductal breast cancer, for example, also involves a gene on the long arm of chromosome 13; Wilms' tumor of the kidney involves a gene on chromosome 11, and small-cell carcinoma of the lung apparently results from defects in a gene on chromosome 3. In each case it appears that both copies of a critical gene are frequently either lost or rendered inactive during the evolution of the tumor-cell clone. This tissue specificity (the association of the loss of certain genes with specific tumor types) suggests that each of

these genes is normally involved in constraining the growth of only a narrow range of cell types in the body.

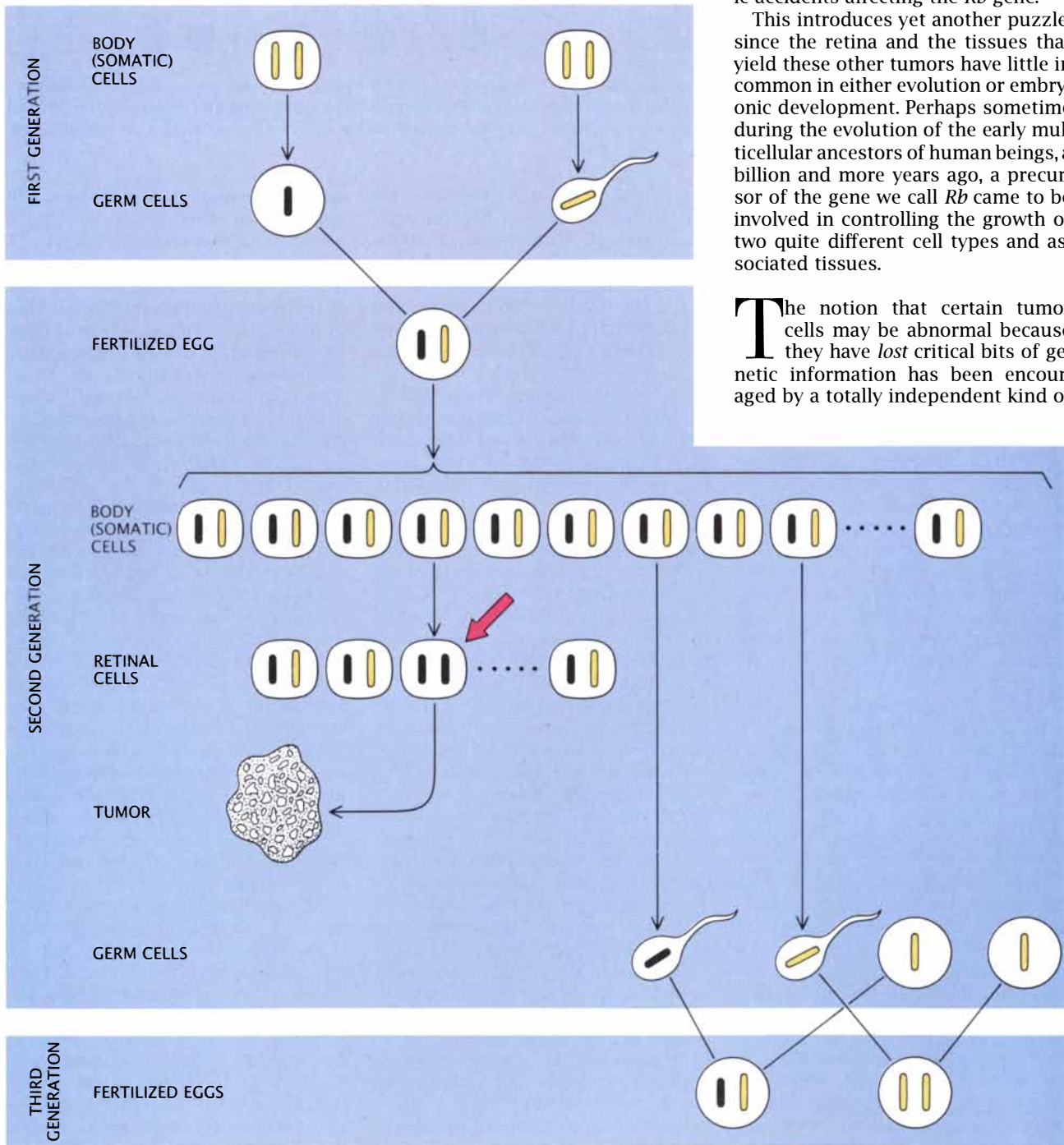
At first it seemed that the range of action of the *Rb* gene would also be limited narrowly to tumorigenesis in the retina. However, careful clinical follow-up of children afflicted

early with familial retinoblastoma has revealed that later in life they incur a greatly increased incidence of tumors that originate in connective-tissue cells—notably osteosarcomas, which arise in bone-forming cells. In other words, mutant copies of the “retinoblastoma gene” predispose to

more than just retinoblastoma. Indeed, recent evidence suggests that observable changes in the *Rb* gene are as frequent in osteosarcomas as they are in retinoblastomas—even in osteosarcomas from individuals with no history of retinoblastoma. In many osteosarcoma patients the tumor seems to arise solely through somatic genetic accidents affecting the *Rb* gene.

This introduces yet another puzzle, since the retina and the tissues that yield these other tumors have little in common in either evolution or embryonic development. Perhaps sometime during the evolution of the early multicellular ancestors of human beings, a billion and more years ago, a precursor of the gene we call *Rb* came to be involved in controlling the growth of two quite different cell types and associated tissues.

The notion that certain tumor cells may be abnormal because they have *lost* critical bits of genetic information has been encouraged by a totally independent kind of



HYPOTHETICAL CASE of familial retinoblastoma is traced at the cellular level. As the result of a genetic accident in the first generation the region carrying *Rb*, the retinoblastoma gene, is deleted from the single chromosome 13 in an ovum (female germ cell). The chromosome (*shaded*) carrying the deletion is inherited by a son and is present in all his body cells, including

retinal cells. A somatic mutation in infancy or early childhood inactivates the second copy of the gene in one retinal cell (*arrow*), and so a tumor develops. The tumor is excised and the patient survives to adulthood. About half of his sperm cells carry the deleted form of chromosome 13, and so about half of his children inherit the predisposition to retinoblastoma.

experimentation, much of it initiated by Henry Harris of the University of Oxford. He applied techniques that enable one to make a hybrid cell by fusing two genetically distinct cells. This is achieved with an agent that causes the outer membranes of neighboring cells to unite, forming one large membrane that envelops the nuclei of both partners. The two complements of chromosomes then merge into one large array carrying twice the usual amount of genetic information. The motive in these forced marriages is to observe how the traits of the two partners blend following their union. Often the genes of one or the other parent cell may dominate in determining the behavior of the hybrid.

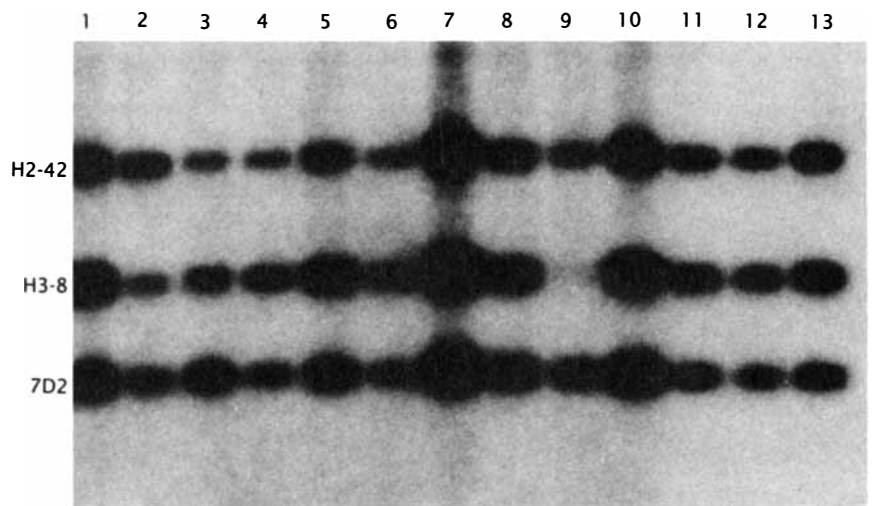
Over the past two decades such experiments have led to the surprising observation that hybrids formed between malignant tumor cells and normal cells often behave like their normal parents, that is, they do not form tumors. This runs counter to intuition, which suggests that virulent tumor cells have traits far more potent than those of their normal neighbors.

An explanation comes once again from the insight that a tumor cell often becomes aberrant through the loss of a critical growth-suppressing gene or genes. In undergoing fusion with a normal cell, the tumor cell regains a growth-regulating gene it lost early in its evolution toward malignancy; the restored gene can reimpose growth control on a cell that has long lacked such control.

A dramatic demonstration of such reassertion of control was reported recently by Eric J. Stanbridge of the University of California College of Medicine at Irvine. His group worked with a number of tumors, among them Wilms' tumor. Fusion of a Wilms' cell to a normal cell yields a nontumorigenic hybrid.

Stanbridge's group managed to introduce a single normal human chromosome 11 into Wilms' tumor cells. The genetically enhanced cells thereupon reverted to normal: they lost the ability to form tumors. This showed, even more directly than the cell-fusion work, that the malignant growth of these tumor cells depends on the absence of a gene or genes normally present on chromosome 11.

The hybrid-cell findings and Stanbridge's result strongly reinforce the impression that a loss of genetic information may be as important for tumor formation as the creation of hyperactive growth-promoting oncogenes. In the long run this realization may open a path toward a therapy based on the



SEARCH FOR *Rb* GENE began when Dryja tested fragments of the DNA of the normal chromosome 13 to see if any of them were missing in retinoblastoma DNA's and so were likely to be part of the gene whose deletion leads to tumorigenesis. This electrophoresis gel shows a critical result. Fragments H2-42 and 7D2 have hybridized with, or bound to, matching fragments of the DNA from each of 13 tumors; having been tagged with a radioactive label, they are visible on the gel as dark bands. The third fragment, H3-8, has similarly hybridized with the DNA of 12 of the tumors—but it has failed to find a match in the DNA of tumor No. 9: the segment of chromosome 13 represented by probe H3-8 is deleted from the DNA of this tumor.

introduction of genes into tumor cells that lack them.

In spite of these major advances, until recently the *Rb* gene was only a theoretical entity, its existence deduced solely from the genetic phenomena I have described. An ultimate goal for cell biologists and biochemists is to understand at a molecular level just how a gene such as *Rb* acts to restrain or inhibit cell growth. The clearest path to such understanding is through the isolation of the gene by molecular cloning. The isolation of *Rb* was a particularly challenging task because the gene's most obvious effects are manifested only when it is absent. It is therefore difficult to devise assays that show directly whether one or another candidate DNA fragment is indeed the sought-after gene.

Thaddeus P. Dryja of the Massachusetts Eye and Ear Infirmary undertook the long-shot quest in 1983, concentrating on human chromosome 13. Marc Lalande and Samuel A. Latt of the Children's Hospital in Boston had created a collection of DNA clones, each derived from a fragment of one or another randomly chosen region of the normal chromosome 13. Dryja sifted through this collection, gambling that one of the fragments might be allied with the chromosomal DNA sequence constituting the *Rb* gene. It was a daunting undertaking: the *Rb* gene is now known to account for only

a thousandth of the total DNA of chromosome 13.

Each of the chromosome-13 fragments served as a "probe" in a DNA hybridization test. The test showed whether a given probe could find a matching segment in the DNA isolated from one or another of a battery of retinoblastoma cells or, alternatively, was not able to find such a matching segment because the probe derived from a part of the chromosome that had been deleted during the formation of a tumor.

Dryja's gamble paid off when one cloned probe was found to come from a chromosomal segment that was fully deleted in two retinoblastoma DNA's out of the 50 or so he examined. This was far from proving that the cloned fragment was even part of the *Rb* gene. It did suggest at the very least that the fragment represented a sequence that lay near *Rb* on the chromosome that had undergone deletion along with *Rb* in the course of the genetic accidents that had triggered these two retinoblastomas.

It remained for Dryja's group, with Stephen H. Friend and others in my laboratory at the Whitehead Institute for Biomedical Research, to establish the precise relation between the cloned fragment and the ostensibly linked *Rb* gene. First we discovered that the cloned fragment was closely related to a messenger-RNA molecule found in normal retinal cells. Mes-

senger RNA (mRNA) is the nucleic acid that transfers information from active genes in a cell's nucleus to the cytoplasm, where the information is read out by the machinery responsible for making proteins. The discovery of a retinal-cell mRNA related to the cloned DNA fragment meant the fragment was (by a remarkable stroke of luck) part of a gene that is actively expressed in normal retinal cells. Significantly, we were not able to detect mRNA related to the fragment in

any of several retinoblastomas. That meant the gene from which the mRNA derived was inactive or absent in the tumor cells—behavior consistent with that of the *Rb* gene.

The possibility that the gene was *Rb* remained to be confirmed. Friend made a DNA copy of the mRNA by the process called reverse transcription. The reverse-transcribed “cDNA” served as a probe with which to survey and map out the entire re-

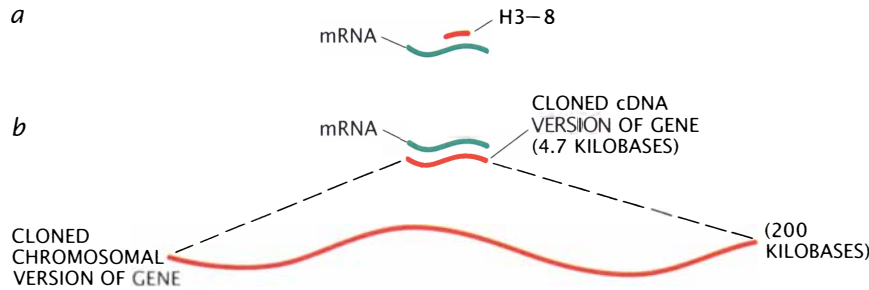
gion on the normal chromosome that was responsible for generating the mRNA—in other words, the gene that might be *Rb*—and to clone it. The cloned gene turned out to be very large, encompassing 200,000 DNA bases. Again by means of nucleic acid hybridization, we studied the configuration of this large chromosomal domain in the DNA's of 60 retinoblastomas and osteosarcomas. In about 30 percent of the DNA samples we found evidence that one copy or both copies of the cloned gene had suffered substantial changes in structure through deletion. (Subtler changes in DNA structure, which can be equally effective in inactivating a gene, would have escaped detection in this analysis.)

We now had evidence that the cloned DNA gene was frequently knocked out in various, independently arising retinoblastomas. But did this cloned gene represent the *Rb* gene itself? The convincing evidence ultimately came from examining the precise configuration of the various deletions affecting the cloned segment [see lower illustration at left]. The goal was to show that the cloned gene encompassed the *Rb* gene, and not an irrelevant gene to the right or left of it along the chromosome.

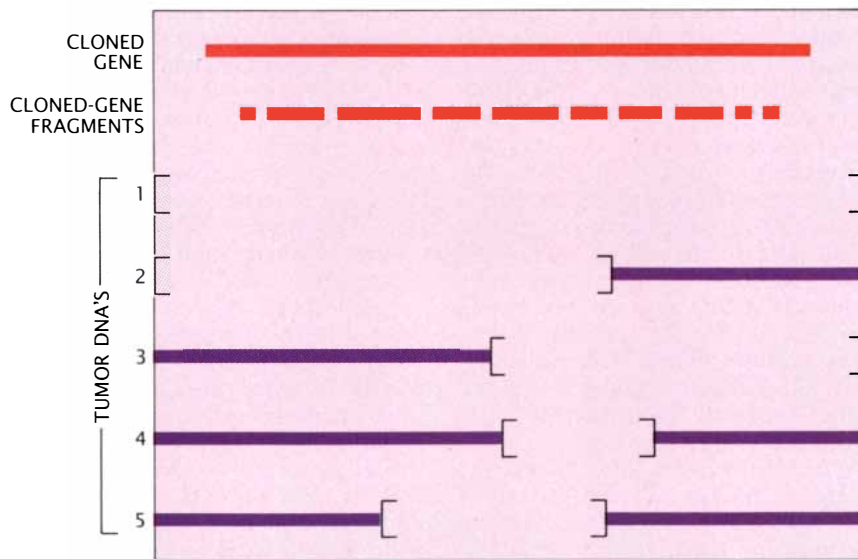
Certain of the mapped deletions caused loss of the entire cloned gene. These were uninformative, since they did not address the critical issue at hand: the cloned gene might just have happened to be deleted along with some other part of the region that included the “intended” target, the *Rb* gene. Three deletions that seemed to involve both the right-hand end of the gene and adjacent, rightward-lying DNA were more meaningful. They indicated that the target for deletion either lay to the right of the cloned gene or was the cloned gene itself. Yet other mutations caused loss of the left end of the cloned gene and other leftward-lying sequences. It seemed increasingly likely that the cloned gene was indeed the common target of these randomly occurring deletions.

The critical evidence came from the discovery of two deletions that began and ended entirely within the confines of the cloned gene. These showed unequivocally that the random deletions leading to retinoblastoma converged on the cloned gene and not on neighboring DNA segments.

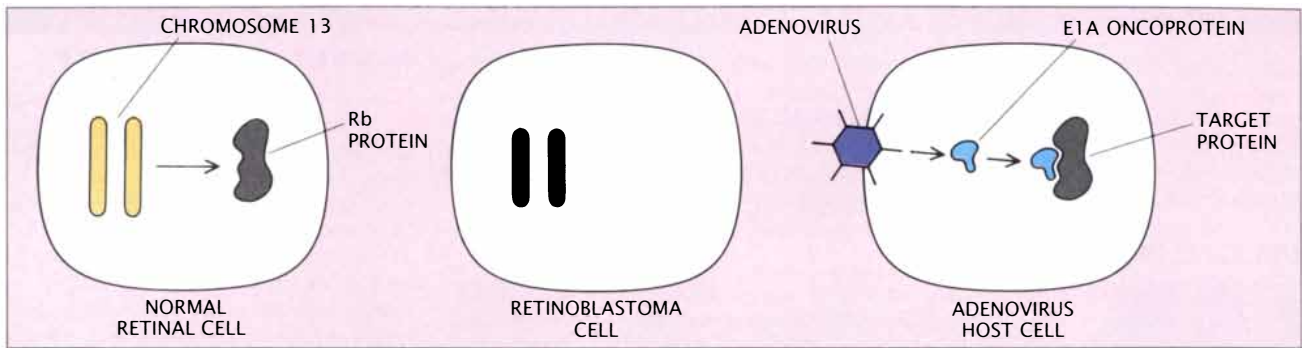
Our work has since been replicated and extended by Wen-Hwa Lee of the University of California School of Medicine at San Diego and by Yuen-Kai Fung and William F. Benedict of the University of Southern California



SERIES OF EXPERIMENTS led to the cloning of a gene and its identification as the *Rb* gene. The messenger RNA of normal retinal cells was probed with H3-8, the fragment that had been shown to be deleted in several retinoblastoma DNA's. The probe discovered a closely related mRNA (a), indicating that H3-8 was part of a gene that is active in normal retinal cells. The mRNA was then reverse-transcribed (b) into a DNA copy (a cDNA clone); this cDNA served in turn as a probe with which to find and clone the long (200,000-base) stretch of chromosomal DNA representing the entire gene that was responsible for having generated the mRNA—a gene that might be *Rb*.



IDENTIFICATION OF CLONED GENE as the retinoblastoma gene was established by seeing whether it—and not a neighboring gene—was the target affected by chromosomal deletions that had triggered retinoblastomas. Fragments of the cloned gene served as probes for mapping deletions in tumor DNA's. The probes found some deletions (1) that eliminated the entire gene as well as neighboring sequences on both sides, and so were not determinative. Some deletions removed the left part of the gene and adjacent leftward sequences (2); such deletions might have caused tumors by damaging either the cloned gene or a different one to the left of it that was actually the *Rb* gene. Other deletions (3) removed the right part of the gene and sequences to the right of it. In a few tumors (4, 5), however, the deletion removed only internal regions of the cloned gene. These deletions showed the cloned gene is the critical target whose inactivation gives rise to a tumor; therefore it is the *Rb* gene.



Rb GENE ENCODES a protein that is found in the nucleus of normal retinal cells (left) but not in retinoblastoma cells (*mid-dle*). The *E1A* oncoprotein of an adenovirus transforms infected cells by binding to a host-cell target protein that turns

out to be identical with the *Rb* protein (right). The fact that the same protein whose absence in retinal cells gives rise to a tumor is also involved in transformation by the adenovirus suggests the protein may be a central growth regulator.

School of Medicine. The aggregate results provide evidence that the cloned gene indeed is the normal *Rb* gene. Most persuasive are the repeated findings that this particular segment of DNA is damaged by major deletions in many different, independently arising tumors.

The ultimate proof of the identity of the cloned gene will have to come from a functional test in which DNA clones carrying intact versions of the putative *Rb* gene are inserted into tumor cells that have no intact *Rb* gene. If the cells thereupon revert at least partially to normalcy, this will argue strongly that the cloned DNA is indeed providing the critical genetic information whose loss triggered tumor formation. Such experiments are currently under way in several laboratories.

Many experimental avenues can be followed once growth suppressors such as *Rb* have been isolated by cloning. Both applied clinical applications and basic research problems come to mind. The clinical utility stems from the ability to use cloned DNA segments to analyze the structure of related sequences in a variety of normal and tumor samples and to detect altered versions of such genes as *Rb*. The reader will recall that mutant *Rb* alleles can be passed from an affected parent to half of the offspring, on the average. A cloned probe could in principle detect defective *Rb* alleles even in the early fetus, providing predictive data on the likelihood of tumor onset later in life.

Beyond the clinical applications loom a number of problems in basic biology. *Rb* is the first growth-suppressing cancer gene to be isolated. The lessons learned from it are likely to prove instructive for an array of genes that act in a similar way, each responsible for constraining the

growth of one or another cell type. The array of these genes already known by virtue of their deletion in certain tumors may represent only the tip of the iceberg. The oncogenes already number upward of 50 genes; the size of the repertoire of these countervailing negative regulator genes cannot yet even be guessed.

The most intriguing question is: What are the mechanisms through which these genes act to limit or shut down normal growth? Some months ago Lee's group reported that the *Rb* gene specifies a protein with a molecular weight of 105,000 that is found in the nucleus of the cell. Nuclear proteins are often involved in regulating the expression of genes.

A strong indication that *Rb* does indeed specify a regulatory protein has come just recently from unrelated work designed to find out how tumor viruses transform the cells they infect. One such virus, an adenovirus, is known to carry an oncogene designated *E1A* into susceptible target cells. The oncogene specifies a protein that reprograms the metabolism of the host cell, eliciting malignant behavior. How does the oncoprotein act?

Workers in Ed Harlow's group at the Cold Spring Harbor Laboratory in New York and in Philip E. Branton's group at the McMaster University School of Medicine in Ontario had found that in a virally transformed cell the viral oncoprotein is complexed with certain host-cell proteins. Presumably the viral protein alters these targets and thus trips the cellular switches that lead to transformation.

One of the targets with which the viral oncoprotein complexes is a host-cell protein whose molecular weight is 105,000. Harlow, Peter Whyte and Karen Buchkovitch noted that this protein has properties similar to those of the *Rb* protein. Together with Jona-

than Horowitz in my laboratory, they went on to show that the two proteins are in fact identical. The adenovirus *E1A* protein, in other words, makes cells malignant by complexing with (and perhaps thereby inactivating) the same protein that is encoded by the *Rb* gene and is missing from retinoblastoma cells. Since the *E1A* protein is a direct regulator of gene expression, the *Rb* protein too must be directly involved in the modulation of gene expression.

It is clear that detailed understanding is only several years away. When it comes, we shall finally see both sides of the coin: how cell growth is turned on and how it is turned off. With this will come new insights into the origins of cancer and into the still obscure mechanisms that allow fertilized eggs to develop into complex organisms such as ourselves.

FURTHER READING

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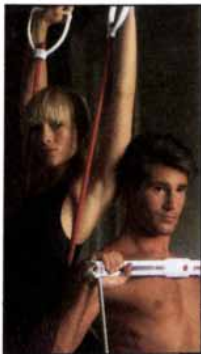


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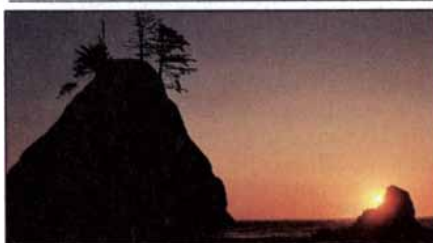


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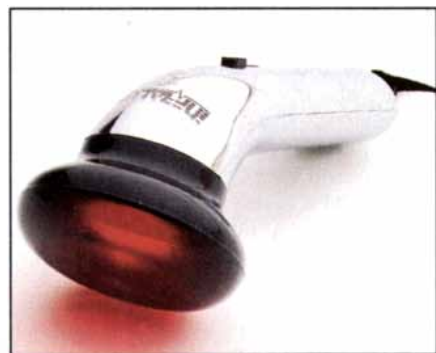
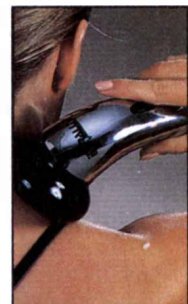
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by Vladilen S. Letokhov

The light spectrum is the language "spoken" by atoms and molecules. Just as different people speak different languages, so each kind of atom or molecule emits and absorbs light of characteristic wavelengths, or colors. By measuring these wavelengths, investigators over the past 100 years have made great strides in understanding the properties of all the elements in the periodic table and of an enormous number of their molecular compounds.

Although such an approach is powerful, it does have limitations. Suppose, for example, one is searching for trace amounts of rare, long-lived radioactive elements in samples taken from river water or the atmosphere. The samples may contain as little as one radioactive atom for every million million (10^{12}) stable atoms and molecules. The individual "voice" of the radioactive atom—the set of characteristic wavelengths of light it emits and absorbs—is too faint to detect above the fray. Standard techniques of spectroscopy, or spectral measurement, fall short of the required sensitivity by a factor of 1,000 or more.

Recently a novel variation on the basic approach has been implemented

that could achieve the necessary sensitivity; it may even mark the beginning of a new stage of research in physics. The new approach, called resonance-ionization spectroscopy, was developed by my colleagues and me at the Institute of Spectroscopy of the U.S.S.R. Academy of Sciences and, independently, by G. Samuel Hurst and his colleagues at the Oak Ridge National Laboratory. Resonance-ionization spectroscopy relies on lasers, intense sources of light that have wavelengths that can be controlled with remarkable precision.

To get an idea of how resonance-ionization spectroscopy works, imagine a polyglot crowd of hundreds of people of different nationalities, say the builders of the biblical Tower of Babel. The crowd represents different kinds of atoms and molecules. Thousands of linguists have studied and classified the languages spoken in the crowd, and now a dictionary exists for each one. Whereas once it would have been necessary to sort through the entire crowd and listen to each language in turn in order to find an individual of a certain nationality, now the crowd can be addressed in the appropriate language, and one can simply ask anyone of the desired nationality to step out of the crowd.

In the same way, lasers having a set of chosen wavelengths can be exploited to detect a desired atom or molecule in a mixture. The wavelengths can be tuned to resonate with, or match, a set of characteristic wavelengths of the atom or molecule in such a way that the light ionizes the atom or the molecule (strips it of one of its outermost electrons). Since the set of wavelengths is unique to each species, none of the other constituents of the mixture will be affected. Once ionized, the atom or the molecular fragments

will have a net electric charge and can be separated from the mixture by applying an electric field.

Resonance-ionization spectroscopy is so selective that it can sense the slightest accent in the spectral language of atoms and molecules. As a consequence, one can detect and separate species that differ only slightly, such as isotopes and nuclear isomers—which are respectively atoms that have the same number of protons but different numbers of neutrons (such as carbon 12 and carbon 14) and atoms whose nuclei contain the same number of protons and neutrons but are in different energetic states.

The sensitivity of the technique suggests an entire range of applications. Investigators might explore the properties of short-lived radioactive nuclei. Or they could detect trace levels of impurities in otherwise pure elements, a task that becomes increasingly important as the circuitry on silicon chips continues to shrink. In practice a solitary rare atom in a sample containing as many as 10^{20} atoms of other elements has been registered.

Why is resonance-ionization spectroscopy such a sensitive technique? To explain its sensitivity, we should recollect that the energies of the electrons of an atom are quantized: the electrons are found only in certain discrete energy levels. An atom loses energy when one of its electrons makes a transition from one energy level to a lower energy level. In the process the atom emits a photon (a quantum of light), which carries away the energy. The wavelength of the photon is inversely proportional to its energy, so that photons associated with radiation of short wavelengths, such as blue light, are more energetic than photons associated

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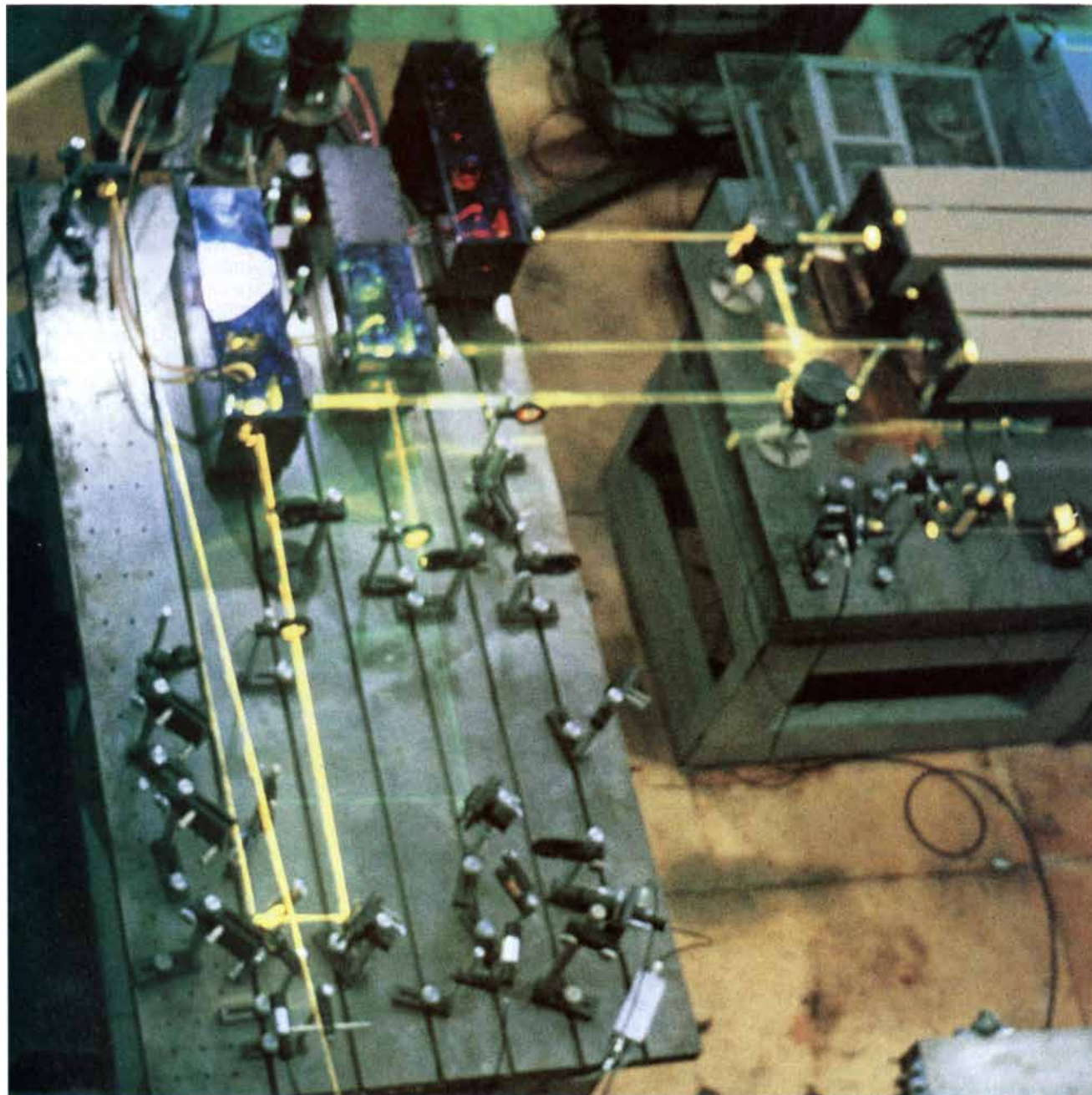
with radiation of long wavelengths, such as red light. An electron can move from one energy level to a higher level if it absorbs a photon, but the energy of the photon must be precisely equal to the difference between the energies of the two levels.

The key to the selectivity of resonance-ionization spectroscopy is that atoms are ionized in a stepwise man-

ner. Instead of using a single, highly energetic "blue" photon to remove an outer electron from an atom, for instance, two or three lower-energy "red" photons are employed. The first one or two photons excite the atom to an intermediate state, so that the electron resides in an intermediate energy level, and the last photon provides the final boost to remove it from the atom

completely. Although the total energy to complete all the steps may be roughly equal for various elements, the probability that any two kinds of atoms will have identical sets of energy levels is zero. It is for this reason that resonance-ionization spectroscopy is so well suited to ionizing individual isotopes of elements.

Another advantage of the approach



PROPERTIES OF ATOMIC NUCLEI can be explored by a technique called resonance-ionization spectroscopy. The wavelengths of a laser are tuned to resonate with, or match, a set of characteristic wavelengths of an atom, so that the light ionizes the atom (strips it of one of its outermost electrons). An applied electric field can then remove the ionized atom from a mixture. The technique can be exploited to explore the struc-

ture of nuclei, since the wavelengths of light emitted and absorbed by an atom depend on the structure of its nucleus. In this laboratory at the B. P. Konstantinov Institute of Nuclear Physics in Gatchina in the U.S.S.R., atoms are sorted according to mass by the apparatus at the top and are irradiated with light of controlled wavelengths from lasers at the bottom. A schematic diagram of the setup is shown at the top of page 57.

is its almost universal applicability. It can be made to work for virtually any substance, if one can form an atomic beam of the substance. In some cases the sample must first be vaporized. By simply heating the sample with a wire filament, a low-power laser or a beam of atoms, one can usually obtain a vapor whose composition reflects that of the original sample.

Finally, the technique is extremely efficient. Measurements can be made within a short period, dispensing with the prolonged observation times characteristic of other spectral methods, in which weak signals from many atoms are collected. The operation time of resonance-ionization spectroscopy is determined by the duration of the laser pulses. In typical experiments the pulses are about 10 nanoseconds (billionths of a second) long. As shorter pulses are exploited, the operation time should be brought down to the range of picoseconds (trillionths of a second) or even femtoseconds (thousandths of picoseconds).

The first successful tests of the stepwise resonance ionization of atoms were done in 1971 at my institution. The work involved rubidium atoms. Since then many laboratories around the world have met with success in applying the technique to a variety of substances.

In 1977, for instance, workers employed the technique to detect single atoms of an element for the first time. Hurst and his colleagues at Oak Ridge carried out the resonance ionization of individual atoms of cesium. The electron stripped from each atom was detected with a Geiger counter, an instrument that produces a measurable current proportional to the number of electrons entering it.

That same year G. I. Bekov and V. I. Mishin of the Institute of Spectroscopy near Moscow ionized sodium atoms that were part of a beam of particles. They used two tunable lasers (lasers with adjustable wavelengths). The first excited the sodium atoms to

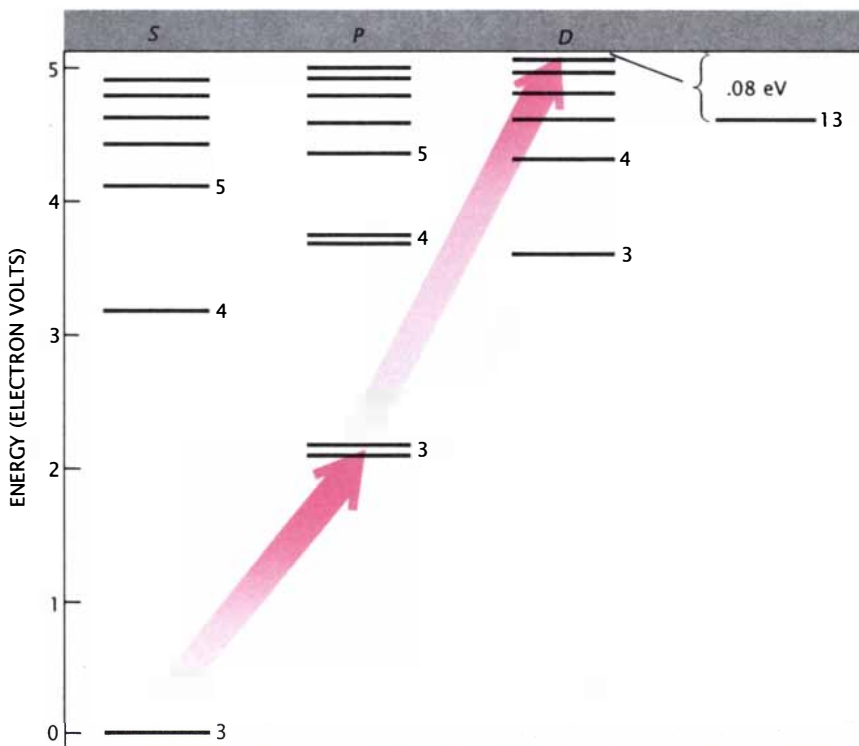
an intermediate state and the second raised them to a highly excited state near the ionization limit. The outermost electrons of such highly excited atoms, which are sometimes called Rydberg atoms, are so weakly bound that the atoms can be ionized easily by a pulse of electric field. In this case the ions were accelerated and deflected by the same electric field that did the ionization, and they were registered by an electron multiplier.

Resonance-ionization spectroscopy has also yielded information about the nature of atomic nuclei. In particular, it is currently being used to measure the mean nuclear radii of short-lived isotopes produced in collisions between protons and fixed targets of matter. The work, which is being done at the B. P. Konstantinov Institute of Nuclear Physics and at the Institute of Spectroscopy, represents a new trend in experimental physics: a blending of laser physics and nuclear physics.

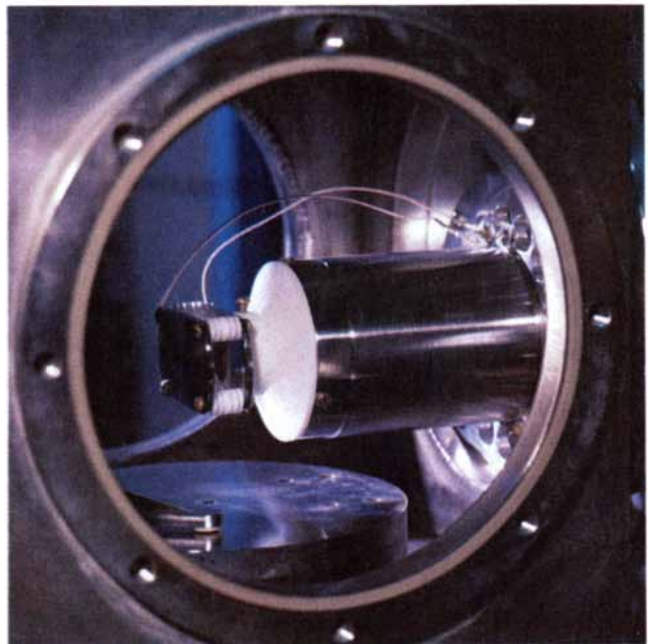
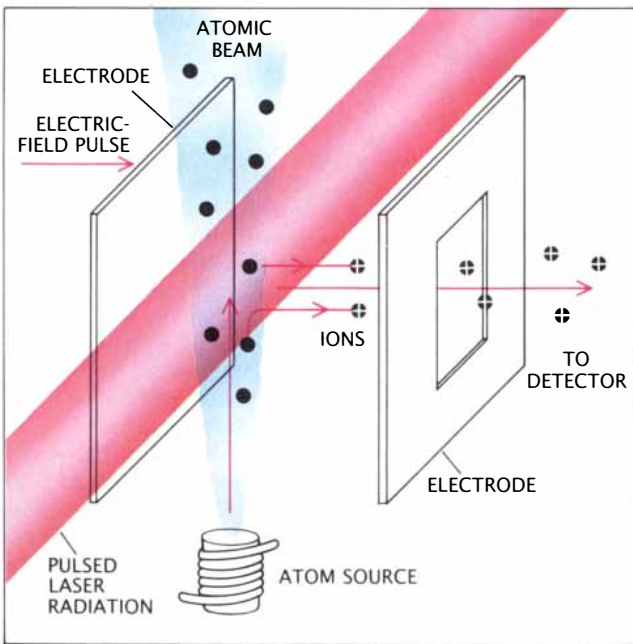
In this study the short-lived elements are allowed to diffuse out of the target in which they are generated and to pass through a separator that sorts them by mass. The resulting mixture consists of elements that have the same mass (the same total number of protons and neutrons) but different atomic composition (different numbers of protons) and isotopic composition (numbers of neutrons). The atoms then pass into a vacuum, where they are irradiated by pulses of light from three tunable lasers. The wavelengths of the lasers are set to select a particular element. By changing the mass of the elements allowed to enter the vacuum, one can compare how the energy levels of an individual element vary as the number of neutrons in the nucleus is changed.

According to theory, the energy levels of an atom depend ever so slightly on the volume of the nucleus. For this reason, measurements of how the energy levels of an atom shift as a function of the number of neutrons in the nucleus can help to determine the radius of the nucleus. This has made it possible to measure the nuclear radii of long-chain short-lived isotopes of europium and a number of the "rare earth" elements in relation to the nuclear radius of the stable isotopes. The results show that as the number of neutrons decreases, the radius first diminishes and then grows larger. This anomalous behavior probably results from nuclear deformation.

The early success of resonance-ionization spectroscopy suggests that in the near future the method should be competitive with existing methods of



CONCEPTUAL BASIS of resonance-ionization spectroscopy is that the energies of electrons in an atom are quantized: the electrons cannot assume arbitrary energies and are found only in certain discrete energy levels. Some of the energy levels of a sodium atom are depicted. Each of the two outermost electrons has its lowest possible energy when it is in its ground state (designated 3s). Such an electron can be stripped from a sodium atom when it absorbs a photon (a quantum of light) if the photon has an energy of at least 5.14 electron volts. (The energy of a photon is inversely proportional to its wavelength: the higher the energy, the shorter the wavelength.) To make the technique as selective as possible, atoms are ionized in a stepwise manner. A sodium atom, for instance, is ionized by exciting the electron first to an intermediate level, 3p (arrow at lower left), and then to a highly excited state, 13d (arrow at upper right); final removal is accomplished by an electric field.



APPARATUS for detecting single atoms is shown schematically (left), together with a picture of the vacuum chamber (right) in which the atoms to be detected undergo resonance ionization. The first stage of analysis is to heat a sample, forming a beam of atoms. The beam travels upward through a re-

gion bounded by two electrodes. Pulses of laser light and pulses of electric field ionize specific kinds of atoms; other kinds of atoms continue traveling upward. The pulses of electric field draw the ions to an electron multiplier (cylinder at right), which counts the number of ions generated in the process.

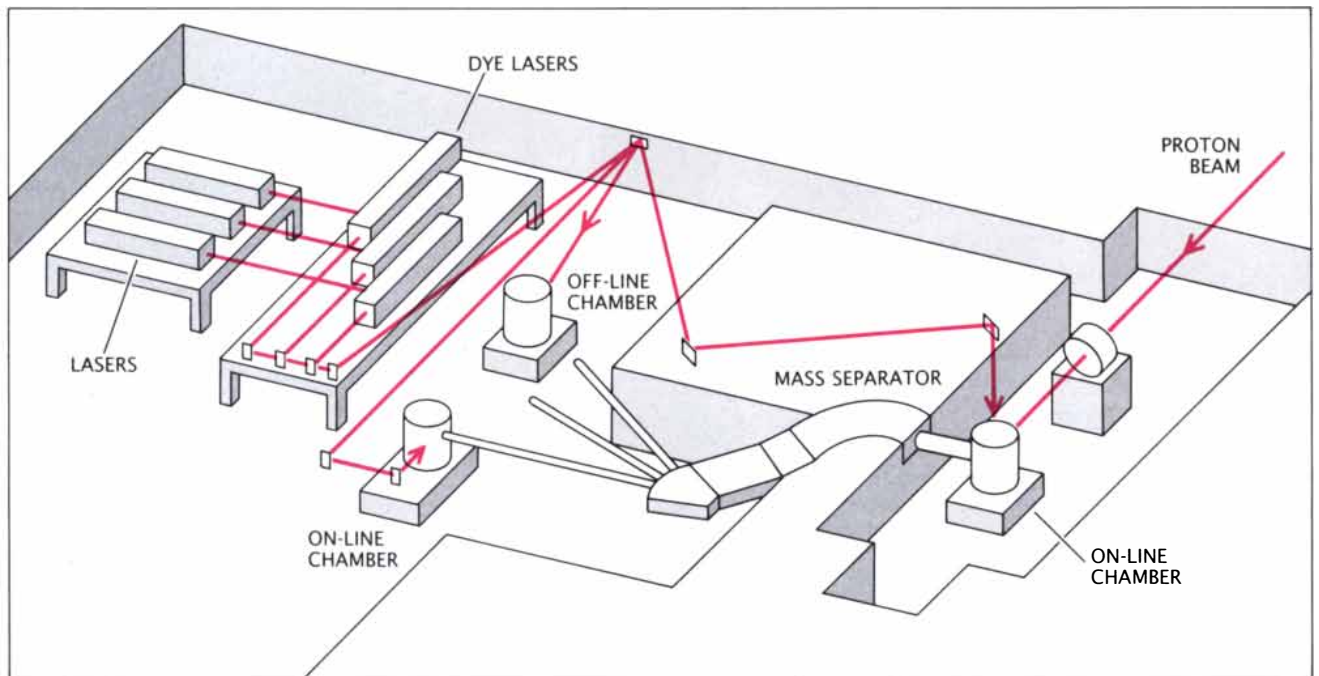
nuclear physics in detecting very rare long-lived radioactive isotopes.

Another application of resonance-ionization spectroscopy is the analysis of trace elements in natural materials of complex compo-

sition, such as seawater, ores, soils and biological tissues. It is now possible to identify traces of elements at a sensitivity level of one part per trillion. In my view this opens up new and interesting possibilities for studying the distribution of ultralow concentra-

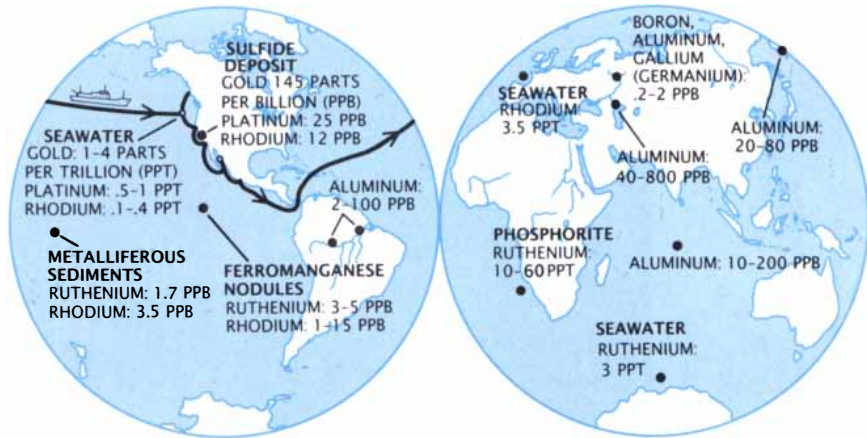
tions of rare elements in the earth's crust and in seawater, and thereby gaining insight into the geological history of the earth.

Knowledge of the distribution of rare elements in seawater is important for oceanography, geology, geochem-



PROPERTIES OF ATOMIC NUCLEI are probed with resonance-ionization spectroscopy. Nuclei are produced by accelerating protons to an energy of one billion electron volts and aiming them at a stationary target. Short-lived nuclei that have life-

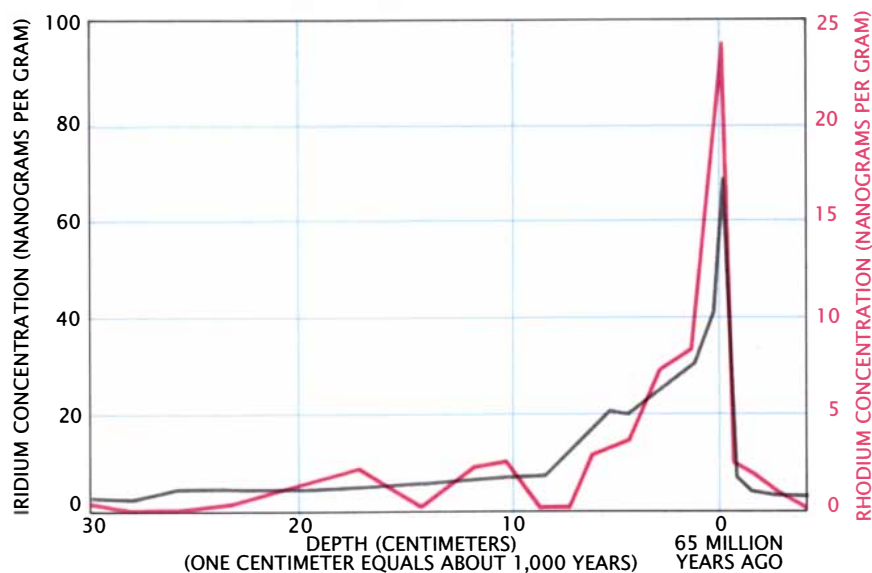
times of from several seconds to several hours are studied in the on-line chamber; longer-lived nuclei are studied in the off-line chamber. The investigations are carried out with pulses of laser light from three lasers that have tunable wavelengths.



