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