TRACE ELEMENTS in seawater, river water and various sediments and deposits were analyzed on shipboard by resonance-ionization spectroscopy during the 12th cruise of the research vessel *Akademik Mstislav Keldysh* in 1986. To enhance the speed of analysis, workers used a sorbent that extracted the noble metals (corrosion-resistant metals such as gold and platinum) from seawater or other solutions. After the sorbent had absorbed the metals, it was incinerated and the ash residue was vaporized by heat in a vacuum to form an atomic beam that could then be subjected to resonance-ionization spectroscopy. These techniques made it possible to obtain, for the first time, data accurate to within one part per trillion concerning the concentrations in oceanic materials of elements in the same chemical group as platinum.

istry and cosmochemistry. Investigations in this area also increase our understanding of the processes involved in the formation of the lithosphere (the hard outer layer of the earth that includes the crust). In addition,

some of these rare elements are noble metals (corrosion-resistant metals such as gold and platinum). Studying the distribution of traces of these elements is therefore of practical as well as scientific value; it could make



RELATIVE CONCENTRATIONS of the elements iridium and rhodium in deposits laid down at the boundary between the Cretaceous and the Tertiary periods (about 65 million years ago) support the hypothesis that the earth was struck by some large extraterrestrial body at that time. The iridium content of the rocks was determined by a technique called neutron-activation analysis, and the rhodium content was determined by resonance-ionization spectroscopy. The concentrations of both elements peak sharply at the boundary between the geologic periods; this observation is significant because the elements are abundant in extraterrestrial bodies and rare in terrestrial rocks. In addition, the ratio between the concentration of iridium and the concentration of rhodium—.34 plus or minus .06—matches the ratio of their concentrations in meteoritic matter (where it varies from .3 to .6). It is not at all similar to the ratio of their concentrations in crustal rocks (where it varies between 1 and 6) or in material from the earth's mantle (where it varies between .7 and .8).

it possible, for example, to find new sources of these metals in the oceans.

Because of the complexity and inconstancy of the composition of seawater and because one cannot store it unchanged for any prolonged period, it is regarded by some investigators as a "living organism," which should be analyzed immediately after sampling. Geologists working on land can rely on the later analysis of samples collected in the field; oceanographers would prefer to be able to make the analyses directly, on shipboard.

The concentrations of noble metals in seawater are extremely low—sometimes less than one part in 10^{-12} —and so measuring them by standard spectral methods would require several stages of concentration, a difficult and inconvenient procedure (particularly at sea). Hence only scarce data are available on the concentrations of noble metals in seawater. The technique of resonance-ionization spectroscopy is a promising alternative.

To make analytical measurements on shipboard, investigators from the Institute of Spectroscopy and the Institute of Oceanology in Moscow have developed an "expeditionary" model of a laser-resonance-ionization spectrometer, which was mounted on the research vessel *Akademik Mstislav Keldysh* for its 12th cruise (in 1986) and used to determine the concentrations of gold and of metals belonging to the same chemical group as platinum in seawater, in suspensions, in sediments, in marine minerals and in sulfide ores. Workers thus obtained a good deal of interesting information and proved that it is possible to make ultrasensitive analyses on board ship without relying on traditional procedures, which are tedious and involved.

Another successful application of ultrasensitive laser analysis has been in the study of rare geological catastrophes. As many readers know, in recent years investigators have amassed a large amount of evidence suggesting that certain extraordinary events of short duration have taken place in geological history. It has been hypothesized that these events came about when large extraterrestrial bodies struck the earth; the collisions seem to have left traces in the form of geochemical and isotopic anomalies, which coincide with major biostratigraphic boundaries.

For example, the most recent such event seems to have taken place about 65 million years ago, near the boundary between the Cretaceous and the Tertiary periods, roughly coinciding

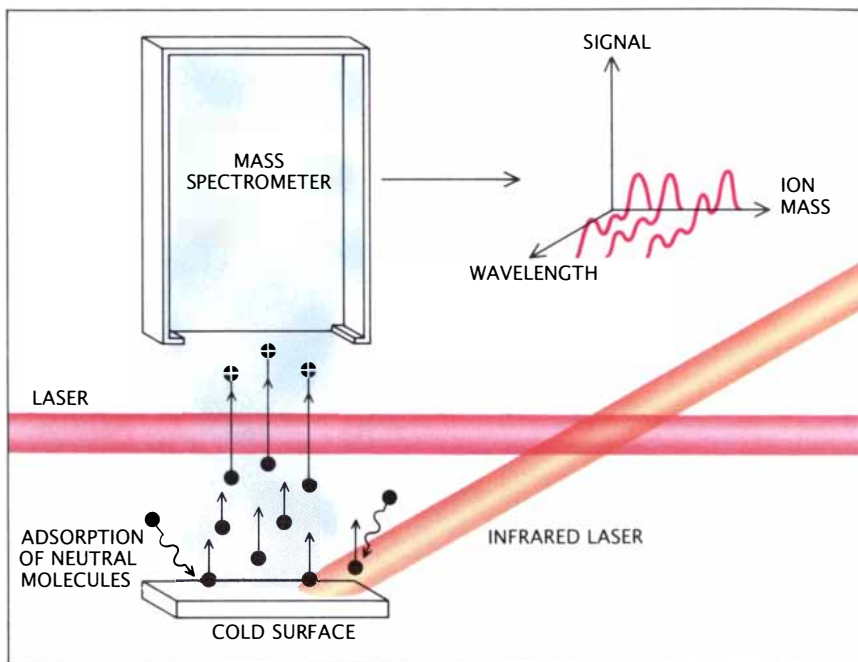
with the extinction of the dinosaurs. In 1980 Luis W. Alvarez and his colleagues at the University of California at Berkeley became interested in this "great Mesozoic extinction"; they examined the concentration of iridium in rocks that had formed at the Cretaceous-Tertiary boundary. Iridium is a convenient indicator because it is abundant in cosmic material (such as asteroids), whereas its concentration in surface terrestrial rocks is several orders of magnitude lower.

The concentration of iridium in sedimentary rocks corresponding to the Cretaceous-Tertiary boundary turned out to be so high that it could not be explained by the gradual accumulation of extraterrestrial material from such "background" sources as micrometeorites and cosmic dust. Iridium anomalies were discovered in more than 50 geologic sections taken from places all around the globe. One interpretation was that the iridium was left by a large cosmic body that struck the earth, setting in motion the events that eventually led to the mass extinction of many of the species that had been dominant.

Some alternative hypotheses suggest that the anomalously high levels of iridium and other elements at the Cretaceous-Tertiary boundary are due to concentration during the course of sedimentation or to volcanic activity. In order to test these hypotheses, it is important to determine precise values for the ratios between the concentrations of various elements and their isotopes in the boundary deposits; it is particularly important to study the concentration of the platinum-group elements, whose concentrations are high in cosmic material and low in terrestrial rocks.

Until quite recently it has been impossible to determine these ratios, because there were no reliable methods for measuring the concentration of platinum-group elements in sedimentary rocks at a sensitivity higher than one part in 10^{-9} . The only exception was iridium, which could be detected in concentrations as small as one part in 10^{-11} by a technique called neutron-activation analysis.

Now, however, laser-resonance-ionization spectroscopy has made it possible to determine with great precision the concentration of any platinum-group metal in geological samples. Investigators at the Institute of Spectroscopy and the V. I. Vernadsky Institute of Geochemistry and Analytical Chemistry in Moscow have measured the ratio between the concentrations of rhodium and iridium in Cre-



TRACE QUANTITIES OF MOLECULES are detected by resonance-ionization spectroscopy. A low-density gas containing molecules to be detected is put in contact with a cold surface. The molecules collide with the surface and are absorbed onto it, accumulating with time. An infrared laser pulse is then aimed at the surface, liberating most of the adsorbed molecules and causing them to rise like a cloud. A pulse from another laser ionizes specific molecules, which are then collected and sorted by mass.

taceous-Tertiary boundary deposits from a section of the Sumbar River valley in the Turkmen Republic of the U.S.S.R. The ratio of the concentration of rhodium to the concentration of iridium in these samples is .34, with an uncertainty of .06. This agrees very well with the ratios typically found in meteorites (between .3 and .6), but it is quite different from the ratios found in crustal rocks (between 1 and 6) and in material from the earth's mantle (between .7 and .8).

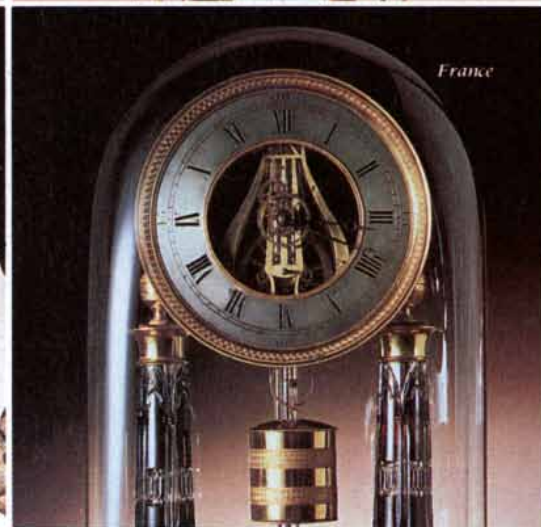
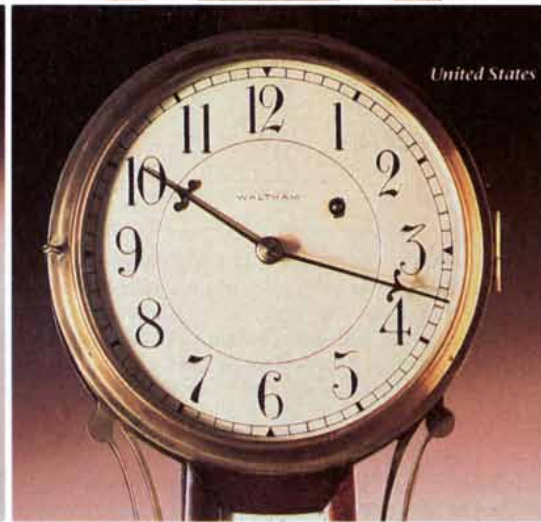
This result gives us reason to believe the concentrations of platinum-group elements at the Cretaceous-Tertiary boundary are not the result of accumulation during sedimentation or volcanic activity. Rather, the data point unambiguously to some extraterrestrial origin for the anomalously high concentrations of iridium and support the hypothesis of Alvarez and his co-workers, namely that the iridium anomaly is the trace of a collision between some large cosmic body and the earth. By determining the ratios between the concentrations of other platinum-group elements, it may even be possible to determine what the extraterrestrial body was—whether it was a chondrite (a stony meteorite), an iron meteorite, a comet or some other kind of object.

Resonance-ionization spectroscopy

is a powerful and exciting technique. Indeed, the technique may eventually enable investigators to meet the formidable challenge put forward by the late Soviet physicist Peter L. Kapitza. In a speech on the future of science at an international symposium held in 1959, Kapitza urged the development of techniques that would "match a dog's sense of smell." With resonance-ionization spectroscopy it should be possible to detect molecules with sensitivity and selectivity that could be matched only by mammalian olfactory organs. In other words, a laser smell analyzer is perhaps in the cards.

FURTHER READING

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THE TECHNOLOGY OF WINNING

An Enthusiast's Guide to the
1988 Summer Olympic Games

Part II of a two-part series
Edited by Chester R. Kyle

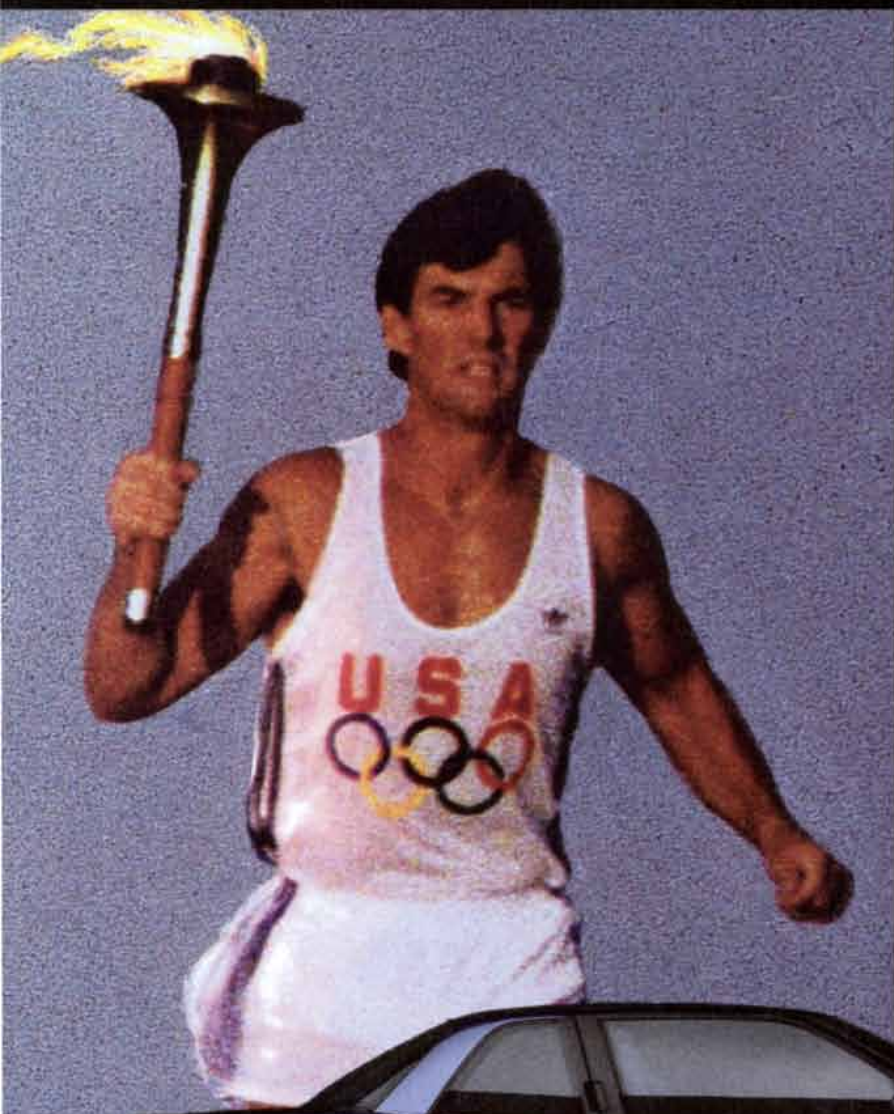


Since the 1950's, a worldwide revolution has taken place in the methods used to coach, train, select and develop athletes. Records have fallen at an unprecedented rate. Sports sciences and equipment technology have made phenomenal gains. In order to stay abreast of world competition, the United States Olympic Committee (U.S.O.C.) has actively initiated programs to help U.S. athletes' chances in the international arena.

These articles are written by scientists and industry leaders who are intimately involved with the recent advances in sports science and technology. Beginning with an overview by Charles Dillman, Director of Sports Science and second in command of the U.S.O.C., the articles provide insights into how science and technology improve athletic performance.

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36 USC 380

THE U.S.O.C.'s SPORTS SCIENCE EVOLUTION

by
Charles J. Dillman

During the 1988 Winter Olympic Games in Calgary, the difference between first and tenth place in the women's downhill event was only 1.42 seconds. Due to the intense competition, there has been a worldwide trend toward taking a more scientific approach to the development and training of elite athletes.

The standard for this approach was set by the Eastern European countries. They first began to build a scientific system for sports development in the 1950's. The results of their scientific work and the high level of academic preparation of their coaches was clearly illustrated at the 1976 Games in Montreal, where the Soviet Union and the German Democratic Republic dominated many events. Since that time, the western world has been trying to catch up. There is no doubt that it will take some time for the western countries to become more competitive due to the formidable lead obtained by the Eastern European countries.

In the U.S., a reorganization and emphasis on amateur sports began in 1978. At that time, the U.S. Congress passed the Amateur Sports Act which established new directions and goals for the American sports system. This legislation designated the U.S. Olympic Committee as the main coordinating body for all amateur sports in the U.S., and gave it the exclusive right to market the Olympic symbols in its efforts to raise funds for the support of amateur sports programs.

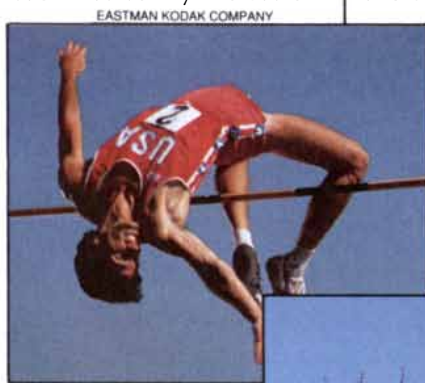
Since 1978, the U.S.O.C. and its 38 National Governing Bodies (NGB's) have been moving very rapidly to develop amateur sport in America and to achieve greater success in the international arena. To accomplish these goals, the U.S.O.C. initiated five major programs: 1) Development/

Funding, 2) Training Centers, 3) U.S. Olympic Festival, 4) Support for World University, Pan Am and Olympic Games and 5) Sports Medicine and Science.

In development funding, the U.S.O.C. provides support annually to each of its 38 NGB's to help them develop their sport, increase the level of participation, train more coaches and officials, conduct competitions, and build facilities. The U.S.O.C. presently has three Training Centers: Lake Placid, New York; Marquette, Michigan; and Colorado Springs, Colorado. A fourth Training Center in San Diego, California has recently been approved and will be operational in 1991. For teams electing to use these training centers, room and board, training facilities and services are provided without charge by the U.S.O.C.

The U.S. now has a domestic Olympic Games, the Olympic Festival, conducted at different locations each Summer except the year of the Olympic Games. The U.S.O.C. also provides support for the selection and final preparation of teams for an increasing number of world competitions. And finally, the U.S.O.C. has made a significant commitment to developing a high level medical and scientific program to assist athletes in all sports.

Initial efforts by the U.S.O.C. to develop a scientific program were begun in 1978 at Squaw Valley, California and Colorado Springs, Colorado. However, these efforts were set back due to the boycott of the 1980 Summer Games and the termination of Squaw Valley as a Training Center. Programs and funding were renewed in 1981 with the major focus of creating a fully integrated core program of sports science in Colorado Springs and a national program of scientific assistance. From 1981 to 1984, laboratories in biomechanics and exercise



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Charles J. Dillman, Ph.D., is Director of Sports Science, U.S.O.C. Assistant Executive Director, U.S.O.C. Programs, in charge of Training Centers, Sports Science, Sports Medicine, International Games Preparation and the Olympic Festival. Specialist in Sports Biomechanics.

physiology were developed and grant programs were established to help selected sports develop their own scientific testing and technology programs.

An evaluation after the Olympics in 1984 indicated that further improvements in performance analysis required a more integrated approach. Thus the concept of sports science was generated where all areas related to performance enhancement would work together to identify the factors that limit an athlete's ability.

This reorganization in Colorado Springs created five departments in sports science—Computer Services, Engineering Technology, Biomechanics, Physiology and Psychology; and five departments in sports medicine—Clinical Care, Education, Nutrition, Drugs and Dental Services. The primary focus of these groups is to provide scientific, medical and educational services to the teams visiting the Colorado Springs Center. In the special elite athlete testing camps, the concept takes an even more integrated view of performance.

Typically, medical exams, nutritional evaluations, vision testing, physiological evaluations, biomechanical analysis and psychological counseling are undertaken over a four-day period. When the testing is complete, the entire medical and scientific team reviews the results with the coach and athlete focusing upon the interrelationships among the areas to determine the strengths and weaknesses of each athlete. Perhaps a poor performance in jumping could be traced to a biomechanical problem or a muscular weakness. The inability to train hard might be related to poor nutritional habits. This multidisciplinary approach increased the power of our testing programs to effectively isolate the real factors that were limiting performance.

While the Core Program in Colorado Springs provides the focal point of the U.S.O.C. efforts in sports science, it is the National Program which has the greatest potential to make widespread significant contributions. The purpose of the National Program is to mobilize scientific expertise in the U.S. and to get various groups involved with NGB's to help them solve their problems. To stimulate an interest in sport, various grant programs have been established in scientific services (standardized testing and evaluation), research, and equipment and technology. These grant programs have been successful in acquiring the services of some leading researchers and technologists for the U.S. Olympic pro-

gram. The results of some of this work are presented in other articles in this section of SCIENTIFIC AMERICAN.

The development of sports science at the Olympic level has received increasing emphasis in the U.S. since its initiation in 1978. Four NGB's had some type of scientific program in 1982. In 1988 there are 26 NGB's that have scientific programs. No research was being funded in 1982. Presently the Sports Medicine Council is funding approximately 20 projects per year. During the past six years the sports science budget has increased tenfold to an annual budget of two million. Significant progress has been made in the U.S. in attempting to develop a sports scientific program.

The main question is, how effective have these programs of scientific assistance been in helping to improve the performances of U.S. athletes in international competition? Perhaps the best evaluation can be made by the people these programs serve—the coaches and athletes. Participants have been asked to evaluate these programs and their response has been very favorable. Typical remarks indicate that the testing and information presented at training camps has been effective in improving training programs and creating an understanding about some complex aspect of performance. When the scientific team can form a good relationship with a knowledgeable coach who is willing to implement some of the recommendations, dramatic improvements in performance are achieved.

Further improvements in the U.S. sports system are needed before we become fully competitive at the international level in all sports:

- **A club system of sport needs to be developed to replace the declining scholastic system.**
- **A national program of coach development and education needs to be established.**
- **A dissemination system for education needs to be developed so new information can reach all levels of sport.**
- **More training facilities are needed for the minor sports.**
- **Of course, more financial assistance needs to be given to each sport.**

Once these aspects of the sports system are enhanced, the present capabilities of the medical and scientific programs will be more effectively utilized.



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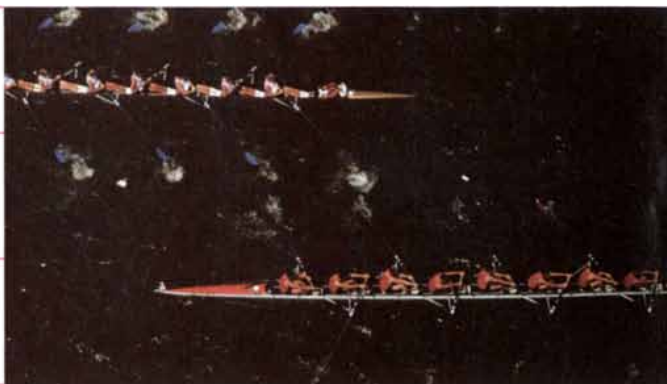
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RACING SHELLS, CANOES AND KAYAKS:



Eastman Kodak Company

LAUNCHING THE NEW FLEET

by
Edward S. "Ted" Van Dusen

For the first time in recent history, the 1988 U.S. Olympic rowing, canoeing and kayaking teams will be using boats designed and built entirely in the U.S. In a concentrated four-year development program sponsored by the U.S.O.C., a new fleet of composite racing shells has been launched that should improve U.S. medal chances in Seoul. Because of the critical dependence of the athlete on equipment, the 26 Olympic boating events are prime candidates for the application of modern technology.

Olympic Rowing, Kayaking and Canoeing

Olympic rowing shells, kayaks and canoes race at speeds from 4.5 to 5.9 meters per second (10-13 m.p.h.) over courses from 500 to 2,000 meters in length. Forward motion occurs as the oars or paddles are planted in the water and the boat is drawn past them. The physical challenge consists in maximizing useful human energy over the race distance, minimizing wasteful motion that may disturb water flow past the boat and balancing a highly unstable craft.

The challenge in designing Olympic rowing and paddling equipment consists of maximizing the propulsion generated by the athlete, minimizing losses from hydrodynamic and aerodynamic drag and accomplishing both within the restrictions imposed by Olympic regulations.

Aerodynamic Drag

Although aerodynamic drag comprises only 12 percent of the total drag on a rowing shell and 9 percent of the total drag on a kayak at racing

speed with no wind, improvements can be very significant. The total drag on racing shells can be reduced nearly 1 percent when the standard round outrigger tubes supporting the oarlocks are replaced with streamlined shapes, and we have fitted several of the U.S. boats with new airfoil riggers. This could result in a lead of about five meters in a 2,000 meter race. Aerodynamic improvements in clothing, oar locks, boat shape and other items are also being investigated.

Hydrodynamic Drag

The hydrodynamic drag on rowing shells, kayaks and canoes consists primarily of frictional drag and pressure or wave drag. Frictional or viscous drag results from the shearing action of water flowing past the hull.

Surface waves are generated by displacement hulls, causing an adverse pressure distribution along the hull. At higher speeds, the drag force created by this pressure increases unevenly in a series of peaks and valleys as the changing wave patterns cause crests or troughs to appear at the stern.

When the wavelength of the waves generated by the boat is the same length as the hull, the boat is said to be traveling at hull speed. The wave drag on very slender hulls is small until a boat reaches about one half hull speed. It then increases gradually as it approaches hull speed, and it increases abruptly as hull speed is attained. Displacement boats can exceed hull speed only if they have high propulsive power or if their hulls are slender.



Brian Hill Photography

Edward S. "Ted" Van Dusen, Ph.D., is President, Composite Engineering Inc., designer and manufacturer in advanced composite construction, including wind turbine blades, rowing shells, kayaks and sail boats. Ocean Engineer and former elite rower.

Slender hulls reduce the amplitude of the wave train so successfully that the wave drag on Olympic rowing shells, canoes and kayaks is only 6 to 15 percent of the total hydrodynamic drag. This enables them to travel up to twice hull speed. As the cross-sectional area of the hull is decreased, the waterline length must increase in order to displace sufficient water to float the boat and crew. Increasing the length of the boat also increases the hull speed.

The decreased wave drag and increased hull speed achieved by long slender hulls carry a double penalty, however. First the long slender hull has a relatively large wetted surface area which increases frictional drag. The designer seeks to minimize total drag by balancing low wetted surface area against low wave drag. Grooved surface films, such as Riblets™ manufactured by the 3M Corporation, can reduce frictional drag, but they have recently been outlawed in international competition. The second penalty is the comparative instability of slender hulls.

With stable boats, the buoyancy and weight forces combine to cause a righting torque as the boat rolls. However, rowing shells and canoes are highly unstable and will capsize if not actively balanced by the rower or paddler. The constant series of adjustments required is much like trying to balance a pendulum upside down on your hand. This feat requires a great deal of skill and its difficulty is increased by the action of wind and waves.

Towing Tank Testing

Few well-documented studies of slender hulls existed prior to 1986 when a group of us began testing rowing shells, kayaks and canoes. During the first phase of this study, a coordinate axis measuring machine was used to study the hull shapes of the most competitive single shells and kayaks.

These measurements, accurate to .1 millimeter, were used to calculate hydrostatic characteristics such as wetted surface area and volume distribution for each hull. Three new kayaks and two new shells were designed to systematically vary these parameters. The five new models, plus four kayaks and four shells, were tested in the towing tanks at Tracor Hydronautics. The total drag on each hull was measured at several different trims (bow up or down) over a wide speed range.

Towing tank tests showed that the drag on one of the new

kayak designs was 1.5 percent lower than the drag on the best existing boat. Two boats copied from this model were delivered to the U.S. kayak team in early 1987. U.S. team members Greg Barton and Norm Bellingham raced the new boats to two gold medals in the Pan American Games and two gold medals in the World Championships in 1987.

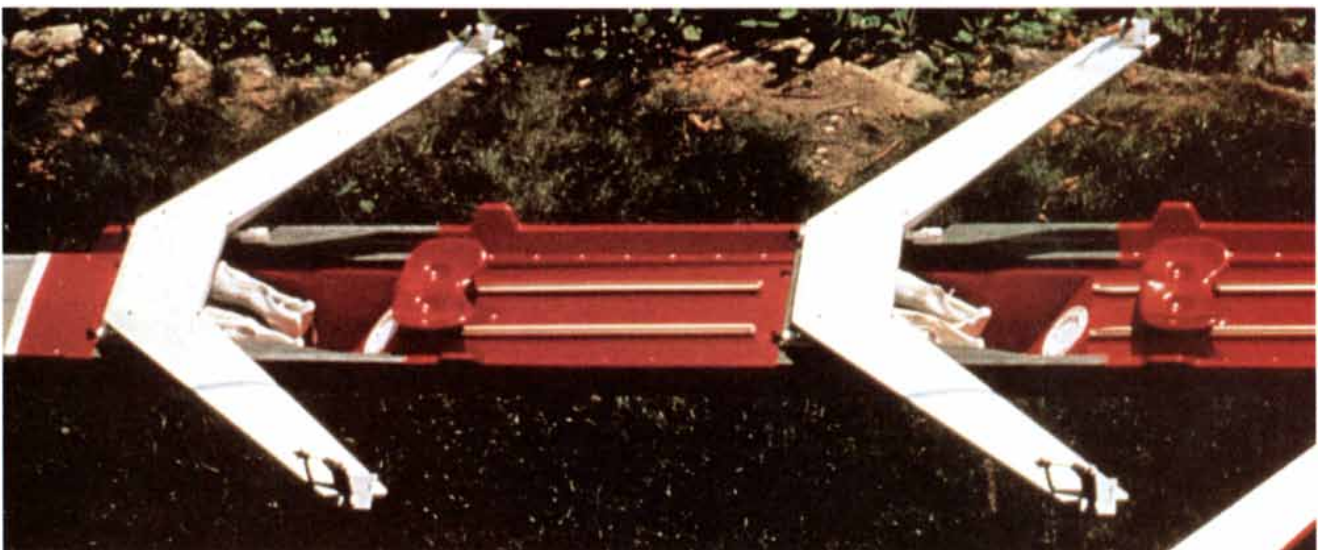
One rowing shell currently being manufactured by a U.S. company outperformed the others in the towing tank, and the tests identified only small improvements for this model. Although only single shells and kayaks were tested, the data showed that larger shells and kayaks could be significantly improved by varying the shape and adjusting the water line length. These improvements are being implemented in the design and construction of a fleet of boats for the U.S. rowing, kayaking and canoeing teams. The hulls of these new boats are constructed for maximum hull rigidity. Very stiff honeycomb-cored carbon fiber composite materials are being used, since hull flexing and vibration can increase turbulence and drag.

The towing tank tests showed that the design and construction of rowing shells and kayaks should be appropriate to the weight and size of the crew. The women's eight-oared shell offered the greatest opportunity for improvement in this area. We are building a women's eight specially designed for the lower average weight and size of a women's crew.

Other recent technological research in rowing and paddling includes the design, construction and testing of lightweight composite kayak paddles by Greg Barton. The weight of the new paddles is less than half the weight of the best wood paddles. Also, the University of California's Livermore Laboratories have developed instrumentation designed to instantaneously measure the power output of a rower, the synchrony of rowers in team boats and physiological parameters such as heart rate. This instrumentation should help to increase the effective power output of individual rowers and crews and aid in team selection.

The difference between an Olympic gold medal and a fourth place finish is often a fraction of a second, and improved equipment can often make this difference. On the other hand, the most technologically sophisticated equipment cannot guarantee an Olympic win. In the end, Olympic medals will be awarded to those athletes who, by their skill, courage and dedication transform technological sophistication into victory.

COMPOSITE ENGINEERING INC.



GAINING THE COMPETITIVE EDGE:



HIGH-TECH TRAINING TOOLS

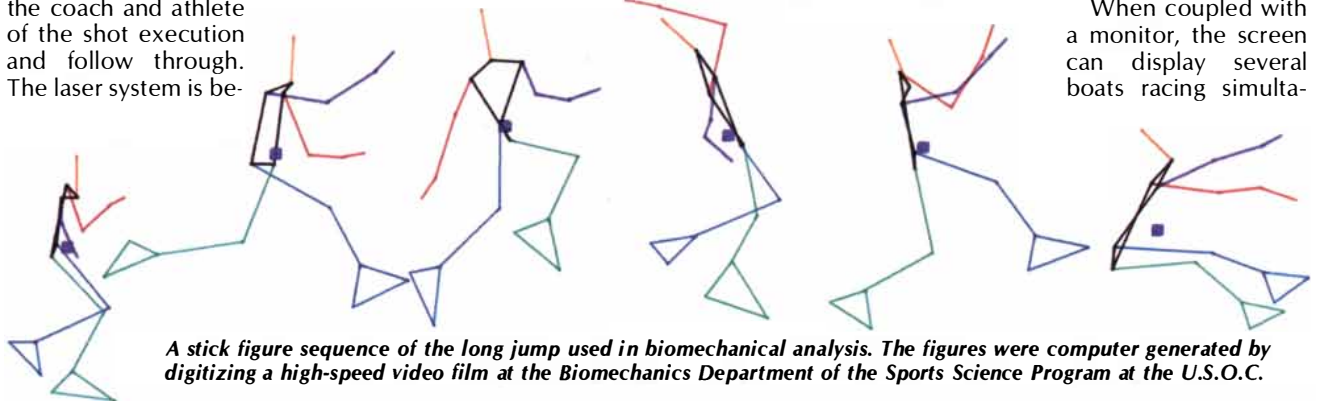
by
Edmund R. Burke

At the Olympic Training Center in Colorado Springs, cyclists ride bicycle simulators for hours, while electronic monitors record their power, efficiency, heart rate and oxygen consumption. Hundreds of elite rowers train and compete indoors using computerized rowing simulators when bad weather keeps them off the water.

Increasingly, the magic of electronics and computers is being harnessed by sports scientists to analyze everything from a pole vaulter's take off to a long jump landing. Nationwide, imaginative high-tech training devices with biofeedback are helping athletes to improve, and coaches to scientifically gauge athletic performance.

Lasers Hit the Bulls' Eye

A team of researchers from industry and the U.S.O.C.'s sports science group have developed a rifle or pistol mounted laser to track the movement of gun sights. The laser, about the size of your thumb, fires an invisible infrared beam at the target, which is recorded by a special video camera. A monitor near the shooter allows the coach to observe the shooter's aim before the gun is fired, and a video recording permits later viewing and analysis by both the coach and athlete of the shot execution and follow through. The laser system is be-



A stick figure sequence of the long jump used in biomechanical analysis. The figures were computer generated by digitizing a high-speed video film at the Biomechanics Department of the Sports Science Program at the U.S.O.C.

ing actively used by the elite shooters on the U.S. team.

Ultimate Indoor Training

Ergometers, devices which measure the power generated by athletes, have been used for decades in training. Stationary ergometers are based on the most common forms of exercise. Treadmills reproduce walking, running or stair climbing. Other machines quite accurately simulate rowing or cycling. Arm-crank ergometers can duplicate the action of paddling a canoe. Since 1986, computer-controlled exercise ergometers have been introduced which greatly expand their value as training and research tools. Two of the most imaginative are in rowing and cycling.

In 1986, former Olympic oarsman Dick Dreissigacker and his brother Pete, along with Dick's wife Judy, (who is a computer specialist) designed a simple and economic computerized rowing ergometer which uses a flywheel and fan for loading. The display screen on the ergometer can selectively register power, speed, stroke rate, time, distance and caloric energy consumption. Almost every competitive rowing program in the U.S. now uses the machine for Winter training or preliminary team selection.

When coupled with a monitor, the screen can display several boats racing simulta-

Edmund R. Burke, Ph.D., is Director, New Product Development, Spenco Medical Corporation. Specialist in sports physiology and training of elite athletes; author of four books and over 100 scientific articles. Former Technical Director, United States Cycling Federation.

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neously. This feature has spawned indoor competitions throughout the U.S., and last year a world championship was held in Boston with over 100 elite rowers competing from all over the world, including a team from the U.S.S.R.

In cycling, an indoor computer-controlled trainer designed by Bruce Sargeant and a group from Frontline Technology simulates wind resistance, hills and inertia to work muscles in the same manner as when riding outdoors. The trainer allows the cyclist to use his or her own bicycle and gives the cyclist immediate feedback of speed, time, cadence, heart-rate, power output and calories burned.

The computer's most notable function is race simulation. The cyclist can choose from a variety of pre-programmed or self-designed road or track courses. The bicycle and the course profile are displayed on the LCD screen, and the pedaling resistance automatically increases or decreases with the speed, rate of acceleration or with climbs and descents.

Video Studies of Motion

Traditionally, biomechanists have depended upon high-speed film to capture detailed images of athletes in competition. However, high-speed video has several advantages over film. It is inexpensive and easy to duplicate, gives instant feedback, records in dim light and allows researchers to imprint simultaneous timing or other data on the videotape. An even greater benefit is that video output can be fed directly to computers for display and analysis.

Under a U.S.O.C. sports sciences program, high-speed video filming is available to all of the Olympic sports. For example, track and field, the sprints, the middle distances, the hurdles, the pole vault, the long jump, the triple jump, the high jump and the hammer throw have been actively filmed and analyzed by U.S.O.C.-sponsored scientists.

Each frame from the high-speed video is converted to a digital computer image, and may be enhanced using techniques developed for satellite imagery. The coordinates of the athlete's joints are marked frame by frame, and the digitized motion sequence is then available for computer analysis. With a second camera, a three-dimensional computerized image can be created that may be viewed from any angle.

For example, elite race walker Mark Fenton's gait was filmed and his digitized images showed that he had a tendency to place his leading foot too far out in front of his center of gravity. This caused him to shift back at impact and decelerate as his foot touched the

ground. By shortening his stride slightly and making other adjustments, Fenton was able to improve his time in the 20-kilometer walk by about 5 percent.

Swimming Treadmill

At the Olympic Training Center in Colorado Springs a new swimming flume has been added to the facilities. The swimming flume, the water equivalent of a wind tunnel, allows the swimmer to swim in place as water is circulated by pumps located at the bottom of the flume. On one side of the flume a window permits observation and video taping of the swimmer. The velocity and temperature of the water in the flume can be accurately controlled.

Flumes are not new, and have been used by top swimmers in other countries for years, but this is the first one available in the U.S. Future work will investigate the four competitive strokes, (the crawl, back stroke, breast stroke and butterfly) for technique, energy cost and active drag. The flume can be used to measure oxygen consumption and aid each swimmer to learn a pace which is most efficient for him or her. It will also be used by competitive kayakers and canoeists to improve their rowing skills.

Athletic Radar

Recently, a series of pulse monitors have come into common use which features a memory function that can be linked to a portable computer. They can be programmed to beep when the pulse reaches a target zone. The units transmit the heart beat from sensors on a chest strap to a watch-size monitor on the wrist. They are used by athletes as a pacing and training tool, and by researchers to study the effect of heart rate on performance.

The most advanced device in this category employs the

ultrasound Doppler effect to measure speed, and using speech synthesis through an ear-phone, it updates the athlete on time, heart rate, distance and speed. Developed by Nike Inc., the monitor can be used in running, cycling, skiing, skating or any sport where speed is critical.

Athletes are now using computerized devices that give real time feedback, as well as other advanced mechanical and electronic training aids to help them improve performance. Other devices make it possible for coaches and scientists to quantitatively measure and analyze performance and to suggest improvements to the athlete. These training tools were unheard of only 10 years ago.

HIGH-TECH TENNIS

For the first time, tennis will be a medal sport in the Olympics. Most of the players will be top professionals who are willing to forego prize money during the Olympic games. The following facts have been provided by tennis technical experts Jack Groppe and Tracy Leonard:

- Mid-size and larger rackets have a high rotational inertia and are therefore more stable on off-center shots. Probably 95 percent of all shots are hit somewhat off center.
- Radar-gun tests have shown that the best professionals can serve the ball from 120 to 140 m.p.h. with an occasional fireball exceeding 150 m.p.h. When a ball bounces it loses from 20 to 50 percent of its speed depending upon the playing surface.
- In professional matches, the average playing time per point is 5.2 seconds on grass, and nearly 10 seconds on clay. Although actual playing time is short, heart rates can go as high as 190 in elite tennis matches, and normally stay high since there is only about 30 seconds for recovery between points.
- When spin is put on a ball, air pressure differences on the surface cause the ball to curve in flight. Top spin drops the ball and underspin lengthens the shot. At high altitudes, low air friction on the ball speeds up the game so much that slower courts and balls are often used to simulate sea level conditions.
- The vibrational frequency of a tennis racket is 70-100 cycles per second (c.p.s.), of the ball, 350 c.p.s. and the strings, 600-700 c.p.s. Tuning the frequency of the racket and strings for maximum energy return is a developing trend in design.—C.K.

THE MODERN TECHNOLOGY OF ARCHERY



by
James L. Easton

Archery is a science, sport and hobby. The best archers can shoot arrows with incredible consistency and accuracy. They must train for long hours to achieve repeatable physical motions of holding, aiming, releasing and follow-through. In World and Olympic competition, archers must shoot for over 30 hours in four consecutive days, so conditioning is vitally important. Today's archer is a finely disciplined and trained athlete.

In the Olympics, men shoot from 30, 50, 70 and 90 meters; women, from 30, 50, 60 and 70 meters. They shoot 36 arrows at each distance. Both men and women can group most of their arrows in a 9.6-inch center that encloses the 10 and nine point scoring areas—known as the gold.

Such unbelievable accuracy is due not only to training and skill, but also to the combined technology of the bow and arrow. Tournament bows and arrows are made of space-age materials. Modern bow limbs use a syntactic foam that is sandwiched between unidirectional fiberglass and carbon fiber. The combination offers lightness,

strength and exceptional speed and stability.

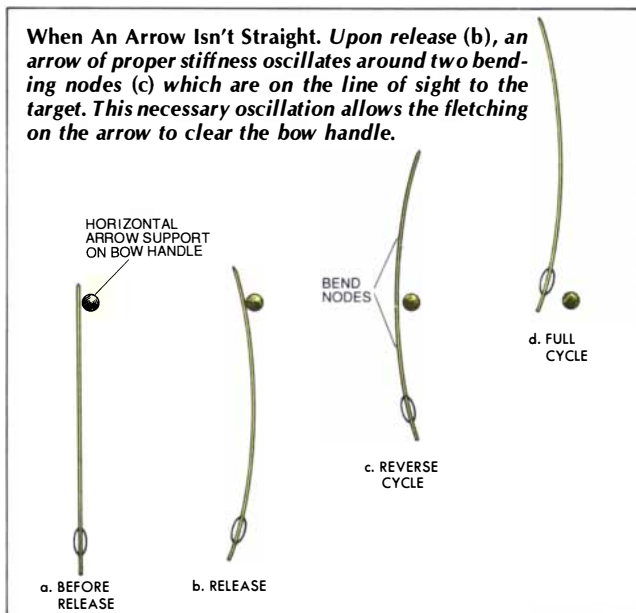
Probably the most critical part of the equipment is the arrow. The best target arrows are made of carbon fiber mixed with fiberglass, or of ultrathin-walled, high-strength aluminum sheathed in high-modulus carbon fiber. But no matter what the arrow material, all the arrows of each size must be straight within .003 inch, weigh the same within plus or minus 1 percent and be the same stiffness within a few thousandths of an inch deflection. They must also be matched in stiffness to their length and the pounds of pull of the bow, and each archer's shooting style.

Identical stiffness is important, because of what is known as the archer's paradox. An arrow must flex in a uniform way to achieve maximum accuracy. Accuracy deteriorates when an arrow is either too stiff or too flexible. The bow accelerates the arrow to flight velocities of over 220 feet per second with enormous forces that buckle the arrow and set up vibrations in the arrow that continue all the way to the target. Yet with the right mix of weight and flexibility, it goes on to hit the mark with remarkable precision.

When the bow string is released, it slides around the fingers with a sideways displacement. This causes the arrow to bend toward the bow and sets up an oscillation which allows the arrow to snake around the bow handle without physical contact, except initially [see diagram at left]. Ideally the arrow will go through nearly one complete bend cycle allowing the fletching to clear the handle.

Technology has dramatically improved the arrow. A recently developed arrow shaft, to be used by U.S. Olympic archers, is a carbon fiber barrel-shaped shaft built on a thin wall (.006 inch) high-strength aluminum core tube. The thinner, lighter ends reduce the overall weight and create a higher frequency vibration that more closely approaches the optimum one full cycle at the moment the feathers or plastic vanes pass the bow. The arrow thus allows a greater margin for error in release technique. Also, the higher velocity of this new shaft, with its shorter flight time, increases accuracy by decreasing the effects of wind and weather on the arrow.

The technology of winning in modern archery has become a combination of the most advanced equipment, the most advanced physical and mental training and that elusive competitive spirit of a winner.



James L. Easton is President, Easton Aluminum Inc., sporting goods manufacturer. Commissioner of Archery, 1984 Olympics. Chairman, International Archery Federation Development and Technical Committee. Member U.S.O.C. Sports Equipment and Technology Committee.

Most people who are missing



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So before you buy just any economy car, check out a Nissan Sentra. You'd be crazy not to.



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SEOUL SHOES:



Eastman Kodak Company

BIOMECHANICAL AND TECHNICAL DEVELOPMENTS IN RUNNING SHOES

by
E. C. Frederick

Shoe designers take second to no one in the engineering challenge competition. Imagine designing a shock attenuating device that must weigh under seven ounces and support and protect a 150-pound bouncing body that slams into the ground with a force three times its weight. And, as if protection from one of these collisions weren't a tall enough order, these shocks occur more than 90 times a minute for as long as two hours.

Add to that spec sheet control for swaying and slipping, and the need to retain these properties over a range of temperatures and humidities, as the runner races over surfaces from sand to concrete.

That's a fair mission statement for a technical running shoe, and we haven't even touched on issues of fit, fashion, color or durability, not to mention the specific tasks which these shoes will perform.

Olympic sprinters accelerate from zero to over 27 m.p.h. with traction forces exceeding body weight and impact forces over 3.5 times body weight. The impact shocks transmitted through the skeleton at sprint speeds are so violent, they can cause headaches or loosen fillings. And leaning into turns at precarious angles can

burst a sprinter's shoe uppers or peel off sole layers.

At the other extreme from these violent power events are Olympic marathon competitors who pound hot pavement for more than two hours and average over 12 m.p.h. Even at these gentler speeds, peak forces will approach three body weights. Each event has its own combination of stresses that footwear must withstand while boosting performance.

Seoul's runners will wear featherweight spike shoes for the sprint events; softer, sturdier, middle distance

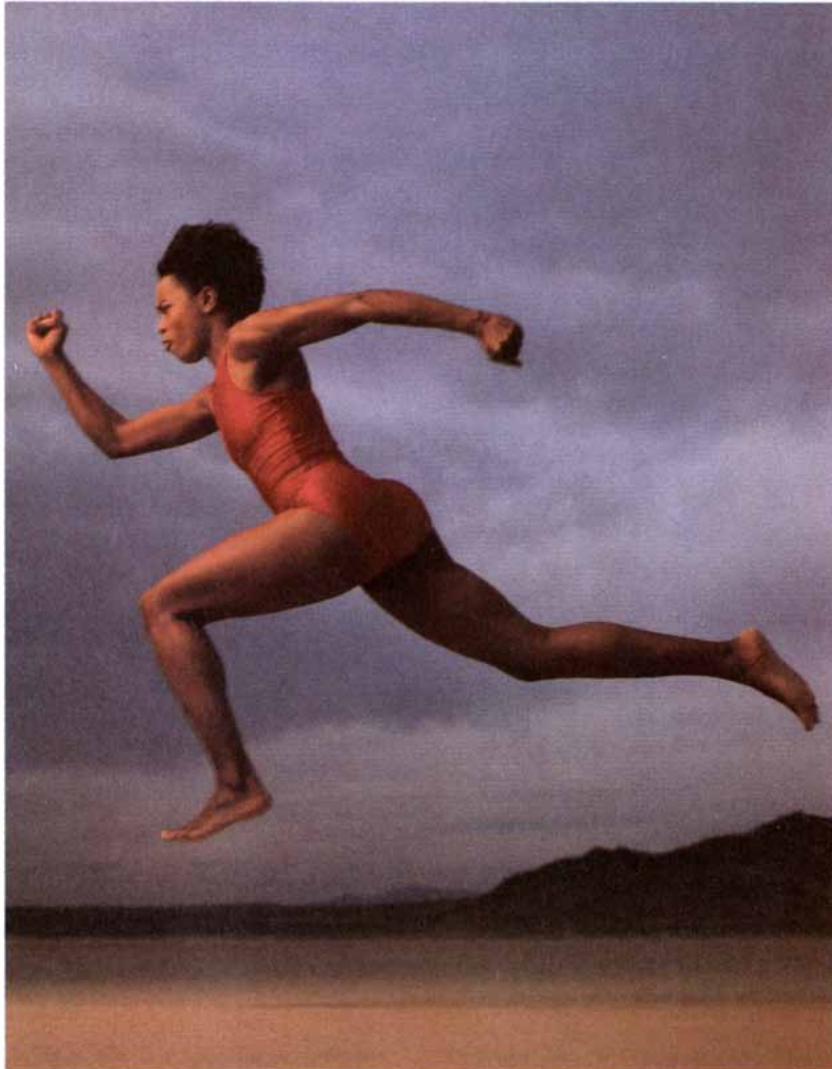
shoes with fewer, shorter spikes for the 800 and 1,500 meters; and distance spikes with more heel lift, and added cushioning and support for the 5,000 and 10,000 meters. Some steeplechase shoes will have mesh uppers that drain between water jumps, and heel pads for bounding over hard stationary barriers. Some sprint shoes have asymmetrical, "centrifugal" forefoot straps to counteract the strain on the foot from running turns counterclockwise.

Marathoners' racing flats may have: graphite reinforced supports; reinforced synthetic rubber outsoles computer-designed to maximize traction and minimize wear and injury; moisture-wicking fabrics; breathable Teflon laminates; and multi-density cushioning systems



Anatomically-based shoe shape includes properly scaled heel widths and molded-in three-dimensional foot contours. 1) Polyurethane-encapsulated, inflated air cushion for shock attenuation and high-energy return. 2) Structural-plastic, cantilevered foot bridge slows pronation velocity. 3) Reinforced leather exoskeleton provides strategic support. 4) Rigid plastic heel counter support tames the rolling heel. 5) Waffle-type lug outsole provides independent suspension and traction while minimizing weight. 6) Upper materials are mesh laminates for shoe climate control and blister protection.

E. C. "Ned" Frederick, Ph.D., is the head of Exeter Research Inc., biomechanics consulting firm serving sports and fitness companies including Nike Inc. Advisor to numerous Olympic athletes including six Olympic medalists. Author, over 100 technical articles and books.



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which control foot movement while attenuating shocks.

This abundance of technology and science leads inevitably to specializations within events. There are shoes for certain surfaces and weather conditions. And most competition shoes are designed to be fine-tuned by changing spike or lacing patterns.

This dizzying array of technological choices that confronts today's athletes becomes even more bewildering when we look at three of the issues occupying today's shoe engineers: cushioning, traction and energetic economy.

Cushioning

Cushioning is provided in proportion to race distance. Shorter sprint races are run on soft polyurethane tracks which provide reasonable cushioning. But shoes for the middle distances and beyond must be good shock absorbers first. Much of their technological content is under the foot to help the body attenuate impact forces and to protect delicate structures within the foot—such as the tiny sesamoid bones under the ball.

Marathon shoes take this to the extreme. Their shock attenuating soles stress durability. Some cushioning systems, such as ethylene vinyl acetate foams provide excellent cushioning early on but compact to the consistency of wood in the later stages of a marathon when runners need all the cushioning they can muster. The cellular structure of molded polyurethane soles seem to stand up better than other foams, and it has become the material of choice for the long run. Polyurethane's extra weight can be compensated for by encapsulating lighter materials such as inflated air cushions or lighter foams.

Traction

When running on slippery or wet surfaces, or changing speed or direction, traction is elevated to priority status. Friction forces over 1.0 times body weight have been measured for a wide selection of flat sole designs, and spikes show even greater forces due to interlocking between spikes and the surface.

Metal spikes are designed to minimize weight and are placed to match the running style. By rule, the spike number is limited to 11, but placement is optional. Titanium is often employed to minimize weight. Numerous spike shapes and lengths are used and plastic nubs are molded into spike plates to enhance the spring back from the track and to add more interlocking.

In fact, the development of traction has come so far that it can be done too well. Spikes can be hard to pull out of today's soft synthetic tracks. So athletes have a variety of spike geometries and lengths at their disposal for particular conditions. But that's not traction's only twist.

A runner's body movements adjust to variations in the surface. These kinematic adjustments change the frictional requirements of running shoes and foil mechanical

friction measurements. For example, when biomechanical studies are used to predict friction on cinder and synthetic surfaces, they give higher frictional coefficients for the cinder surfaces and lower coefficients for synthetic surfaces than do equivalent mechanical measurements.

Kinematic adjustments are an important thread that runs through studies of shoe biomechanics, confounding many attempts to simplify the technical aspects of sport shoe design. While daunting, this factor also presents a great opportunity for innovation not only in cushioning and traction but in the enhancement of running economy as well.

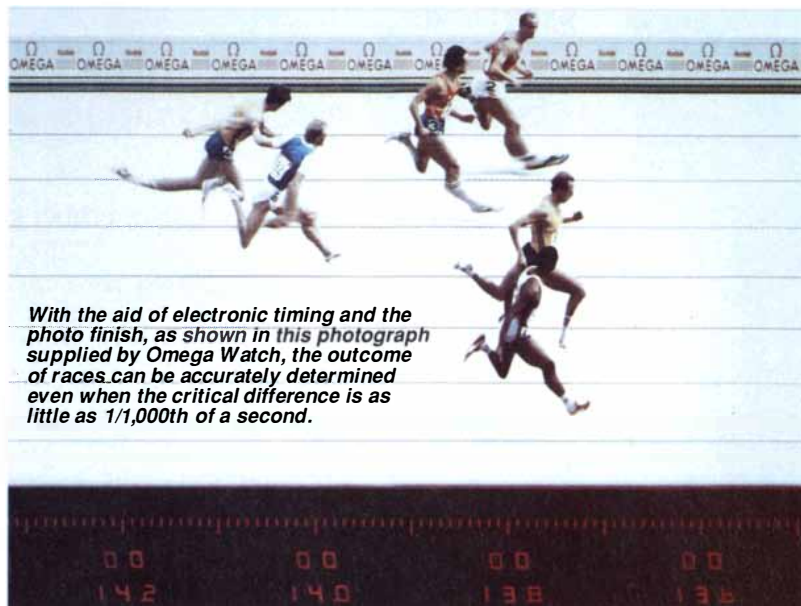
Running Economy

The easiest way to lower energy consumption is to reduce shoe weight. Because the running foot undergoes extreme changes in potential and kinetic energy, it costs more to carry extra weight on the foot than any other part of the body. For every 100 grams carried on each foot, about 1 percent more energy is consumed. Light-weight materials and composites as well as minimal support systems are being used to lower this cost.

To a point, softer soles also lower energy cost. To absorb the increased shock of hard soles, limbs flex more but this means additional energy expenditure. So, the body does less work to cushion footstrike with softer shoes.

Another promising strategy to lower energy consumption is to improve the springlike properties of cushioning materials. The viscoelastic nature of sole materials allows only about half of the energy they absorb to be returned. It may be possible to tune the shoe's cushioning to the runner to return a higher percentage of this energy. However, a complex maze of kinematic adaptations and the body's tendency to adjust its stiffness make it difficult to sort out the best way to tune cushioning. Another possibility currently in vogue is to use more resilient cushioning materials, but we don't know how much of this added energy return can actually be used by the running body.

The abundance of shoe design possibilities coupled with the body's tendency to adjust in predictable ways to shoe mechanical characteristics give us a new way to manipulate human movement for better and safer performance. Therein lies the most provocative result of scientific studies of footwear and the key to many future improvements.



With the aid of electronic timing and the photo finish, as shown in this photograph supplied by Omega Watch, the outcome of races can be accurately determined even when the critical difference is as little as 1/1,000th of a second.

"The Space Station," a special advertising section in the July issue, included a discussion of scientific uses of a space station by Thomas M. Donahue. The section was not meant to imply support of the NASA Space Station by the National Academy of Sciences.

*For Bill Demby, the difference means
getting another shot.*



When Bill Demby was in Vietnam, he used to dream of coming home and playing a little basketball with the guys.

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THE FLIGHT OF THE JAVELIN



by
Mont Hubbard

All of us, at one time or another, have attempted to throw something as far as possible. This act exhibits one of our fundamental relationships with the earth, the struggle against gravity. This struggle is dramatically represented by the four Olympic throwing events: shot put, hammer throw, discus and javelin. All four events differ in throwing technique, in the projectile weight and in the importance of aerodynamic forces on the flight. The ratio of the maximum possible aerodynamic force during flight to the weight is roughly 600 times as large in the javelin throw as it is in the shot put. Indeed, the javelin has such a small specific gravity (.64) that it floats in water, and it flies so efficiently that it can be thrown farther in air than it could be in a perfect vacuum.

The importance of aerodynamics in the javelin throw makes it an ideal subject for theoretical analysis. For the past four years, at the University of California at Davis, we have been using computer analysis to study the flight of the javelin under a grant from the U.S.O.C. We have used wind

tunnel tests, aerodynamics and physics to predict what constitutes an ideal throw.

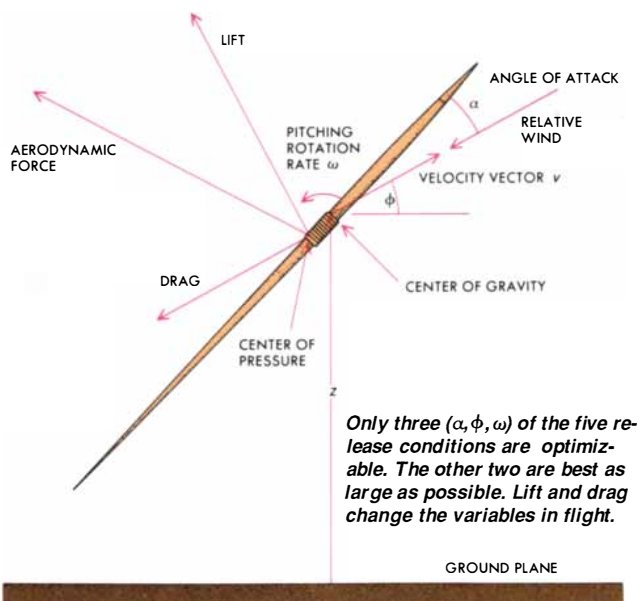
The javelin throw became an event in the modern Olympics in 1906, and world records have increased greatly since then, roughly doubling in 80 years to 104.8 meters in 1984. These advances can be attributed to an improved level of athlete selection, skill and training, as well as to innovations in javelin design.

The progress of javelin world records has been highly erratic. In the early 1950's, because of the expense of replacing shattered wood javelins, engineer Dick Held built the first aluminum javelin for his brother Bud, a Stanford javelin thrower. Using the new javelin, Bud Held broke the existing world record by over 20 feet. The new Held javelin was a brilliant innovation, not because it was made of aluminum, but because Held had cleverly altered the traditional shape, employing aerodynamics to improve the javelin's flight. This led to a cycle of rules changes which attempted to suppress new aerodynamic designs, and new designs which attempted to exploit the rules.

By 1986, athletes and equipment had improved to such an extent that javelins were being thrown out of the stadium and into the stands endangering the spectators. This led to a rule change effectively banning aerodynamic javelins which "sailed." Since 1986, the world record has dropped about 20 meters.

It is the shape of the javelin which determines the air flow patterns around the surface during flight, and thus the resulting aerodynamic forces and torques. Air flowing past a javelin induces pressure and shear stress over its entire surface, the net result of which is the aerodynamic force. This force is commonly resolved into components called lift and drag which are perpendicular and parallel to the relative wind direction. Their effective location is the center of pressure.

The magnitudes of the forces are proportional to the product of four factors: air density, the square of the relative wind speed, the projected area of the javelin and the lift and drag coefficients, C_l and C_d . In turn, these coefficients and the location of the center of pressure depend heavily on the angle of attack, the angle between the javelin and the relative wind direction. Most of us have experienced this phenomenon. If we hold our hand out of a moving car



Mont Hubbard, Ph.D., Professor of Mechanical Engineering, University of California at Davis is a researcher in the computer modeling and optimization of sports including the ski jump, pole vault, high jump, bobsled and javelin throw.

window, small changes in the angle of attack dramatically change the lift and drag.

Because the center of pressure is not, in general, at the center of gravity of the body, the aerodynamic force exerts a torque about the center of gravity and causes angular acceleration. This angular acceleration results in a changing pitch attitude during flight; the nose gradually rises and then falls. This changing attitude and the changing relative wind direction as the javelin approaches and recedes from its zenith, cause continuous changes in the angle of attack (and hence the lift, drag and pitching torque) during the flight.

Once released from the thrower's hands, the trajectory is completely determined by the state of the javelin at release (its position, orientation, velocity and rotation), together with the forces which act during flight. The forces in flight are themselves functions of these states during flight. We have been able to calculate the entire trajectory of a javelin by solving the equations of motion numerically in a computer using only the release conditions and force profiles from wind tunnel studies.

By assuming that the trajectory lies in a vertical plane, the important launch conditions are reduced to five: the height of the center of gravity above the ground, the magnitude of the velocity and its angle from horizontal, the angle the javelin makes with horizontal and the pitching rate of the javelin (nosing up or down). The first two have no optimal values because throwing faster and releasing higher always increase the range, all other factors being the same. World class javelin throwers can launch a .8 kilogram javelin at 30 meters per second (67 m.p.h.) with a mean acceleration of over 40 g's.

The other three release conditions may be optimized to maximize the range. We have calculated the optimal release conditions numerically on a computer by systematically searching in the space of release conditions. Contrary to the 45 degree angle which would give a maximum range

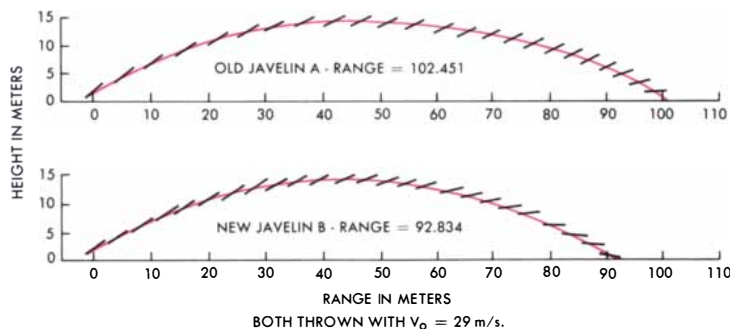
in a vacuum, the optimal release angle at which a javelin should be thrown is about 30 degrees for both the old style aerodynamic javelin and the new model. For the old javelin, we found the initial angle of attack should be about 5.9 degrees, while the pitch rotation should be about 9.2 degrees per second nose downward. A 1983 world record javelin throw by Tom Petranoff was analyzed on video film, and the launch conditions of this throw almost exactly matched calculated values.

For the new style javelin, the calculated release conditions are quite different. The ideal pitch rotation is nose upward at three degrees per second while the angle of attack is a negative two degrees. If an error of a few degrees per second were made in the pitch rotation of the old style javelin it would fall 20 meters short, even when launched at the same world class velocity of 30 meters per second. The new javelin is much less sensitive. Thus, the "lucky throw" is no longer such a factor in elite competition.

The theoretical optimal release conditions can be used as an aiming point by the throwers, but are of little value if athletes have no information about their actual release conditions. For this reason, we have developed a system capable of providing rapid feedback in the javelin throw.

A high-speed video camera (200 frames per second) films about 10 points on the javelin during the first .2 second after release. A powerful, fast computer automatically digitizes the 40 video frames to calculate precisely the two-dimensional coordinates in the plane of motion for all 10 points as functions of time. From the coordinates it is possible to estimate the set of release conditions.

The speed of the computer allows the thrower to view the data within roughly three minutes after the throw, soon enough for the information to be used to modify and improve the next throw. We are just beginning long term studies with individual javelin throwers to understand better how the system may be used to enhance performance.



Rule restrictions instituted in 1986 severely limit contribution of lift to range. For equal release velocities of 29 meters per second, the old javelin (top) could have large angles of attack and lift late in flight, but the new one (bottom) always noses over and flies only about 90 percent as far.

HIGH-TECH POLE VAULT POLES

The pole vault is a startling example of how technology can raise athletic performance. The pole vault record has increased four feet since 1961, to 19 feet, 9-1/4 inches. Until the 1950's, vaulters used stiff bamboo poles and landed in sawdust pits. Then in 1960, Herb Jencks of the U.S. introduced the flexible fiberglass pole and vaulting records headed for the sky.

Jencks, a manufacturer of fiberglass fishing poles, built a new deep sea tuna pole about 10 feet long, and over one inch in diameter. As a lark, his son, a 100-pound junior-high-school pole vaulter, took one of the tuna poles, fit wood plugs in the end and tried vaulting with it. Surprisingly, he topped his best height by several inches.

A fiberglass pole bends several feet in the middle, storing energy so athletes can hit the vault box much

faster without excess shock. The pole springs back at the top of the swing, catapulting the vaulter over the bar. Jencks soon began building poles for local high-school vaulters and later for all comers.

Today's poles are computer designed to bend in one direction, and are matched to the weight, take-off speed and hold technique of each vaulter. Any pole is legal as long as it has been commercially available to all competitors for at least six months. The present world record holder, Sergei Bubka of the Soviet Union, uses an American pole made by Spirit UCS.

In addition to the pole, modern foam pits cushion falls, and synthetic surfaces add spring and traction to the runup and takeoff. This high-tech combination has spawned the rapid jump in vaulting heights.—C.K.

INNOVATIONS IN CYCLING TECHNOLOGY



by
Chester R. Kyle

In Olympic bicycle racing, cyclists struggle to overcome the relentless force of aerodynamic drag. At racing speeds of over 30 m.p.h., wind resistance is more than 90 percent of the total retarding force against a bicycle and rider. The remaining 10 percent is the rolling friction of bicycle bearings and tires.

Cycle racers can lower wind resistance in several ways. They use an uncomfortable crouched racing position so that the body is more streamlined and has less frontal area. They wear smooth form-fitting costumes and tear-drop shaped helmets. They also slipstream behind other riders. By drafting, the required power output drops by more than 30 percent, so riders travel in a pace line or pack to conserve energy. They frequently switch the lead, going into oxygen debt while in front, and recovering while drafting.

In the Olympic cycling time trials, where the pace is steady and predictable, equipment can make a huge difference in performance. Here, single racers or teams of four

compete against the clock at 1,000 meters, 4,000 meters and 100 kilometers. In the past few years, time trial bicycles have undergone a revolution in technology.

So called "funny bikes," introduced in 1984, were a radical departure from tradition. They have feather-light Kevlar disk wheels that cut the wind resistance of a normal wheel in half, as well as upturned "bull-horn" handlebars that put the rider in a sleek aerodynamic position and airfoil shaped tubes that streamline the air flow over the frame.

The bikes are designed with the same attention to detail as a jet aircraft. Using hidden cables, wing shaped handlebars, disk sprockets, tiny front wheels (that allow team members to draft closer), narrow 200 p.s.i. Kevlar tires weighing less than 1/4 pound each, strapless pedals that attach directly to the shoes and special aerodynamic components, the bikes can cut minutes from the time in 100 kilometers. Since 1984, cyclists have broken almost every time trial record in the world using the new bikes.

Designed by scientists in the U.S. and Italy, who performed extensive wind tunnel tests, the funny bikes have a dramatically lower wind resistance. In the 1984 Olympics the Italians and Americans topped the world in technology. Since then the other cycling countries have caught up, and dozens of manufacturers worldwide are now producing similar aerodynamic bicycles and components.

Now, in 1988, the Italians and Americans have once again introduced significant improvements in time trial bicycles. The U.S. team bikes, built by Mike Melton, Director of the Technical Center of Huffy Inc., weigh less than 16 pounds. The frames are made of advanced aerodynamic composite graphite tubes and weigh only 3.3 pounds. This airfoil shaped tubing, manufactured by True Temper, is stiffer and much lighter than steel.

Italian professional bike racer, Francesco Moser, recently pedaled more than 31 miles in one hour to break the world indoor record using a remarkable custom bicycle with an enormous 42-inch rear disk wheel and a tiny 24-inch front wheel. The huge rear wheel has a much lower rolling friction than a normal 27-inch wheel and the small front wheel cuts wind resistance and weight substantially. In combination with the American composite bicycle, Moser's strange machine may trigger a new round of exciting changes in cycling technology.



Chester R. Kyle, Ph.D., is a sports equipment consultant. Designer of 1984 Olympic bicycles and clothing for the U.S. cycling team. Member U.S. Olympic Sports Equipment and Technology Committee. Founder, International Human Powered Vehicle Association.



TO A RADAR GUN THEY LOOK EXACTLY ALIKE.

Forget the fact that the car on the left is a legendary performance car. And that the one on the right is a wagon.

A radar gun doesn't notice minor details like that. It focuses on only one thing: speed.

And from that point of view, the Porsche 944 and the Volvo 740 Turbo Wagon look remarkably similar.

In fact, in repeated quarter-mile tests, they came up with virtually identical numbers—both in elapsed time and miles-per-hour. In 0-60 tests, the

*BASED ON INDEPENDENT ACCELERATION TESTS. © 1988 VOLVO NORTH AMERICA CORPORATION

Volvo wagon actually came out ahead of the Porsche.* Which is no small feat for *any* car, much less a wagon.

It's no wonder *Road & Track* magazine called the 740 Turbo Wagon the closest thing to a five-door sports car.

Which all goes to prove that the Volvo 740 Turbo Wagon is something very rare indeed:

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The Insulin Factory

The pancreatic beta cell is a factory for the production of insulin. New investigative techniques give an unprecedented view of the hormone's manufacture and pathway to the blood

by Lelio Orci, Jean-Dominique Vassalli and Alain Perrelet

Every cell in the human body is a chemical plant. Among the many products manufactured for export are hormones: messenger proteins that carry instructions from their site of production by way of the bloodstream to other cells throughout the body, where they regulate a variety of functions. One hormone is insulin, whose primary role is to control the transport of glucose, the body's main energy source, from the bloodstream into the cells where it is burned. An insulin deficiency impairs the body's ability to get glucose into the cells. As a result glucose accumulates in the blood, leading to the condition known as diabetes—more specifically type I, or insulin-dependent, diabetes. Uncontrolled, diabetes can have devastating consequences for the eyes, kidneys and blood vessels, and it severely reduces life expectancy.

In the light of insulin's importance, it is of considerable interest to understand how this hormone is manufactured and exported to the bloodstream. For some 20 years our laboratory at the University of Geneva has been largely occupied with the study of the insulin factory. The investi-

gation bears on more than the manufacture, processing and secretion of insulin. Because insulin is a protein, a description of insulin production can serve as a model of the secretory pathway followed by many proteins in a variety of cells throughout the body.

Where does the body manufacture insulin? A partial answer to the question was found a century ago. In 1889 two German physiologists, Joseph von Mering and Oscar Minkowski, showed in a classic series of experiments that the removal of the pancreas—an abdominal gland that releases digestive enzymes into the gut—leads to diabetes. Further experiments carried out in the first quarter of this century indicated, however, that damage to the pancreas did not always lead to diabetes: as long as minute islands of distinctive cells, which did not contain digestive enzymes, were left intact, the disease was prevented. These islands had been discovered in 1869 by a German medical student named Paul Langerhans, and so they were known as the islets of Langerhans.

The mysterious factor preventing diabetes, which apparently arose in the islets, was named insulin from the Latin *insulae*, or islands. Only in 1921 was insulin actually isolated by Frederick G. Banting and Charles H. Best and their colleagues James J. R. Macleod and James B. Collip at the University of Toronto; the year 1922 saw the first use of pure insulin to treat a young diabetic.

By the early part of this century, then, production of insulin was localized to the islets of Langerhans. Although approximately a million islets are scattered throughout the pancreas, they make up only about 1 percent of the total pancreatic weight. In spite of this small presence, the islets have an important role in the control of metabolism: in addition to insulin they produce three other hormones—glucagon (a protein that counteracts

insulin and raises blood sugar), pancreatic polypeptide (which regulates the release of pancreatic digestive enzymes) and somatostatin (a protein that inhibits the release of all islet hormones).

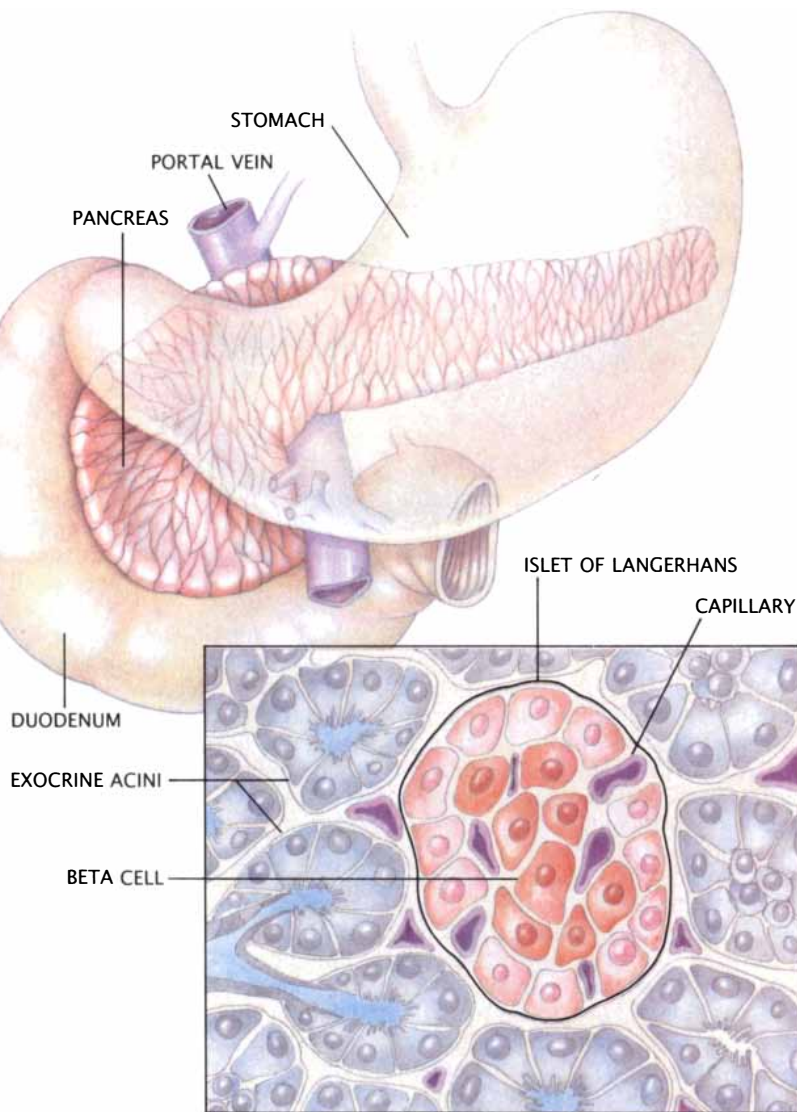
Each islet of Langerhans contains some 3,000 hormone-producing cells. By exposing islet sections to antibodies that specifically recognize the various islet hormones and by labeling each antibody with a fluorescent molecule, it has been shown that each hormone is manufactured in a different type of islet cell. The insulin-producing cells, known as beta cells, make up more than 70 percent of the islet-cell population and secrete insulin directly into the bloodstream. This mode of secretion is referred to as endocrine. Secretion by a duct (as the pancreas secretes its digestive enzymes into the gut) is referred to as exocrine.

Protein Synthesis

Synthesis of any protein begins in the cell nucleus with the activation of the stretch of DNA—the gene—that specifies the protein's composition. The gene is copied into a strand of another nucleic acid, RNA. The RNA in turn is processed into a form called messenger RNA, which is sent out into the cytoplasm of the cell. There it acts as the blueprint for the manufacture of proteins: it instructs small, dense bodies called ribosomes to assemble amino acids in a precisely defined sequence to build up the prescribed protein chain.

The protein secreted by the beta cells, insulin, consists of two separate amino acid chains, the A and B chains, linked by disulfide bridges. Precisely how this protein is assembled was unraveled in the 1960's through the pioneering work of Donald F. Steiner and his collaborators at the University of Chicago. They immersed the beta cells in amino acids that had been

LELIO ORCI, JEAN-DOMINIQUE VASSALLI and ALAIN PERRELET are professors of histology and embryology at the University of Geneva Medical School. Orci earned his M.D. at the University of Rome in 1964 and in 1966 went to the University of Geneva, where he is currently chairman of the department of morphology. Vassalli is a native of Geneva, where he completed his medical education in 1972. He then spent nine years at Rockefeller University, receiving a Ph.D. in biochemistry before returning to Geneva to take his present position. His hobbies include sailing and skiing. Perrelet also hails from Geneva, where he studied medicine and earned an M.D. in 1969. After a postdoctoral stint at Rockefeller, he returned to Geneva to his current position. He also maintains an interest in ornithology and botany.



PANCREAS is an abdominal gland tucked under the stomach. Much of it is dedicated to the production of digestive enzymes, which it secretes into the intestine by way of a duct; the process is known as exocrine secretion. Dispersed throughout the pancreas are the islets of Langerhans (*inset*), which contain the insulin-producing beta cells. Insulin is secreted not into a duct but into blood capillaries and thus into the general circulation; the process is known as endocrine secretion. The capillary blood is collected by the portal vein (*blue*) to be distributed throughout the body.

labeled with a radioactive isotope. The cells incorporate the amino acids into proteins, which can be traced by their radioactive tagging. It was then possible to separate, analyze and identify the tagged proteins by subjecting them to a chemical process called chromatography. It became obvious that insulin was actually synthesized as part of a larger protein—a precursor that Steiner and his co-workers termed proinsulin. From Steiner's investigation and the work of many others who have studied the manufacture of proteins destined for secretion, the following general picture emerged.

The ribosomes actually do not synthesize insulin or even proinsulin but

a larger precursor molecule called proinsulin: proinsulin with a short additional amino acid sequence. The ribosomes that assemble proinsulin are attached to the exterior of an elaborate network of flattened sacs lying outside the cell nucleus. The sacs, or cisternae, feed into one another, so that the network is actually one continuous, convoluted pouch: the endoplasmic reticulum. Because the ribosomes give the endoplasmic reticulum a bumpy appearance, the network is often termed the rough endoplasmic reticulum, or RER.

The pre-sequence of proinsulin directs the protein from the ribosome across the RER membrane. As soon

as the preproinsulin reaches the lumen, or interior, of the RER, the pre-sequence is detached by cleaving enzymes manufactured by the ribosomes for this purpose. The enzymatic cleavage of preproinsulin leaves within the RER proinsulin, a molecule that encompasses the amino acid chains of insulin and a connecting peptide, or C peptide, that links the end of one chain to the beginning of the other. Eventually, as we shall explain below, the C peptide will be cleaved away to yield insulin [see illustration on page 89].

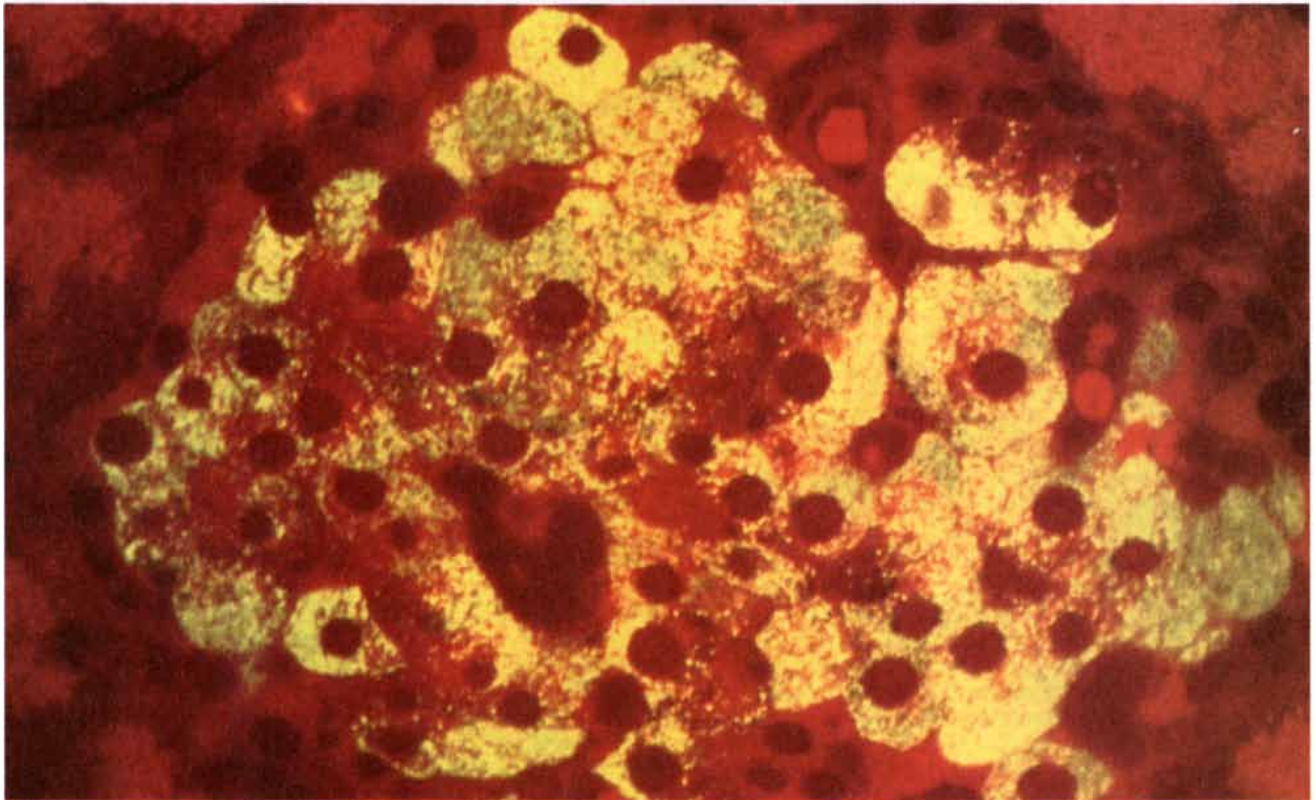
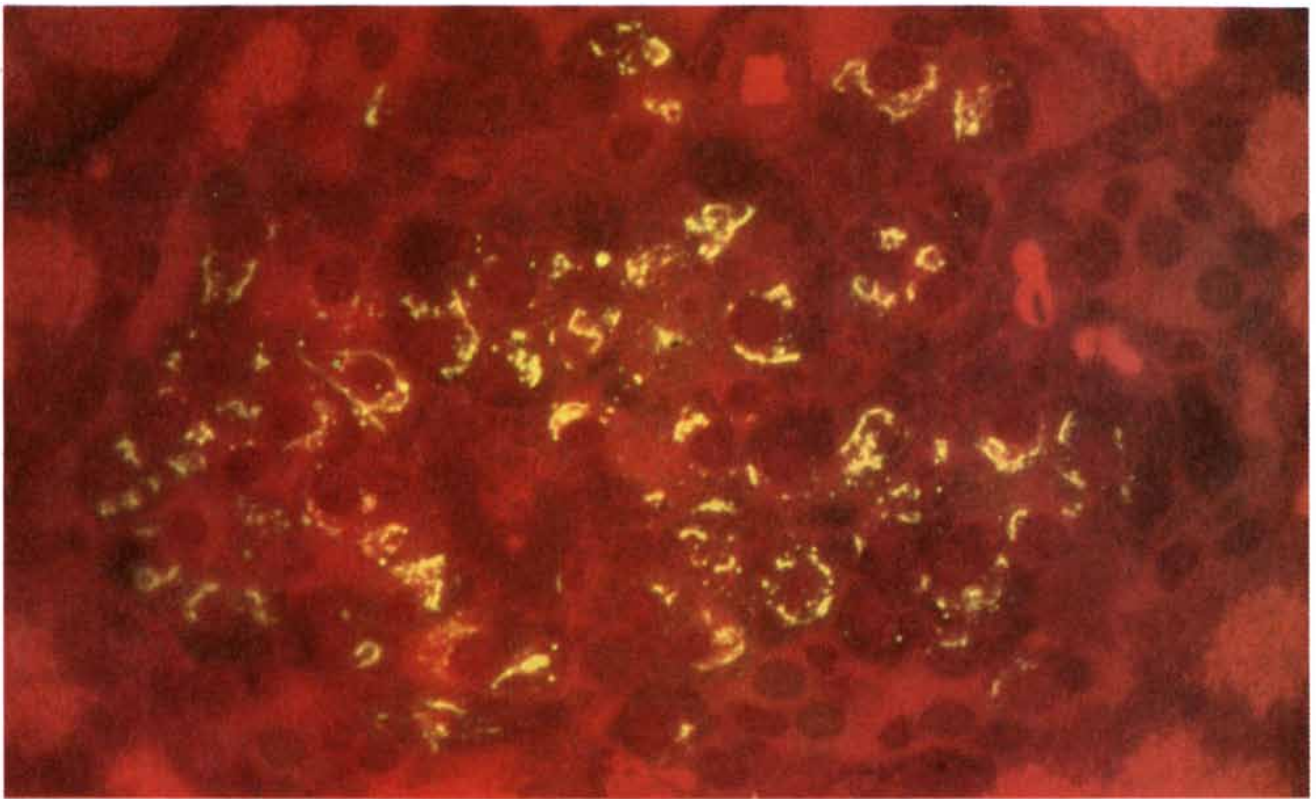
Autoradiography

To determine the exact location of the proteins within the beta cell after they are synthesized on the RER, radioactive tagging must be combined with the technique of high-resolution autoradiography, pioneered in the 1960's by George E. Palade and Lucien G. Caro, then at the Rockefeller Institute for Medical Research. As before, tissues are immersed in radioactively tagged amino acids. At various times thereafter cells are sliced into thin sections. Each section is covered with a sensitive photographic emulsion so that the position of the radioactive isotopes can be superposed on the structural details of the cell as revealed by the electron microscope. At each stage, once again, the actual composition of the protein is determined by chemical analysis.

We have applied this technique extensively to trace the insulin-synthesis pathway. Autoradiography reveals that immediately after five minutes of labeling most of the tagged molecules are in the RER. Chemical analysis of these molecules by chromatography shows that at this time they are predominantly proinsulin, which again indicates that preproinsulin is cleaved into proinsulin almost as fast as it is formed.

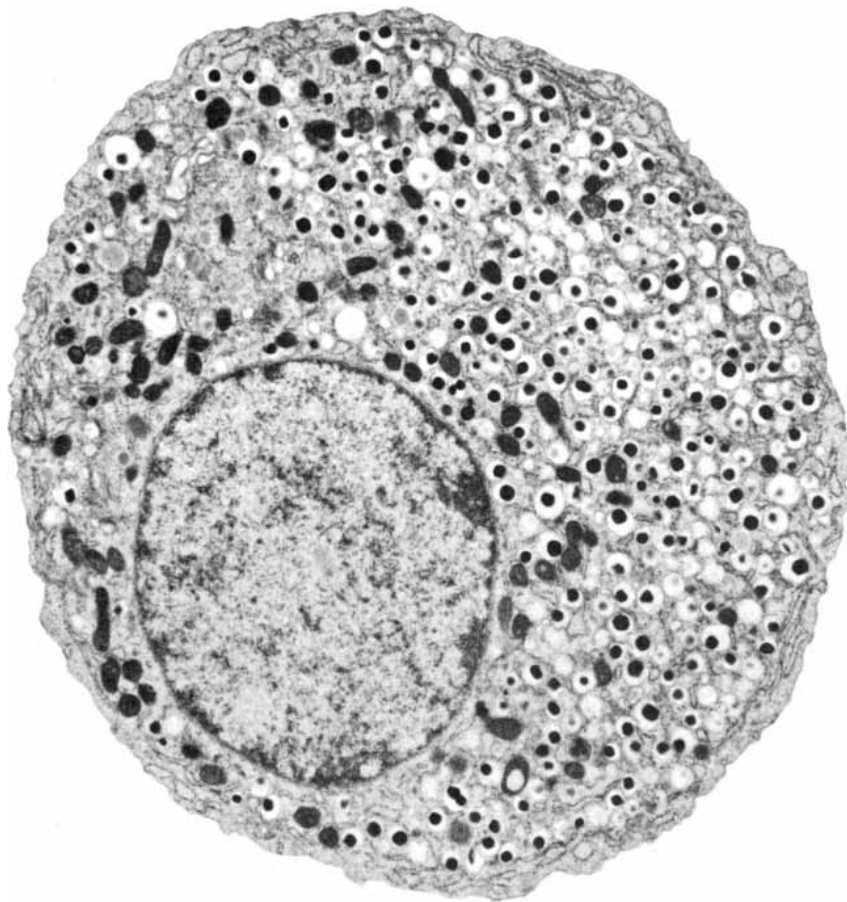
Fifteen minutes later autoradiography shows that the majority of the tagged molecules are found in another region of the beta cell, the Golgi complex. We shall describe the function of the Golgi apparatus in detail below. For now, we point out only that the Golgi, like the RER, is composed of cisternae but that these cisternae are not adorned by ribosomes or extensively connected to one another; instead they are arrayed somewhat like a stack of pancakes.

Continuing to trace the radioactive isotopes, one discovers that about an hour after tagging they have moved past the Golgi complex and are found



INSULIN FACTORY is in the pancreas, where the specialized beta cells are clustered in small regions called the islets of Langerhans. The two photomicrographs are of adjacent tissue sections from a single islet. Each slice, enlarged here 1,100 times, contains numerous sectioned beta cells; their nuclei are the dark red circular patches. One slice (*top*) was exposed to a monoclonal antibody that binds to proinsulin, a precursor of insulin. The antibody was tagged with a fluorescent yellow dye.

The glow reveals that the proinsulin is concentrated around the beta-cell nucleus, suggesting that it resides in the Golgi apparatus: an organelle that sorts proteins and routes them to different destinations in the cell. The other slice (*bottom*) was exposed to a fluorescent antibody directed against insulin. Insulin is seen to be much more widely distributed, indicating that it is primarily associated with the secretory granules that carry the hormone from the Golgi to the cell membrane.



BETA CELL loaded with insulin is enlarged 6,500 diameters in this electron micrograph. The numerous circular vesicles containing dark blobs are the uncoated secretory granules in which insulin is stored, ready to be released from the cell if the level of glucose in the bloodstream increases. The parts of the beta cell that are not involved in insulin manufacture are not easily seen in this micrograph.

in another component of the beta cell: small, round vesicles that are dispersed between the Golgi complex and the cell membrane. Analysis of the contents of these secretory granules, as they are called, shows that by now the mature insulin has been generated; the connecting peptide has been cleaved from the proinsulin, leaving the two-chained insulin molecule.

The Golgi Region

Where exactly has the transformation from proinsulin to insulin taken place? Good candidates are the Golgi complex and the secretory vesicles, and so it is prudent to back up and take a closer look. When this region is examined in suitably enlarged electron micrographs, two distinct types of secretory granules are seen in more or less close proximity to the Golgi stack. The first type are termed coated secretory granules because of the striking coat of bristles covering their outer membrane. The bristles themselves are made of a

protein called clathrin, which is often associated with membrane movement (and in particular with the pinching off of membrane segments, which we shall describe below). Coated secretory granules contain a moderately dense protein filling, which is observed to be uniform over the entire granule. They are seen in close proximity to the Golgi apparatus and sometimes may actually be seen

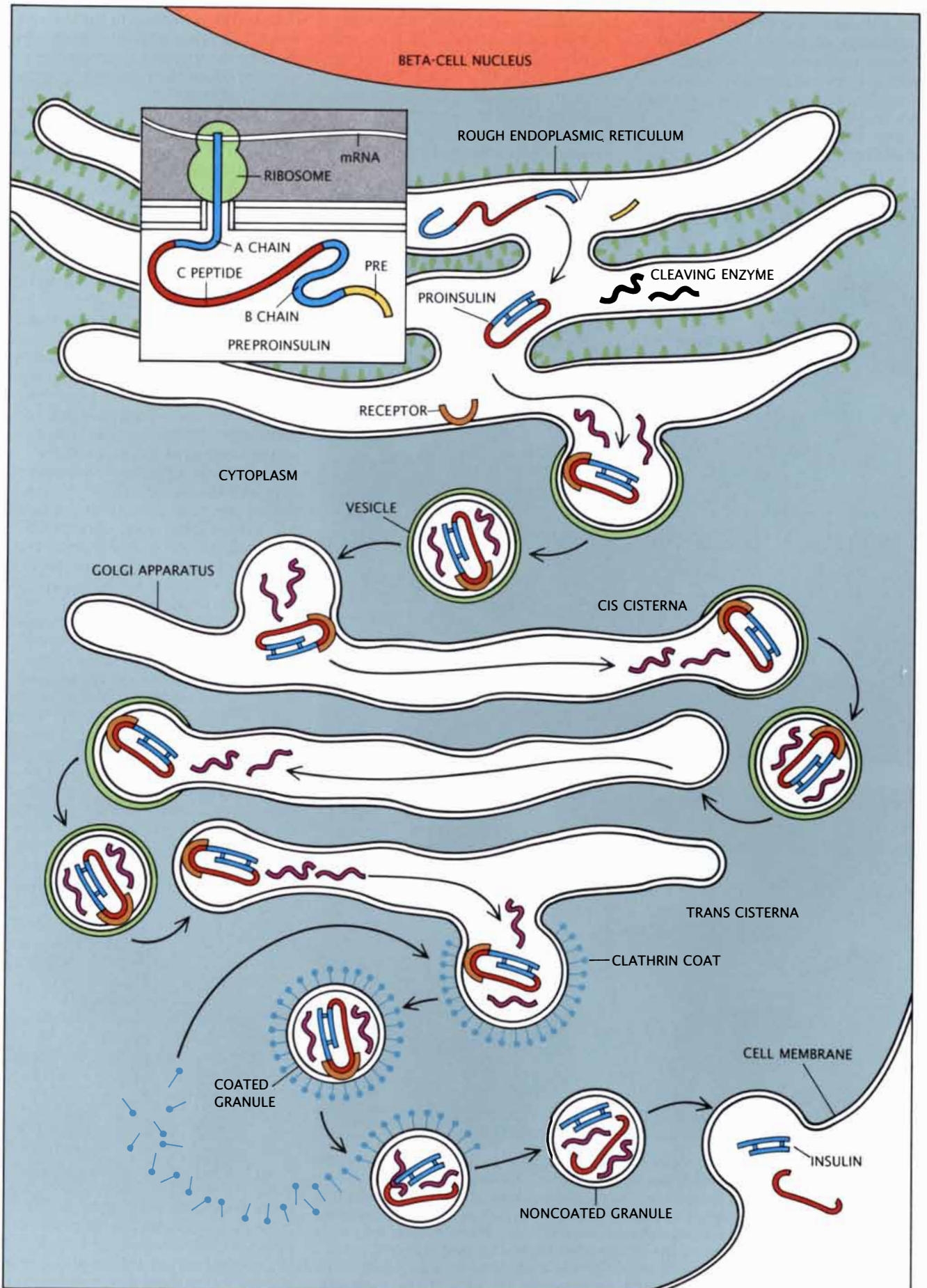
ASSEMBLY LINE for the production of insulin begins in the beta-cell nucleus, where the gene encoding the precursor molecule preproinsulin is transcribed into RNA. Messenger RNA is exported into the cytoplasm; here it instructs ribosomes docked at the rough endoplasmic reticulum (RER) to assemble amino acids to form preproinsulin. The pre-sequence (*yellow*) is probably cleaved off as preproinsulin passes into the RER, leaving proinsulin, which is composed of the amino acid sequences that will form insulin (*blue*) linked by a connecting peptide, or C peptide (*red*). Proinsulin, probably bound to receptors (*brown*), and cleaving enzymes (*purple*) are transferred in small vesicles to the *cis*, or near, side of the Golgi apparatus. They move to the end of the first cisterna, or Golgi sac; the end buds off to form a vesicle that moves to the next cisterna and fuses with it. These vesicles bear a distinctive membrane coat (*green*). When the *trans*, or far, side of the Golgi is reached, a vesicle coated with the protein clathrin (*blue bristles*) pinches off to become a coated secretory granule. In the coated granule, cleaving enzymes start to remove the C peptide from the proinsulin molecule to yield insulin. This process is accompanied by acidification of the granule's content and shedding of the clathrin coat; the result is the formation of noncoated granules, which contain mostly insulin to be released at the cell membrane.

pinching off from a dilated cisterna.

The second type of granules are far more abundant, and these granules are found scattered throughout the cytoplasm of the beta cell. Their protein filling is denser than that of the coated granules and is separated from the granule membrane by a clear halo. Unlike the first granule type, these have no clathrin coat, whence their name: noncoated granules. The fact that the coated granules are in close proximity to the Golgi cisternae and are occasionally seen to bud off from them, whereas most noncoated granules are situated farther from the Golgi stacks, suggests that the coated granules are precursors of the noncoated ones.

This suspicion has been confirmed by a number of experiments. Autoradiography shows that the radioactive proteins peak in the coated granules approximately 30 minutes before they peak in the noncoated ones. Furthermore, chemical analysis has shown that at the time the radioactive proteins peak in the coated granules, about half of the proinsulin has been converted into insulin. In other words, it appears that the conversion of proinsulin into insulin is linked to the coated granules.

Recently, in a series of crucial experiments carried out with Ole Madsen of the Hagedorn Research Laboratory at Gentofte in Denmark and Max Storch of the University Medical Clinic in Freiburg, West Germany, we have been able to demonstrate directly that the coated granules are the site of proinsulin-into-insulin conversion. Our experiments combine the high magnification of electron microscopy with precise labeling. An antibody directed against proinsulin is linked to very fine gold particles, which are electron-opaque and so stand out sharply in electron micrographs [see illustration on page 92]. When beta cells are sectioned and the slices are exposed to



the gold-labeled antibodies, two compartments of the cell are found to be rich in proinsulin: the Golgi stack and the coated granules. Noncoated granules are found to be extremely low in proinsulin.

The argument has recently been made airtight by a second experiment,

very similar to the previous one except that the antibody is specific for insulin rather than proinsulin. This experiment reveals that insulin is absent from the Golgi stack, is detectable in small amounts in the coated granules and is most abundant in the noncoated granules. The coated granules must

then be the primary site for the conversion of proinsulin into insulin; by the time they become noncoated granules the conversion process is essentially complete.

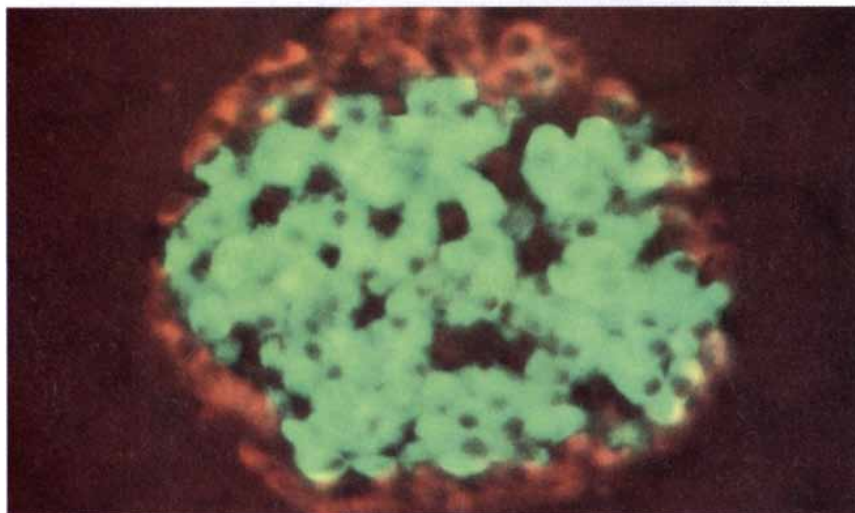
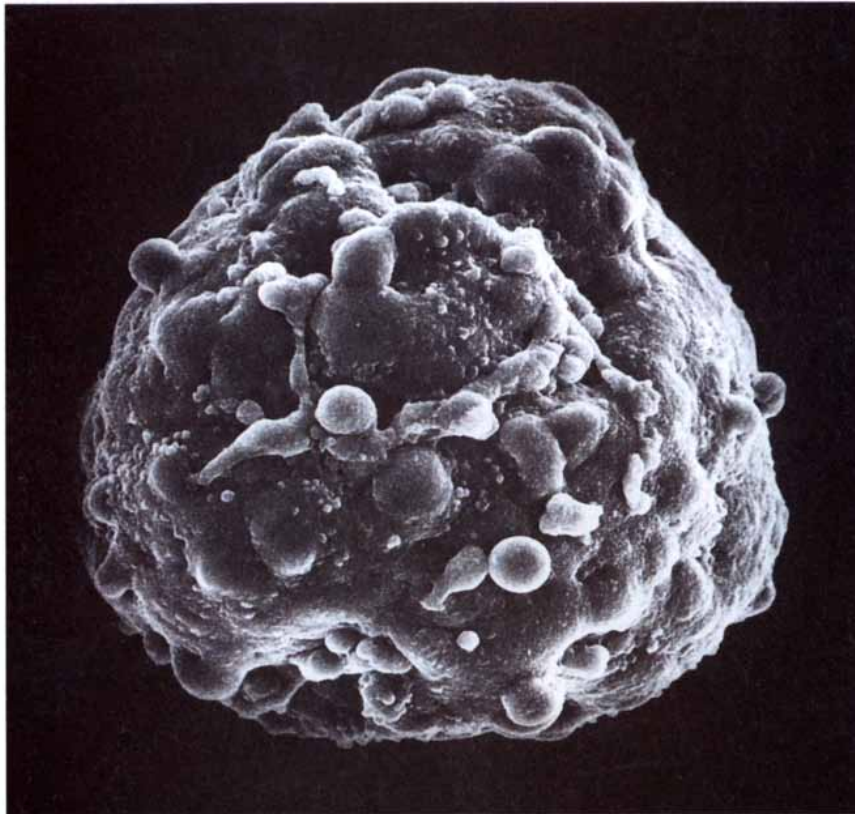
Although the Golgi cisternae themselves contain no insulin, passage through the stack must be a critical stage in the entire process, because the Golgi apparatus funnels proinsulin into the coated secretory granules, where the actual conversion into insulin takes place. The role of the Golgi apparatus becomes clearer when one considers how proteins are transported across this organelle.

There is a steady flux of small vesicles that bud off from the endoplasmic reticulum and carry a wide variety of newly synthesized proteins toward the Golgi stacks. On reaching a stack, the vesicles fuse with the cisternal membrane nearest the RER. (This side of the Golgi stack is known as the *cis* pole, from the Latin for "on the same side as.") On the far side of the stack (called the *trans* pole, from the Latin for "across"), the Golgi cisternae display bulbous or dilated extremities, which bear clathrin bristles and in which a dense protein content is often visible; these are the outpocketings that pinch off to become the coated secretory granules.

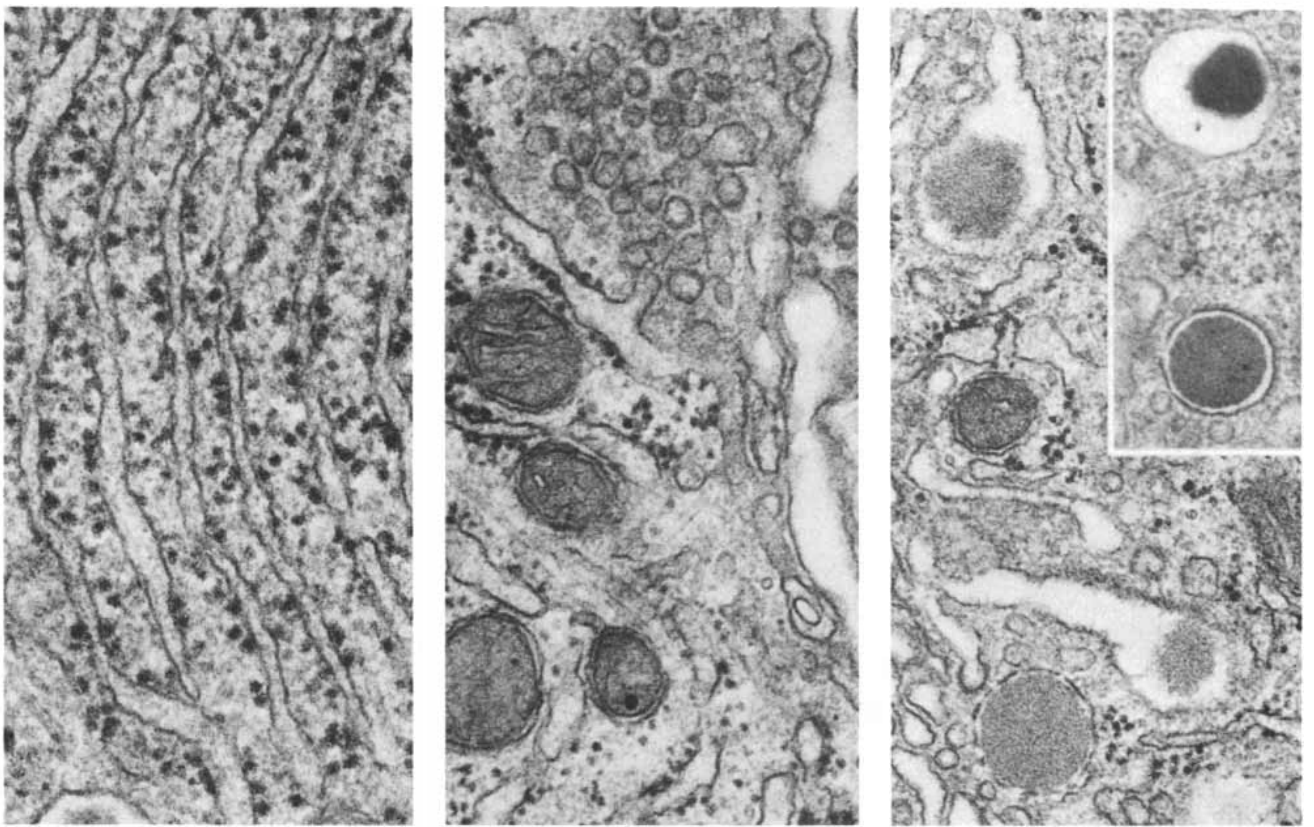
The mechanism by which proinsulin, as well as other proteins manufactured in the RER, travels within the Golgi stack from the *cis* to the *trans* pole is currently the subject of intensive research. Recently, in collaboration with James E. Rothman of Princeton University, we have observed that the transfer of protein from one Golgi cisterna to the next is carried out by "microvesicles," which are similar to the vesicles that carry proteins from the RER to the *cis* pole of the Golgi stack. The current model of the intra-Golgi transport is that the microvesicles pinch off from the end of one cisterna, travel to the next and fuse with it; that process is repeated until the *trans* pole is reached. Like the coated secretory granules, the microvesicles also have a coated membrane, but the coat is not clathrin; neither its function nor its composition is at present understood.

Postal Sorting

As we have mentioned, the Golgi body receives a wide variety of proteins from the RER, each of which must then be routed to a precise destination within the cell. To get an idea of the complexity of this process, one should bear in mind that in addition to

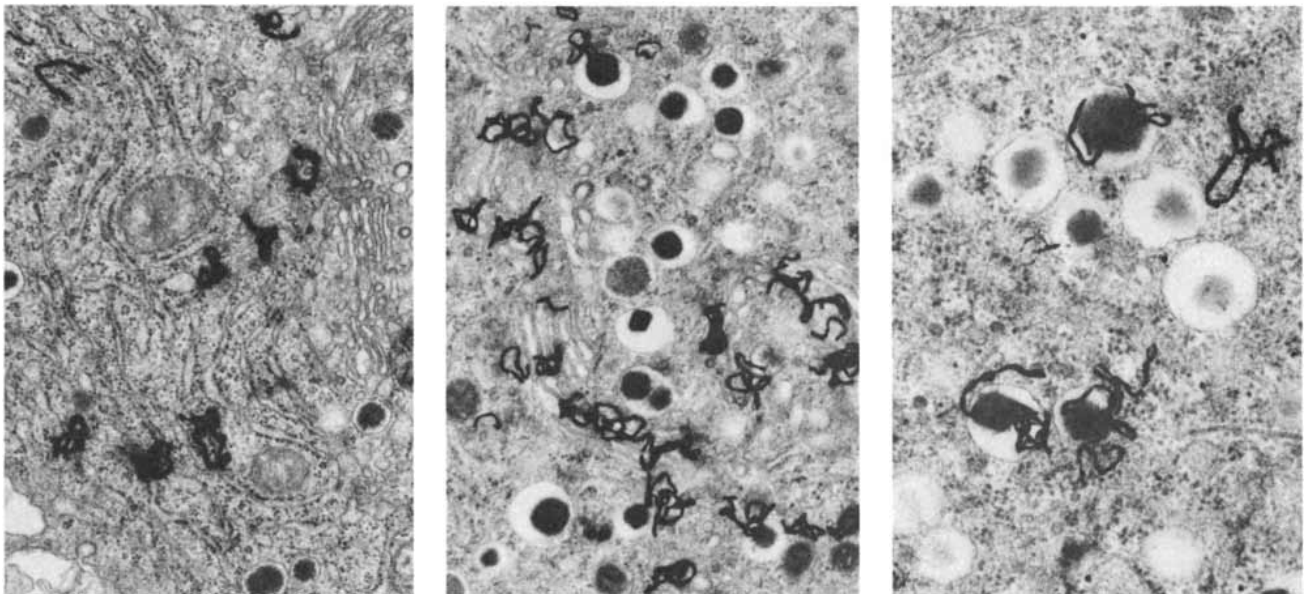


ISLET OF LANGERHANS appears as an irregular ovoid body in a scanning electron micrograph (*top*), enlarged 960 diameters. About a million islets are scattered throughout the pancreas. Cells in the islets produce several hormones, including glucagon and insulin. In the photomicrograph (*bottom*, 525 diameters) fluorescent antibodies (*green*) directed against insulin show that insulin-containing beta cells characteristically occupy the center of the islet. Antibodies (*red*) directed against glucagon show that the glucagon-producing cells are at the islet's periphery. Cells producing pancreatic polypeptide and somatostatin are also at the periphery.



ELECTRON MICROGRAPHS show the successive regions of the insulin factory magnified 81,400 times. The RER, visible in the panel at the left, consists of the endoplasmic reticulum (*elongated sacs*) adorned by ribosomes (*small dense bodies*). Transfer of proinsulin to the Golgi stacks is accomplished by small

vesicles that bud from the RER and then merge with the Golgi cisternae (*middle panel, top*). In the panel at the right a coated granule (*dense body at bottom*) has budded off from a dilated *trans* cisterna of the Golgi apparatus. Inset in the right-hand panel shows a coated and a noncoated granule in more detail.



AUTORADIOGRAPHY locates radioactively labeled proteins in electron micrographs. Beta cells are supplied with a radioactively labeled amino acid, which they incorporate into proinsulin. A photographic emulsion consisting of silver bromide crystals in gelatin is then placed over thin tissue sections to record the positions of the labeled molecules at a given time. Photographic development of the emulsion yields the black, spaghetti-like grains at the site where the emulsion has been

exposed to radioactivity. Immediately after the cells have been exposed for five minutes to the labeled amino acids, most of the newly synthesized radioactive proteins are found in the RER (*left*). Ten minutes later most are found in the Golgi region (*middle*); one hour after labeling most of the labeled amino acids are in the secretory granules (*right*). Chemical analysis shows that the processing of proinsulin to insulin takes place between the Golgi apparatus and secretory-granule stations.

insulin, whose eventual destination is the bloodstream, other proteins are sent to the beta-cell membrane and still others are routed to various organelles within the beta cell. What is more, some of the proteins destined for the cell membrane seem to reach their target continuously, without the need for any specific stimulus. (Such proteins are referred to as "nonregulated" or "constitutive.") Other proteins, such as insulin, are referred to as "regulated" because they are secreted only when an adequate stimulus—

for instance glucose—reaches the beta cell. The Golgi is responsible for keeping track of both types of proteins.

For this addressing system to work properly, it is believed the Golgi apparatus is equipped with receptors that are specific for regulated proteins. Although they have not been directly observed, we have hypothesized that such receptors bind proinsulin to the inner side of the Golgi membrane and transport the hormone to the *trans* cisterna. Once the proinsulin has been collected there, the dilated end of the

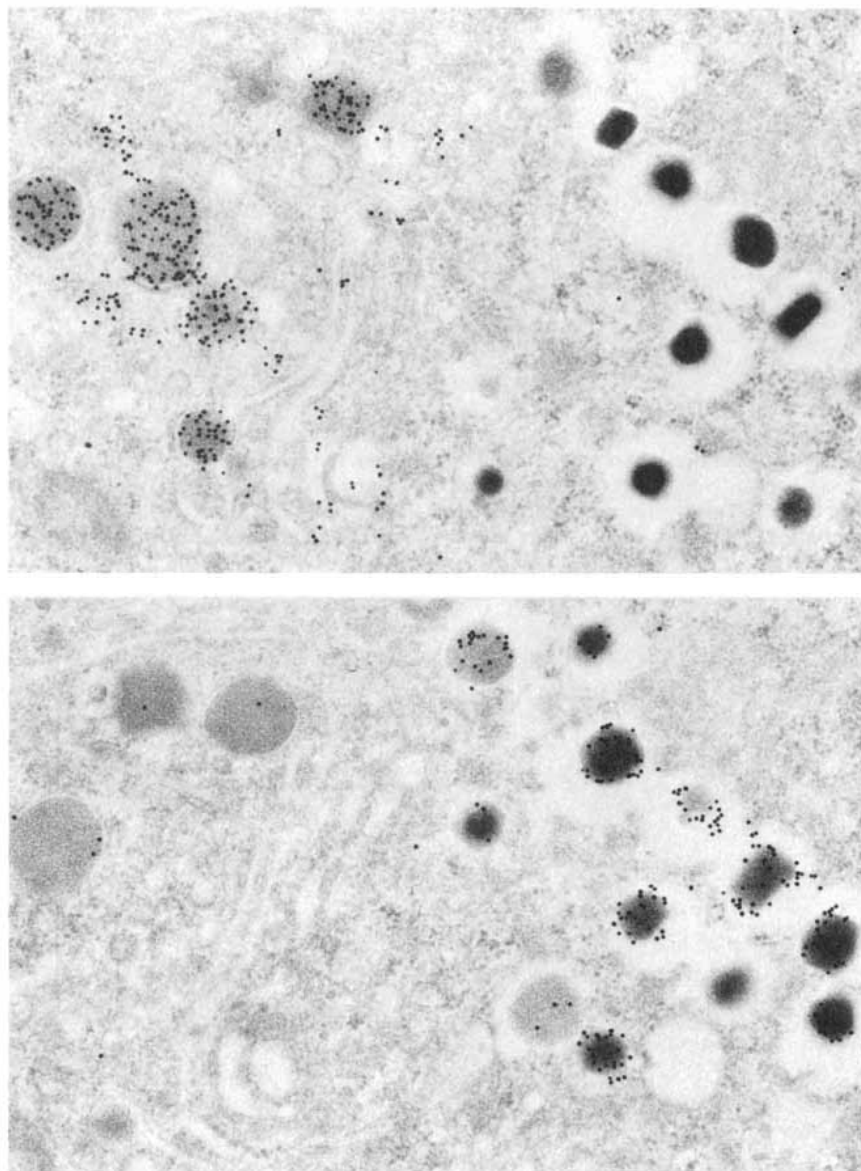
cisterna pinches off to become a coated secretory granule. This hypothesis is based on the fact that electron microscopy shows proinsulin to be localized along the inner side of the Golgi cisternae; in the secretory granule, however, the proinsulin is distributed uniformly through the granule, which may indicate that the proinsulin has detached itself from the putative receptors and thus from the granule membrane.

Hsiao-Ping H. Moore, Michael D. Walker and Regis B. Kelly of the University of California at San Francisco and Frank Lee have recently cast a very interesting light on the problem of Golgi sorting. They cultured endocrine cells from the pituitary gland. Into these cells, which normally secrete the hormone adrenocorticotropin (ACTH), they introduced the DNA sequence that encodes proinsulin. The pituitary cells were thus "tricked" into manufacturing proinsulin along with ACTH. Moore's group found that ACTH, like proinsulin, is secreted in a regulated way. In collaboration with Moore, we have subsequently discovered ACTH and insulin in the same pituitary-cell secretory granules. In other words, the Golgi body did not distinguish between proinsulin and ACTH; it routed them to the same destination. This indicates that cells other than beta cells are also equipped with receptors that sort proteins to secretory granules. It also strongly suggests that a given receptor can recognize a number of regulated proteins.

The crucial problem remaining today is to identify the putative receptor in the Golgi stacks and find the exact site on the protein to which it binds. Collaborating with Sharon K. Powell, Charles Craik and Moore, we have taken a first step in this direction. By modifying the DNA that encodes proinsulin and then injecting the altered DNA into the beta cell, we can make the cell produce "mutant" proinsulin. We have found that the deletion of the C-peptide sequence from proinsulin does not affect the correct sorting of proinsulin to the secretory granules. We are currently investigating the deletion of other parts of the proinsulin molecule to determine exactly which domain (or domains) controls the sorting process.

Regulated vs. Nonregulated

One might ask whether the nonregulated, constitutive proteins mentioned above follow the same pathway as proinsulin. In collaboration with Moore's group we have directly ob-



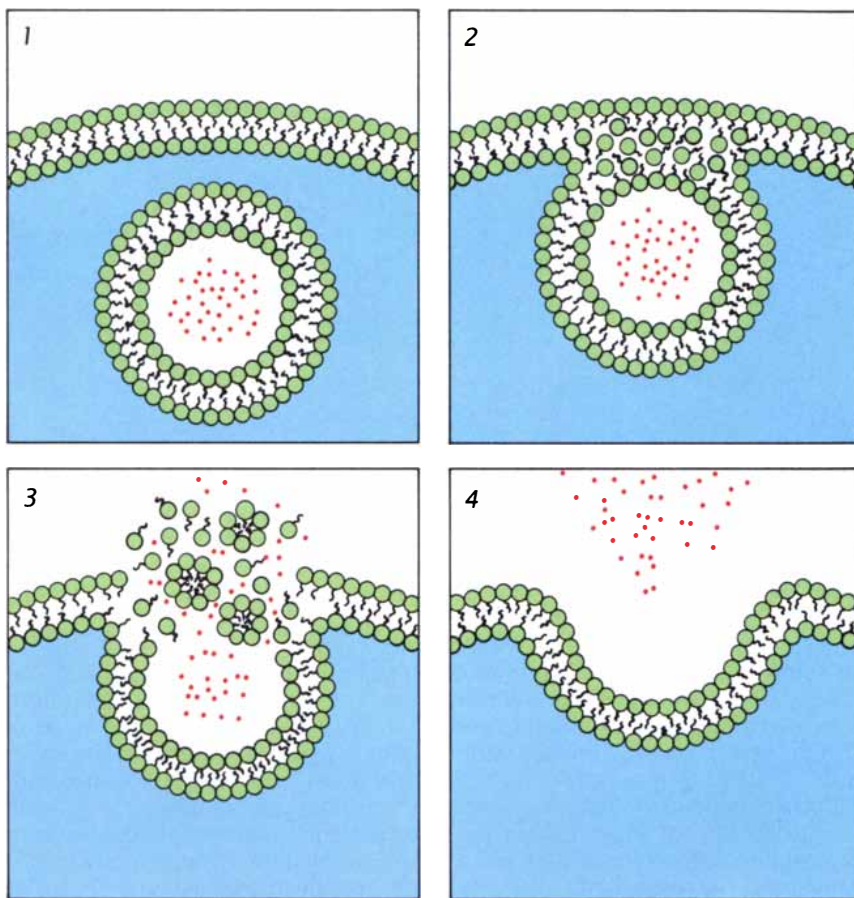
EXACT SITE at which the hormone proinsulin is converted into insulin was identified in these electron micrographs by labeling two consecutive thin sections of the same beta cell with gold-labeled antibodies (*small black dots*), which are in turn directed against proinsulin (*top*) and against insulin (*bottom*). Proinsulin is found only in the Golgi complex and coated secretory granules; insulin is most abundant in the noncoated granules and appears in small quantities in coated granules. One concludes that proinsulin-to-insulin conversion starts in the coated granules and proceeds as they become noncoated granules. The magnification is 39,400 diameters.

served the route followed by one protein, hemagglutinin, which is exported to the cell surface constitutively. Hemagglutinin is synthesized by the beta cell when it has been infected with an influenza virus or, in commoner language, given a cold. The hemagglutinin is then transported to the cell membrane, where it is incorporated into burgeoning new viruses that go on to infect other cells.

By simultaneously localizing proinsulin and hemagglutinin, we were able to pinpoint the exact site where the regulated and the nonregulated secretory pathways diverge. Whereas the two proteins coexisted in most cisternae of the same Golgi apparatus, hemagglutinin was not found in the dilated part of the *trans* cisterna where proinsulin concentrates. Afterward hemagglutinin was found not in the coated granules but in smooth, clear vesicles that move to the cell membrane. This experiment therefore directly identifies the *trans* Golgi cisterna of the beta cell as the site where proinsulin is sorted from the constitutive protein hemagglutinin.

We now return to insulin manufacture. As discussed above, the final generation of insulin from proinsulin in the coated granules requires the cleaving away of the connecting peptide. Consequently for every insulin molecule created, a molecule of C peptide is generated and carried along with insulin in the secretory granules. It is also likely that the cleaving enzymes, which are synthesized by ribosomes on the RER, themselves follow the same route as proinsulin from the RER through the Golgi stacks in order to reach the coated secretory granules. If the cleaving enzymes are continuously present, why is the proinsulin cleaved into insulin only when it reaches the coated granules? In other words, why are the cleaving enzymes activated only at that late stage?

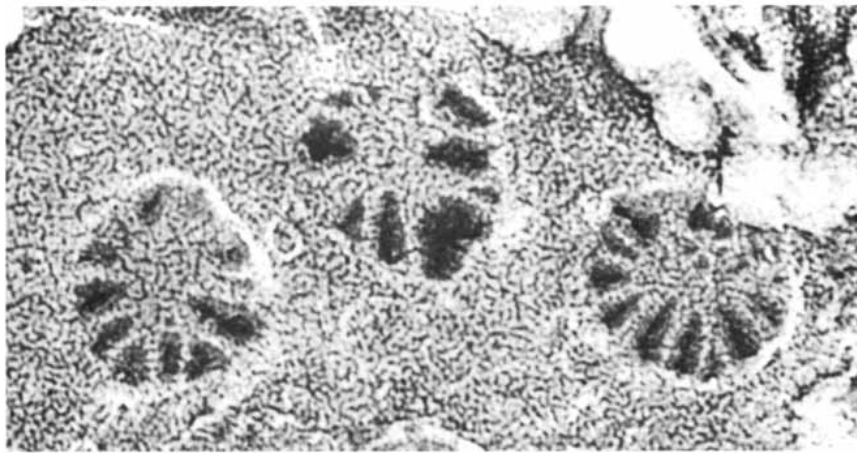
In collaboration with Richard G. W. Anderson of the University of Texas Health Science Center at Dallas, we have recently come up with what may be the answer to this question. Our experiments revealed a gradient of increasing acidification from the coated to the noncoated granules and that the gradient is inversely correlated with the amount of proinsulin found in the granules. This strongly suggests that one important factor in activating the cleaving enzymes is the progressive acidification of the interior of the coated granules. Indeed, one of the enzymes thought to be involved in proinsulin cleavage is most active, at least in the test tube, at acidic pH. Fur-



SECRETION OF INSULIN requires that the membrane of the noncoated secretory granule fuse with the beta cell's outer membrane, as is shown here. The insulin is thus delivered across the cell membrane without ever breaking it, maintaining the integrity of the cell. The release of insulin in this way is termed exocytosis.



EXOCYTOSIS is captured in an electron micrograph. One secretory granule, enlarged here 71,000 diameters, is about to fuse with the beta-cell membrane and release insulin into the space surrounding the cell (*left*). Another granule has opened out and insulin is being secreted (*right*). Each secretory granule liberates some 800,000 insulin molecules outside the cell. The continual fusing of granules with the cell membrane would enlarge the beta cell's surface if material were not recycled; recycling takes place as patches of the cell membrane fold inward and bud off to form vesicles that are transported into the cell. This process is termed endocytosis.



ROSE WINDOWS resembling those found in a medieval cathedral are the pores in the thin endothelial-cell walls of blood capillaries. To enter the bloodstream after leaving the beta cell, insulin may have to pass through the wedge-shaped slits in these diaphragms (here enlarged 270,000 diameters in an electron micrograph), which are composed of thin fibrillar spokes radiating from a central mesh.

thermore, a number of alkaline molecules, such as ammonium chloride, which accumulate in the granules and thereby neutralize the contents, inhibit the cleavage of proinsulin.

Up to this point we have examined the production of insulin from preproinsulin and proinsulin as these proteins pass through the RER, the Golgi stacks and the coated granules. We now turn to the actual secretion of the freshly produced insulin.

Insulin Secretion

Together with the C peptide and a small residue of uncleaved proinsulin, insulin is stored in the mature non-coated granules, ready to be secreted in response to an appropriate stimulus, such as an increase of the glucose concentration in the blood. Not all of the hormone manufactured by the beta cell will be ultimately secreted, however. En route to the cell membrane where secretion takes place, some of the granules will fuse with lysosomes, the ubiquitous scavenger organelles of cells. That leads to the total breakdown of insulin in these granules. No rationale is known for this seemingly uneconomical process, in which a fraction of the synthesized insulin is destroyed in the very cell of its origin. Whether lysosomal degradation serves to regulate the amount of the hormone available for secretion or is a method for disposing of defective granules remains to be seen.

For insulin to be delivered into the bloodstream there still remains a formidable task: the passage of the hormone across two impermeable barriers, the granule membrane and the

membrane of the beta cell itself. Nature's solution to this problem is both simple and elegant. With the electron microscope one sees that as the secretory granule comes into close proximity with the cell boundary, the granule membrane fuses with that of the beta cell. In this process, called exocytosis, the granule membrane is made part of the cell membrane and the content of the granule is released into the bloodstream. The remarkable aspect of the membrane fusion is that it allows insulin to be secreted while maintaining the continuity of the beta-cell membrane at all times. All cells that secrete proteins do so by means of exocytosis.

The reader may have recognized that sustained fusing of the granule membranes to the cell membrane would result in continual enlargement of the cell surface—unless another process existed to counteract it. In fact, the very act of exocytosis activates the reverse process, endocytosis: segments of the cell membrane invaginate and pinch off to form endocytic vesicles, which are dispatched to various sites in the cell for recycling or degradation.

The final question that remains to be answered is how the insulin, after secretion into the extracellular space, gets into the bloodstream to be distributed to its various target cells around the body. The beta cells in the islets of Langerhans are surrounded by an abundance of blood capillaries. To reach the bloodstream, insulin must cross the thin capillary walls, or endothelium. In endocrine glands, such as the pancreas, the endothelial cells are pierced by numerous circular pores or fenestrations. Each

pore is covered by a thin diaphragm.

In collaboration with Elaine Bearer of our group, we have used an improved freeze-fracture technique in conjunction with electron microscopy to observe the endothelial pores in great detail. This procedure makes possible a full frontal view of the surface of the cell membrane. We find that each pore resembles the beautiful rose window of a cathedral: the diaphragm is composed of an array of thin fibrils radiating from a central mesh to delineate wedge-shaped channels. It is appealing to envision this rose window as a dynamic regulator of hormonal traffic across the capillary walls.

In conclusion, we have described the intracellular journey of insulin from the site of its synthesis, the rough endoplasmic reticulum, to the site of its release, the beta-cell membrane. Throughout this journey the critical roles played by the Golgi apparatus and the clathrin-coated secretory granules in the sorting and processing of proinsulin have been evident. Many questions remain unanswered, but the information accumulated in recent years on the general layout and assembly line of the insulin factory has opened the way to a fuller understanding of hormone secretion and its regulation in molecular terms.

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A Close Look at Halley's Comet

The armada of spacecraft that flew by the comet two years ago provided spectacular images and data that continue to yield quantitative information about the nature of the faithful visitor

by Hans Balsiger, Hugo Fechtig and Johannes Geiss

The month of March, 1986, will long be remembered for some of the most spectacular rendezvous in the history of planetary science. In that month an armada of space probes (two of them Japanese, two Soviet and one European) encountered Halley's comet. Their aim was ambitious: to analyze for the first time the gases and dust in the immediate vicinity of a comet and to photograph its nucleus—the tiny solid body hidden inside the comet's head.

Halley's comet is not only the most famous and historically the most important of comets but also one of the best-suited to such encounters. In contrast to comets making their first recorded appearance, Halley's comet has an orbit that is sufficiently well known for a probe to be directed close

enough to the nucleus to obtain good data. Moreover, the strong emission of gas and dust from the comet suggests that it retains much of its original icy and dusty components. In other words, the comet probably consists of pristine material, and so it reflects the conditions prevailing when the solar system was born. Comets having shorter mean periods than that of Halley's comet—which is just under 77 years—are more frequently subjected to erosion by solar radiation as they pass near the sun. They are therefore less likely to offer such a window on ancient times.

The undertaking was a complete success. While the Japanese probes *Sakigake* and *Suisei* made measurements in the region of the "shock front" ahead of the nucleus, the Soviet probes *Vega-1* and *Vega-2* penetrated to within 9,000 kilometers of the nucleus and the European probe *Giotto* actually approached to within 600 kilometers. The great effort and financial investment of these projects paid off: the investigators, from all over the world, made on-the-spot measurements of the physical and chemical processes that account for the spectacular phenomena accompanying a comet on its journey through the inner region of the solar system. Over the past two years the scientific community has digested and analyzed the large body of data that was acquired.

Our discussion will be based primarily on the results obtained by *Giotto*, since we know these results best and since this spacecraft flew closest to Halley's nucleus. The data from the other space probes are equally important for obtaining a complete picture of the cometary phenomena, because those probes produced data complementary to those of *Giotto*. We shall therefore include their findings in the discussion wherever they are needed.

A prerequisite for the success of the

Giotto mission was a flight path that took the probe as near as possible to the nucleus while ensuring that neither the probe itself nor its stability was adversely affected by gas or dust. The calculated risks taken by the planners of the *Giotto* mission proved to be worthwhile. It was during the few minutes just before *Giotto's* closest approach that some of the crucial measurements were made. So close to the nucleus, the molecules detected in gas and dust were to a large extent preserved in their original form, unchanged since the comet's formation.

In a sense, then, the flight of *Giotto* represented a path back through time to the epoch when comets were born. How and when were they formed? According to prevailing theory, the birth of the solar system, including the comets, began about 4.6 billion years ago, when the universe was about two-thirds its present age. Interstellar matter—probably in the form of a dark molecular cloud—reached a sufficient density to initiate a gravitational collapse. Angular momentum was conserved in the collapse, so that a rotating disk of matter emerged. The sun and the planets were gradually built through the process of accretion.

A widely accepted scenario for the origin of the comets was developed in 1950 by the Dutch astronomer Jan Oort. The orbits of the comets that have long periods and the amounts of gas they emit when they are close to the sun led Oort to postulate that these bodies, which are the smallest in the solar system, originally formed in large numbers in the region of the outer planets, beyond the orbit of Jupiter. Many of the comets later escaped into interstellar space as a result of perturbations of their orbits by the outer planets. A number of the comets, however, were concentrated in a cloud lying between .5 light-year and two light-years from the sun, at the edge of the region dominated by the sun's gravitational attraction.

HANS BALSIGER, HUGO FECHTIG and JOHANNES GEISS worked together on the planning, execution and data analysis of the *Giotto* mission. Balsiger, professor of extraterrestrial physics at the University of Berne, is principal investigator of the ion-mass-spectrometer (IMS) team. He has also worked at Rice University and at Lockheed's Palo Alto Research Laboratories. Fechtig, director of the Max Planck Institute for Nuclear Physics in Heidelberg and honorary professor at the university there, is a member of the particle-impact-analyzer (PIA) team. He has also worked at the University of California at San Diego, the Air Force Cambridge Laboratory in Bedford, Mass., and the Harvard-Smithsonian Astrophysical Laboratory. Geiss, who is a member of the IMS team, is director of the Berne Physical Institute and professor of physics at Berne, and he is also associated with the Max Planck Institute for Aeronomy in Lindau. He has been active at the universities of Chicago and Miami, at the Goddard Institute for Space Studies in New York and at the Johnson Space Center in Houston. Geiss is a foreign associate of the U.S. National Academy of Sciences and a foreign honorary member of the American Academy of Arts and Sciences.

The so-called Oort cometary cloud was then disturbed, over billions of years, by the gravitational forces of passing stars, which either ejected comets into interstellar space or injected them into orbits that pass relatively close to the sun. Solar radiation

and the solar wind (the stream of electrically charged particles flowing from the sun) cause these latter comets to develop a coma—a spherical cloud of gas and dust—and a tail. The dust particles in the coma and the tail scatter light, and molecules in the gas are

excited by solar radiation, which causes them to luminesce. The comet thus becomes visible.

The source of the gas in the coma and tail is probably icy material consisting of volatile substances that the comet has taken up and preserved



HALLEY'S COMET, photographed on March 19, 1986, from the island of Réunion in the Indian Ocean, appears brightest at its coma: the cloud of gas and dust surrounding the nucleus. Behind the coma are a straight, bluish ion tail and a curved,

diffuse dust tail. The ion tail is caused by the interaction between cometary gas and the solar wind (the stream of charged particles issuing from the sun); the dust tail results from the radiation pressure of the sun on cometary dust particles.

over billions of years. As a comet passes the sun, the icy substances on the side exposed to the sun sublime and release a gas mixture that expands into interplanetary space, contributing to the coma and the tail. The molecules in this mixture are then gradually dissociated and ionized (stripped of an outer electron) by ultraviolet radiation. The resulting gas of electrically charged particles is called a plasma.

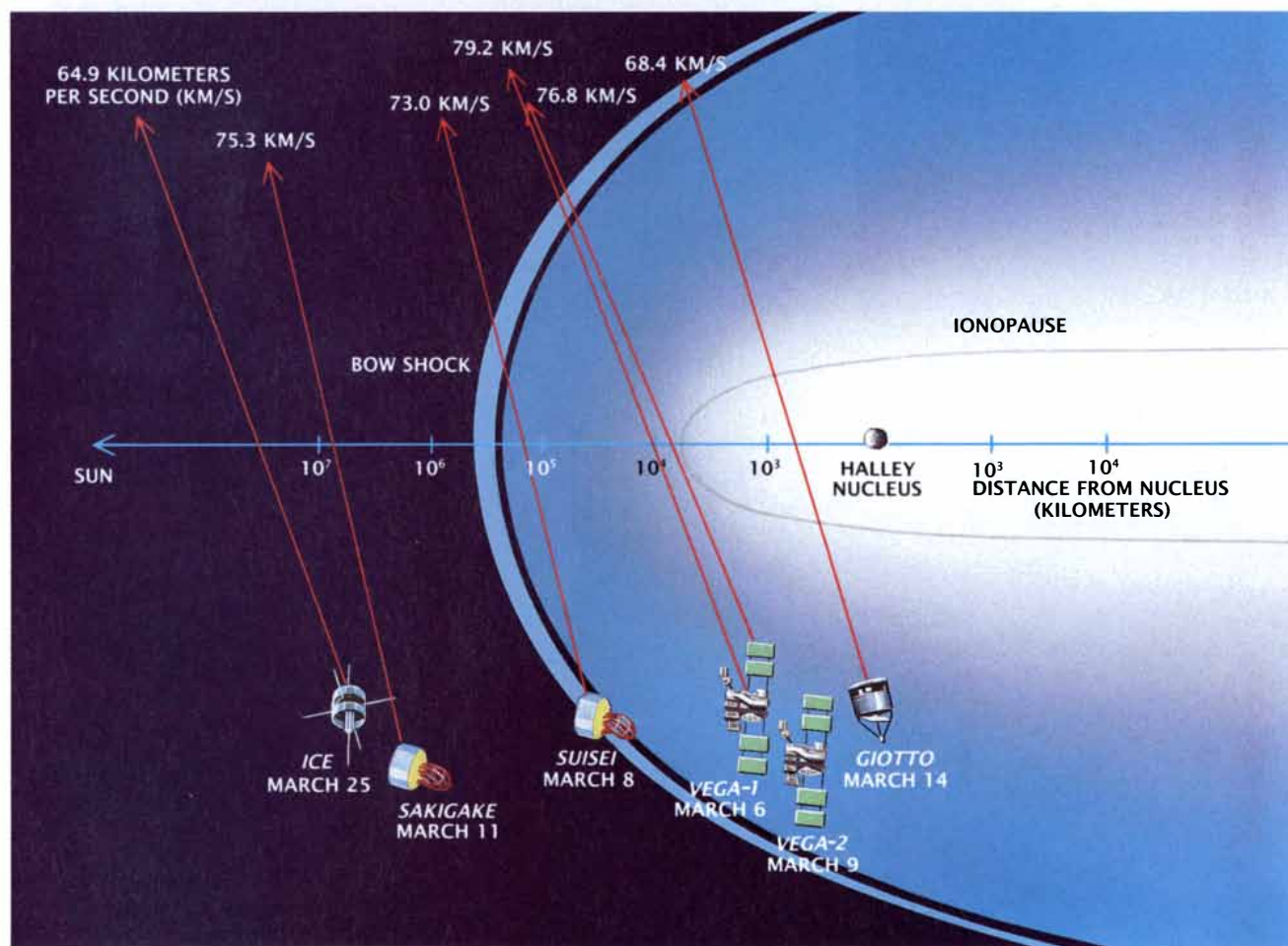
Hence the coma is a mixture of neutral and ionized gases. The inner coma, close to the nucleus, is composed predominantly of neutral molecules and atoms. Farther from the nucleus the coma is dominated increasingly by ions. Each kind of molecule or atom requires a specific amount of time to become ionized, and each moves away from the comet at a specific speed; as a result each species reaches a characteristic dis-

tance from the comet before it is ionized. For example, atomic hydrogen, which is produced when water molecules are dissociated, travels at a relatively high speed and therefore retains its neutral form over distances of up to 10 million kilometers from the nucleus. As soon as the neutral atoms and molecules are converted into ions and electrons, they come under the influence of the electric and magnetic fields carried by the solar wind.

Essentially correct interpretations of the interaction between the plasma of the solar wind and the plasma of the comet were given by the German astrophysicist Ludwig Biermann in 1951, the Swedish physicist Hannes Alfvén in 1957 and later by many others. Their predictions have now received on-the-spot confirmation from the observations made by the five Halley probes and by the American probe *International Cometary Explorer (ICE)*,

which in the fall of 1985 traveled through the tail of comet Giacobini-Zinner [see "The Structure of Comet Tails," by John C. Brandt and Malcolm B. Niedner, Jr.; *SCIENTIFIC AMERICAN*, January, 1986].

The precise data collected by these probes in the immediate vicinity of the comets have now made it possible to replace the general ideas with a quantitative description. To study the interaction of the comet plasma with the solar wind—an interaction similar to those that play important roles in the evolution of the atmospheres of planets and their satellites—*Giotto* carried a number of instruments [see illustration on page 100]. Instruments designated JPA, RPA and EPA measured the energies and directions of motion of particles, while others (IMS and NMS) distinguished the various kinds of particles. Also on board was a magnetometer (MAG) that measured the dis-



SIX SPACE PROBES flew by Halley's comet in March, 1986. Four of them—the Soviet *Vega-1* and *Vega-2*, the Japanese *Suisei* and the European *Giotto*—passed the sunlit side of the nucleus at distances of between 600 and 150,000 kilometers. The first photographs of a cometary nucleus were made, the gas and dust streaming away from the comet were investigated

and interactions between the comet and the solar wind were studied. In addition the probes *Sakigake* (from Japan) and *ICE* (from the U.S.) gathered data in the solar wind, upstream from Halley's comet. *Giotto*, which was equipped with a dust shield, was the only probe to penetrate the ionopause, which bounds the region of pure cometary gas surrounding the nucleus.

turbances in the interplanetary magnetic field caused by the comet. In addition the magnetometer registered the electromagnetic waves produced by the collision of the solar plasma with the plasma of the comet.

As far as eight million kilometers from the cometary nucleus the *Giotto*s began to register a population of protons distinct from those in the solar wind. The velocities of the protons in this population showed that the particles were actually newly ionized hydrogen atoms from the comet's coma. The magnetic field of the solar wind carries such protons away from the sun along spiraling trajectories. The same is true for other, heavier ions newly created by photoionization. The momentum of the solar wind as it streams toward a comet must therefore be shared by an ever increasing number of particles, many of which are relatively heavy. This momentum transfer is called mass loading, and it causes the solar wind to slow down gradually.

At a distance of 1.1 million kilometers from the nucleus, the particle detectors and magnetometer registered, as expected, a shock front arising from the interaction of the plasma of the solar wind with the plasma of the comet: the speed of the ions in the solar wind decreased and their temperature (the extent to which the velocity of individual ions varied randomly from the average velocity of all the ions) increased dramatically at the same time. The thickness of the shock front—the distance over which the speed of the solar-wind ions decreased and their thermal velocity increased—was 40,000 kilometers.

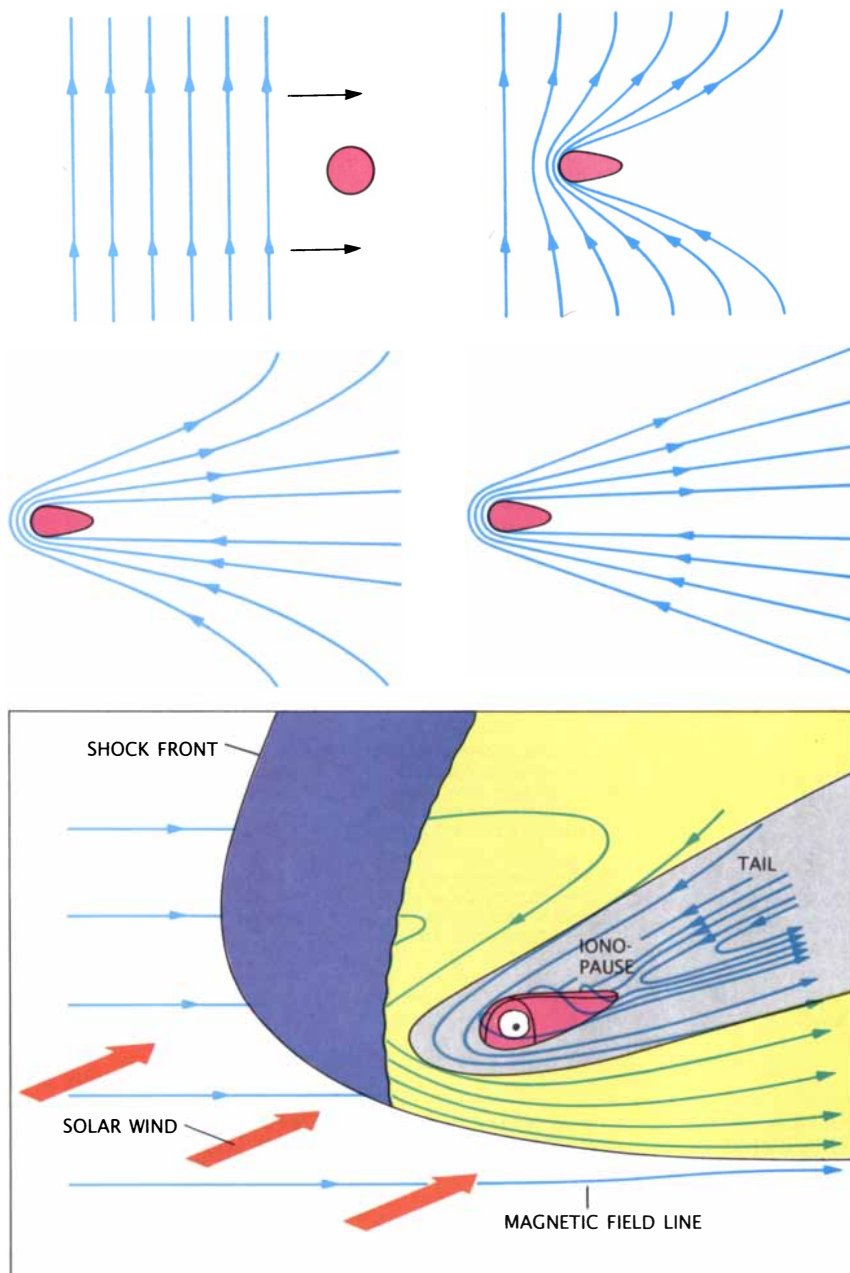
The shock front does not form an actual barrier between the solar wind and the cometary ions; the solar wind merely becomes turbulent there. The final barrier that keeps the solar wind from streaming closer to the nucleus is formed by the slow-moving gas of cometary molecules and ions at the so-called ionopause. Neither the ions of the solar wind nor its magnetic field is able to pass through this barrier into the pure cometary gas beyond it, and they "pile up" outside. Hence the magnetic field increases as one approaches the ionopause: *Giotto's* MAG instrument measured a maximum field strength of 60 nanoteslas at a distance of about 16,000 kilometers from the nucleus. (For comparison, the strength of the interplanetary magnetic field outside the coma was eight nanoteslas, and the strength of

the earth's magnetic field at the poles is approximately 60,000 nanoteslas.)

Because the magnetic field lines get stuck, as it were, at the ionopause, they become draped around it. This effect creates the ion tail, which consists of ions from the solar wind and cometary ions flowing along the drawn-out field lines.

Giotto was the only probe to penetrate through the ionopause into the comet's ionosphere. About 4,600 kilometers from the cometary nucleus,

Giotto's instruments showed the magnetic field falling to zero and the temperature of the ions decreasing from about 2,000 degrees Kelvin (degrees Celsius above absolute zero) to about 300 K. (about room temperature). These declines marked the ionopause. Before the mission, no one was prepared to predict the position of this boundary between the turbulent mixture of solar-wind ions and cometary ions and the pure, cold cometary ionosphere; the values of the variables



INTERACTION between a comet and the solar wind is shown. Magnetic field lines "frozen" in the solar wind are unable to penetrate the ionopause, and so they pile up in front of it and drape around it (top). On the side of the comet facing away from the sun an ion tail forms. The bottom part of the illustration depicts the interaction in three dimensions, as deduced from measurements made during *Giotto's* flyby.

determining the position of this discontinuity were simply not known.

The *Giotto* mission made particularly significant contributions in determining the composition of the neutral and ionized gases in the coma, thanks to the sensitive instruments on board and to the daringly

close approach to the nucleus. The measurements of the gases were important to make; the fraction of volatile materials in the nucleus probably represents about half or more of the total mass of the comet. Such material has largely been lost from the terrestrial planets, the earth's moon and meteorites.

During *Giotto's* flight through the coma, the NMS determined that gas was issuing from the nucleus at a rate of about 20 tons per second. For comparison, the total mass of the comet is about 100 billion tons. Analysis and interpretation of the data are far from complete, but quite a few of the "parent," or original, molecular species of the cometary gas have already been determined. A combination of results from the NMS (which measures the abundances of neutral molecules), from the IMS (which determines the proportions of ions) and from optical instruments (the optical probe experiment, called the OPE, and various instruments on Vega, on earth-orbiting satellites and on the ground) leads to the conclusion that the gas is roughly 80 percent water, 10 percent carbon monoxide, 3 percent carbon dioxide, 2 percent methane, less than 1.5 percent ammonia and .1 percent hydrocyanic acid. Some heavier ions of various kinds were detected by the RPA, the NMS and the IMS, as well as by instruments on Vega, but the nature of the corresponding parent molecules has not yet been determined.

The measurement of carbon monoxide done by the NMS produced a particularly interesting result: the abundance of carbon monoxide in relation to the other gases increases with distance from the nucleus. This means either that carbon monoxide as a gas is released from the comet's nucleus unevenly or that a relatively large amount of it is released from small dust particles within 10,000 kilometers of the nucleus as they are heated by sunlight. The latter explanation would imply that the carbon monoxide is remarkably well retained by the dust grains, probably within larger molecules or polymers.

Isotopic measurements made by the NMS revealed relative abundances of isotopes of sulfur and oxygen that agree to within experimental uncertainty with the abundances on the earth and in meteorites. In the water of Halley's comet, as on the earth and in meteorites, there is a greater proportion of heavy hydrogen than there is in interstellar gas.

The other, nonvolatile part of the comet's mass can be sampled in the form of cometary dust. Originally embedded in the ice of the cometary nucleus, the dust particles are driven away from the nucleus as the ices sublime and the gases expand. The trajectories of the particles within the coma are determined by the initial

EXPERIMENT, ACRONYM	SCIENTIFIC OBJECTIVES	PRINCIPAL INVESTIGATOR, LEADING INSTITUTE
CAMERA HMC	To produce high resolution photographs of the nucleus and of the gas and dust.	H. Uwe Keller Max Planck Institute for Aeronomy, Lindau
NEUTRAL MASS SPECTROMETER NMS	To determine the composition, density and velocity of the neutral gases and of low-energy cometary ions.	Dieter Krankowsky Max Planck Institute for Nuclear Physics, Heidelberg
ION MASS SPECTROMETER IMS	To determine the composition, density, energy and angular distribution of the ions in the solar wind and in the cometary plasma.	Hans Balsiger University of Berne
DUST MASS SPECTROMETER PIA	To determine the composition and mass of cometary dust particles.	Jochen Kessel Max Planck Institute for Nuclear Physics, Heidelberg
DUST-IMPACT-DETECTOR SYSTEM DID	To determine the abundance and mass distribution of dust particles.	J. Anthony M. McDonnell University of Kent
PLASMA ANALYSIS 1 JPA	To determine the energy and angular distribution of ions with high time resolution; to determine the composition of pick-up ions.	Alan Johnstone Mullard Space Science Laboratory, Holmbury, St.Mary
PLASMA ANALYSIS 2 RPA	To determine the energy and angular distribution of electrons with high time resolution; to determine the composition of cold clusters of ions.	Henri Rème Center for the Study of Space Radiation, Toulouse
ENERGETIC PARTICLES ANALYZER EPA	To determine the energy and angular distribution of high-energy charged particles (those with energies above 20 kev).	Susan M. P. McKenna-Lawlor St. Patrick's College, Maynooth
MAGNETOMETER MAG	To measure the magnetic field with high time resolution.	Fritz M. Neubauer University of Cologne
OPTICAL-PROBE EXPERIMENT OPE	To measure the distribution of gas and dust (CN and OH).	Anni Chantal Levasseur-Regourd National Center for Scientific Research, Verrières-le-Buisson
RADIO-SCIENCE EXPERIMENT GRE	To measure the density of gas and dust along the trajectory of the spacecraft.	Peter Edenhofer University of Bochum

INSTRUMENTS on board the European Space Agency's probe *Giotto* are characterized here. The table lists the name, scientific objective and principal investigator of each.

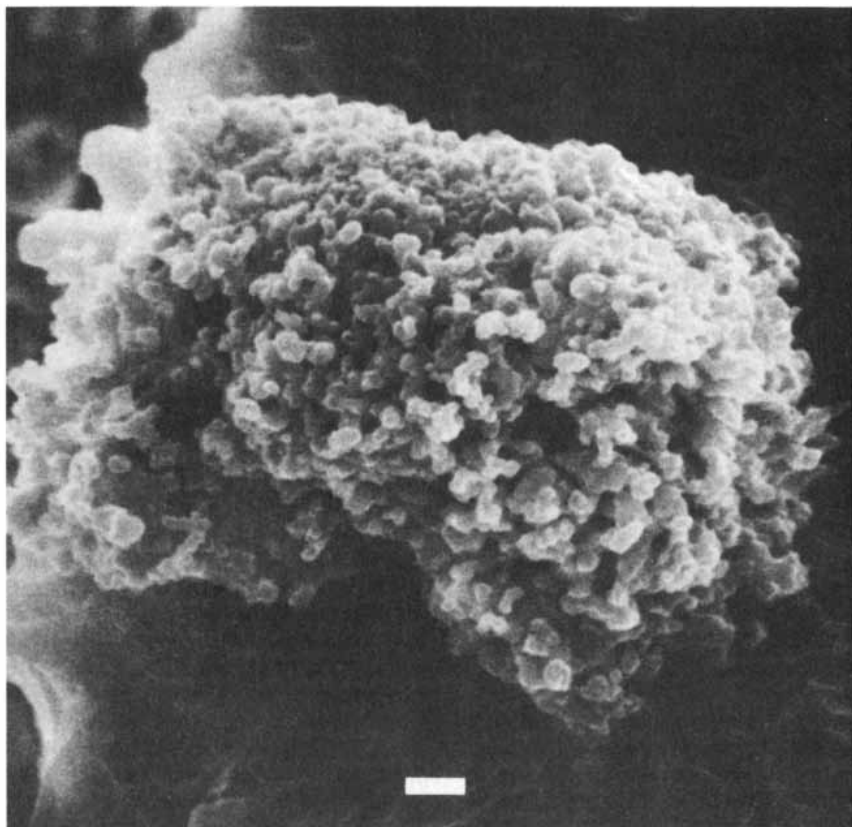
direction in which they leave the nucleus (the direction of the gas outflow) and by the direction of the sun's radiation pressure.

For the smallest particles—those having a diameter of less than a micrometer, or a millionth of a meter—the sun's radiation pressure dominates over its gravitational pull. These particles are driven away from the sun, producing the dust tail that is clearly visible in many comets. For larger particles the gravitational pull of the sun overcomes the radiation pressure, and so the particles stay near the orbital path of the comet. Since the particles are emitted from the nucleus in various directions, they orbit the sun at somewhat different speeds. In the course of time a wide stream of particles is formed, and the stream spreads out continuously along the orbital path. That is how a meteor stream is created. Such a stream is more commonly known as a meteor shower, because of the appearance it takes when it enters the earth's atmosphere. Some of the particles survive the friction of the atmosphere. For some time such particles have been collected in the stratosphere, providing investigators with the first clues to the structure and composition of cometary dust.

Halley's comet has created a meteor stream that is encountered by the earth twice per year, and hence gives rise to two annual meteor showers: the Orionids in October and the eta-Aquarids in May.

When *Giotto* traveled through Halley's coma, dust was being emitted at a rate of between three and 10 tons per second. This estimate is based on measurements of the sizes and masses of the dust particles encountered by the probe, as determined by the DID instrument, and on the rate at which the probe slowed down, as measured by the GRE. If the comet suffers such a high rate of loss only during the few months when it is close to the sun, then it must lose on the order of 100 million tons of material during the course of each orbit. With a total mass of 100 billion tons, Halley's comet can look forward to hundreds of happy returns!

The particle-impact analyzers on board *Giotto* (the PIA) and *Vega-1* and *Vega-2* analyzed the chemical composition of thousands of dust particles, which had diameters ranging from .1 micrometer to 10 micrometers. The dust is a mixture of a light substance consisting of hydrogen, carbon, nitrogen and oxygen and a heavy, stony



BROWNLEE PARTICLE, a dust particle found in the earth's atmosphere, probably originated from dust shed by comets into interplanetary space. The composition of Brownlee particles corresponds to that of the stony component of cometary dust particles. Their loosely packed structure gives them a quite low density (about a gram per cubic centimeter) in spite of their stony composition. The white bar at the bottom corresponds to a length of one micrometer, or a millionth of a meter.

material consisting mainly of magnesium, silicon, iron and oxygen.

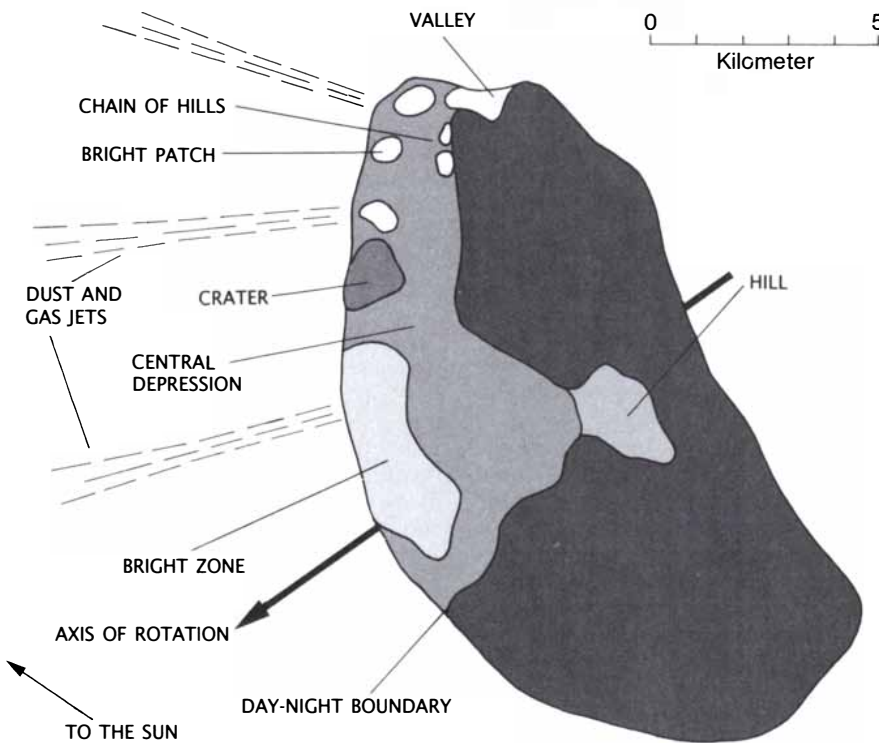
From grain to grain there are large variations in the ratio of the light material to the stony material. It came as a surprise that the light material survives for a comparatively long time when the dust particles are warmed in sunlight. Obviously some of the light material takes the form of polymerized organic substances, which seem to act as a glue, binding together smaller dust particles to form larger ones. The extremely small size of the cometary grains and their physical and chemical characteristics are reminiscent of certain models that describe interstellar dust grains [see "The Structure and Evolution of Interstellar Grains," by J. Mayo Greenberg; *SCIENTIFIC AMERICAN*, June, 1984].

The ratios of the distinct isotopes of individual elements—carbon, magnesium, silicon and iron—in the cometary dust are in overall agreement with the isotopic ratios typical of the entire solar system. The same agreement was found in the gas phase; this result

is one of the primary indicators that the dust in Halley's comet originated from the same material as the rest of the solar system.

Undoubtedly the highlight of the *Giotto* voyage to Halley's comet was the close approach of the spacecraft to the source of the gas and dust: the nucleus itself. Before the Halley missions no cometary nucleus had ever been photographed, because nuclei are relatively small and are veiled by a coma. Nevertheless, investigations of comas had made it possible to deduce a considerable amount about the nuclei.

Now the missions to Halley's comet have beautifully confirmed the essential features of the accepted model of cometary nuclei: the "dirty snowball" model. That model was developed some 40 years ago by the American astrophysicist Fred L. Whipple. He postulated that the nucleus is a single, solid object composed of water ice, other ices and dust particles. Whipple assumed that the nucleus is not en-



NUCLEUS of Halley's comet was photographed by the Halley Multicolor Camera on board *Giotto*. The image at the top is a composite of six photographs. Color was added artificially. The map at the bottom indicates relevant features of the nucleus.

tirely compact but instead has a loosely packed structure. He further assumed that the side of the nucleus exposed to the sun releases gas and dust homogeneously from a large area. The photographs made by *Giotto* support the basic features of Whipple's model, but they also disclose some real surprises. The surface of the nucleus of Halley's comet is irregular and full of pits. Bright jets, or streams, of gas and dust gush from the surface of the nucleus. Furthermore, the chemical data obtained by *Giotto* and *Vega* show that the nucleus is actually made up of three components: the ices, the stony component and a heat-resistant light material that probably contains polymerized organic compounds.

Based on the photographs, the dimensions of the nucleus have been estimated as being roughly 16-by-eight-by-eight kilometers. The shape is reminiscent of a peanut or a potato. By combining photographs from *Giotto* and *Vega-1*, a three-dimensional model of Halley's nucleus was constructed and a volume of about 500 cubic kilometers was derived. With a mass of roughly 100 billion tons, this leads to a density estimate of from .1 to .3 gram per cubic centimeter. (Water has a density of one gram per cubic centimeter.)

The surface area of the nucleus is approximately four times larger than had been thought. This means that the albedo (the percentage of incident sunlight that is reflected) is considerably lower than originally supposed. The low albedo (4 percent) means that Halley's comet is the darkest of all known bodies in the solar system.

A further surprise is that the jets appear to be emitted from a relatively small fraction—about 10 percent—of the comet's total surface. Nearly 90 percent of the surface was inactive at the time of the observations. Much of the surface is apparently covered with a crust of unknown thickness and structure. Before the space missions, jets were recognized as a source of gas and dust emissions from the nucleus, but their dominant role has been identified only as a result of the photographs taken by the space probes. It is now thought that virtually all the gas and dust that leaves the comet does so in the form of jets.

The ultimate goal of analyses of the gas and dust in the coma is to determine the chemical composition of the nucleus. The composition of the coma is not necessarily the

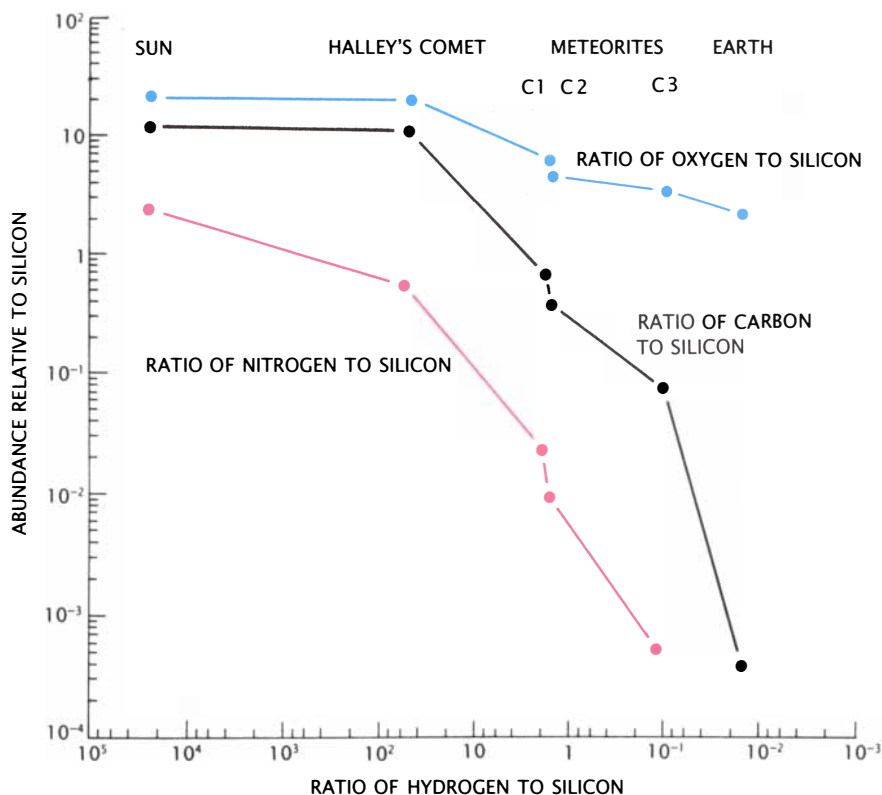
same as that of the nucleus, since the composition of the gas and dust that jet from the nucleus may depend on local conditions at the sources of the jets. Nevertheless, the mixture of elements that was present in the material emitted by the comet during the flybys of *Vega-1*, *Vega-2* and *Giotto* has yielded valuable information about the composition of the nucleus, and several conclusions can already be drawn from the data.

In the first place, the proportion of volatile elements is much higher than it is on the earth and in meteorites; this is consistent with the comet's having formed in the cool outer reaches of the solar nebula.

Secondly, the abundances of carbon and nitrogen and of molecules containing these elements are most significant. In the hydrogen-rich environment of the solar nebula, chemical reactions tend to produce compounds such as methane and ammonia, in which these elements are in a "reduced" state; that is, they are bound to hydrogen atoms. It came as a surprise that in the material emitted by the comet these two compounds are quite low in abundance. Instead a considerable fraction of the carbon is in oxidized form (bound to oxygen atoms), and there is much less nitrogen than might be expected. This indicates that chemical reactions in the outer parts of the solar nebula were not very efficient at rearranging the carbon- and nitrogen-containing molecules.

Indeed, the findings resemble what might be expected in dense interstellar clouds, where the low temperatures lead to unusual chemistry. In these interstellar clouds neutral molecules cannot readily react with one another; the chemistry is therefore dominated by reactions between neutral molecules and the small traces of ions that are present. As a consequence, in the gas phase of the clouds nitrogen is found mainly in its molecular form, carbon is usually found in the form of carbon monoxide or related substances and condensable molecules are enriched in deuterium (a heavy isotope of hydrogen).

These chemical features are apparent in the mixture of volatile substances in Halley's comet. In the comet's water, deuterium is from five to 10 times more abundant than the interstellar average, and the NMS team found much carbon in the form of carbon monoxide. The low abundance of nitrogen reflects the peculiar chemical form nitrogen assumes in interstellar clouds. Molecular nitrogen is



RELATIVE ABUNDANCES of key elements in material emitted by Halley's comet are compared with their abundances in other bodies. The ratio of dust to gas at the source (the comet itself) was assumed to be two to one. Relative abundances of elements in the comet are close to those in the sun, whereas the relative abundances found in the earth and in three classes of the meteorites known as carbonaceous chondrites are not. This result confirms the hypothesis that comets consist of very primitive material, depleted only in the volatile elements hydrogen and nitrogen.

hard to bind or condense; either this nitrogen was lost from the comet or it was not even incorporated in the comet in the first place.

These findings, after they have been refined and analyzed further, should help our attempts to reconstruct the origin of the solar system. At least in the outer parts of the early solar system, physical and chemical processes must have been so gentle that chemical bonds that are older than the sun have survived the formation of the solar nebula (and, of course, the formation of Halley's comet). Hence the chemistry of comets provides us with a link between the solar system and its ancient ancestor, an unnamed dark interstellar molecular cloud dispersed long ago.

The results obtained by the Halley probes represent an important step forward in our understanding of the nature of comets, and by extension of the solar system as a whole. Probes to other comets will

undoubtedly follow. In particular, the data sent back by *Giotto* from deep within Halley's coma demonstrate that it would be worthwhile to bring samples of cometary material back to the earth for analysis by modern laboratory techniques.

FURTHER READING

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The Fossils of Montceau-les-Mines

Some 300 million years ago central France lay at the Equator. The paleoecology of this bygone world has been reconstructed from a superb fossil cache

by Daniel Heyler and Cecile M. Poplin

The final part of the Paleozoic era, some 300 million years ago, was a time of transition. The Carboniferous period, when the continents were gathered in several landmasses near the Equator and a hot, humid climate sustained the swamp forests that gave rise to the major coal reserves of today, was drawing to a close. The world was about to enter the Permian period, when humid heat would give way to a cooler, more arid climate and the first reptilian ancestors of mammals would begin to populate the continents.

Central France was then a region of hills covered with giant ferns and conifers, interspersed among lowlands patterned with rivers, lakes and lagoons. Millipedes, scorpions, insects, salamanderlike amphibians and reptiles crawled on the land, and the waterways teemed with worms, crustaceans, mollusks and ancestral sharks and fishes. When these creatures died, their bodies sank to the bottom of swamps, where they were preserved and eventually fossilized.

Some of these fossil plants and animals were unearthed during the 19th century at Montceau-les-Mines, a coal

basin situated northeast of the Massif Central, a mountain range formed during the Paleozoic at about the same time as the Appalachians. It was only about 10 years ago, however, that strip-mining of the Montceau coal seams revealed the magnitude of the fossil deposit. Many paleontologists now agree that it is one of the richest discoveries of the past decade. Galvanized by the imminent destruction of the site, local amateur paleontologists converged on the mine. Weekend after weekend they raced to save fossil material before it would be destroyed by strip-mining machinery.

Working with the Paleontological Institute at the Museum of Natural History in Paris and the Natural History Museum in Autun, near Montceau, they harvested 7,000 shale slabs and more than 100,000 nodules, most of them bearing fossils. They carefully recorded the location and orientation in which each nodule was found. Later, when the fossils had been identified, it would be possible to reconstruct their distribution in the fossil beds. This was the first time such precise, modern excavating methods had been employed on such ancient deposits.

The mine, no longer operational, has been filled in. For the scientists involved, the enormous task of examining the rescued specimens is still under way. About a fourth of the nodules have been opened, and nearly 22 percent of them have yielded well-preserved fossil animals. Many specimens proved to be in excellent condition; they included such animals as insect nymphs and soft-bodied worms, rarely found in a fossilized state. A research effort coordinated by us and supported by the National Center for Scientific Research (CNRS) made it possible to assemble an international team of specialists to examine this

first lot of fossils. The workers have been able to reconstruct the main features of the site's plant and animal community as well as of its environment. To date nearly 300 species of plants and pollen and 16 classes of animals representing about 30 genera have been identified.

The fossils represent a slice of the earth's geological past that stretches from the end of the Carboniferous to the beginning of the Permian. During that time the region's tropical climate gave way to a more temperate one, accompanied by changes in the flora and fauna that made them better adapted to the drier climate. Thus the deposition documents the transition of species over a critical period in earth history.

The fossils of the Montceau basin are either shale deposits, formed when animals and plants were flattened between layers of silt, or nodules. The process by which the latter came about is not completely understood, but it is thought that an organism can act as a nucleus around which fine sediments accumulate to form the nodule. Nodule fossils—also found at contemporaneous sites such as Mazon Creek near Chicago and at later ones such as the Triassic site in Madagascar and the Cretaceous site at Ceará in Brazil—are more three-dimensional and so give a clearer picture of an organism's physical form.

The zoological groups represented in the Montceau fossils vary considerably in the number of individuals. For several reasons, however, the numbers do not accurately reflect the faunal populations in the basin at the time. First, soft-bodied animals tend not to be preserved as readily as animals with hard parts, such as shell or bone. Second, the speed of the strip-

DANIEL HEYLER and CECILE M. POPLIN are paleontologists at the Museum of Natural History in Paris (Unité Associée 12 of the National Center for Scientific Research). They share an interest in Upper Paleozoic vertebrates. Heyler specializes in fossil fishes, amphibians and tetrapod footprints from continental basins of western Europe, in particular France. Poplin studies mainly North American fossil fishes. She has also worked on European and Chinese fishes and primitive mammals from Mongolia. Montceau researchers not mentioned in the article include J. Doubinger, G. Gand, Jean R. Langiaux and M. D. Sotty.

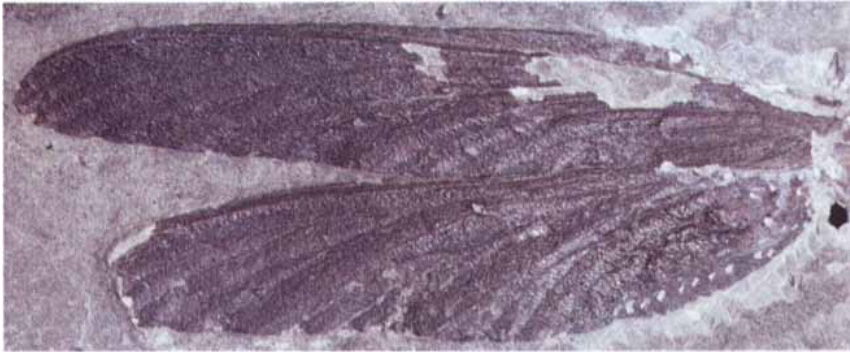
mining made it impossible to collect all the fossils. Last, the mine is only a part of the entire geological basin. Nevertheless, for sheer quantity, quality and diversity of specimens, Montceau can be compared to the famous, contemporaneous site at Mazon Creek and the Bear Gulch, Mont., site (where the fauna is about 15 million years older).

The oldest layers at Montceau were deposited at the end of the Carboniferous period, which began 345 million

years ago and lasted for about 65 million years. The period accounts for the world's coal reserves. Coal formation slowed as the climate became cooler and drier during the succeeding Permian period, which began 280 million years ago and lasted for 50 million years. Hence coal from the Permian is scarce. The transition between the Carboniferous and the Permian periods is not marked by an abrupt geological change and so is not recorded as a stratigraphic boundary.

One must turn to paleontology and in particular to paleobotany in order to assign a deposit to the transition.

It was the fossil flora more than the fauna that enabled the lower layers at Montceau to be dated to the Stephanian (the last stage of the Carboniferous) and the upper layers to the Autunian (the first stage of the Permian). The evolution of the flora throughout Montceau bears witness to the change in climate that took place between these two geological periods.



ANIMALS that lived during the Upper Carboniferous period, 300 million years ago, are preserved in these fossils found at Montceau-les-Mines. Exquisitely preserved fore wing and hind wing (*top left*) belonged to an extinct insect, *Microdictya heyleri*. A cockroach nymph (*bottom left*) is one of many insect nymphs found at the site. An onychophore (*top right*), an unusual animal sharing features of both worms and arthropods, is preserved in a nodule. Its existing descendants resemble velvety caterpillars. A Paleozoic scorpion (*bottom right*) resembles its modern descendants; its venomous vesicle and sting are visible.



STRIP-MINING exposed layers of fossil-bearing coals at Montceau-les-Mines, about 300 kilometers southeast of Paris. Approximately 7,000 shale slabs and 100,000 nodules were excavated over two years by local amateur paleontologists. Most of the nodules remain unopened in the attic of the Natural History Museum in Autun.



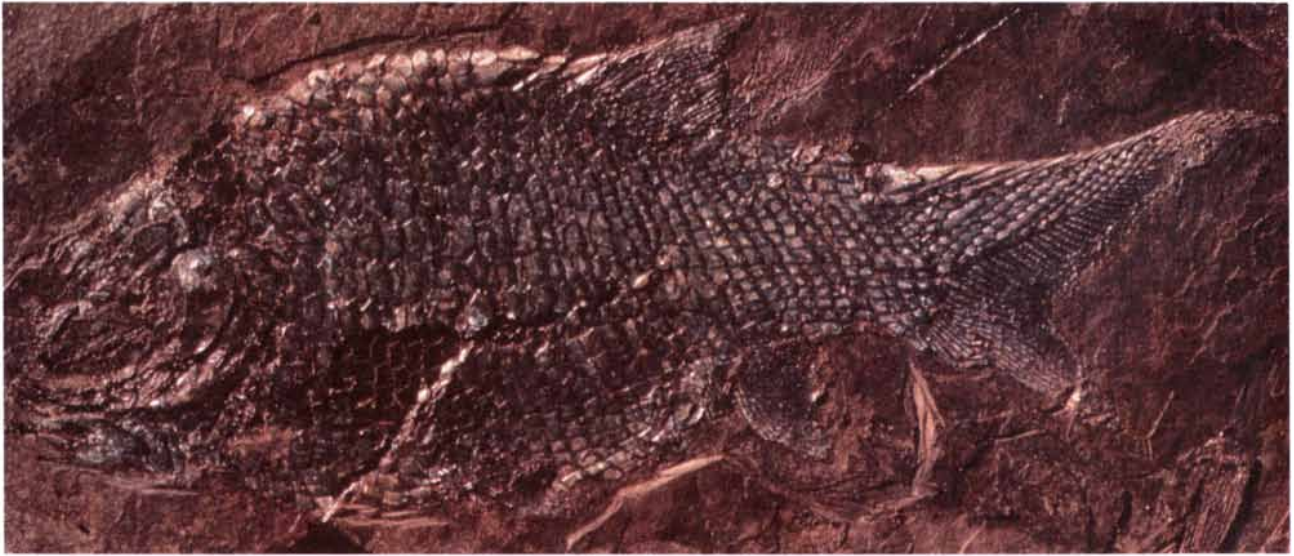
CALAMITES (left), which resemble modern horsetails, grew to the height of trees in the Carboniferous forest. These plants lacked flowers and seeds; they reproduced by means of spores. A giant seed fern (right) reproduced with minute seedlike ovules.

Fossil plants are abundant at Montceau. Nearly 300 species belong to the ancient groups that preceded the seed-producing modern flora. Some resemble giant horsetails and ferns, which loomed as tall as trees in the Carboniferous forest. At Montceau these plants left some trunks in situ and many leaves. They reproduced by means of spores. The common plants of the genus *Alethopteris* also resembled giant ferns but reproduced by means of an ovule, or seedlike organ. Known as seed ferns, this group, which lived mainly during the Carboniferous and the Permian, is important for understanding the evolution of seed plants. More highly evolved plants, such as the first conifers, were also on the scene; they had appeared during the Upper Carboniferous. In increasingly recent strata at Montceau, conifers tend to replace the other groups, probably indicating the advent of a drier, cooler climate.

Of the Montceau fauna, arthropods are by far the most numerous and well-preserved group. By the end of the Carboniferous this phylum had already diversified into half a dozen or so primitive classes. The aquatic arthropods are undoubtedly the most numerous; crustaceans alone represent 43 percent of the fauna examined to date. The latter were studied by Sylvie Secrétan of the Museum of Natural History in Paris, Frederick R. Schram of the San Diego Natural History Museum and W. D. Ian Rolfe of the University of Glasgow. They include 2,000 specimens of syncarids—primitive shrimp-like creatures that still exist—and ostracods, minute crustaceans that have bivalve shells and survive today in both fresh and salt water. Robert Feys of the French Bureau of Geological and Mineral Research studied the estherias, another bivalve crustacean.

The euthycarcinoids, a rare group of aquatic arthropods resembling millipedes with tails, drew the attention of specialists when they were discovered at Montceau; the finding subsequently led to the discovery of the same genus (*Sottyxerxes*) at Mazon Creek. Also found at Montceau were 45 specimens of xiphosurans, which have been identified but not yet studied; this group includes the horseshoe crab.

The terrestrial arthropods at Montceau include the principal groups living today. They are millipedes, studied by John E. Almond of the University of Cambridge, as well as spiders and scorpions. The scorpion fossils, studied by one of us (Heyler) and his col-

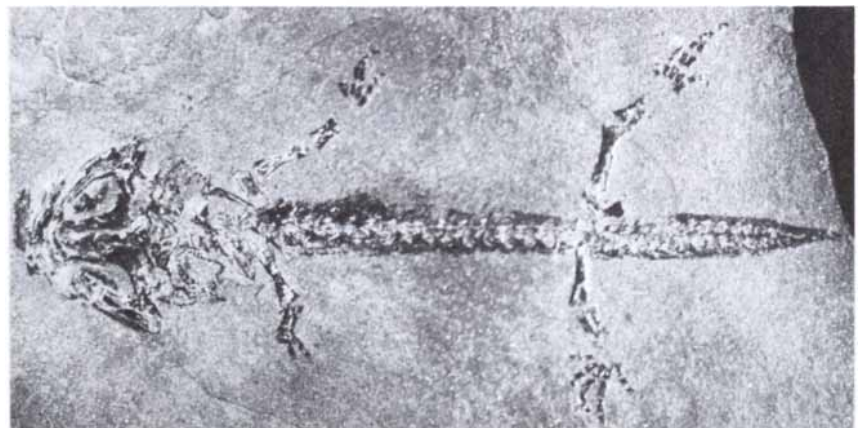


FOSSILS OF ACTINOPTERYGIAN FISHES were found in the Autun Basin; similar specimens were discovered at Montceau, some 50 kilometers distant. Lakes in the two basins were probably once connected. This fish was covered with enamellike scales.

league at the Museum of Natural History in Paris, Maxime A. Vachon, in many cases are beautifully preserved, complete with the venomous vesicle and sting. An extinct group of terrestrial arthropods, the arthropleurids, was also found. They resemble huge sow bugs and have been found only in Carboniferous basins. The five individuals from Montceau, studied by Derek E. Briggs of the University of Bristol, are the smallest, most complete arthropleurids found to date; they probably belong to a new species.

The insects, studied by Laurie Burnham at Harvard University, are surprisingly varied. Insects first appear in the fossil record at the beginning of the Upper Carboniferous, some 320 million years ago. Yet they are represented by eight orders at Montceau, which records a time just 20 million years later. These fossils, dating from a time when land plants and other life-forms were diversifying, represent an important stage in the evolution of insects. Montceau has yielded a large number of immature insects, many with developing wing buds. It is hoped that these nymphal forms, currently under investigation, will provide clues to the evolution of insect wings.

One astonishing discovery was of two fossil onychophores, animals that bear a superficial resemblance to large caterpillars. Today these animals are exceedingly rare and live in Central America, the Caribbean and the Indo-Australian region. Much ink has been spilled over their affinities: they share characteristics of both annelid worms and arthropods, and for a while it was



FOSSIL FOOTPRINTS (*top*) record the passage of an early amphibian or reptile. Its tail trailed behind, leaving a sinuous trace. Fossils of larval branchiosaurus (*middle*), an early amphibian, were found concentrated at the same spot in a Carboniferous stratum. They resemble tadpoles of modern amphibians. This specimen is two centimeters long. Fossils of more mature animals that had developed legs (*bottom*) are rare at Montceau. This branchiosaurus specimen is seven centimeters long.

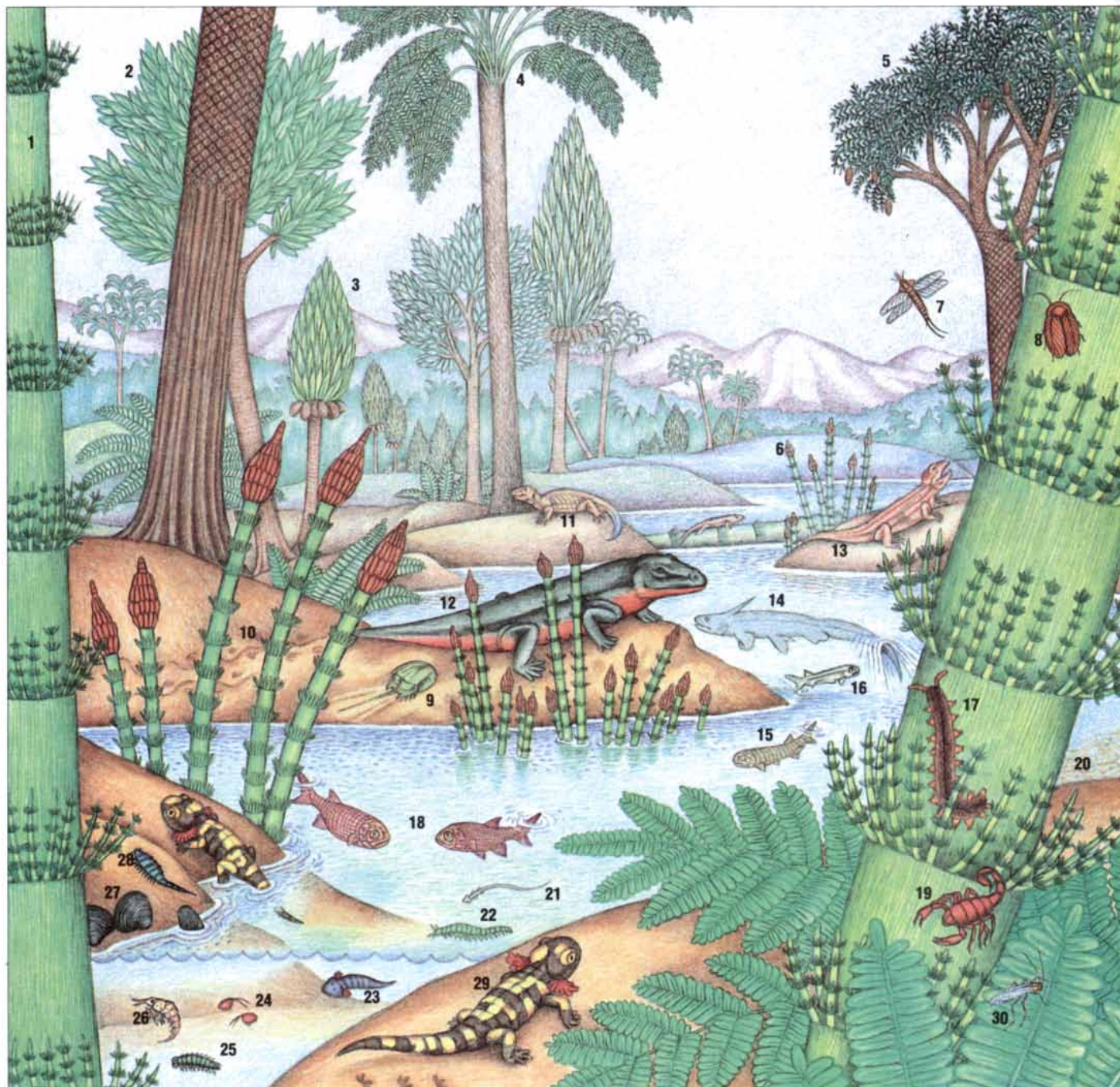
thought they might be ancestors of all arthropods. This hypothesis, however, seems to have been abandoned. In any case, the onychophores are true relics of the early Paleozoic, apparently having undergone little morphological change in nearly 500 million years.

Other invertebrates include bivalve mollusks, studied by Claude Babin of the University of Brest. These animals, found in great abundance at Montceau, all belong to a single species, *Antraconaia lusitanica*, which was

widespread at the time in Europe, from Poland to the Iberian Peninsula. This mollusk is one of the classic stratigraphic fossils that made it possible to date the layers in which they were found at Montceau to the Upper Carboniferous. More unusual was the discovery of polychaete annelids, segmented worms that typically have fleshy, paddlelike appendages protruding from each segment. The bodies of these animals are made up entirely of soft tissue, but thanks to the

exceptional preservation in the nodules, 72 individuals have been found.

The vertebrates found at Montceau belong to at least four classes: bony fishes, cartilaginous fishes, amphibians and reptiles. Fish are the most numerous. The acanthodians, the first jawed fishes in the fossil record, are represented at Montceau by specimens from 20 to 50 centimeters long. These enigmatic fishes have tails resembling those of sharks.



DIVERSE LIFE-FORMS inhabited the hot, humid landscape of France's Massif Central during the Upper Carboniferous. The region was dotted with hills, rivers and lakes. Fossilized remains suggest that these plants and animals inhabited an

Their fins are supported by sharp spines; a predator would have found them most uncomfortable to swallow. These fishes vanished without descendants 250 million years ago.

A second group is the Xenacanthida, distant cousins of ancestral sharks. These freshwater predators prowled the coal swamps during the Upper Carboniferous and Lower Permian. Xenacanth was the giant of the time, reaching three meters in length, but those from Montceau were rather

small, never exceeding one meter. Their numerous sharp teeth indicate that they were great hunters. They have a strong, serrated spine at the base of the skull, which most likely served as a defensive weapon.

A third group, the actinopterygians, is represented at Montceau by eight species. In appearance they evoke their remote descendants such as carps, sardines and tunas, but they possess numerous primitive characteristics such as their cranial anatomy and their thick, enamellike scales, which must have given these fishes a rather rigid appearance.

The amphibians at Montceau resemble small salamanders. One region in the deposit yielded a fossilized group of gill-bearing larvae, similar to the tadpoles of extant amphibians. Fragments of larger skeletons found elsewhere at Montceau probably belonged to full-grown animals similar to those identified at other contemporaneous deposits. Except for these, few bones of amphibians or reptiles have been found at Montceau.

These creatures did, however, leave numerous footprints, which are preserved in the shales. Such footprints record the location of shores: riverbanks and the edges of lakes and lagoons. Unlike carcasses, which may have been swept far from their point of origin, prints remain in place from the day they were formed. They show fingers, claws and sinuous lines drawn by a tail trailing in the mud as an animal made its way to the water. The tetrapod spoor at Montceau reveal that many species of amphibians and reptiles lived together there. The number of prints, however, yields no information about the actual abundance of a species, because a single individual could have left many traces in the course of a day.

Animals were not the only makers of fossil prints. Our team also often found imprints of falling rain, ripple marks left by running water and the cracked pattern of drying mud. These are important indicators of climate, revealing intervals of dryness alternating with rainfall. Such records preserve changes on tiny time scales, as brief as a season, a week or even a day.

What kind of environment did the plants and animals of Montceau inhabit? The faunal evidence tells a contradictory story. Many of the animals, such as the polychaete worms and some of the aquatic arthropods, lived in salt water, like their modern descendants. Moreover, fossils resembling those from Mont-

ceau have been found at Mazon Creek in sediments known to have been marine. Yet other aquatic animals are characteristic of lacustrine, generally freshwater environments. Onychophores today are found in humid, tropical forests near rivers, and extant amphibians live only in fresh water. Arthropleurid and estheria fossils have been found in freshwater Carboniferous basins in Europe and North America. Finally, there is no doubt that millipedes, spiders, scorpions, insects and reptiles are mainly terrestrial.

This confused picture of the Montceau environment was resolved with the help of the humble bivalve *Anthraconaia*. At Montceau the fossil mollusk's two shells are usually found linked by the hinge. The preservation of the fragile hinge shows that the shells of dead animals were not transported before being buried. It is even possible that living animals were entombed abruptly by the rapid deposition of sediment. The small size of the specimens, together with the elongated shape of their shells, indicates that the environment was somewhat poor in organic nutrients. Rapid sedimentation and a scarcity of nutrients indicate that Montceau lay at an estuary, where the flow of fresh river water alternated with brackish tides.

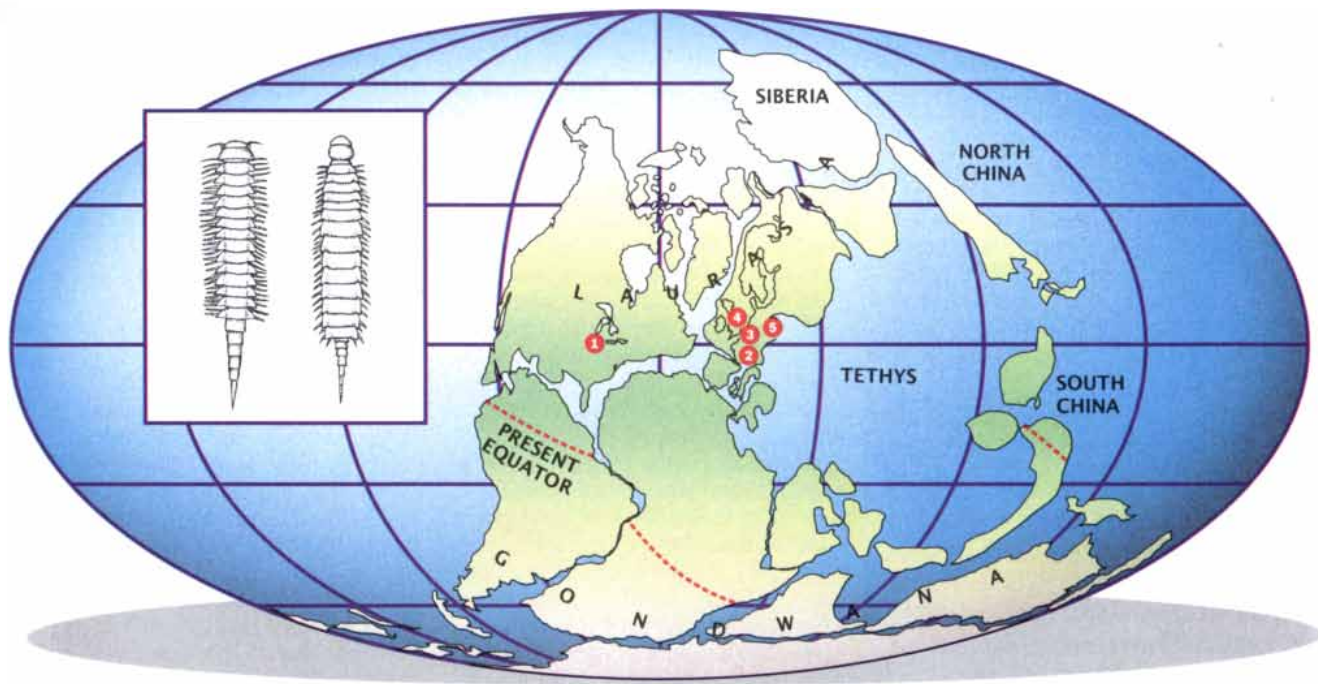
The aquatic faunas also disclose something about the larger-scale geography at the time. Fossil fishes at Montceau are closely related to fishes excavated from lacustrine basins in the nearby Massif Central region, less than 200 kilometers away. The lakes must have been linked at times, perhaps by flooding, enabling aquatic species to migrate from one place to another. As the floodwaters ebbed, the lakes became separated once again. Such minor events might leave no traces visible to a geologist working 300 million years later, but paleontological evidence suggests that the different environments must have been connected in some way.

If the Montceau region was dotted with lakes, where was the sea? Most geologists think the sea at the end of the Carboniferous was far south of Montceau. How, then, does one explain the presence of marine animals at Montceau and in the Massif Central? One possible answer is that the lakes were salty, the residue of epicontinental seas that had submerged the region before the sea level dropped.

The Montceau fossils show clear evidence of a marked change in climate during the period they span. Comparison with contemporaneous deposits elsewhere indicates this was not a



estuarine environment. Species shown in this scene are not all drawn to scale.



LANDMASSES lay well south of their modern positions during the Upper Carboniferous and were gathered into two protocontinents: Laurasia (which later split into North America, Europe and much of Asia) and Gondwana (Africa, Antarctica, Australia, India and South America). At the time, Mazon Creek (1), Montceau-les-Mines (2), the Saar Basin (3), Great Britain (4) and Bohemia (5)—all of them present-day fossil sites—lay near the Equator. Mazon Creek was closer to Europe than it is today,

which explains why its fauna resembles the fauna found in Europe. The discovery at Montceau of a new eurycarinoid species, *Sottyxerxes multiplex* (left), led workers to reexamine Mazon Creek fossils and to recognize the presence of the related species *Sottyxerxes piekoeae* (right) there. The map shows China split into northern and southern blocks; an alternate theory, recently espoused by paleobotanists, holds that the blocks had fused long before, during the Lower Carboniferous.

local or regional phenomenon. The fossil evidence at Mazon Creek tells virtually the same story. This site preserves an estuarine environment similar to Montceau and contains outcrops dating from the Westphalian epoch (somewhat earlier than the oldest beds at Montceau) up to the early Permian. Fossils from similar sites in Great Britain, Bohemia and the Saar Basin in Germany also support this scenario of changing climate.

Why do localities so distant from one another today share similar fossil life-forms? If one plots these sites on a paleogeographic map showing the position of the continents at the end of the Carboniferous period, the reason becomes obvious. At that time Europe, North America and much of Asia were joined in a single landmass, which geologists call Laurasia. A narrow sea, the Tethys, separated Laurasia from Gondwana, a vast protocontinent consisting of the future southern continents. There was no Atlantic Ocean and therefore Mazon Creek was much closer to Europe than it is now; more-

over, the sites lay near the Equator. These factors account for the climatic similarity of their fauna.

Laurasia and Gondwana have since drifted apart and broken up into the modern continents. Europe and North America became separated by the Atlantic Ocean. Most important, the continents migrated northward (except for Australia and Antarctica, which drifted southward). Consequently the Equator was no longer in Laurasia but in Gondwana; during the Permian it was already south of Mazon Creek, the Massif Central, the Saar Basin and Bohemia. This history explains the climatic evolution seen at Montceau.

Montceau has now been established, together with Mazon Creek and the Bohemian sites, as a typical reference site for the paleontology of Laurasia at the Permocarboniferous limit, but much remains to be done. The attic of the Natural History Museum in Autun is filled with cases holding thousands of unopened nodules. Study of the material will yield a precise picture of the local conditions of life and fossil deposition and help to specify the anatomical details needed to trace the

evolution of various species—information that is badly needed for this period in earth history. The investigators may find animals known from other sites but new to Montceau; these would add to knowledge of paleogeography. Each discovery will add yet another piece to the picture of the evolution of life on this planet.

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Plasma-sprayed Coatings

The hot, high-speed flame of a plasma gun can melt a powder of almost any ceramic or metal and spray it to form a coating for protection against corrosion, wear or high temperature

by Herbert Herman

In 1970 a student project I was supervising led to a happy accident. The student's assignment was to study the properties of aluminum oxide, a refractory (heat-resistant) ceramic, that had been melted and rapidly solidified. He faced two challenges: heating the substance to well above its melting temperature of about 2,000 degrees Celsius and then cooling it very rapidly. For a heat source he turned to the plasma gun, a device that had been invented in the 1950's and had served in industry for melting and forming deposits of metals and ceramics. In order to solidify the aluminum oxide quickly he planned to spray a thin layer of the molten material on a cool substrate.

The strategy worked in every detail but one. When powdered aluminum oxide was introduced into the hot, high-velocity flame of a plasma gun, it melted and was propelled onto a target of steel that had been roughened to hold the deposit as it accumulated. There it quickly cooled into a solid coating. At the time, however, we wanted to study the properties of the ceramic alone, free of any substrate. Yet the ceramic turned out to be impossible to remove, even with a chisel! We had stumbled on plasma-sprayed coatings, an existing but largely undeveloped technology.

HERBERT HERMAN is professor of materials science at the State University of New York at Stony Brook. He earned his doctorate from Northwestern University in 1961 and then did postdoctoral work at the University of Paris (Orsay) as a Fulbright scholar and at the Argonne National Laboratory. He went on leaves from his posts at the University of Pennsylvania and at Stony Brook to serve as a Ford Foundation Professor in Industry at the Western Electric Company and as a liaison scientist at the Office of Naval Research in London. Herman is editor-in-chief of *Materials Science and Engineering* and chairman of the thermal-spray division of ASM International.

Since then my laboratory and many others have been studying this coating technique intensively. My students and I now plasma-spray coatings of ceramics, metals and even polymers; we do so in air, in a vacuum and even under water, from hand-held guns and guns mounted on electronically controlled robot arms. The laboratory activity mirrors the wide variety of industrial applications that have emerged. In aircraft engines plasma-sprayed metallic coatings protect turbine blades from highly corrosive environments, and plasma-sprayed ceramics insulate other engine parts from high temperatures. Plasma-sprayed coatings are also found in internal-combustion engines, in power plants, in industrial machinery and in many other areas where technology places extreme demands on materials. As those demands increase and as theoretical and practical mastery of plasma spraying grows, the realm of applications is certain to expand.

Plasma spraying is by no means the only way to apply a protective coating; the alternatives range from procedures as simple as galvanizing to more sophisticated techniques such as vapor deposition, in which the coating material is vaporized and allowed to condense onto the substrate atom by atom. But plasma spraying can melt and apply a variety of materials, including refractory ceramics, at a high rate (in some cases more than 50 pounds per hour). The technique also carries much less risk of degrading the coating and substrate than many other high-temperature processes do, because the gas in the plasma flame is chemically inert and the target can be kept fairly cool. And yet a plasma gun can be only a little more cumbersome than a paint sprayer.

Plasma spraying has evolved in many details since 1970, but the basic design of the plasma gun has changed little. It consists of two

electrodes: a cone-shaped cathode inside a cylindrical anode, which extends beyond the cathode to form a nozzle. An inert gas—usually argon with an admixture of hydrogen—flows through the space between the electrodes, where it is ionized to form a plasma. A tube directs powdered coating material into the jet of plasma that develops in the nozzle. Water circulates through passages in the anode and the cathode to prevent the fierce heat from melting them.

The gun begins operating when a pulse of current creates an arc (an electrically conducting channel in a gas) across the gap between the electrodes. A steady direct current of many hundreds of amperes at a potential of 50 volts or so then sustains the arc. As the arc forms, electrons are torn from the atoms of gas; the electrons and the positive ions they leave behind are accelerated toward the anode and the cathode respectively. These rapidly moving particles collide with other, neutral atoms or molecules in the gas, dissociating any molecules into their constituent atoms and ionizing the atoms. In this way the gas within the arc is transformed into a collection of ions and energetic electrons: a plasma. The stream of gas that flows between the electrodes stretches the arc, so that in its course from one electrode to the other the arc loops out of the nozzle of the gun as a plasma flame.

Most of the electric power consumed by the gun—typically from 20,000 to 80,000 kilowatts—initially flows into the freed electrons in the plasma rather than into the positive ions. In tenuous plasmas, such as the glowing gas in a neon sign, collisions between the energetic electrons and the slow-moving positive ions are rare and little energy is transferred. The positive ions remain sluggish and the plasma, even though it is energetic, stays cool. The plasma of a plasma gun, however, is about 1,000 times

denser than the low-pressure plasma in a neon tube. Frequent collisions transfer energy from the electrons to the positive ions, accelerating them until the plasma reaches a kind of equilibrium. The result is a thermal plasma, in which the energy of the electrons has been turned into enthalpy, or heat content. A high enthalpy is associated with a high temperature; in a plasma gun the temperature can approach 15,000 degrees C.

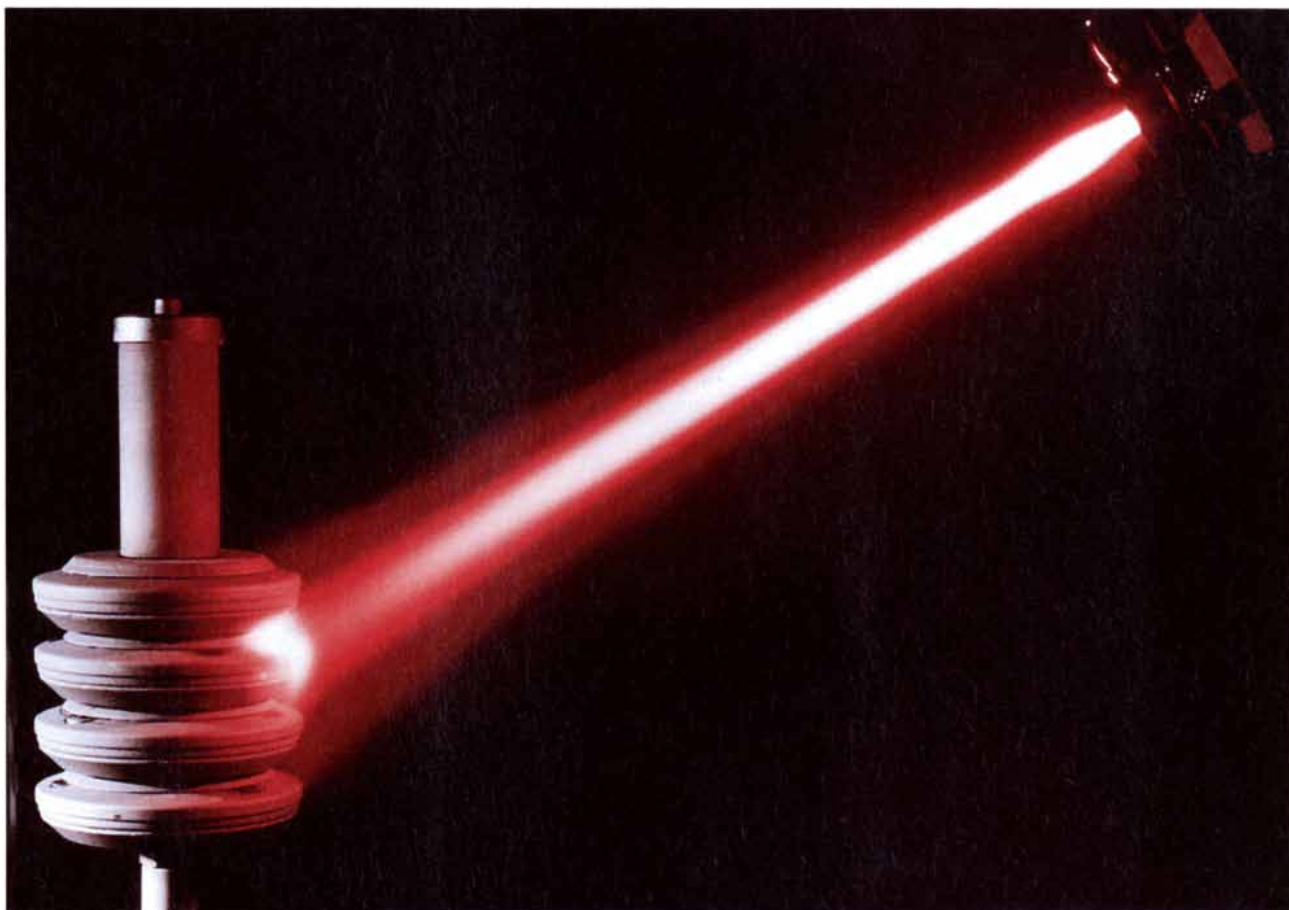
In addition to the enthalpy reflected in its high temperature, the plasma contains enthalpy associated with the ionization of the gas atoms and (a necessary first step for some gases) the dissociation of molecules into their constituent atoms. A plasma of hydrogen, whose molecules must be dissociated into their two atoms before they can be ionized, has a higher enthalpy at a given temperature than a plasma of argon, in which the atoms are independent to start with. Thus hydrogen added to the argon in a plasma gun increases the heat content

of the flame, and hence the gun's power and its ability to melt refractory materials.

The high temperature of the plasma generates high pressure, which is supplemented by two effects related to the plasma's electrical conductivity. Near the water-cooled walls of the anode the plasma gives way to a sheath of cooler gas that is not ionized and so is not conductive. The non-conductive layer narrows the plasma channel by forcing toward the center of the orifice the electric field lines that loop through the plasma from electrode to electrode. This so-called thermal pinch effect is supplemented by a magnetic pinch. The electric field threading the jet of plasma is accompanied by a magnetic field, which encircles and constricts the jet. Together these pinch effects increase the pressure, temperature and velocity of the plasma. Depending on the geometry and power of the gun and the flow of gas, the plasma flame can reach supersonic speeds.

The powdered coating material, carried in a stream of gas such as argon, is injected into the flame either within the nozzle or as it emerges from the outer face of the anode. What happens next, provided conditions are right, is simple in outline. The flame accelerates the particles, and they are melted by its high temperature, probably supplemented by heat given off as ions recombine and molecules reassociate on the surface of the particles. The molten droplets are propelled onto the target surface, where they solidify and accumulate to form a thick, tenaciously bonded protective coating.

For the process to succeed, however, a number of delicately balanced criteria must be satisfied. The particles must take enough heat from the hottest part of the flame—near the anode face—to melt thoroughly, but not so much that they overheat and vaporize. At the same time the droplets cannot linger in the flame; they must be traveling fast enough to flatten and spread out when they strike the target, flow-



PLASMA FLAME coats copper disks with tungsten to make X-ray-machine "targets," which release X rays on being bombarded with electrons. An electric arc in the plasma gun generates the flame by ionizing argon gas, converting it into a plasma. The tungsten powder is injected into the flame at the

nozzle of the gun, where the ions and electrons of the plasma are recombining. The flame, at a temperature of nearly 15,000 degrees Celsius, melts the particles and propels them onto the target. In this case spraying is taking place in a low-pressure, oxygen-free atmosphere to avoid degrading the metals.

ing into crevices and tightly gripping the surface.

A broad array of variables affect particle heating and acceleration. The heat content and velocity of the plasma flame play a critical role; they reflect such characteristics of the gun as its geometry and power level together with the composition and flow rate of the plasma gas. How effectively a given flame melts and accelerates the powder in turn depends on the kind of coating material and the size and shape of the particles. For a given coating material and gun there is an optimum particle size. Particles much smaller than the ideal will overheat and vaporize; much larger particles will not melt and may fall from the flame or rebound from the target.

The way the particles are fed into the flame also affects their melting and deposition. The pressure of the carrier gas must be adjusted to blow the particles into the flame but not through it. The angle of injection is critical as well: downwind injection minimizes the disruption of the flame

by the influx of particles and increases their velocity, whereas injection in the upwind direction gives the powder more time to take heat from the flame.

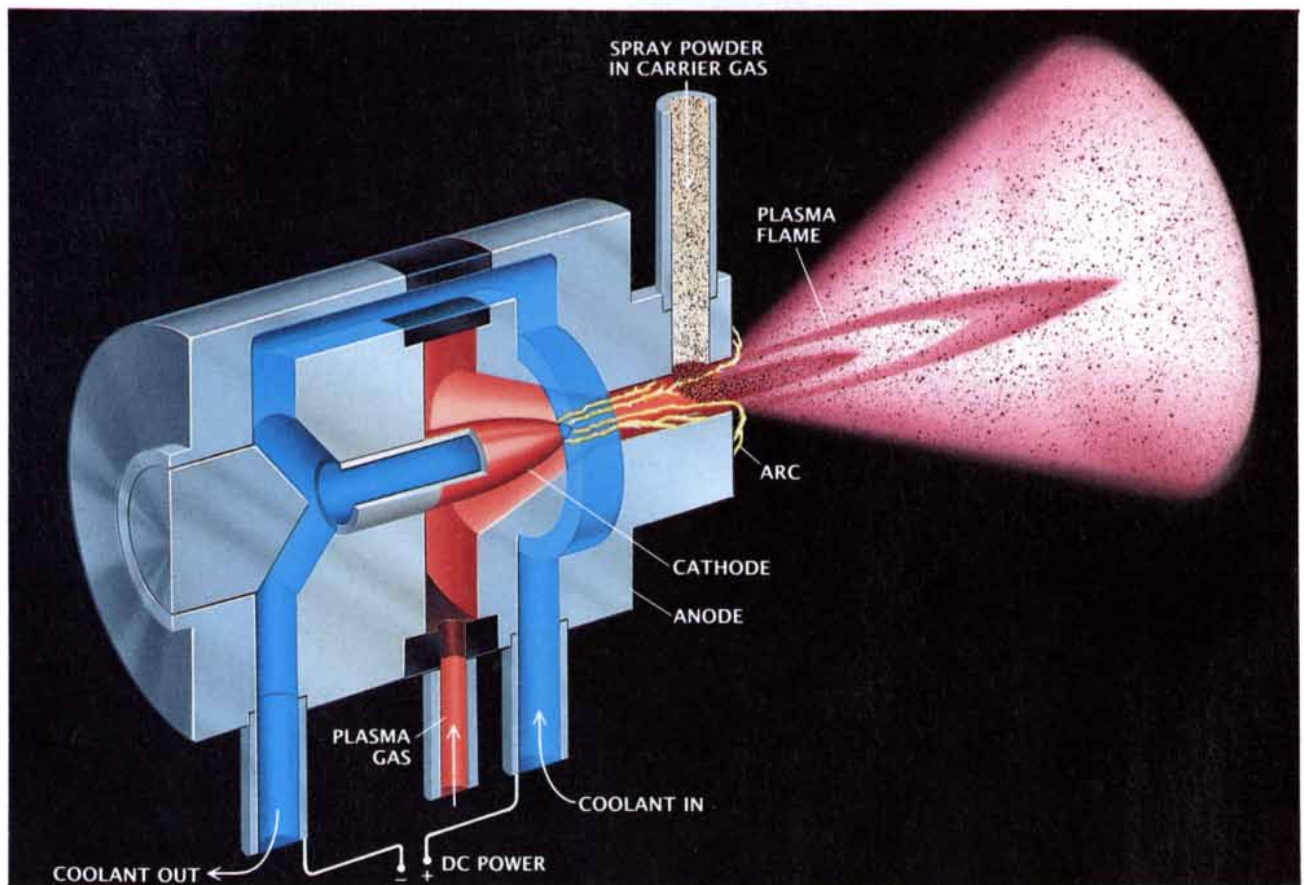
If the spraying is done in air, the particles begin to cool and slow down as they collide with air molecules after leaving the plasma flame. One more factor in the coating process, then, is simply the distance from the gun to the surface to be coated, which typically varies between five and 10 centimeters for spraying in air.

Until recently manipulating these variables—and many others—to produce a high-quality coating was at best a matter of informed guesswork. Now, in an effort to develop a theoretical foundation for designing plasma-spray systems, fundamental studies of the interaction of particles and the plasma flame are under way at various laboratories. At the University of Limoges, for example, Pierre Fauchais and his colleagues have carried out extensive studies of gas and particle velocities in the jet. These investigations and others like them rely on

laser Doppler techniques, in which the frequency shift of laser light reflected from the moving particles serves as a measure of their velocity.

To study the velocity of the gas itself, the Limoges group “seeded” the flame with very small particles of aluminum oxide, about three micrometers (millionths of a meter) in diameter. Such particles presumably accelerate rapidly and have little effect on the flow of gas, and so they can serve as reliable markers of gas behavior. By probing the seeded flame with a laser, the workers found it emerged from their gun at about 600 meters per second (almost twice the speed of sound) but then slowed continuously.

The group also studied particles with sizes of between 18 and 46 micrometers—a size range typical of many coating materials. The workers noted that larger particles responded more slowly to the accelerating gas and reached lower maximum velocities. On the other hand, all the particles, once accelerated, lost speed more slowly than the gas itself. At about



PLASMA GUN ionizes a stream of gas and injects powdered coating material into the resulting flame. An inert gas (red), mostly argon, flows through the space between a conical cathode and a ring-shaped anode. There the gas is ionized by

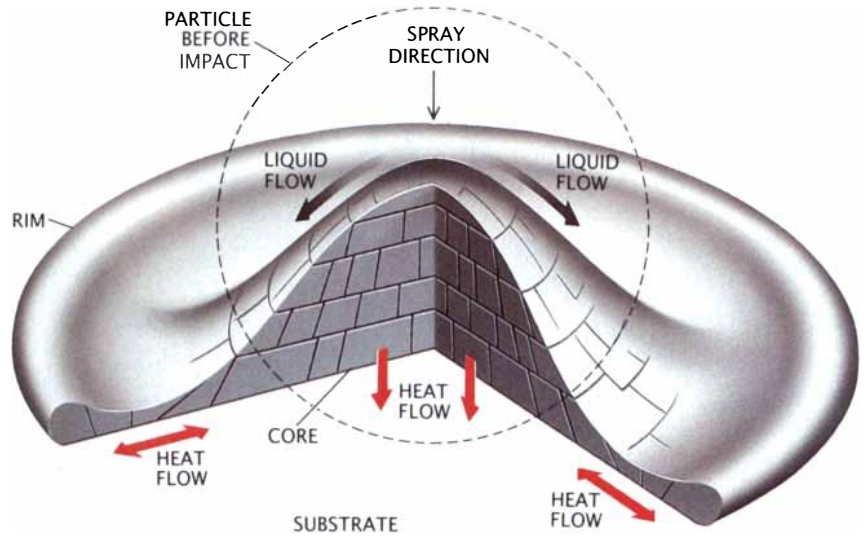
an arc, sustained by a powerful direct current. The resulting plasma jets out through the nozzle and sweeps up powdered spray material fed by a carrier gas (brown). Cooling water (blue) circulates through the gun to prevent it from melting.

seven centimeters from the gun nozzle the 18-micrometer particles had reached a maximum velocity of 260 meters per second, and they were still traveling more than 200 meters per second at 15 centimeters.

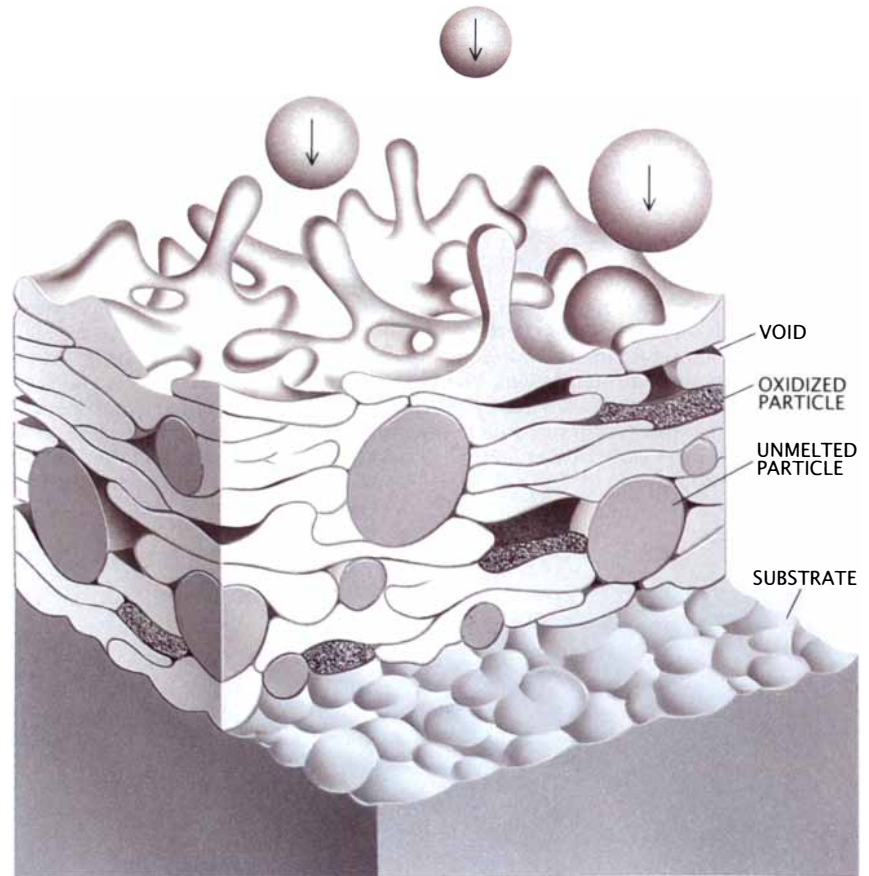
When the initial fast-moving droplets of coating material arrive at the target, they strike a surface that has usually been roughened beforehand by machining, grit blasting or abrasion. They solidify into the microscopically tortuous shape of the roughened surface, locking onto its irregularities. Particles continue to rain down at a rate of perhaps a million per second, accumulating into a coating at a rate that depends on the area to be covered and how fast the gun moves over the surface. To understand the process better we studied single “splats”—solitary droplets that have solidified on a surface—and complete coatings under the microscope. We relied on transmission electron microscopy for examining the internal structure of particles and coatings; scanning electron microscopy revealed overall shapes and textures.

Transmission electron micrographs of single splats showed that their internal structure—a mosaic of crystalline grains—contains many flaws, suggesting that each particle solidifies extremely quickly, in perhaps a millionth of a second. From the orientation of the grains and the overall shape of the splats, we developed a description of the process. As the impacting droplet flattens out on the surface, the substrate acts as a heat sink, and a solidification front moves upward through the splat. A low mound of solidified material forms and the remaining melt spills off it, finally hardening into a raised rim.

The result of this process, repeated many millions of times, is a layer of material that can range in thickness from 10 micrometers to many centimeters—a deposit thick enough to be removed from the substrate and employed as a bulk material. Ordinarily, however, the substrate has been roughened and the coating is firmly anchored to it by mechanical bonding. Other processes that are less well understood can also anchor plasma-sprayed coatings. Some coatings form chemical bonds with their substrates, and metallic coatings can establish a bond as the heat of plasma spraying (the workpiece can reach 200 degrees C. unless it is cooled with jets of air) enables atoms of the coating and the substrate to interdiffuse.



SPLAT results when a microscopic droplet of molten coating material strikes a surface, flattens out and solidifies. The author and his colleagues studied single splats by scanning and transmission electron microscopy. From the shape and orientation of the internal crystalline grains they concluded that as a splat solidifies, heat is lost to the substrate beginning at the center, which strikes the surface first. A solidified core forms, and remaining melt spills off it and hardens into a raised rim.



BUILDUP of a plasma-sprayed coating is a chaotic process. Molten particles spread out and splatter as they strike the target, at first locking onto the irregularities of the roughened surface and then interlocking with one another. Voids result as the growing deposit traps air. In some cases particles overheat in the flame and become oxidized; other particles may not melt and simply get embedded in the deposit.

The forces holding together the individually solidified splats in the coating are the subject of intense investigation. It is certain that successive splats interlock mechanically, at least. In metal coatings interdiffusion may also take place, and in some ceramic

coatings an analogous process called sintering can unify the deposit.

A micrograph showing the surface of a plasma-sprayed deposit intended to serve as a high-performance coating can be dishearten-

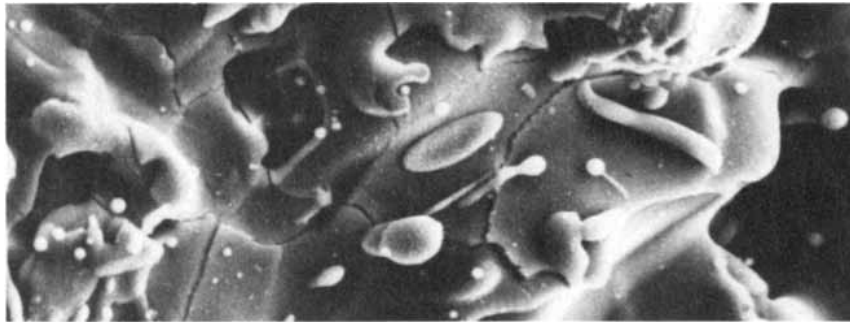
ing. Ceramic coatings in particular reveal a multitude of flaws. They are riddled with cracks formed as the ceramic cooled and are honeycombed with voids filled with air trapped in the deposit. Such flaws can doom a coating exposed to mechanical stress. If they extend all the way through the coating, they also make it useless for protection against corrosion.

Strangely, it is porosity that suits plasma-sprayed ceramic coatings to one of their most important applications: as thermal-barrier coatings, which are insulating coatings for metal parts exposed to very high temperatures in gas turbines and other kinds of engines. For one thing, porosity increases a ceramic's insulating ability. Moreover, because a ceramic is brittle in the first place, pores do not weaken the material but instead toughen it by interrupting the propagation of the cracks that inevitably form as the material is strained. They thereby give thermal-barrier coatings the ability to survive the mechanical stress that results from repeated exposure to high temperatures in the combustion section of an engine.

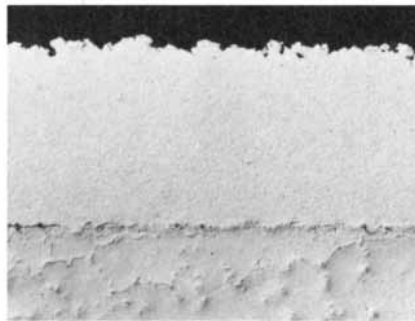
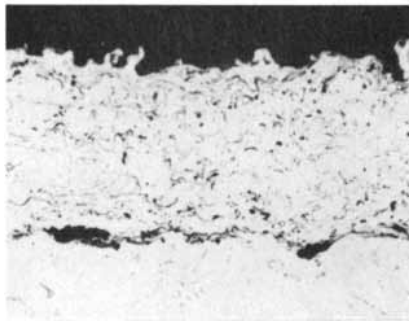
The function of a thermal-barrier coating, in fact, is to allow those temperatures to be raised still higher. The efficiency of any heat engine increases as its combustion temperature is raised. Yet aircraft turbine engines, for example, already function at temperatures that approach the operational limits of the superalloys from which combustion chambers, blades for turbines and other high-temperature parts are made. One way to exceed the apparent barrier is to replace the metal parts with components made of refractory ceramics, but the brittleness of ceramics and the difficulty of making high-quality ceramic parts have hampered this strategy.

By acting as a thermal insulator, on the other hand, a surface layer of ceramic a quarter of a millimeter or more in thickness can protect an engine's metal parts when its operating temperature is raised. Thermal-barrier coatings, usually made of oxides based on zirconium, are now found in the combustion sections of aircraft engines, marine gas turbines and large, stationary gas turbines that generate electric power. The piston caps, cylinder liners and exhaust ports of large diesels powering trucks, boats and locomotives have also been plasma-sprayed with ceramics to raise the engines' operating temperature and, it is hoped, their efficiency.

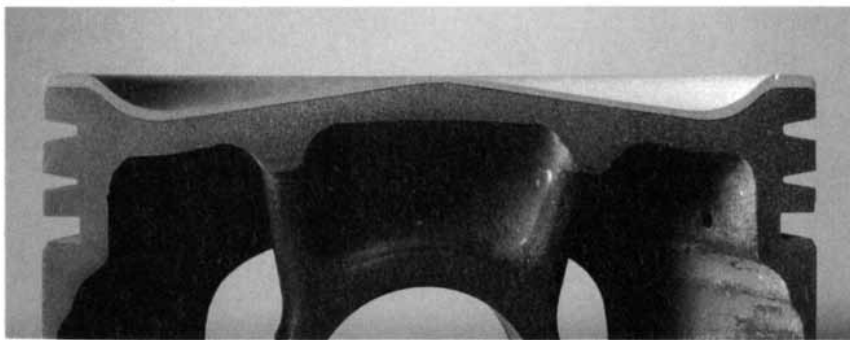
Service in an engine means repeated cycling between room temperature



CERAMIC COATING of plasma-sprayed aluminum oxide is enlarged about 2,500 times in a scanning electron micrograph. Spatters from impacting droplets have solidified on the surface, which is webbed with cracks formed as it cooled and contracted. Such preexisting cracks can toughen ceramic coatings by arresting the growth of other cracks that develop when these brittle materials are subjected to strain.



CROSS SECTIONS of plasma-sprayed coatings reflect the spray environment. These two optical micrographs show coatings of the same material, enlarged some 100 diameters: an alloy of cobalt, chromium, aluminum and yttrium, sprayed on steel in air (*left*) and in a vacuum (*right*). The coating sprayed in a vacuum (actually a low-pressure atmosphere of an inert gas) is much denser and more homogeneous than the coating sprayed in air, which contains voids and oxidized patches. In a vacuum the droplets travel faster and spread out more thoroughly when they strike the surface; in addition there is no air to be trapped in the coating or to react with it.



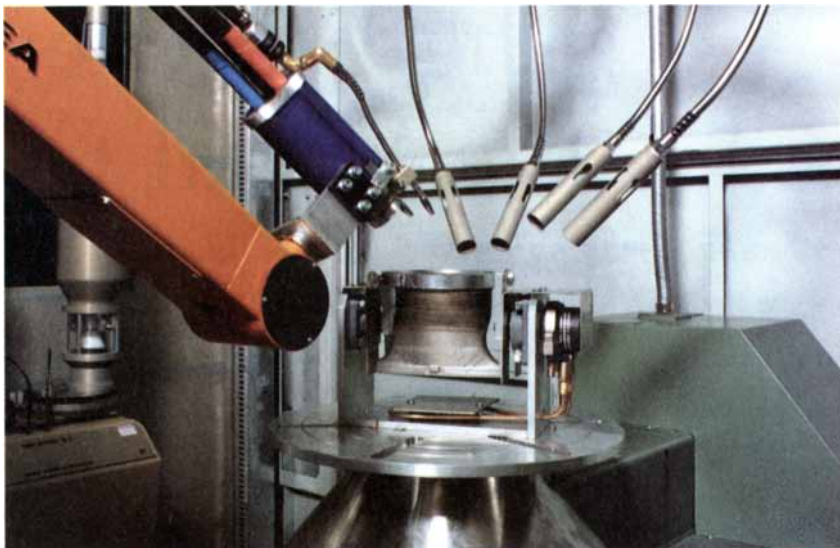
PISTON CAP, shown is cross section, is clad in a 2.5-millimeter-thick coating of plasma-sprayed ceramic. The ceramic, an alloy of zirconium oxide and yttrium oxide, is a thermal-barrier coating: it acts as an insulator, allowing the engine's operating temperature to be raised while protecting the underlying metal of its components. A higher operating temperature is thought to increase an engine's efficiency.

and perhaps 1,000 degrees C., resulting in strains that are compounded by a drastic difference in the rates at which the ceramic and the underlying metal expand or contract with temperature changes. Crack-stopping voids enable a thermal-barrier coating to survive this regimen. By retaining lubricants, pores also benefit some plasma-sprayed coatings designed to protect against wear, such as the layer of aluminum-titanium oxide with which many piston rings are clad. Such voids can be fatal, however, to many wear-resistant metallic coatings and coatings meant to prevent their substrate from corroding or oxidizing.

One way to achieve a void-free coating is to spray it in a chamber from which air is excluded, leaving only a low-pressure atmosphere of the plasma gas. In such "vacuum" plasma spraying no air can be trapped in the coating, so that one source of voids is eliminated; in addition the droplets, unhampered by air resistance, are deposited at higher velocities than they are in air and so spread flatter and thinner when they strike the surface. As a result vacuum plasma spraying yields a dense, void-free coating. The technique also makes it possible to plasma-spray metals such as zirconium, titanium and niobium, which would oxidize if they were heated in air, and to heat oxidation-sensitive metallic coatings and substrates so that they can bond by interdiffusion.

One widespread use of vacuum plasma spraying is producing the thin coatings of metal, generally only .08 millimeter in thickness, that protect turbine blades from oxidation. Such coatings, usually made of a complex alloy of nickel, cobalt, chromium, aluminum and yttrium, also serve as a first layer on many engine components that later are given ceramic thermal-barrier coatings. In that role they are known as bond coats, and besides protecting the metal part from oxidation they absorb some of the strain that results from the mismatch between the thermal-expansion rates of the part and the ceramic coating.

Like any simple and versatile technique, plasma spraying is giving rise to numerous variants and refinements. Plasma-spray equipment has been one focus of development. Workers in Czechoslovakia have produced high-powered (250-kilowatt) guns, meant for spraying material at a very high rate, in which water swirls around the internal diameter of the nozzle to cool it and constrict the flame. Plasma-Technik Sulzers AG in



ROBOT ARM (orange) holds a plasma-spray gun (blue) in position to apply a ceramic thermal-barrier coating to an aircraft-engine component; the four silvery nozzles direct jets of cool air at the metal to prevent it from overheating while it is treated. Plasma spraying has found its widest industrial application in the aircraft industry. The photograph was made at Plasma-Technik Sulzers AG in Wohlen, Switzerland.

Wohlen, Switzerland, has developed automated systems that can intricately manipulate the gun and the workpiece in order to coat complex shapes such as turbine blades. Recently the Metco division of the Perkin-Elmer Corporation in Westbury, N.Y., devised a gun that has a movable cathode, which makes it possible to adjust the power of the gun by varying the characteristics of the arc instead of by adding a secondary plasma gas, such as hydrogen. Manufacturers have also introduced mechanisms that feed several different powders into a gun and can gradually substitute one powder for another as the spraying proceeds in order to produce a coating whose composition and properties change across its thickness. Some workers are even experimenting with a plasma gun of a radically different design, in which a rapidly alternating electric field generated by a radio-frequency coil replaces the arc as the plasma source. These so-called RF plasmas do away with electrodes and the possibility of contaminating the coating with material eroded from them.

Investigators are also applying the technique to new materials. The General Electric Company is using vacuum plasma spraying to make freestanding components: intricate aircraft-engine parts formed by plasma-spraying a superalloy on a removable substrate. Other workers spray ceramic particles or fibers and a metal powder simultaneously to produce a strong, stiff composite material: the ceramic particles

dispersed in a matrix of metal. In a joint program with workers at the U.S. Naval Research Laboratory and Metco, my colleagues and I have fabricated a thick film of high-temperature superconductor by plasma-spraying the compound in the form of a powder—a strategy that could play an important role in the manufacture of future superconducting devices.

At the same time we and other investigators continue to extend our grasp of the underlying phenomena: the plasma flame, the encounter between the plasma and the powdered coating material, the deposition, solidification and buildup of the material, and the behavior of coatings in their intended environments. By achieving a good theoretical grounding we can hope to continue creating plasma-sprayed coatings to satisfy the most stringent requirements of industry.

FURTHER READING

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The Discovery of the Visual Cortex

Soldiers who suffered head wounds in the Russo-Japanese War were among those who contributed to the identification of the brain's visual center and the first description of its organization

by Mitchell Glickstein

A person who has perfectly healthy eyes can be blinded by damage to the back of the brain. The reason is simple: the rearmost (occipital) lobes of the two hemispheres that constitute the cerebrum (the uppermost part of the brain) form a major center for vision. They contain what is known as the primary visual cortex. If this cortex is destroyed, the brain will not be able to detect the vast majority of the visual signals transmitted from the eyes.

The explanation may be simple, but the fact that a discrete part of the cerebral cortex (the sheet of gray matter that covers the cerebrum) is devoted to vision was far from easy to uncover. Indeed, the process of discovery spanned more than a century. The history leading to the identification of the primary visual cortex is fascinating in its own right, mixing ingenuity, astute observation, folly and failure. It is also important for what it led to: an ever increasing understanding of how the brain functions and how people see.

When a person looks at something, light coming from the object produces a scaled-down image of the object on the retina: the array of photoreceptors and connected nerve cells at the back of the eye. The retina translates the image into nerve impulses, which are

carried over the cablelike optic nerve to the brain [see illustration on page 122]. The primary targets of this nerve are two collections of nerve cells deep in the brain called the lateral geniculate ("kneelike") bodies. The optic nerve transmits visual signals from the right side of the visual field to the lateral geniculate body in the left hemisphere, and it transmits signals from the left side of the visual field to the right hemisphere.

The lateral geniculate bodies then relay the signals to the occipital lobe on the same side of the brain, and specifically to the primary visual cortex, which does an initial analysis of the image and transmits selected information about it to other regions of the brain. Those regions in turn analyze the information further, interpret it and make use of it to control the movements of the eyes or limbs.

The path leading to the discovery of the primary visual cortex began in the late 1700's—about 50 years before the cell was recognized as the basic structural and functional unit of plants and animals, and more than 100 years before the specialized properties of nerve cells (the building blocks of the brain and the spinal cord) were described. Lacking such knowledge of cells, investigators in the late 18th century had little concept of how the brain functions, but they had made good headway in describing its general appearance.

For example, in 1783 the Scottish anatomist Alexander Monro II published a textbook that accurately (and beautifully) showed the major subdivisions of the brain, including the gray cortex of the cerebrum and the underlying white matter. Nevertheless, the cortex was depicted as a uniform sheet of gray without any substructure.

Today the cortex is known to be divided into layers, each of which differs in the type of nerve cells it contains and the packing of both cells and nerve fibers: the long, signal-carrying "axons" that extend from cell bodies.

The image of a featureless cortex became outdated at about the same time Monro's text was published. Seven years before the book appeared, an Italian medical student at the University of Parma named Francesco Gennari began a detailed study of the brain. Gennari, who was just 24, hardened brains with ice, examined the surface features and then cut and dissected the specimens in order to describe both superficial and deep structures. He published his observations in a 1782 monograph titled *De Peculiaribus Structura Cerebri*, printed by the famed publisher and typographer Giambattista Bodoni.

In his book, which at the time was relatively obscure, Gennari noted that the cortex is not uniform. Rather, the gray matter is divided by a whitish layer—a line in cross sections—that parallels the surface of the brain.

RUSSO-JAPANESE WAR of 1904-5, depicted in this 1904 woodcut, contributed indirectly to the understanding of human vision. During the war a Japanese physician named Tatsuji Inouye examined Japanese soldiers (*right*) who had bullet wounds to the head and correlated the site of injury with the patient's visual losses. He thereby determined how different parts of the visual field are mapped onto the main vision center of the brain: the primary visual cortex. Inouye's studies were possible because the Russians had introduced rifles that used smaller, faster bullets. These penetrated the skull without shattering it, allowing many soldiers to survive their injuries and to cooperate with Inouye.

MITCHELL GLICKSTEIN is professor of neuroscience at University College London and is on the external scientific staff of the Medical Research Council. He earned a doctorate in experimental psychology from the University of Chicago in 1958 and held positions at the California Institute of Technology, the Stanford University School of Medicine, the University of Washington School of Medicine and Brown University before moving to London.

He was surprised. As he put it: "None of the anatomists I happened to read have taught that in addition to the cortical and medullary substance there is in the brain another substance which I am accustomed to call the third substance of this organ." (The "medullary" material is the white matter under the cortex, which is now known to consist primarily of nerve fibers sheathed in a whitish substance known as myelin. The "third substance," Gennari's stripe, probably consists of myelinated axons as well, ones that transmit signals within the occipital lobe.)

In addition to discovering the myelinated stripe that bears his name, and hence recognizing that the gray matter is subdivided, Gennari also realized that the cortex looks different in different regions of the brain. In particular, he found that the white line, which sometimes appears "as a single stripe, sometimes [as] two independent parallel stripes," is difficult to see in sections of the front part of the brain but "can be detected more and more clearly in the posterior part"—specifically in the region that is now known to be the primary visual cortex. A footnote indicates that Gennari first saw the stripe on February 2, 1776.

Thus, working with the simplest of

tools, well before new staining methods opened the way to the microscopic study of the brain, Gennari initiated the field of cerebral architectonics: the study of regional differences in cortical structure. Yet because he was not well known, his role in the discovery of the variable white stripe in the brain was not widely acknowledged until a century later.

Meanwhile two others claimed, or were credited with, the stripe's identification. Samuel Thomas Soemmering, professor of anatomy at the University of Göttingen, insisted that he had described the band four years before Gennari had, in a book published in 1778. Soemmering had indeed mentioned a stripe in his book, but he described it as yellowish and placed it in the cerebellum, where there is no such stripe. What Soemmering saw was probably either one of the layers in the gray matter covering the cerebellum or an artifact of the method he employed to examine the brain.

In spite of Soemmering's claim, credit for the discovery of the stripe usually went to the eminent French anatomist Félix Vicq-d'Azyr. In 1786, four years after Gennari's monograph appeared, Vicq-d'Azyr described the white line and its location in his massive and beautiful *Traité d'Anatomie*.

Because of the Frenchman's prominence, the line came to be known as the stripe of Vicq-d'Azyr. Not until 1882, when the Austrian anatomist Heinrich Obersteiner reviewed the dates of Gennari's and Vicq-d'Azyr's contributions, was the band rechristened the stripe of Gennari.

Gennari is now one of the most cited anatomists of all time, yet his name is for the most part unfamiliar to the people of the city he lived in and even to most scholars at the university where he made his discovery. Moreover, until I became a visiting professor at the University of Parma in 1983 little had been written about his life. Because of the paucity of information, I collaborated with Giacomo Rizzolatti of the university's Institute of Human Physiology to learn more about Gennari's personal history.

We found that he was born some 25 kilometers from Parma, in the tiny village of Mattaleto, which is in the foothills of the Apennines. After finishing medical school in 1776 and earning a place in the College of Physicians, he established a medical practice and pursued the anatomical studies that led to his book. A year after the book was published, he was granted a stipend to continue his research at the university, but he published nothing



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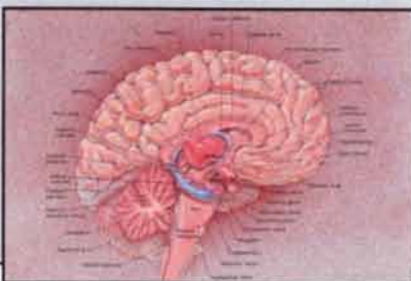
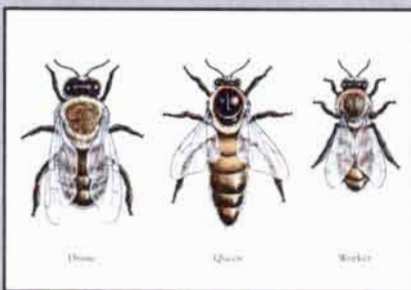
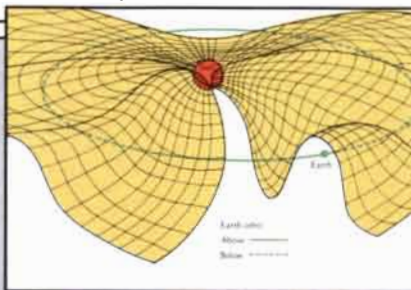
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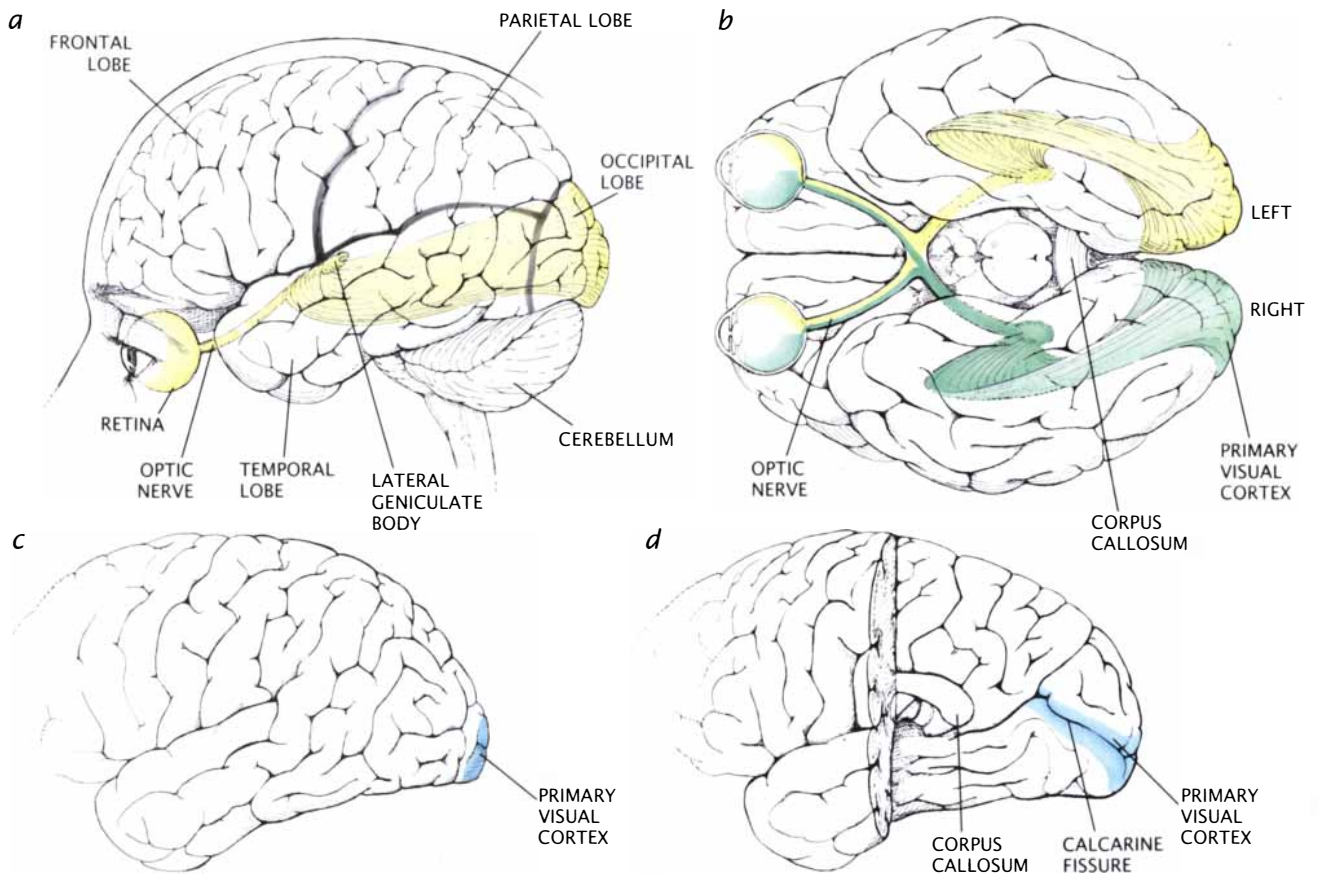
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BASIC PATH of visual signals through the brain is shown from the side (*a*) and from below (*b*). The retina of the eye converts light from an observed object into nerve impulses and relays them by way of the optic nerve to a collection of nerve cells deep within the brain called the lateral geniculate body. From there the impulses travel to the primary visual cortex, which is in the occipital, or rearmost, lobe of each hemisphere. Signals from the right side of the visual field (*yellow*) go to the

occipital lobe of the left hemisphere, and signals from the left side of the field (*green*) go to the right hemisphere. The primary visual cortex (*blue in details*) constitutes a fraction of the cerebral cortex (the convoluted sheet of gray matter that blankets the hemispheres). It consists of a small part of the outermost surface of each occipital lobe (*c*) and a much larger part of the medial surface (*d*)—the inner surface, facing the opposite lobe—including a groove called the calcarine fissure.

else. Gennari died, impoverished and ill, at the age of 45, after years of trouble and misery brought on in part by compulsive gambling.

Before he lost his way in life, Gennari was a remarkably astute scientist. He realized that the structural variations he had found in the cortex probably reflected differences in function, but he had no way of knowing what those functional differences might be.

Serious experiments into cortical function began not long after the publication of Gennari's monograph. In the typical experiment investigators produced lesions in the brain of animals and studied the resulting deficits. These experiments, combined with the observations of the deficits found in human beings who had suffered brain damage, led by 1850 to the recognition that the cerebral cortex is essential for normal movement, sensation and thought.

Nevertheless, there was as yet no compelling evidence for making the next crucial connection, namely the realization that specific lesions lead to specific functional deficits. In fact, the very idea of cortical localization was given a bad name by a pseudoscientific fad known as phrenology, which started in the first half of the 19th century. Franz Joseph Gall, a prominent anatomist who worked in Vienna and later in Paris, taught that the brain is composed of as many individual regions as there are psychological faculties. He argued that the shape of the skull reflects the form of the brain under it, and that personality and character traits—such as cruelty and a love of food—can be evaluated by palpating the head. Gall's disciple Johann Spurzheim expanded the scheme and attracted some support from physicians as well as an enthusiastic popular following.

Such experimental evidence as there

was in the first half of the 1800's seemed to point away from localization. For example, the French physiologist Pierre Flourens reported that a lesion in the forebrain of animals resulted in a mixture of effects; a single lesion might leave an animal with sensory deficits, difficulty understanding what it saw and felt, and difficulty initiating movement. He therefore concluded that sensation, perception and volition cannot be separated, that whatever controls them is diffused throughout the cortex. "Unity is the great principle, it is everywhere, it dominates all," he announced. "The nervous system therefore forms one unitary system." Sensible opinion favored Flourens.

In the third quarter of the 19th century three discoveries finally made the concept of localization attractive once again. In 1861 the French physician Pierre Paul Broca reported that a lesion in the left frontal lobe of one

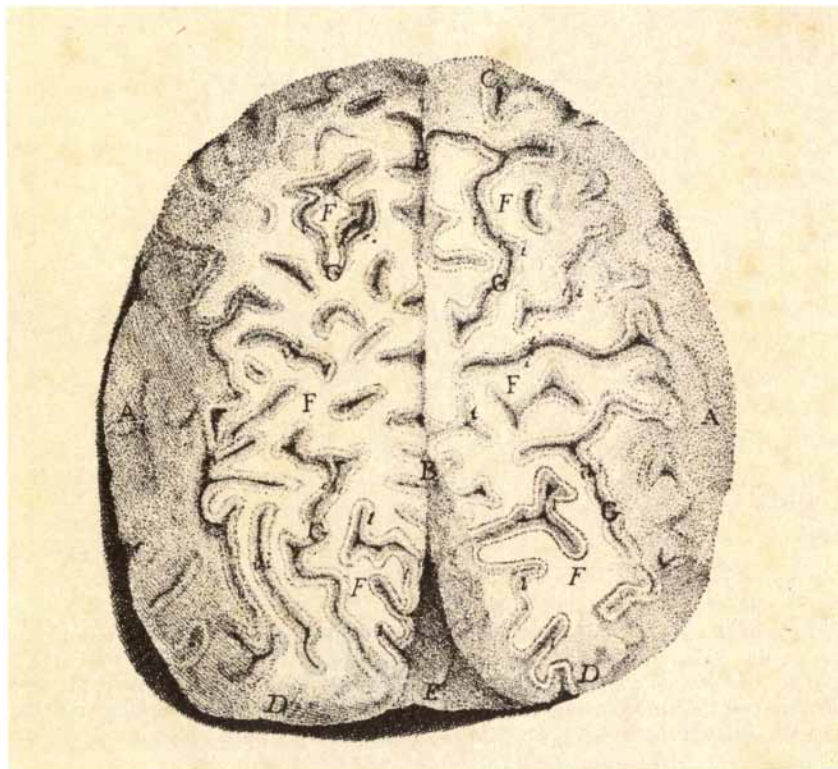
of his patients resulted in a permanent speech disorder. A few years later John Hughlings Jackson, a London neurologist, described a type of epileptic seizure that begins with a rhythmic movement of one body part and then spreads to neighboring regions in a definite sequence. The pattern was suggestive of a brain organization in which adjacent brain regions control adjacent parts of the body.

Then in 1870 the German physiologists Gustav Theodor Fritsch and Eduard Hitzig did an experiment that was arguably the single most important factor in initiating new investigations of cortical localization. They electrically stimulated discrete areas of cortex in the frontal lobe of a dog and found that the stimulus produced the movement of a limb or some other body part on the opposite side of the body. The surgical removal of an area whose stimulation had resulted in movement in a limb made the animal clumsy when moving the same limb. Interpretations of this experiment varied, but one reasonable explanation held that in spite of earlier claims to the contrary at least one part of the cortex is specialized for the control of a specific function: movement.

The search was on for regions that control other functions, particularly vision. The first person professing to have identified the center for vision was the British neurologist and physiologist David Ferrier, who initially worked in laboratory space made available at the West Riding Lunatic Asylum in Yorkshire and then moved to King's College London.

By systematically noting the effects of alternating current on the brains of animals, Ferrier confirmed that stimulation of certain parts of the brain resulted in specific kinds of movement. At King's College, where he concentrated on monkeys, he also found that stimulation of an area known as the angular gyrus, which is located in the parietal lobe, caused the eyes to move. The finding suggested to Ferrier that

STRIPE OF GENNARI, a white layer (*l*, top) within the gray cerebral cortex, is shown in a 1782 illustration of a horizontal section of the brain. The illustration appeared in a monograph (*bottom*) by the stripe's discoverer, Francesco Gennari. The observation of the stripe, which is most prominent in the primary visual cortex, was the first recognition that the cerebral cortex has structural subdivisions, and it led Gennari to speculate—correctly—that the cortex in the back of the brain might have a unique function.



FRANCISCI GENNARI

PARMENSIS

MEDICINAE DOCTORIS COLLEGIATI

DE PECULIARI

STRUCTURA CEREBRI

NONNULLISQUE EJUS MORBIS .

PAUCAE ALIAE ANATOM. OBSERVAT.

ACCEDUNT .

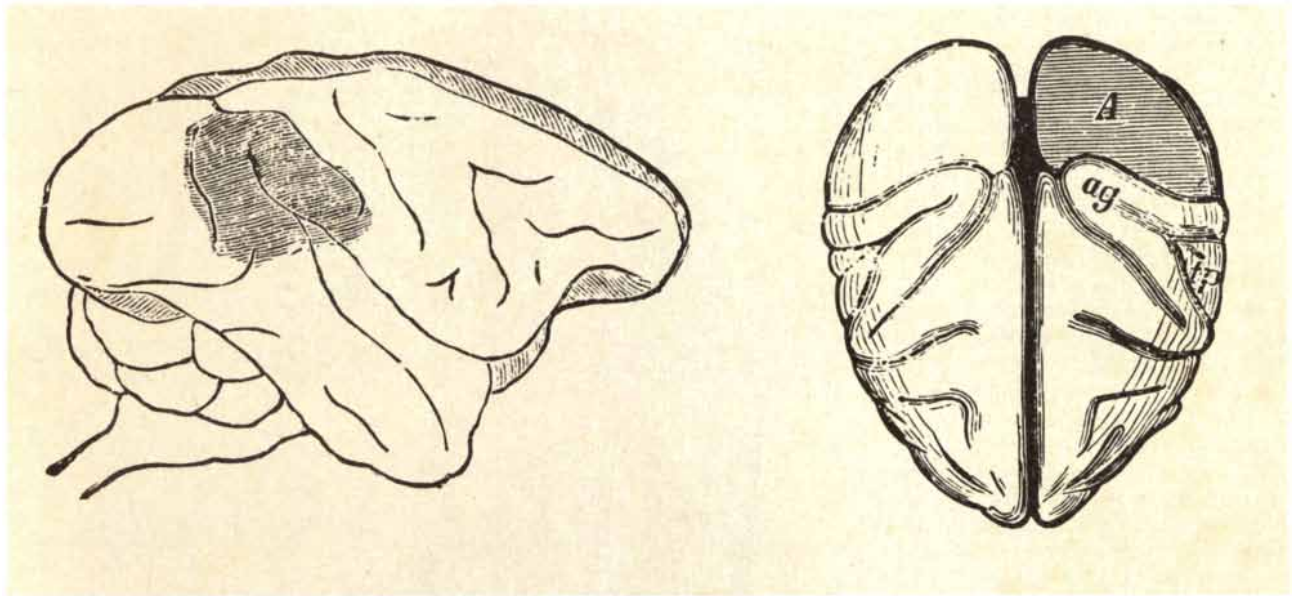


PARMAE

EX REGIO TYPOGRAPHEO

M. DCC. LXXXII.

CUM APPROBATIONE .



LESIONS made in the brain of monkeys initially yielded contradictory information about the location of the main vision center of the brain. In 1876 a British neurologist named David Ferrier reported that the removal of a region in the parietal lobe known as the angular gyrus (*triangular shaded area, left*)

blinded monkeys. He suggested that the region is the seat of vision. Hermann Munk, a German physiologist, strenuously disagreed; his studies, which he discussed in an 1881 publication, indicated that the occipital lobe (*area A, right*) is responsible for vision. Later work ultimately proved Munk was correct.

the angular gyrus might well be the sought-after visual area of the brain.

To test his idea further, he removed the angular gyrus and observed the response of the monkeys. Excising the gyrus from only one side of the brain seemed to leave the monkeys unable to see in the eye opposite to the lesion; if both gyri were removed, the animals seemed to become completely blind.

Ferrier's evidence for the total loss of vision was largely anecdotal. He reported, for example, that one monkey, which was particularly fond of tea, seemed unable to locate a cup placed right before its eyes.

"On placing a cup of tea close to its lips it began to drink eagerly," Ferrier reported to the Royal Society of London in 1875 and in his book *Functions of the Brain* in 1876. "The cup was then removed from immediate contact, and the animal though intensely eager to drink further, as indicated by its gestures, was unable to find the cup, though its eyes were looking straight towards it. This test was repeated several times with exactly the same result. At last on the cup being placed to its lips, it plunged in its head and continued to drink though the cup was gradually lowered and drawn half way across the room." Lesions of the occipital lobe did not produce a comparable handicap; hence Ferrier had no reason to think that the occipital lobe was important for vision.

Ferrier's conclusions were contro-

versial. His most bitter opponent was Hermann Munk, a German professor of physiology at the Berlin Veterinary School, who had begun his own experiments soon after Ferrier started his. Munk correctly reported that damage to the occipital, not the parietal, lobe is responsible for blindness. He found that removal of the occipital cortex from one side of the brain made monkeys hemianopic: unable to see one side of their visual field. Because each eye lost half of its vision, Munk concluded that both eyes must be connected to both the right and the left hemispheres of the brain. He also reported that removal of the occipital cortex on both sides of the brain produced total blindness.

Munk was not gentle to his opponent. In an 1881 publication he records two sets of comments he had made earlier to the Physiological Society in Berlin: "In my first communication on the physiology of the cortex which I made in March of last year I did not say anything about Ferrier's work on the monkey because there was nothing good to be said about it."

When he was asked to express his views at a later session, however, Munk seems to have had quite a bit to say. He first listed several of Ferrier's conclusions, including not only his assertion that the angular gyrus is the visual center in the monkey but also his idea that the occipital lobe is the seat of hunger! Then he stated that

Ferrier's declarations "are worthless and gratuitous constructions since the operated animals were examined by Mr Ferrier in quite an insufficient manner and only at the time of general depression of brain function. If I have gone too far in this statement which is based on a general survey of Mr Ferrier's experiments it was up to me to restore the injury, the sooner the better. However, as the experiments show now I have said...rather too little than too much. Mr Ferrier had not made one correct guess, all his statements have turned out to be wrong."

The acrimony between these two investigators was so strong that the psychologist and philosopher William James noted in his 19th-century psychology textbook that "the subject of localization of functions in the brain seems to have a peculiar effect on the temper of those who cultivate it experimentally...Munk's absolute tone about his observations and his theoretical arrogance have led to his ruin as an authority."

Munk, as it turns out, escaped ruin, and he continues to be recognized for having demonstrated clearly that the occipital lobe has a unique role in vision. Even so, Ferrier's work merits further attention, both because questions remain and because the results he obtained did provide a clue to the visual organization of the brain.

Why is it that Ferrier did not see a clear loss of vision after lesions were made in the occipital lobes of monkeys, and what was happening to the animals that seemed to be blinded by lesions of the angular gyri? Ferrier's failure to blind his monkeys by damaging the occipital lobe in both hemispheres is not hard to explain. In almost every instance he removed a large part of each lobe—the section found behind a deep groove known as the lunate fissure. This would have eliminated most of the primary visual cortex but not all of it. Even if just a few millimeters of cortex remained, the animal would have retained a good deal of its vision because, as will become clear below, relatively small amounts of the primary visual cortex map a rather large extent of the peripheral visual field.

Ferrier's monkeys probably lost central vision, then, but they would not have been blind. Presumably they compensated for their visual losses to a great degree. Monkeys quickly learn to exploit whatever sight remains after a brain injury, and they are aided in this effort by their ability to move their eyes and head quickly. Munk, for his part, probably produced blindness by including in his lesions more of the medial face of each lobe: the inner surface that faces the opposite hemisphere. Much of the primary visual cortex is on the medial surface.

As to why monkeys that lacked angular gyri seemed to be blind, Ferrier's descriptions of the animals' activity indicate that he had unwittingly discovered not the visual center of the brain but a region that is of major importance for the control of visually guided movement: the faculty that enables one to, say, reach accurately for a raspberry on a bush or walk down a busy street without bumping into

anyone or anything. Ferrier's monkeys could no longer guide their movements according to what they saw, and that is why they had difficulty reaching food placed in front of them.

Ferrier himself must have eventually recognized his mistake. In his first experiments he had allowed his monkeys to live only three or four days after surgery because infection was inevitable. Later, when he adopted the sterile surgical procedures of Joseph Lister, which allowed the monkeys to survive and heal, he realized the monkeys did not stay "blind." His description of the monkeys as they recovered makes it clear that the major effect of his operation was to produce deficits in visually guided movement.

While Ferrier pursued his studies of the angular gyrus, Munk's conclusion that the occipital lobe is the seat of vision gained support. By 1890 Edward Albert Sharpey-Schäfer, professor of physiology at University College London, had replicated Munk's results, and physicians had reported many cases of patients who suffered partial blindness following damage to the occipital lobe.

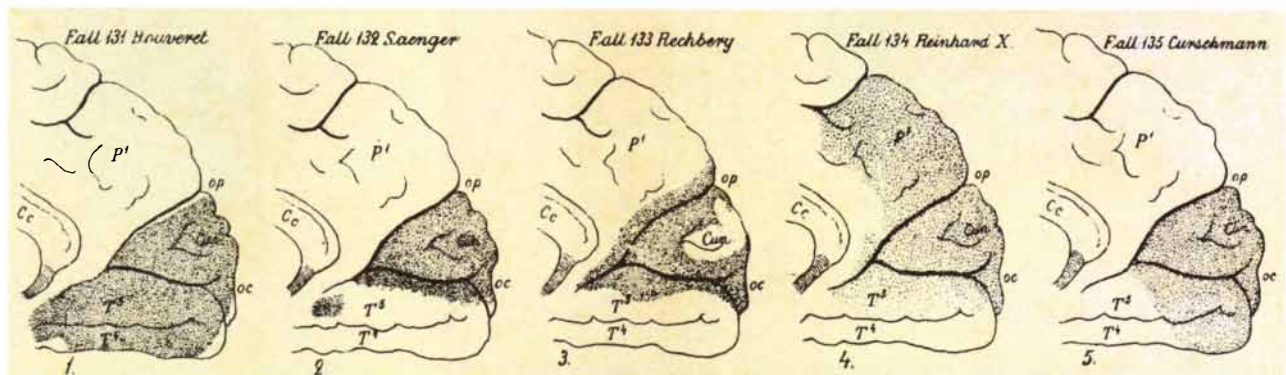
The Swedish neuropathologist Salomen Eberhard Henschen of the University of Uppsala summarized the clinical story in 1892. He assembled all the available papers meeting two criteria: they described cases in which brain damage had led to the loss of the right or the left half of the visual field, and they included an autopsy report on the site of the brain damage in the affected hemisphere. In every case the damage included the region of the occipital cortex that surrounds and includes a groove prominent on the medial surface of both hemispheres: the calcarine fissure. This region contains the part of the cortex in which Gennari's stripe is most visible.

Thus, after more than a century, Henschen confirmed Gennari's early suspicion that the cortex with the prominent stripe—the striate cortex—has a unique function. Indeed, Henschen had finally demonstrated that the striate cortex is no less than the primary visual center of the brain.

If the visual world is mapped onto the striate cortex, how is the map arranged? Henschen correctly observed that the lower visual field is mapped onto the upper bank of the calcarine fissure and that the upper visual field is mapped onto the lower bank. He also proposed that the center of the visual field is mapped onto the forward part of the striate cortex and that the periphery of the visual field is mapped onto the rearward parts. This proposal was incorrect.

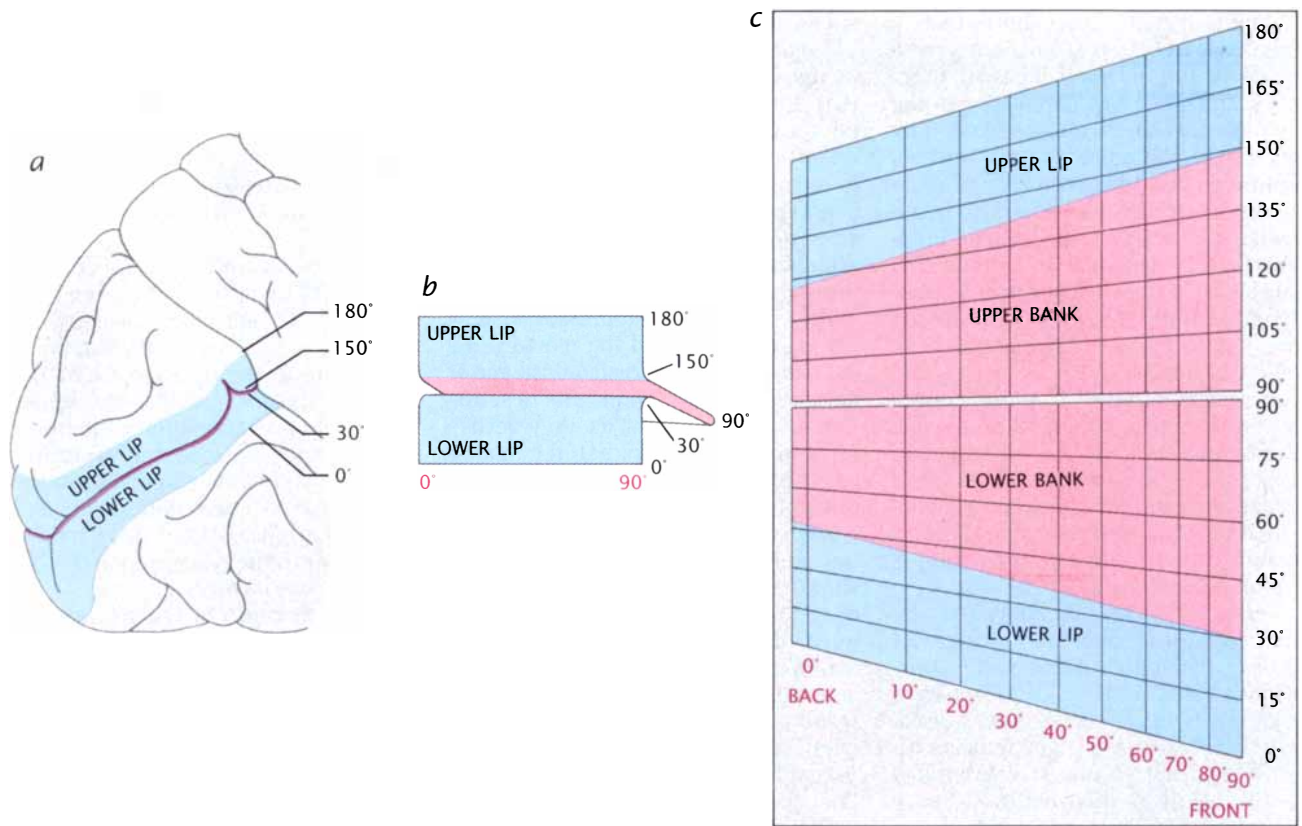
Henschen came to the wrong conclusion because the data at his disposal were not fine enough: the patients on whom he had based his conclusions had large lesions. What was needed was a series of patients who had partial damage to the striate cortex and had lost the ability to see one or another region of the visual field. Such cases are a by-product of wars, and the next war arrived in due course.

In 1904 and 1905 troops of the Imperial Russian Army fought the Japanese in several bitter campaigns in Asia. The war involved more than 500,000 soldiers, and its casualties provided a young Japanese physician named Tatsuji Inouye with enough data to develop the first reasonably accurate scheme showing how the visual field is represented in the human brain. Inouye eventually reversed Henschen's proposed mapping pattern; he showed that the central part of the visual field projects to the back of the visual cortex and the periph-



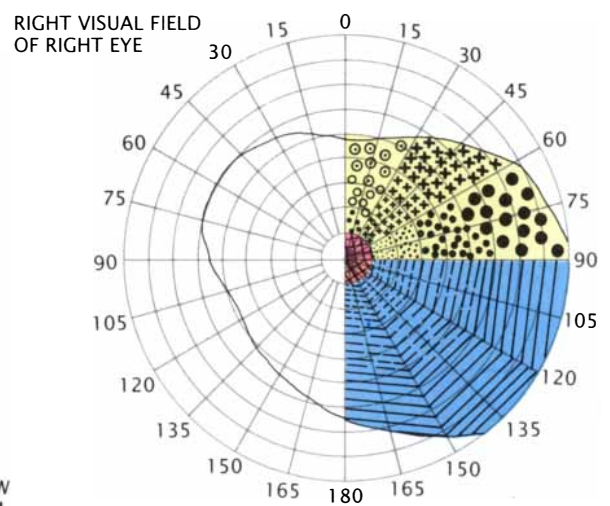
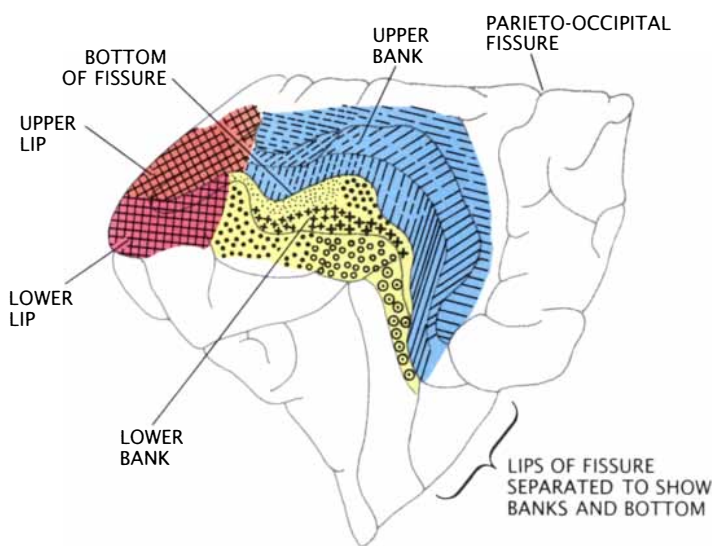
SITE OF BRAIN DAMAGE (shaded regions) in partially blind patients was mapped by a neuropathologist named Salomen Henschen in 1890. These drawings, showing the medial sur-

face of the occipital lobe, represent a few of the many cases he studied. His work helped to confirm Munk's suggestion that the vision center of the human brain is in the occipital lobes.



INOUE'S SCHEME showing how the visual field is mapped onto the primary visual cortex—that is, onto the lips (*blue*) and banks (*pink*) of the calcarine fissure—was published in 1909. (Here the right side of the visual field is mapped onto the occipital lobe (*a*) of the left hemisphere.) Inouye described locations in the visual field (not shown) by a coordinate system in which the horizontal axis is calibrated in degrees of “azimuth,” from -90 degrees on the left to 90 degrees on the right, and the vertical axis shows “elevation,” from zero degrees at the top to 180 degrees at the bottom. The center lies at zero

degrees azimuth and 90 degrees elevation, and the right side of the visual field corresponds to the points to the right of the vertical axis. To make the scheme Inouye spread the fissure (*b*), revealing its banks; he then mapped azimuth (*red*) along the fissure's horizontal dimension and elevation (*black*) along the vertical axis (*c*). The diagram shows that the center of the visual field is represented at the rear of the occipital lobe, whereas more peripheral parts are represented toward the front of the lobe. It also reveals that a disproportionately large amount of the visual cortex is devoted to central viewing.



ANOTHER SCHEME showing how the visual field (*color*) maps onto the visual cortex in the occipital lobe was developed by Gordon Holmes in 1918. (The center of the visual field lies at the center of the grid.) The images are Holmes's, although his symbols have been redrawn and color and new labels have

been added for extra clarity. His scheme quickly supplanted Inouye's because it is easier to grasp and shows that the area of cortex devoted to the center of the visual field is disproportionately large in the vertical as well as the horizontal direction; Inouye's diagram showed only horizontal magnification.

eral visual field projects to the front.

In spite of his contribution to neuroscience, Inouye has been virtually ignored for many years, an oversight that David Whitteridge, a colleague of mine from the University of Oxford, and I hope to correct. We recently tracked down the 1909 monograph Inouye wrote (in German) and translated it into English; we also got in touch with his family in Japan to learn more about his personal history.

Inouye, who was born in Tokyo in 1881, completed his medical studies at the University of Tokyo and began work under a prominent ophthalmologist in the year before the Russo-Japanese War broke out. He became a physician in the army, where he examined a number of Japanese soldiers who had lost some vision as a result of head wounds from bullets. He also examined soldiers referred to him by other physicians, and he studied one Japanese soldier injured in the Boxer Rebellion of 1900 in China.

The creation of Inouye's scheme was facilitated by the fact that the Russians had introduced an entirely new rifle, the Mosin-Nagant Model 91, which shot bullets that had a higher muzzle velocity (620 meters per second) and a smaller diameter (7.6 millimeters) than the bullets of earlier wars; the new bullets often penetrated the skull without shattering it. The patients lost consciousness for periods lasting from a few hours to several days after they were injured, but they recovered enough to cooperate in Inouye's studies. (They had a personal reason to do so: their pensions were based on how much visual damage they had suffered.)

Inouye based his description of the cortical map on data from 29 patients. For each patient he made a careful plot of the visual field of each eye (the right eye normally sees a slightly different image from the one the left eye sees) and pinpointed the site of injury on the skull. In order to determine exactly which part of the brain was damaged, he identified each bullet's entry and exit points and calculated the area of brain that would be damaged assuming a straight trajectory through the brain tissue. He had satisfied himself that the assumption was reasonable by analyzing cases in which a soldier had been hit while firing from a prone position. The bullet entered and left the skull and then reentered the body in the shoulder or the forearm. In such cases the three wounds were consistently in a straight line—another consequence of the high-velocity Russian bullets.

In addition to correcting Henschen's error about the orientation of the map, the scheme that resulted from Inouye's efforts revealed a fundamental fact about the organization of the striate cortex: the proportions of the image are not preserved when the image is mapped onto the cortex. Inouye did not depict the mapped proportions entirely correctly, but he did recognize that a disproportionately large fraction of the striate cortex is devoted to the central visual field, as might be expected from the fact that the macular region of the retina (the region of central focus) has a high concentration of visual cells.

Inouye died just 12 years ago at the age of 96, but his work has long been overlooked, in part because during World War I the renowned British neurologist Gordon Holmes and his colleague William Tindall Lister produced a more accessible and refined diagram of the way in which the visual cortex maps the visual field. That figure has since been widely reproduced.

Holmes and Lister developed their scheme in much the same way as Inouye had: they were assigned to British military-base hospitals, where they studied the visual losses that followed injury to the occipital lobe. Although their findings for the most part agreed with Inouye's, they disagreed with him on one major point. Inouye, along with a number of investigators before and since, found that patients rarely lost a complete half of the visual field when they had widespread damage to the left or right occipital lobe. Rather, they continued to see a small region in the center—the part that falls directly on the macula—suggesting that the central region is mapped twice, once on each side of the brain.

Holmes and Lister vigorously denied that such "macular sparing" occurred; they believed all cases of apparent macular sparing were caused by incomplete damage to the occipital lobe. Who was right? Macular sparing probably does exist, but no single explanation accounts for all cases.

The work of Holmes and Lister essentially completed the chapter of history devoted to the discovery of the primary visual cortex and the initial description of how it functions. I should mention, however, that they and the other people mentioned in this article were by no means the only important players in the decades-long drama; I have singled out only a few of the major figures, concentrating on those who have gotten too little credit for their contributions.

In the years since the introduction of Inouye's and Holmes's schemes much has been learned about the organization of the cerebral cortex in general and the striate cortex in particular. For instance, the areas of cortex adjacent to the striate cortex and beyond it on the temporal and parietal lobes are now known to have a predominantly visual function and to receive their major input directly or indirectly from the striate cortex. In monkeys and human beings roughly half of the cerebral cortex is devoted to processing the visual image.

The study of the brain's role in vision is by no means complete. One major task for the future is to elucidate the specific functions of the extrastriate areas: How does the visual system process color, form and movement? How is such information used to recognize familiar objects and to guide the body's movements?

Many workers look more to the future than to the past as they pursue such issues, and yet a knowledge of history helps to keep the often frustrating process of investigation in perspective. As is true in almost every new research area, progress was slow initially, before technical and theoretical advances made many of the fundamental discoveries possible. Laboratory research with animals then clarified a previously chaotic view of brain organization. That research sometimes led to erroneous conclusions, but further experiments confirmed the facts and resolved the puzzles. The results have led clinicians to a better understanding of their patients' disorders and ushered in an era of prolific research into the remarkable workings of the human brain.

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SCIENCE AND BUSINESS

Patent Medicine

New patents challenge Congress and courts

On the outskirts of Washington, D.C., sits the U.S. Patent and Trademark Office. On long shelves and in wood cases, it houses the more than 4.75 million U.S. patents issued since 1790. In recent years this venerable office has seen a new kind of patent: genetically modified living matter, ranging from microorganisms to mammals. Although the courts have ruled that such patents are legal, a lively debate continues on Capitol Hill about the appropriateness of patenting life. Meanwhile, companies holding the patents worry about the extent of their legal protection.

The stakes in these debates are high. "Patents are vitally important to both the pharmaceutical and biotechnology industry," says David J. Mugford, associate general counsel at Schering-Plough in Madison, N.J.

"Over \$1.7 billion has been spent on biotechnology research and development and the results can be copied relatively easily," adds George B. Rathmann, chief executive officer at Amgen in Thousand Oaks, Calif., and chair-



Living controversies, teaching manufacturing, counsel on change, melodious computers

man of the Industrial Biotechnology Association. The companies developing products through recombinant-DNA techniques have therefore come to rely heavily on patents as a way of protecting their investments, he says.

Originally the Patent Office was unwilling to patent living organisms. But in 1980 the Supreme Court ruled that Ananda Chakrabarty, a scientist at General Electric, was entitled to a patent for his novel strain of bacteria that digested oil slicks. The decision set a legal precedent and spurred investment in commercial genetic-engineering research. It showed that companies could gain ownership rights to the fruits of their labor. "The Chakrabarty decision set the stage for Genentech's public offering and was directly linked to our ability to start this company," Rathmann says.

Although in theory the Chakrabarty ruling cleared the way for patenting any life forms except human beings, the Patent Office continued to move cautiously. In 1985 the office's Board of Appeals and Interferences reaffirmed that all plants could be patented. Two years later an application for an oyster with multiple sets of chromosomes raised the issue of patenting higher life forms. Again the Board of Appeals said the Patent Office could issue a patent for the organism. (The application was actually rejected as too "obvious," however.) Last April, the Patent Office awarded the first patent for "transgenic non-human mammals" to investigators from Harvard University for a mouse that incorporates a human gene.

As a result of those decisions, patenting life forms is legally acceptable, says Reid G. Adler, an attorney with Finnegan, Henderson, Farabow, Garrett & Dunner in Washington, D.C. Nevertheless, that has not stopped an-

imal-rights advocates, some farm coalitions and environmentalists from petitioning Congress to ban animal patents. Some worry about the morality of patenting life; others ask whether farmers will have to pay royalties on the progeny of patented animals. Still others fear that releasing new organisms into the environment could cause serious ecological disruptions. Although Congress has held hearings on the issue of patenting life, calls for a moratorium on patenting organisms have won little support.

Congress is nonetheless trying to come to grips with many of the other concerns. In mid-July the House Subcommittee on Courts, Civil Liberties and the Administration of Justice approved a proposal from Representative Robert W. Kastenmeier (D-Wisc.) that would exempt farmers and researchers from paying royalties on the progeny of patented animals. In another bill, Kastenmeier proposed that the U.S. Department of Agriculture and the Environmental Protection Agency issue permits to those who wish to develop transgenic livestock or release genetically altered animals into the environment.

The nature of biotechnology patents has raised other questions as well. Most of the patents awarded to companies exploiting recombinant-DNA techniques have been for unique processes, rather than for products such as animals or organisms. Patent holders would rather have exclusive rights to a product than to a process, notes Iver P. Cooper, associate general counsel for the Association of Biotechnology Companies, since it is far easier to detect and prove infringement on a product than on a process. But so far much of genetic engineering has been aimed at making known drugs such as insulin more easily and cheaply than is possible through conventional techniques; consequently, a majority of companies hold process patents.

Not surprisingly, companies are eyeing one another's processes for making the same product with suspicion. A landmark case in this area is likely to be the ongoing dispute between Amgen and Genetics Institute in Cambridge, Mass. By employing recombinant-DNA technology, Amgen created an organism that produces erythropoietin (EPO), a protein that regulates the rate at which red blood cells are formed. Three months before Amgen



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received its patent, Genetics Institute won a patent giving it rights to a more conventional process for making EPO as well as to the product EPO itself. Each company now claims the exclusive right to EPO.

Process patents have also been a source of international friction. While product patents receive the same protection outside the U.S. as they do domestically, process patents do not. Under what Cooper describes as a "quirk" in U.S. law, foreign companies manufacturing in plants outside the U.S. can employ a U.S.-patented process and sell the resulting product in the U.S. without paying royalties. Because of the number of process patents "the issue is extremely important to biotechnology," Mugford observes. What took a U.S. inventor five years can be replicated abroad in a matter of days, Rathmann adds.

Only if a U.S. company can prove a foreign importer has inflicted "economic damage" on domestic industry, will the International Trade Commission bar importation of the product. But proving economic damage is difficult, according to Cooper. Moreover, the U.S. company will not receive any compensatory payment even if damage is proved. Congress has debated extending protection to process patents since the Johnson Administration; this year it may act. Legislators hoped to have a bill ready for the President in early September.

As Congress and the courts have wrestled with the implications of biotechnology, the Patent Office has faced its own challenges. The office has been flooded with more biotechnology applications than it could manage, and applicants have often waited more than four years for a patent. This problem was exacerbated when many examiners qualified to review biotechnology applications were hired by the private sector. The Patent Office has also come under much criticism from Congress for its prototype computer database of patents; the work has taken more time and more money than anticipated.

Slowly, however, the Patent Office is getting back on course, say industry leaders. According to Mugford, the office has made great strides in organizing a special group to handle biotechnology and in hiring and training more examiners. The office has also proposed that biotechnology applications include the long sequences of DNA bases that describe the genetic makeup of an organism in machine-readable form, preferably on floppy discs. This will enable examiners to check by

computer for genetic similarities between an organism described in an application and organisms that have already been patented. For now, examiners continue to scan the copies of patents kept in the traditional wood cases.

—Elizabeth Corcoran

Making Manufacturers

M.I.T. aims to teach manufacturing principles

Although it is barely September, 20 first-year graduate students have been toiling over assignments for three months. At the same time, several dozen business leaders and professors are trying to thrash out their future curriculum. All are part of an experimental master's degree program that the Massachusetts Institute of Technology hopes will eventually change the way companies manage manufacturing.

For two years, with no summer vacations, the students will take enough courses to earn master's degrees in both engineering and business administration, focused on manufacturing issues. Along with attending regular classes at the Sloan School of Management and the engineering school, they will participate in seminars based partly on talks from leaders in business and technology and on tours of local manufacturing plants.

At the heart of the program are six-month thesis projects that teams of students will undertake at manufacturing plants. Their problems will be "real"—such as how to cut the time it takes to get a product to customers—and will be jointly picked by companies, faculty and students, says H. Kent Bowen, a codirector of the program and a professor in the engineering school. "We hope that they [the students] will see the intellectual challenges and career opportunities in manufacturing," he adds.

That would be a change. In recent years, fewer than 5 percent of the graduates from the top U.S. business schools have taken jobs in production and operations. In contrast, consulting and—before the stock market crash—investment banking have each claimed roughly 20 percent of the graduates.

It is not just that MBA graduates long for careers in finance, say business school administrators. Few companies have promoted production and operations managers as rapidly as they have promoted managers in finance and marketing. "It used to be, in the 1950's, that the road to success for

the CEO was through manufacturing," says Arnaldo Hax, a deputy dean at Sloan. "Perhaps in the long run we may recapture that."

Industry, too, has been searching for ways to enhance manufacturing. "We're concerned about what it takes to make ourselves competitive," says William C. Hanson, vice-president of manufacturing for Digital Equipment in Maynard, Mass. That concern spurred nine corporations, led by Boeing, Digital Equipment and Kodak, to agree to provide people, time and reportedly \$30 million for the M.I.T. program. This money covers the tuition and monthly stipend for all joint-degree students; it will also fund the research projects of some 30 M.I.T. faculty members from the engineering and management schools. The investigators will explore manufacturing issues chosen jointly with industry.

Marrying the study of engineering and management is certainly not a new idea. Cornell University initiated a small, five-semester program offering a joint master's degree in engineering and business in 1985. More typically, though, graduate engineering programs have simply encouraged students to take a few business courses, while business schools have required students to take one "operations" course that covers everything from assembly lines to customer relations.

M.I.T.'s engineering school and Sloan administrators, however, felt that the informal ties between engineering and management "missed the mark," Bowen says. Even MBA candidates with bachelor's degrees in engineering "get overwhelmed by accounting or strategic management and forget to tie in the technology," he adds. And so four years ago the dean of the engineering school began to campaign for the program that is now under way.

Although one program may not make much difference, "we hope other, similar programs will follow," Hanson says. The M.I.T. program will be a "multimillion dollar investment over five years" for Digital Equipment, he says, "but compared to the size of the problems, that's not very big." —E.C.

Change Artist

Consultant offers framework for corporate change

These days, many chief executive officers are struggling to change their companies to exploit new technology or improve their competitive edge. Over the past eight years,

a number of them—from James R. Houghton at Corning Glass Works to David T. Kearns at Xerox—have turned to David A. Nadler, president of Delta Consulting Group in New York City.

Most of Nadler's work goes unpublished; clients come through referrals. He offers no pat solutions. "I can tell you what your problem is, but I can't fix it," he says. "It's more powerful if I give you a framework for solving it."

At the center of Nadler's framework are two visions of the corporation. On the one hand, he sees it as a system. Inputs, such as consumer demands, stiffening competition and the advent of new technology, force the system to change internally. If the changes are made skillfully, they will yield a change in output, such as greater efficiency. On the other hand, Nadler argues that the system is a human one, running on the skills and enthusiasm of thousands of individuals. Consequently, sending down orders from the head office without considering how they will affect individuals below does not work, he says. Instead changes must maintain the "congruences," or the way individuals fit together with the tasks at hand and the formal and informal ways things get done.

Pamela P. Flaherty, a senior human-resources officer at Citibank, says she has often watched Nadler describe his framework and help his listeners quickly fit it to their situation. People feel that they have found the solutions themselves, Flaherty adds, "even though he's orchestrated it." As a result "you come away energized."

Consider one example Nadler will talk about: infusing Xerox with the importance of quality throughout the company. In the early 1980's Xerox found itself battered by Japanese competition. Eighteen trips to Japan convinced Kearns that the only way to fight back was to improve quality radically. "His problem was: How do you get 100,000 people to work differently?" Nadler recalls.

According to Paul A. Allaire, president of Xerox, Nadler approaches problems with an intimate knowledge of the experiences of other chief executive officers who have made similar changes. Because "he recognizes that companies have informal structures" that direct their operations, Allaire adds, Nadler helps companies tailor his framework to address their most pressing problems.

With Nadler, Xerox began by creating a team of 17 "quality executives," one from each major unit of the company. They held workshops on how to change tasks and formal structures to

improve quality as well as on individuals' hopes and fears about the shift. Every other week the representatives would return to their groups to let them know about the changes. As a result individual employees throughout the company had enough time to adjust to the changed environment and develop new informal structures. Xerox became a textbook example of how to restore a company's competitive edge.

Nadler also relies heavily on technology. During meetings at Delta's headquarters, Nadler may quietly type notes that are immediately displayed on a common computer monitor. Through his judicious notewriting, say participants, Nadler subtly guides—not dominates—the discussion.

Nadler's skill in shaping group dynamics reflects his diverse background. In his early years, when he hoped to follow in his father's career in the foreign service, he earned a bachelor's degree from George Washington University in international relations. But he became intrigued with management; a master's degree from the Harvard Business School and a Ph.D. in psychology from the University of Michigan eventually led to a job as an associate professor at Columbia University's business school in the mid-1970's. When he became frustrated with academia, he took a year's leave of absence to try full-time consulting. He has not returned to the classroom since.

—E.C.

Silicon Minstrels

These computers ain't just whistling Dixie

Night and day a team of computers is waiting to serenade you. Just give it a call and it will play a ragtime melody, improvise on a five-string banjo and sing scat—all over the telephone. It has even been known to accept collect calls.

For more than two years Bellcore in Morris Township, N.J., has funded these computer recitals. Why? "There are some kinds of research that really benefit the culture but don't show a profit," investigator Peter S. Langston, who dreamed up the project, asserts. "This is one of them." From Bellcore's vantage, Langston's research pulls together advanced computer software and novel sound-transmission techniques, according to Stuart I. Feldman, who supervises Langston.

Langston's work is premised on a simple observation: a rock-music afi-

cionado forced to listen to Beethoven and a lover of classical music subjected to Led Zeppelin may not like what they hear but will concede that it is music rather than simply noise. Langston is looking for a few common syntaxes, ideally in the form of simple algorithms, common to all music. Imposing such algorithms on snippets of random noise would then make the brief intervals sound like music even though they would lack content or theme. Such were the humble beginnings of what describes itself as "Peter's weird music demo."

Call the appropriate number. (It usually circulates by word of mouth in the research community.) "Hi!" answers a computer-generated voice. "This is Eddie, your computer-music phone friend. Oh boy, you are really, really going to like this music, I can tell." After the listener chooses the short, medium or long demo, Eddie turns over the show to his colleague, "Eddie, but you can call me Mom." Then begins an assortment of "musical" interludes ranging from 10 seconds to two minutes in duration. All are "performed live": once a phone call is connected, the music synthesizers in Langston's laboratory start to swing.

Between passages Eddie interjects brief descriptions of the work. One tidbit relies on "fractal interpolations of an eight-note theme," Eddie chirps. "First the eight-note theme is played and then successively more elaborate interpolations are played until things really get out of hand." Six passages based on random numbers have a pulse more often heard in discotheques than in research labs.

Most of Langston's experiments are run for listeners at Bellcore; the recitals took to the phone lines when Eddie was connected to a computer-controlled telephone-switching experiment, also at Bellcore. To date Eddie has performed for almost 10,000 callers from eight countries. Langston does not plan to program the system to record feedback from listeners, however, until he sharpens Eddie's musical prowess.

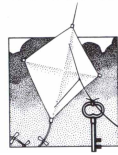
In addition to furthering investigations on the phone system and computer software, Eddie is bettering Bellcore's reputation as a place that sponsors interesting albeit offbeat research, Feldman says. He agreed to let Eddie accept collect calls to help spread the word, or rather the song. Sadly, however, when Bellcore learned of *Scientific American's* interest in Eddie, it canceled the collect-call service.

Even so, for a good time, you can call: 201-644-2332.

—E.C.

THE AMATEUR SCIENTIST

Shock-front phenomena and other oddities to entertain a bored airline passenger



by Jearl Walker

When an airliner is at cruising altitude, air sweeps past it at several hundred miles per hour. You look through the onrush of air every time you watch the passing landscape and clouds through an airplane window. Yet your view is normally so clear that you may well forget about the ferocious flow of air just outside the window.

The flow is quite noticeable, though, if you are sitting behind the wing and look at the landscape through the highly turbulent exhaust from a jet engine. The chaotic variations of air density within the exhaust alter the direction of the light rays reflected from the ground. The rays are refracted randomly by the turbulent gases and what you see is a wobble dance of features in the landscape. The dancing is diminished when the plane is on the ground, because then much less air flows through the engine.

There are some less obvious clues that sometimes reveal the flow of air past an aircraft in flight. In her book *Science from Your Airplane Window* Elizabeth A. Wood describes one subtle tip-off: objects on the ground may appear distorted when light rays from

them pass near the front of the wing. Wood first noted such distortion when she was seated near the leading edge of the wing and peered down at a long road that cut across the landscape at an angle to the wing. As the airplane proceeded over the landscape, the road seemed to slide gradually out of sight under the wing. Although the road was straight, the segment of it immediately in front of the wing always seemed to be bent toward the wing [see illustration below].

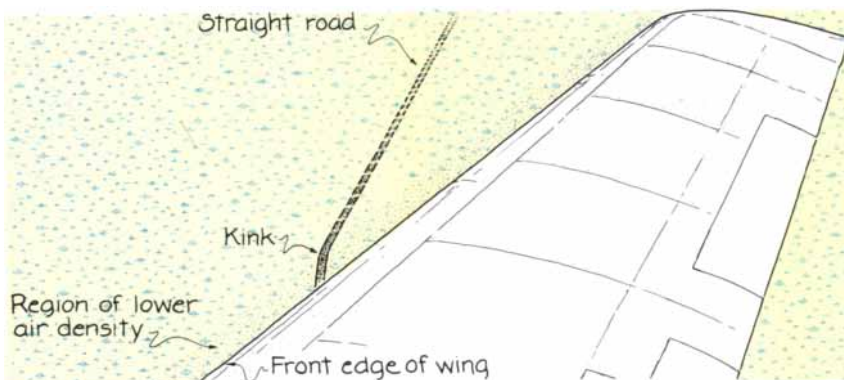
The kink in the road was an illusion. As a wing moves through the air some of the air is forced up over it; the speed of that air increases and its density decreases. The changes begin somewhat in front of the wing. When Wood viewed the road along the front edge of the wing, she intercepted rays that traversed the region of lower-density air there. The variation in density refracted the rays slightly upward. Now, when a light ray enters your eye, you automatically extrapolate it backward to perceive its source without considering any bending it may have undergone on its way to you. Such was the case with Wood and the refracted rays. The deflection of the rays toward

the vertical made part of the road seem to be nearer the wing than it was. Since rays coming from the road farther from the wing did not pass through the lower-density air and were not bent, their origins were seen correctly. The apparent kink in the road was the point where the undistorted image of the road joined the displaced image.

Although this is certainly the right explanation of the illusion, one detail bothered me for some time: the reduction in air density near a wing seemed to be too small to refract most of the rays by any perceptible amount. I assumed that the refraction works as follows. A ray is refracted when it crosses the boundary of the region of lower-density air. When it enters the lower part of the region, it is refracted somewhat toward the boundary. Since the ray is initially angled upward, the refraction makes it a little more vertical. Thereafter the ray travels in a straight line across the region until leaving it, whereupon it is refracted somewhat away from the boundary; again the refraction rotates the ray toward the vertical. What bothered me was the fact that if the air density is only moderately lower near the wing, refraction is significant only when a ray passes through the boundary at a glancing angle; the few rays that had that angle of approach hardly seemed capable of creating the illusion.

I finally realized my error by taking a closeup view of the displaced bit of road. Starting at the kink position, the size of the illusory shift of the road increases steadily with proximity to the wing, suggesting that the air density decreases steadily as the wing surface is approached. In the presence of such a density gradient, a light ray is refracted throughout its traversal of the region near the wing, and so it follows a curved path [see bottom illustration on opposite page]. A ray that originates near the illusory kink has a short journey through the region and curves only slightly; a ray from the part of the road that is most displaced penetrates the region deeply, and so it curves more. The nonuniform deflection of the rays produces the nonuniform displacement of the road between the kink and the wing.

I can see a related illusion when I am seated just behind a wing and gaze over it. I pick out a large building in the approaching landscape and keep watching it as it seems to come closer to the wing. As it is about to disappear under the wing, it suddenly becomes distorted and seems to flow toward the wing, disappearing a little before it



The bent-road illusion

"should" disappear [see top illustration on next page]. By raising my head to bring the building back into view, I can repeat the disappearance act. At first I wondered if I was seeing only a confusing composite of my direct view of the building and a fleeting reflection of it out on the front edge of the wing. I checked by gradually raising my head to keep a building right at the edge, thus momentarily freezing the scene for study. There was no reflection: the image of the building was in fact distorted—stretched toward the wing.

The distortion was due to the same trick of refraction that kinked Wood's view of the road. When the lower part of the building's image neared the wing, it suddenly sank in my view because light rays from it were refracted into a curved path by the density gradient just above the wing. For a moment the image of the building elongated like drooping molten glass. When the top of the image also sank, because its light rays were curving through the density gradient, the entire building rapidly disappeared before it should have. The wing seemed to have sucked the building in like a vacuum cleaner.

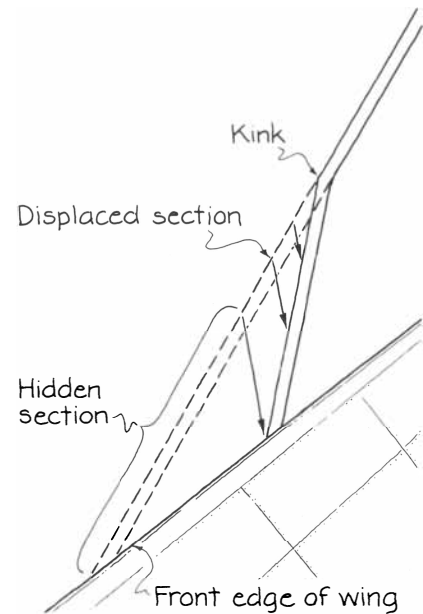
How does your view of the wing itself escape distortion? After all, when you look down on it, you intercept rays that have climbed through the density gradient. There is no distortion because the rays traverse the density gradient for too short a distance and at too steep an angle to curve significantly. That may be a good thing: if wings were distorted much on airliners, flights would be more unnerving than they are now.

Wood suggested another way in which refraction might alter what is seen over the wing. Although most airliners fly slower than the speed of sound, the airflow over the top of the wing may actually exceed the speed of sound. When it does, a shock front forms that extends one or two meters upward from the wing. It is like a narrow, transparent, porous wall stretching out along the wing; it may extend the full length of the wing or be broken up into several short sections. The air density is low in front of a shock front and higher behind it. One cannot see the shock front on the wing, of course; after all, it is just air. Wood proposed, however, that one might be able to infer its presence because under some conditions its refraction of sunlight could cast a dark band on the wing.

An independent observation of such a band was reported in 1983 by Antony Hewish of the University of Cam-

bridge. He had been flying at high altitude in a Boeing 727 with the sun about 25 degrees above the tip of the wing near him. The band ran along most of the length of the wing and was from one to two centimeters wide (he compared it to the diameter of the rivets on the wing). A narrower, brighter band lay just behind the dark one. Mild turbulence jostled the bands, and sometimes multiple bands appeared. When the aircraft descended and slowed, the pattern slid toward the front of the wing, faded, narrowed and disappeared. Apparently the decrease in airspeed over the wing first diminished and then eliminated the shock front giving rise to the bands.

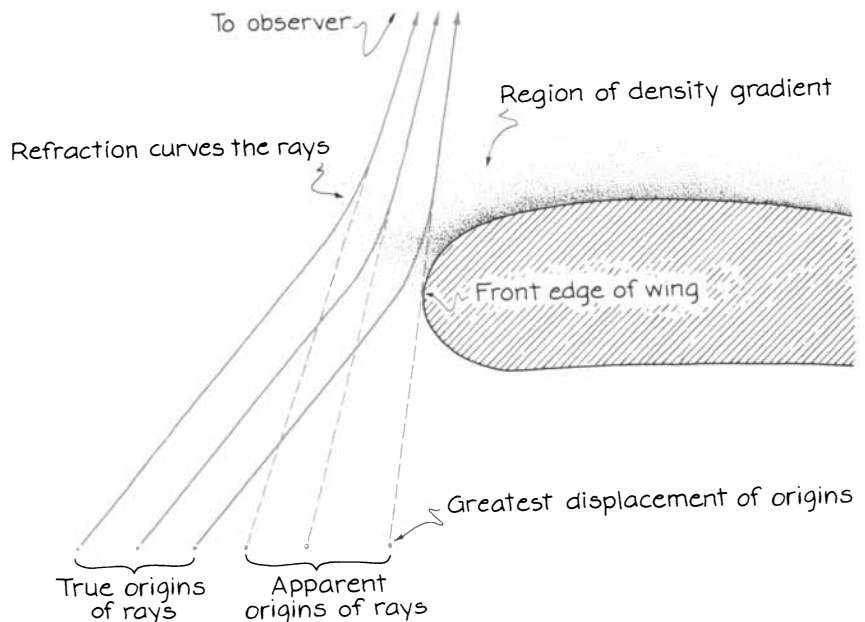
How were the bands Hewish saw formed? Consider a sun ray that pierces the front surface of the shock front at a glancing angle [see bottom illustration on next page]. Since the sun is 25 degrees above the wingtip, the ray is angled downward. As it passes through the shock front it is refracted slightly upward (and also slightly away from the fuselage), so that it reaches the wing somewhat closer to the trailing edge (and a bit farther out on the wing) than it would have in the absence of a shock front. The spot on the wing illuminated by the refracted ray is bright; the spot it would otherwise have illuminated is dim. If many rays along the length of the shock front are thus deflected, the bright spots form a bright band and the dim spots form a dark band. Bands could also be produced if sun rays pierced the rear of the shock front and so were



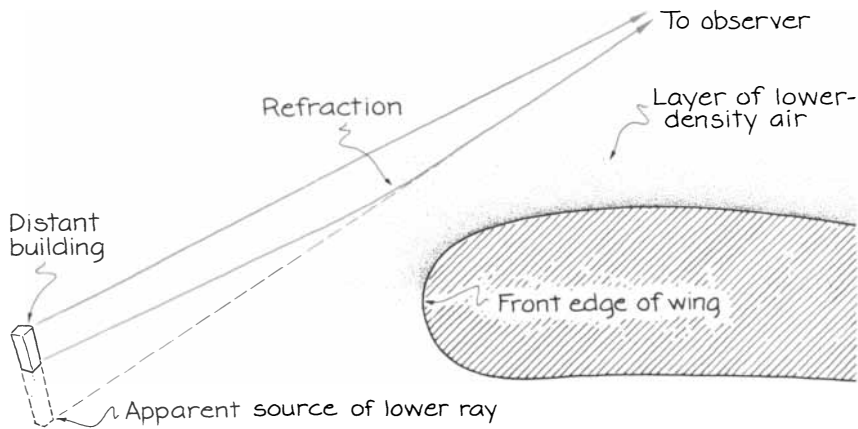
A magnified view of the road illusion

deflected toward the leading edge of the wing.

The explanation is plausible but flawed: it ignores the possibility that the spots that should be dim may in fact be illuminated by other rays passing through somewhat lower points on the shock front. In order for bright and dark bands to form, the shock front must either be curved or have a steep density gradient across its narrow width. Either condition can focus the rays like a lens so that a bright band falls on the wing. The dark band, then, is a strip where the focusing



Refraction through a density gradient



How a building appears to sink

prevents rays from reaching the wing.

I searched for such bands on the wings of aircraft long and diligently but without luck. Then, on the day after I completed the first draft of this column, I saw them. I was seated well in front of the wing; the plane was at 38,000 feet. The sun was somewhat in front of the wing. When I looked back at the wing, I noticed an odd line on it. At first I thought the line was only an edge of one of the metal sheets on the wing, but then I saw that it shimmered slightly when the wing shook in the turbulence. Was the line due to a shock front? Suddenly the pilot banked the aircraft, bringing the wing up and turning us so that the sun was about 25 degrees above the wingtip. The line sharpened into distinct bright and dark bands. My excitement probably startled fellow passengers.

When the plane leveled out, the sun was still above the wingtip but at a larger angle. The bands were then less distinct. As I watched them for the

next half hour, gradual changes in flight direction brought the sun somewhat behind the wing, and the bands became fuzzy and finally disappeared.

This fortuitous experiment helped me to understand why the bands are so rare. For them to form, sun rays must skim through a shock front, because only then do the rays undergo appreciable deflection. That means the sun must be approximately above the wingtip; the ideal angle of elevation seems to be about 25 degrees, which must have something to do with the way the shock front curves vertically. When the sun is too far ahead of the wing or behind it, or too high above the wingtip, either the bands do not form or they are too faint to be seen by a casual observer.

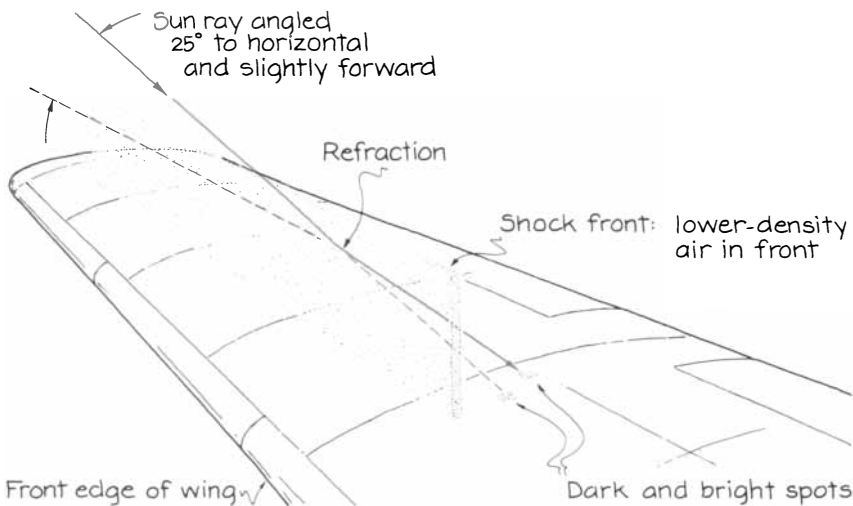
The appearance of the bands may also depend on the air temperature. For a shock front to develop, the airflow over a wing must exceed the speed of sound. Since the speed of sound is lower in colder air, per-

haps only fast planes flying through very cold air develop extensive shock fronts over the wings.

Recently I spotted another peculiar optical display that was probably caused by a shock front. I had the luxury of being on a nearly empty flight and could sample the view from several window seats over a wing. I happened to be on the opposite side of the aircraft from the sun when I noticed a dark vertical band near the leading edge of the wing. As I moved my head forward the band moved toward the wingtip. At first I thought the band was caused by an imperfection in the window, but when I moved forward to the next window seat, I saw the band again, this time out on the wingtip. Clearly its position was linked to the angle at which I viewed the wing. Still skeptical, I scrutinized the band while keeping my face pressed to the window. When the plane encountered mild turbulence that shook the wing gently, the band wiggled to and fro over the wing. Since my eyes were not moving with respect to the window, the dance had to be caused by something happening out on the wing and not by a blemish in the window.

From some points of view in the two window seats I saw two bands. By moving my head I could make one band pass the other one. I gradually began to realize that I was looking through one or two shock fronts that sat out on the wing. But how did the fronts form these bands? They differed from the bands seen by Hewish and predicted by Wood because they fell across my eyes (and presumably the nearby part of the fuselage) and not on the wing; from any window seat other than those two I would not have seen them. Also, since I was on the opposite side of the airplane from the sun, the bands could not be due to any refraction of direct sunlight.

After the flight I developed a plausible explanation for this second kind of band. Suppose there is a shock front that is curved horizontally, with a convex surface facing the leading edge of the wing. If I look at the wing almost tangentially along the shock front, I intercept rays that come from details on the wing beyond the shock front and may be refracted when they pass through the front. Consider two adjacent details. A ray from the one on my right might undergo only a small refraction because it enters the front at a large angle [see bottom illustration on opposite page]. A ray from the detail slightly to the left might be refracted more, because, owing to the front's curvature, it enters at a glancing angle.



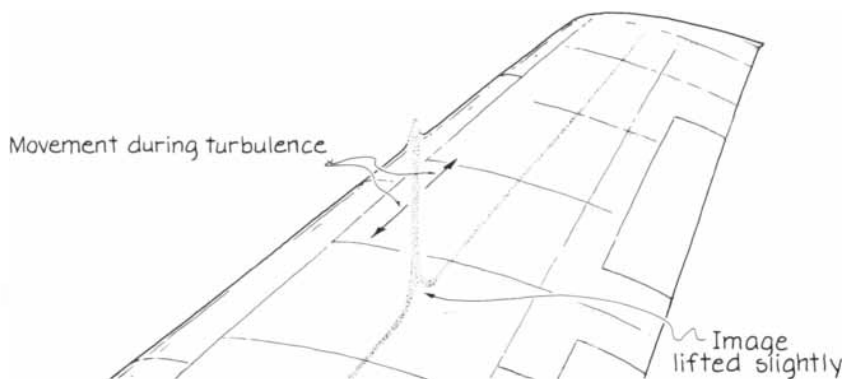
Refraction by a shock front

When I mentally extrapolate the rays backward, the detail on my left appears to be displaced to the left of its true position. The detail on my right undergoes less displacement. The light rays from the region between the two details are then spread over a larger angle in my view than they should be, and that region appears to be dim. Since the shock front stands one or two meters high, I see a dark vertical band of about the same height out on the wing.

The model seems to explain two other aspects of what I saw. The leading edge of the wing and other features along the wing were warped upward near the dark band, apparently because when rays from those features passed upward through the shock front and into the higher air density, they were refracted slightly downward, away from the surface of the shock front. My mental extrapolation of them back onto the wing then produced the illusion that they originated slightly above their true origin. The model also explains why the dark band moved when I did. The band was visible only when I looked almost tangentially along the curved surface of the shock front, so that I intercepted rays that entered the front at a glancing angle and therefore underwent perceptible refraction; other angles of view through the front involved rays that were insignificantly refracted. If I moved my head forward, the place along the front where my view was almost tangential shifted toward the wingtip because of the horizontal curve of the shock front; so, consequently, did the dark band.

The next time you sit on the shady side, watch the plane's shadow soon after takeoff. At first the shadow is large, but it seems to shrink steadily as you ascend. The shrinkage is an illusion. Because the shadow is formed by almost parallel rays of light from the sun, it must be the same size regardless of your distance from the ground. (The rays are not precisely parallel because the sun is a disk in our field of view rather than a point, but I shall neglect that fact.)

The shadow seems to shrink when you ascend simply because its angular width decreases with distance. When the angle is too small and the shadow too faint, the shadow disappears. You might see the shadow again if you fly over a cloud that is not too far below the airplane. Recently I flew over an array of clouds scattered at many different altitudes below the plane. As the distance between me and the clouds kept rapidly changing, the ap-



A strange band seen on the wing

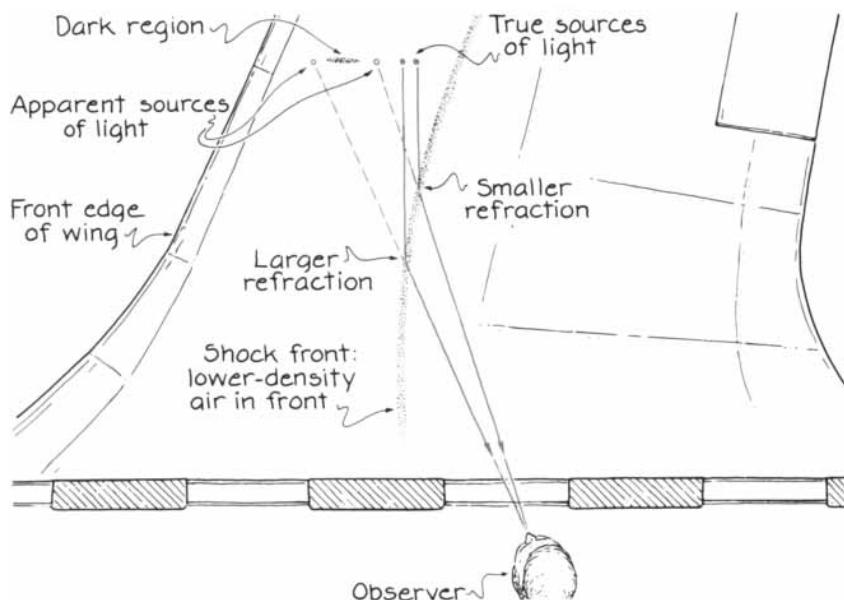
parent size of the airplane's shadow fluctuated wildly.

In the past several years Gordon Lundskow of Rochester, Minn., and Robert T. Chilcoat of the State University of New York at Syracuse have written to describe a peculiar feature that is sometimes seen at an aircraft's "shadow point." Lundskow had been watching the shadow on the ground until it disappeared when the plane had climbed to about 20,000 feet. In the shadow's place a bright spot appeared. Chilcoat observed a similar bright spot that traveled over the ground, always staying (as the shadow had stayed) diametrically opposite the sun. When a cloud below the airplane got in the way, the spot disappeared. You may sometimes see some such brightening even if the shadow is present; in that case the brightness surrounds the shadow.

The brightening at and near the shadow point is called heiligenschein. Its causes are varied, but in every case something on the ground scatters sunlight back in the general direction of the sun. When you look at the shadow point or close to it, you intercept some of the bright return of light.

FURTHER READING

SHOCK-WAVE PHOTOGRAPHY IN TUNNEL AND IN FLIGHT. F. E. Lamplough in *Aircraft Engineering*, Vol. 23, No. 266, pages 94-103; April, 1951.
 SCIENCE FROM YOUR AIRPLANE WINDOW. Elizabeth A. Wood. Dover Publications, Inc., 1975.
 SUBSONIC FLOW. Milton Van Dyke in *An Album of Fluid Motion*. The Parabolic Press, 1982.
 IN-FLIGHT MOVIES. A. Hewish in *Nature*, Vol. 306, No. 5939, page 118; November 10, 1983.



An overhead view of the shock front

COMPUTER RECREATIONS

Old and new three-dimensional mazes



by A. K. Dewdney

"... a labyrinth constructed by Daedalus, so artfully contrived that whoever was enclosed in it could by no means find his way out unassisted."

—*Bulfinch's Mythology*

Most mazes are two-dimensional, so that if we look down on them, we are able to work our way through their intricate twists and turns. But we cannot look down, so to speak, on three-dimensional mazes: upper levels obscure lower ones. We have no alternative but to feel our way—either literally or figuratively—along complex passages.

There are both old three-dimensional mazes and new ones. Given its leg-

endary difficulty, Daedalus' labyrinth of yore must have been three-dimensional. Its stygian darkness serves as an appropriate setting for an exploration of maze-solving techniques, including an extension of the famous right-hand rule employed in the solution of two-dimensional mazes. As for modern mazes, those that are constructed by M. Oskar van Deventer are not only three-dimensional but also invisible! They lead to a fascinating reconstruction problem: When can three two-dimensional mazes define a single three-dimensional one?

Daedalus constructed his notorious labyrinth for Minos, the powerful king of Crete. The king did not intend the

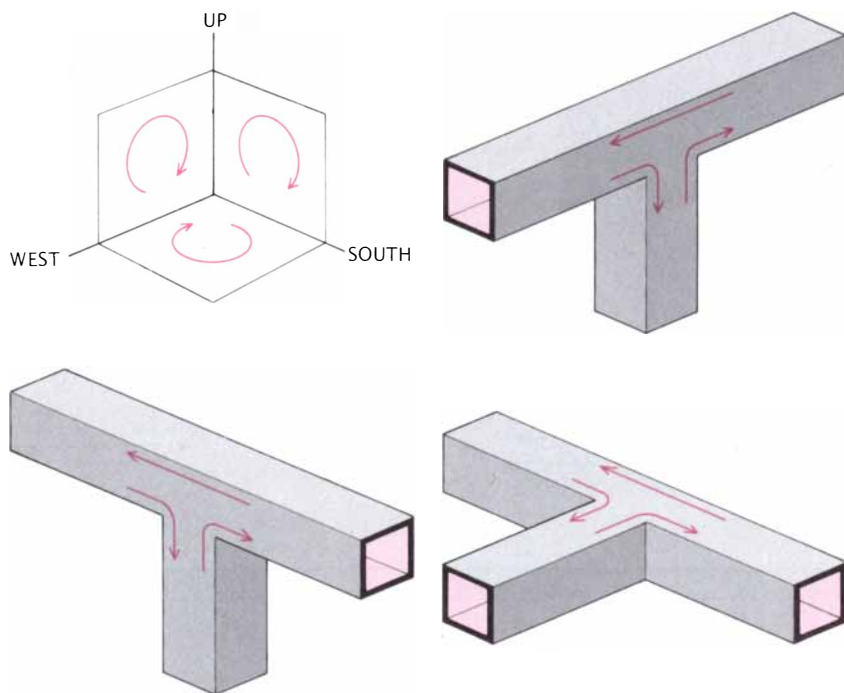
maze for recreational purposes, however. The maze served to confine seven youths and seven maidens sent to him by Athens each year as tribute. No amount of intelligence would serve the hapless victims as they crept along its damp, dark passages seeking the way out. But that was not the worst of it: a fierce and horrendous creature, known as the Minotaur, inhabited the labyrinth. The Minotaur, which had a human head and the body of a bull, devoured the poor young Athenians who were trapped in the structure.

Only Theseus, the fabled Greek hero, solved the labyrinth and in doing so killed the Minotaur. He tied a length of thread provided by the king's daughter (who secretly loved him, of course) to the outside of the labyrinth and unwound the thread as he wandered the passages searching for the Minotaur. After slaying the Minotaur, he merely followed the thread back to escape from the labyrinth.

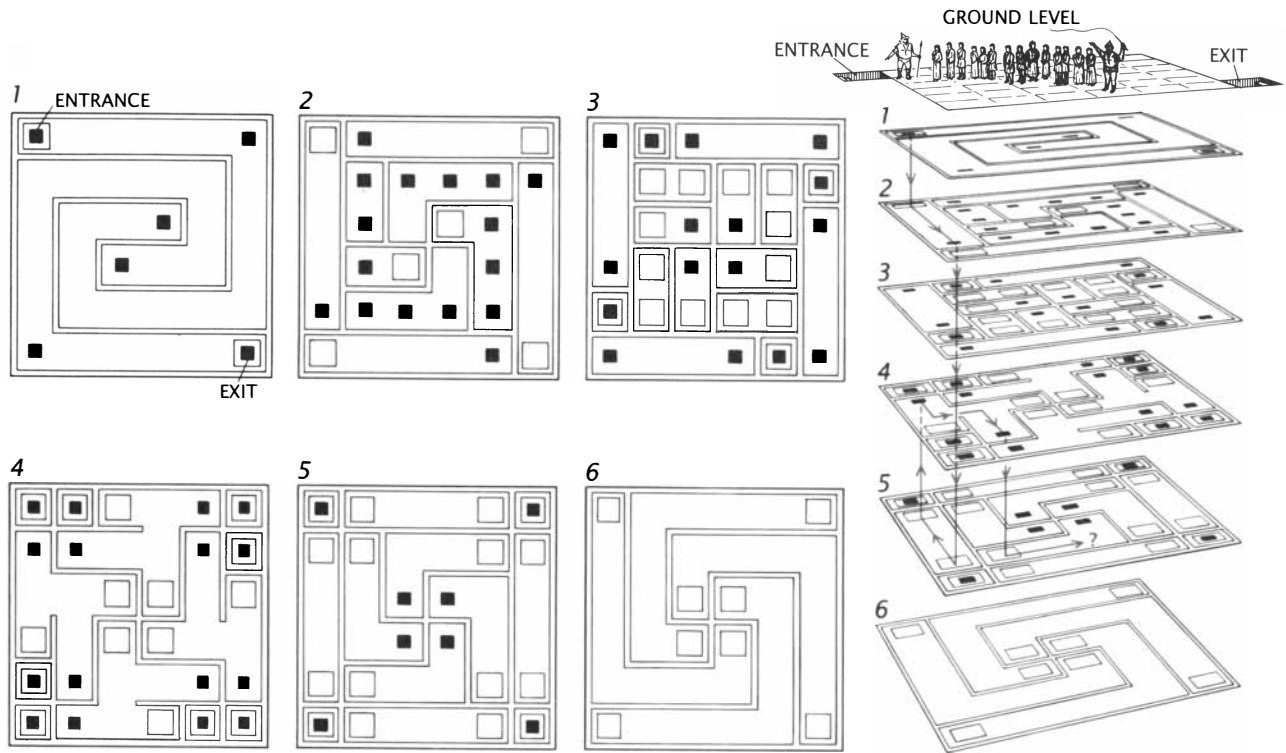
What would have happened if Theseus had been absentminded and had forgotten to secure the thread before entering the labyrinth? Could he have escaped some other way? One possibility would have been for him to tie the thread to the slain Minotaur before setting out in search of the exit. The thread would then at least have enabled him to return to the same starting point (the carcass of the monster) after each unsuccessful probe into Daedalus' cunning labyrinth. But the thread alone would not have guaranteed an eventual exit from the maze. How would Theseus have remembered which passages he had already explored?

That depends on whether Theseus' memory was internal or external. If it was internal, he might simply have remembered the turns he took at each junction he encountered. If it was external, he might have placed some token at each junction as a record of transversal. Personally, I think the latter form of memory is the likelier one, and so we shall allow Theseus a number of one-drachma coins.

Every time Theseus came to a junction of three or more passages, he would have examined the floor at the entrance to each passage. If a coin was already there, he would not have entered that passage. If no coin was there, he would have entered. After entering he would immediately have put a coin down within view of the junction. Some readers will no doubt object that Theseus could not possibly have seen the coins because of the utter darkness in the labyrinth. It therefore seems reasonable to allow



The triple right-hand rule for three-dimensional mazes



The reconstruction of Daedalus' labyrinth and a possible path (color)

him some form of ancient fire-making apparatus, such as a cigarette lighter.

In following the procedure just outlined, Theseus might well have been forced to backtrack. If, for example, he had come to a dead end or a junction where all passages had coins at their entrances, he would have had to retrace his steps. Is it possible that in the course of backtracking Theseus might have encountered nothing but non-enterable junctions? In other words, could he have been caught in an infinite loop? For the benefit of those who like to think for themselves, I shall not answer the question. Suffice it to say that the basic method I have outlined is widely applied in modern computing for searching through data structures; it is called a depth-first search.

It might have happened that our intrepid hero had no coins or—worse yet—no cigarette lighter. How could he then have solved the maze? Luckily there is a method for escaping from the maze without external memory. Moreover, executing it would not have taxed Theseus' brain any more than carrying out a depth-first search. I call this method the triple right-hand rule.

Ordinarily two-dimensional mazes can be solved by the so-called right-hand rule: on entering the maze one keeps a wall continuously on one's right, no matter how the passages may twist and turn. If a passage forks, one

turns down the right-hand corridor. If a passage comes to a dead end, one simply turns around—keeping a wall on one's right. Eventually one will emerge. Astute readers will have noticed I did not state explicitly that one would emerge at the exit. If the exit happens to be in the middle of the maze (as it is in many paper-and-pencil exercises), one might well come out where one entered after a tiring application of the right-hand rule. But re-emerge one must. The reason is very simple: abiding by the rule enables one never to retrace one's steps. If no part of the wall that defines the maze's passages is ever retraced, it follows that eventually one must run out of wall, so to speak, at an opening. (The exception is the case in which the walls of the maze form a completely closed circuit, but in that case there would be no opening in the wall where one could have entered.)

A variation of the right-hand rule can be applied in solving three-dimensional mazes, including the cruel labyrinth of King Minos. To make things simple, I assume all passages in the maze have a square cross section and are quite straight, except at bends where they make 90-degree turns. In addition, I assume the passages run precisely east-west, north-south or up-down and are therefore perpendicular to one another. I also assume

only two types of junction are formed wherever three passages come together: a T junction and a three-way corner.

Let me now take the reader groping along the passages in order to explain the operation of the triple right-hand rule. No gyroscope is necessary; gravity tells us which way is up and which is down. The other four directions are remembered by keeping track of our turns as we make our way through the three-dimensional maze. If we enter the maze facing east, for example, a turn to the right leaves us facing south; after another turn to the right we would be facing west, and so on.

The triple right-hand rule is applied at a T junction only after we identify the plane in which the junction lies, since each of the three possible planes has a specific "handedness" assigned to it [see illustration on opposite page]. Imagine a clock stuck on a surface parallel to the plane of the T junction. We arbitrarily call the direction in which the hands of a clock turn "right," and we will consistently turn in that direction in the labyrinth.

In the case of three-way corners the rule must be modified somewhat. (Is that the Minotaur bellowing in the distance?) Say that up-down passages have direction 1, north-south passages direction 2 and east-west passages direction 3. If one enters a three-way corner along direction 1, one leaves

along direction 2. If one enters along direction 2, one leaves along direction 2, one leaves along direction 3. Even Theseus might have guessed that if he enters a three-way corner along direction 3, he ought to leave along direction 1. That is all there is to the triple right-hand rule.

The rule happens to satisfy a general criterion for solutions: no passage would be traversed twice in the same *direction*. Does the triple right-hand rule guarantee success? I contend that it does, but only if the maze has one possible path connecting entrance to exit. If the maze has more than one possible solution, I more modestly propose eventual emergence from the maze—through either the exit or the entrance.

Of course, there is no guarantee that Theseus would have emerged from the labyrinth had he started following the triple right-hand rule only after dispatching the Minotaur. But if he had used the rule from the moment he entered the maze and if the struggle with the Minotaur had not disturbed his memory, he would eventually have emerged a hero into the daylight. Theseus would not have cared whether he had left by the entrance or the exit!

With these rules in mind readers may feel ready to try solving a three-dimensional labyrinth. After some extensive research into the matter I offer nothing less than a reconstruction of Daedalus' original labyrinth. The re-

construction is displayed on the preceding page. Its six levels are all underground. The top level (level 1) lies just under the heavy stone slabs of the courtyard of King Minos' palace. Two of the slabs are missing, revealing holes. The reader is shown into the maze at one of those holes by a burly servant of King Minos. The reader might eventually emerge at the other hole, for that is the labyrinth's exit. Between entrance and exit lie perhaps a few adventures and misadventures.

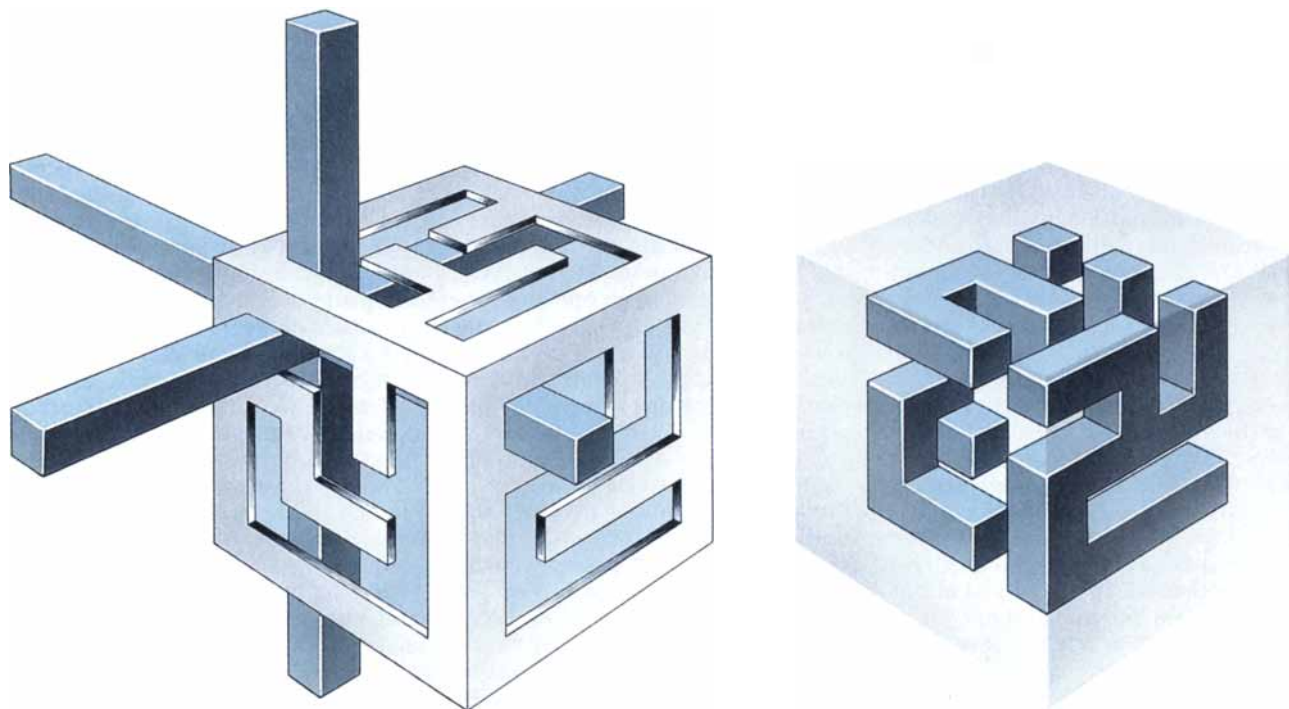
The six levels of the labyrinth reflect the origin of its design: a cube consisting of six cells on a side. All horizontal passages appear as passages normally do in maps of two-dimensional mazes. Vertical passages, however, appear as solitary squares. A would-be Theseus may go from one level to the level below by clambering down a hole depicted as a black square. He or she will then emerge in the corresponding cell in the underlying level, where the reader will find a larger white square on the map—the hole through which he or she came. Naturally, when a reader wants to go up, he or she must go to the nearest white square. Sometimes one sees a black square inside a white one. This simply means that from that particular position in the labyrinth it is possible to go either up or down.

There are several possible paths from entrance to exit in the labyrinth.

Some readers will be content to find just one of them; others may want to search for the shortest solution path as measured in cells traversed. To make it a bit more adventurous, I have added a Minotaur to the labyrinth. It stands at the one spot where it is guaranteed to intercept any innocent explorer. I shall mention in a future column the first five readers who report the spot to me.

Among the more modern types of three-dimensional maze are two that stand out. The first is visible, the second invisible. The visible maze is a clear plastic cube that contains an arrangement of intersecting, perforated walls. A steel ball rolls along passages created by the walls. The solver holds the maze, manipulating it so that the ball rolls until it eventually reaches the "finish" position. Such a maze, made by the Milton Bradley Company, was a favorite in game stores a decade ago. Today a similar puzzle, called Miller's Maze, is available at Toys-"R"-Us stores.

The other kind of modern maze comes from the workshop of van Deventer in Voorburg, The Netherlands. He calls one of his productions a *holle doolhof*, or hollow maze. The terminology is perfectly reasonable: his mazes are wood boxes that contain absolutely nothing! Not a passage or wall can be seen within, but a three-dimensional maze nonetheless exists in the box.



A simple van Deventer maze (left) and its projective cast (right)

The secret lies in the sides of the box. They are two-dimensional "control mazes": wood surfaces in which slots have been cut. A cursor consisting of three mutually perpendicular wood spars registers one's position in the hollow maze. Each spar passes from one side of the box to the other, sliding along the slots of the control maze on each side. Not surprisingly, the two control mazes on opposite sides of the box are identical. In this way van Deventer can produce a single three-dimensional maze from three pairs of two-dimensional mazes.

In the simple example shown on the opposite page one starts with the cursor in one corner of the box and tries to manipulate it into the opposite corner. Each spar is pushed into and pulled out of the box, automatically moving the other two spars (if possible) along slots in their respective control mazes. It might seem that to solve a hollow maze one merely solves each of the three control mazes. But this is not so. Although each of the control mazes can be easily solved, the hollow maze is quite difficult.

The difficulty lies in the fact that possible moves on one control maze may be blocked by another control maze. Moreover, it is not clear in which order the cursor's three spars should be pushed or pulled. There may be several possible moves at any given position of the cursor. To solve the maze one might as well close one's eyes and "feel" one's way through it. In such a mode the invisible maze within the box takes on a new, tactile reality.

The invisible maze can in principle be made visible by tracing the slots of three mutually adjacent control mazes onto a solid cube of material that can be carved. When the tracing is complete, all "nonmaze" material is cut away from the solid. The control mazes must of course have the same orientation as they do on the original van Deventer maze.

Since the process is largely imaginary to begin with, I equip myself with a laser saw in carrying it out. Positioning the saw directly over one of the cube's faces, I simply follow the traced lines, cutting straight through the solid as I go. When the cutting is complete, I gingerly push all the unwanted material out of the cube. It slides away, leaving a three-dimensional form that corresponds to the slots of the control maze. After the same process is repeated for the other two faces, the solid that remains is in effect a "negative" of van Deventer's implicit maze: the allowed passages are represented by solid posts and beams. I call it a

projective cast. Readers can see a rendition of one on the opposite page.

Two fascinating questions revolve around projective casts. First, when do three two-dimensional mazes yield a projective cast of a viable three-dimensional maze? Second, when does a projective cast yield three projections that are viable two-dimensional mazes? The term "viable maze" ought to be defined. It refers to a maze in which all passages have unit width and there is a path from the "start" to the "finish" position. (A viable three-dimensional maze that results from three two-dimensional control mazes, it seems to me, ought to be called a van Deventer maze.) Other conditions could readily be suggested, but they would relate to the aesthetics of good maze design; the proposed definition will do for a start.

One can experiment with very simple control mazes and still be quite confounded by what emerges in three dimensions. For example, one can construct a van Deventer maze from rather trivial control mazes consisting of 3-by-3 cellular matrices in which certain adjoining cells have been removed. Readers might enjoy starting with three 3-by-3 control mazes having L-shaped slots in various orientations. How many combinations result in van Deventer mazes?

The other question addresses the opposite issue: When does a three-dimensional maze yield three viable control mazes as projections? Both questions have practical importance for van Deventer. An answer to either one greatly simplifies the process of designing his mazes. Van Deventer himself confesses to having done a great deal of actual cutting and trying in coming up with more complicated hollow mazes. Readers with something to say on the subject should write to van Deventer directly at the following address: p.a. Dr. Beguinlaan 44, 2272 AK Voorburg, The Netherlands. A creative response might well result in a second look at van Deventer mazes in this department.

The invisible professor appeared in this department in May to draw a number of classic examples from the infinite variety of trigonometric and algebraic curves. Among the many readers who had made prior acquaintance with the professor were some who had interesting comments to make.

Abe Achkinazi of Bell, Calif., has proposed a date between the invisible professor and Lucy, the Hewlett-Packard color plotter in the mathematics

laboratory of the California State University at Northridge. The professor might enjoy Lucy's Lissajous figures. Achkinazi has a program that draws straight lines between corresponding points on a pair of such figures. In this way Lucy produces wild curves clad in a kind of moiré sheen.

Tom Dorn of Vancouver, British Columbia, recommends his own program BUMBLEBEE. It incorporates the following parametric equations in which the constant a can be varied:

$$\begin{aligned}x &= 2 \sin(at) \\ y &= e^{t \sin t}.\end{aligned}$$

Temple H. Fay of the University of Southern Mississippi finds polar curves, which are plotted in terms of coordinates (r, θ) rather than (x, y) , useful in teaching calculus. The professor plots a butterfly with the aid of sine, cosine and exponential functions:

$$r = e^{\cos \theta} - 2 \cos(4\theta) + \sin^5(\theta/12).$$

Commercial and quasi-commercial interest runs rampant in the area of curves. There are products aplenty to aid the amateur charter of curvilinear complexity. For example, David E.-B. Kennedy, a mathematics teacher at the Langley Secondary School in Langley, British Columbia, is enthusiastic about the Casio fx-7000G calculator-plotter. This hand-held marvel displays miniature stepped plots of virtually any function on a 1.5-by-2-inch display.

SPIA, an apparently comprehensive mathematics program, allows users to construct and plot formulas of almost any type. Moreover, it includes special manipulations such as Fourier transforms for those who want to understand signal processing. Interested readers can write to Moonshadow Software, P.O. Box 5974, Baltimore, Md. 21208.

Finally, I have heard from a shadowy organization called MAL (an acronym for Maths Algorithm Library) at P.O. Box 531, Wynnum, Brisbane, Q 4178, Australia. An amusing flyer promises MALTreatment to readers interested in MALfunctions. MALpractice is easy, according to MALadministrator Dr. P. ffyske Howden.

FURTHER READING

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BOOKS

Advice by a science adviser on how to give science advice



by Lord Zuckerman

SCIENCE AND TECHNOLOGY ADVICE TO THE PRESIDENT, CONGRESS, AND THE JUDICIARY, edited by William T. Golden. Pergamon Press (\$49.95; paperbound, \$24.95).

Harold Macmillan, one of Britain's most distinguished prime ministers, once observed that the politician has to run hard to keep up with the scientist. At the time, his attention was focused on the quest for a treaty banning the testing of nuclear weapons, and he was finding it difficult to follow the arguments that were then raging about the problem of differentiating underground explosions from natural disturbances in the earth's crust. He might have said the same thing about half of his other political worries: in one way or another all were affected by scientific and technological considerations.

It was not always that way for politicians. In Britain the uneven distribution of the wealth that was generated

by the industrial and agricultural revolutions of the 18th century changed the structure and politics of the country only slowly, and the changes that did take place came about relatively peacefully. Moreover, what was happening in Britain had little immediate impact on other countries. In those days the extent to which a country cultivated and exploited science was as much its own business as was the way it was governed.

The situation today is different. Wherever they first surface, major innovations very soon have repercussions over the entire world, whether by stimulating new demand, closing down old industry, moving high-cost and labor-intensive manufacture from richer to poorer countries, or stimulating the sale of arms. The consequences of major technological innovations are experienced around the world almost as fast as they are in the country where they emerge. It took decades for news of the steam engine to spread from the U.K., where the machine was perfected, to most other parts of the world. Today detailed information about current high-technology developments of corresponding magnitude is available worldwide in no time at all. Telecommunications, artificial satellites and computers have seen to that.

Furthermore, there was no debate about the interaction of science and government when James Watt perfected the steam engine in the latter half of the 18th century. Today the exploitation of nuclear power not only is of major concern to national governments but also has to be monitored by agencies of the United Nations. No longer are questions of the relation of science to government or of so-called science policy—or of the place of the scientific adviser in the machine of government—parochial issues that can be dealt with within national boundaries.

William T. Golden, the editor of *Sci-*

ence and Technology Advice, thinks the administrative machinery whereby advice on science and technology issues comes to the president of the U.S., Congress and the judiciary is not all it could be. In true democratic fashion he invited 84 men and two women (one of the latter a well-known judge and the other a Nobel-laureate biophysicist) to give their views about how the situation could be improved. His contributors were chosen for their "wisdom, experience, and love of country, without regard to political affiliations." Given their diversity of experience, it is hardly surprising that no single view emerges about what best needs to be done. The most interesting contributions are those of six men who at one time served as presidential science adviser. They all make it clear that the job was anything but simple.

It was the shock occasioned by the launch in 1957 of the first Sputnik by the U.S.S.R that stimulated President Eisenhower to appoint James R. Killian, Jr., president of the Massachusetts Institute of Technology, as the presidential science adviser, and to set up at the same time a President's Science Advisory Committee (PSAC). Eisenhower's reason was that he needed impartial help in deciding among the numerous proposals he was receiving about how to react to the "threat" that Sputnik posed.

George Kistiakowsky, who replaced Killian in 1959 and served until the Kennedy Administration took over in 1961, told Golden that he and Killian had a relatively easy time in dealing with these matters. They were matters in which the president had an immediate "substantive and political" interest. Moreover, Eisenhower was ready to accord his scientific adviser the authority of his own name in dealing with the officials who directed the scientific and technological affairs of executive departments—not only Defense but also the smaller specialized agencies concerned with space, energy and the environment.

What also helped was that Kistiakowsky, like Killian, got on well with other cabinet officers in the White House. He had been left with no doubt that for the Government to be effective it was essential that the team around the president include a science advisory organization and a science adviser of "the right caliber," just as the president had to have legal and economic advisers. The man or woman selected for the top post had to be someone in whom the president had

LORD ZUCKERMAN has had a distinguished career as an investigator and notable experience as a science adviser to government. He was educated at the University of Cape Town and University College Hospital, London, and then embarked on a research career in vertebrate zoology, including innovative studies of the social life of baboons. He next turned to endocrinology—he was the author of a 1957 *SCIENTIFIC AMERICAN* article on hormones. During World War II he studied the wounding effects of bombs and, as chief strategic adviser on air operations to Supreme Headquarters Allied Expeditionary Forces, developed plans for selective destruction of the communications network of northwestern Europe. From 1960 until 1966 he was chief scientific adviser to the Secretary of State for Defence; from 1964 to 1971 he served as chief scientific adviser to the British government. In 1969 Lord Zuckerman was named professor at large at the University of East Anglia, where he is now professor emeritus.

sufficient confidence to delegate the "authority to speak for the president in defined areas."

Jerome B. Wiesner, who served as President Kennedy's science adviser, is of the same opinion. He sees the president as playing "a central role in balancing the priorities of the nation, especially those aspects that are dominated by the Federal Government, as is the case with science and technology." He had been vested by the president with the same authority Eisenhower had accorded his advisers: total oversight of "all science and technology programs in the Government and in related education programs."

A large part of Wiesner's and PSAC's work continued to be screening the "avalanche" of new military and space projects that confronted the president. He and PSAC played an important role in the deliberations that led up to the Partial Test Ban Treaty of 1963. Although he may not have taken part in discussions of the foreign policy and defense matters that were the particular concern of McGeorge Bundy, the president's special assistant for national security, and of Secretary of Defense Robert S. McNamara, he was certainly not "shut out" from them (as Kistiakowsky suggests he was) to the extent to which Henry Kissinger saw to it that President Nixon's science adviser, Edward E. David, was later ignored. Kissinger had no need for scientific advisers.

"Basically," as Wiesner points out, "the question of who provides the advice boils down to a competition for control of presidential decisions." Wiesner also warns that it is useless to tender advice to someone who either does not want advice or does not like the advice that is tendered.

It was for this reason that President Nixon in 1973 abolished PSAC and the position of science adviser. Nixon took the step because some members of the committee had made public their disagreement with the views he was entertaining at the time about the merits of anti-ballistic-missile systems and about the need for supersonic air transport. The members who had spoken out had violated a convention of confidentiality that Wiesner says had governed PSAC's deliberations up to then. (There was, however, no leakage of classified information.)

Almost alone among the contributors to Golden's anthology who held the position of science adviser to the president or had been members of PSAC, Edward David does not favor the reinstatement of the committee.

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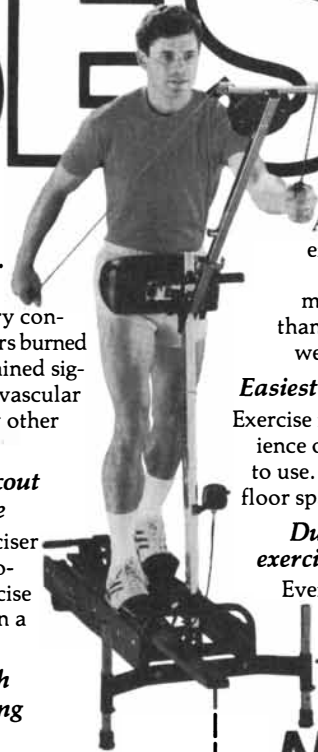
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His main criticism is that it had become "part of the political fabric of the White House." The science adviser and the members of PSAC were being selected, he suggests, in the same way as political appointees—the implication being that no one was selected if it was known that he was hostile to the president's political views. In some quarters it was therefore thought that PSAC did not provide "politically neutral, objective advice."

For example, industrialists with an interest in big defense contracts did not like judgments on their affairs being made behind the committee's closed doors. If PSAC gave the thumbs down to some ambitious and costly project that had been submitted to the president for approval, and he accepted the committee's advice, those who had wanted the verdict to go the other way would be bound to cry "Foul!" For this reason and others David puts forward the novel proposal that PSAC and the office of the science adviser should be replaced by a "Federal Contract Research Center." This would be a "private, nonprofit corporation chartered to work exclusively for the Federal Government," to which any member of the White House staff could turn for advice. If a president thought he needed a personal science adviser as well, that would be up to him.

George A. Keyworth II, who for five years was President Reagan's science adviser (the post had been reinstated by President Carter), is also lukewarm about having a science advisory committee that reports directly to the president. As he sees it, PSAC brought about its own demise when it began publicly to advocate "political actions" that were contrary to what the president wanted (something that Keyworth, as a major protagonist of the Strategic Defense Initiative, certainly avoided doing!).

There were no risks of this happening in the case of the so-styled White House Science Council, which Keyworth set up as an advisory body to himself. Keyworth also discovered that "the science advisory mechanism is most active—and most important" not at the presidential level but at the level of the White House senior staff. To ensure the proper implementation of science and technology policy, Keyworth's major recipe for change would be a new executive Department of Science and Technology, under whose "managerial roof" all major science programs of other departments would be brought.

Only two of the contributors to the

book were at the receiving end of the advice tendered by the PSAC machinery: ex-president Ford and McGeorge Bundy. Bundy agrees with Edward David that the White House is no place for anyone who does not enjoy the president's trust. That is clearly a necessary specification for a chief science adviser. Contrary to what David advocates, however, Bundy is strongly of the opinion that it is time to reestablish PSAC in its original form and to appoint as science adviser a person of standing in the world of science. The adviser should, as I. I. Rabi once put it, be someone who could serve as "a spokesman *of*, not *for*, the scientific community," someone with the right personality to work with the president's other top officers, and with the prestige to recommend to the president, as members of PSAC, appropriately eminent individuals in the world of science.

President Ford wisely reminds the reader that "personal taste" will always play a major part in determining how presidents deal with scientific matters and scientific advice. Scientific and technological judgments necessarily have to be taken into account in reaching decisions on many matters, but even where they are critical, as in defense and energy, they may be overshadowed by other considerations. President Ford also warns that a president's list of priorities is always subject to sudden change because of "surprises." Yet without the "competent technical assistance" that can be provided by "a strong White House science and technology office," a president "could, and probably would, make serious errors of judgment affecting our nation's future security, health and prosperity."

It would have been alarming had President Ford said anything different. At the same time what he says does not indicate just how the presidential need for scientific advice can be most effectively satisfied, or just where a central scientific organization should focus its attention. Some issues are obvious, and clearly they apply to all countries.

First, it is generally agreed that in the interests of national welfare and security it is necessary to encourage the growth and spread of scientific knowledge. A central scientific advisory body should be in a position to advise the chief executive on whether or not the country's educational institutions are turning out enough adequately educated manpower to fill the jobs that determine the well-being of

the nation. A president, a prime minister or a general secretary has to feel confident that everything that can usefully be done to satisfy this objective is being done, given the resources that can be made available. Equally, he must understand that what cannot be done is to legislate for the emergence either of scientific geniuses or of the revolutionary new scientific ideas that are likely to have the greatest beneficial impact on the nation's future.

Second, it should be the business of the top science adviser and a central advisory committee to help the head of government deal with the major new technical issues that so often float up to the top levels of government for decision. The need for the kind of scientific help that President Eisenhower felt he had to have in dealing with big defense projects has also not disappeared. In fact, it has widened with the emergence of ever more problems that have to be dealt with scientifically. These include—to mention only a few—previously unsuspected problems in environmental control and in ensuring the safety of new classes of drugs and agricultural chemicals, and problems relating to genetic engineering, to the disposal of radioactive waste, to air safety and to AIDS. All these issues, and many more, call for balanced scientific advice at the top. Many of them can be dealt with effectively only by international scientific cooperation.

On the other hand, some issues clearly do not come into the purview of a central scientific advisory establishment—in particular those political matters where scientists may have views as ordinary citizens but bring no specialized knowledge to bear. For example, it is not for a scientific adviser to say that in the interests of social justice the level of unemployment benefits should be raised.

There is, however, a gray area. Almost immediately after my own appointment in 1960 as a full-time scientific adviser to the British government, Kistiakowsky and I arranged to meet twice a year (each accompanied by a few selected colleagues) to discuss matters of our own choosing, without according our deliberations any official status. These meetings continued through the period when Wiesner and then Don Hornig and Lee DuBridges served successively as presidential science adviser, that is to say for some 10 years.

The agenda for our first meeting, which took place in London, focused on NATO defense policy and on the

proposed treaty to ban nuclear tests that was then under discussion. In the diary Kistiakowsky later published, he wrote that when the U.S. Joint Chiefs of Staff saw our report, they would “hit the roof because we definitely poached on their territory.” Worse, we had come to conclusions about NATO policy that challenged current military doctrine. He also records that before he could invite me to Washington for our second meeting, he had to seek the approval not only of General Goodpaster, the president's defense aide, but also of the Secretary of State and the Defense Secretary.

I was under no such constraints. As the government's chief scientific adviser, I had a free hand to decide what items of government policy were affected by scientific considerations and, having studied the matter, to decide whether to proffer my views either to the prime minister or to other cabinet ministers, senior civil servants or the military. Needless to say, I had more formal statutory duties as well.

Obviously the size and content of the gray area for a central science adviser will always vary in accordance with the way a president or a prime minister goes about his business, and with the personalities involved. Differences in the constitutional patterns of different countries also make it certain that there cannot be a uniform blueprint that sets out how a central scientific organization should be organized. The system has changed more than once over recent years in the U.S. So it has in the U.K. and in other countries. Departments and ministers of science, of education and science and even of technology have come and gone. Official international conferences have been called to consider how to bring scientific awareness into the top councils of government, but there is still no single view of how that can best be done.

What is clear, as is pointed out by Harvey Brooks, a distinguished physicist who served for many years on PSAC and who contributes to Golden's volume, is that top scientific advisers and members of PSAC's should always distinguish between what he calls “policy for science” and “science for policy.” They need, in other words, to distinguish between governmental decisions relating to the growth and effective application of scientific knowledge, and decisions that relate to general government policy and that are affected by scientific considerations.

In my view, PSAC in its heyday was a far more effective scientific advisory

body than the Central Advisory Council on Scientific Policy, the corresponding institution in the U.K. The U.S. committee, unlike the British council, dealt with defense matters and was kept informed about many affairs of state where it was regarded as useful to ventilate the views of an independent body of scientists. There were other reasons, essentially constitutional, for the British top Advisory Council's being unable to act like a PSAC. In particular there was the fact that in the U.K. the separate departments of state are not extensions of the presidential executive arm but empires that operate on their own (although subject to overall government policy and to the financial constraints, agreed on at cabinet level, imposed by the Treasury).

There were also differences between the position of the president's adviser and my position as chief scientific adviser. Once appointed, and until my retirement, I served a succession of governments, Conservative and Labour alike, but always with direct access to the prime minister of the day. As his adviser I had to deal directly with departmental ministers of cabinet rank and with their officials. Throughout my period of service I was not debarred from giving—and indeed was often encouraged to give—my views on matters of national security policy that seem to have been taboo for the president's science adviser. My responsibilities also brought me into direct contact with the central scientific organizations of several other countries, and in particular with PSAC.

Still, regardless of the administrative differences in the way we worked, and of the degree of license we enjoyed, I would judge that Kistiakowsky, Wiesner and I dealt in much the same way with the science-dominated problems that concerned our respective governments. Many issues (such as those that fell into the “environment” category) were usually noncontroversial. Others (such as the political problems that today are posed by AIDS or holes in the ozone layer, and with which our successors have to contend) called for a great deal of specific inquiry. A few (such as the SDI in the U.S. today) were inherently and overwhelmingly controversial. It is problems that fall into the last category that have drawn most fire from critics of the relations between a president and his scientific advisers.

What, then, determines the degree of faith and trust a president has in the man he appoints as his science

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adviser? Why does a president sometimes take his scientific advice from someone he has not appointed publicly to any position of authority?

The issue of political partisanship, independence and objectivity will always remain an open question. In dealing with it I would, however, commend the British system as a better model than the American. The post of chief scientific adviser to the British government follows civil service rules. Whatever party was in power, I served impartially, as all civil servants do. I was never expected to express—and never did express—a view about domestic issues that were the subject of party political debate. Nor was it ever expected that I would trim my own views about defense, or any other matters of policy with which I was concerned, to suit the views of the reigning party.

As far as I know, no rule or principle debarred members of PSAC, whatever their political affiliation, from continuing to serve from one presidency to the next, Republican or Democratic. Why should the same practice not apply to all presidential science advisers, given that an incoming president wants to retain his predecessor's appointee and that the latter wishes to continue? There is more than one precedent for this in the case of non-scientific U.S. cabinet officers. At the very least, such a practice would minimize any suspicions of a science adviser's lack of political impartiality. Anyhow, I cannot think that Edward David's Federal Contract Research Center would fare any better than a PSAC when it comes to accusations of bias and prejudice. That comment also applies to "science courts," to which it has been proposed that major controversial technical issues should be referred: some people would always feel that bias had played a part in the choice of the judges.

In short, it is all but impossible to give precise meaning to such terms as "independence" and "objectivity" as they apply to science advisers and to PSAC's. To some extent the issue of independence is taken care of by the fact that members of a PSAC or a Central Advisory Council on Scientific Policy are unpaid. Moreover, it is not difficult to set out a job specification for the post of chief scientific adviser and to list criteria that the successful appointee should satisfy. But in the end it is chance, the unpredictable interrelations of all who advise and the receptivity of the person who is advised that determine the outcome. The sci-

entific adviser's job is to consider and advise. Advising demands the exercise of judgment, whose quality may or may not be determined by "objectivity." Whether or not the scientist's advice is accepted, it should, as Rabi puts it, be understood and considered.

For his part, the science adviser needs to remember that there are other advisers who may be proffering different advice on the same issues on which he is commenting, and that their views also need to be understood and considered. But whatever else, a scientist's advice should never be trimmed to accord with what the president likes or dislikes.

There is, of course, no reason why a scientist who has kept himself informed about what is happening in the world at large should prove any less able to serve as director of the National Security Council than a lawyer or a businessman or an academic social historian. Throughout Winston Churchill's years as Britain's prime minister, he turned for advice more to his physicist friend Professor F. A. Lindemann, later Lord Cherwell (whom he appointed to his cabinet both during and after the war), than he did to any of his other ministers.

Science, as Rabi said, has become "the basic element, the novel element in our culture over the last four or five hundred years." We have, he said, "to live with it congenially," otherwise it could destroy us. The "we" is all of us. The problem that all countries now face is how to build up a "college" of scientists of standing who have enough intellectual curiosity, enough flexibility of mind, to serve as advisers at the center of government and at the same time to retain the trust and respect of the scientific community of which they are members.

Many of the political problems that will determine man's fate are conditioned by technical considerations that have no respect for national boundaries. Mr. Golden made "love of country" one of the criteria by which he selected his contributors. Love of country in the sense of narrow patriotism is no longer enough. What matters more is whether scientists can help their political leaders to steer us through the next few decades into a future that is less beset by conflicting nationalistic aspirations than the present is—a future in which science is brought to bear, and brought to bear internationally, on the emerging and still undisclosed environmental and other problems that will determine the survival of our species.



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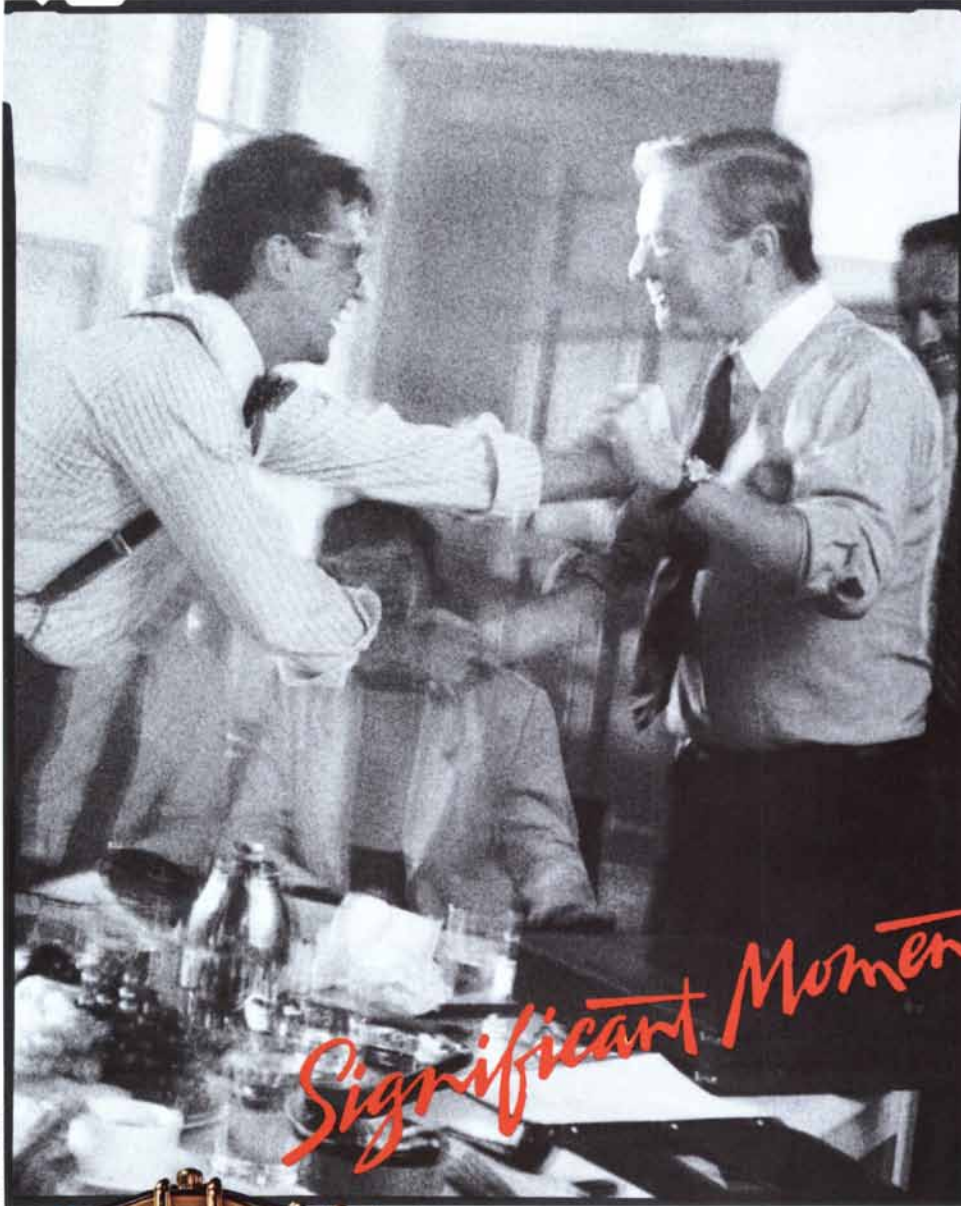
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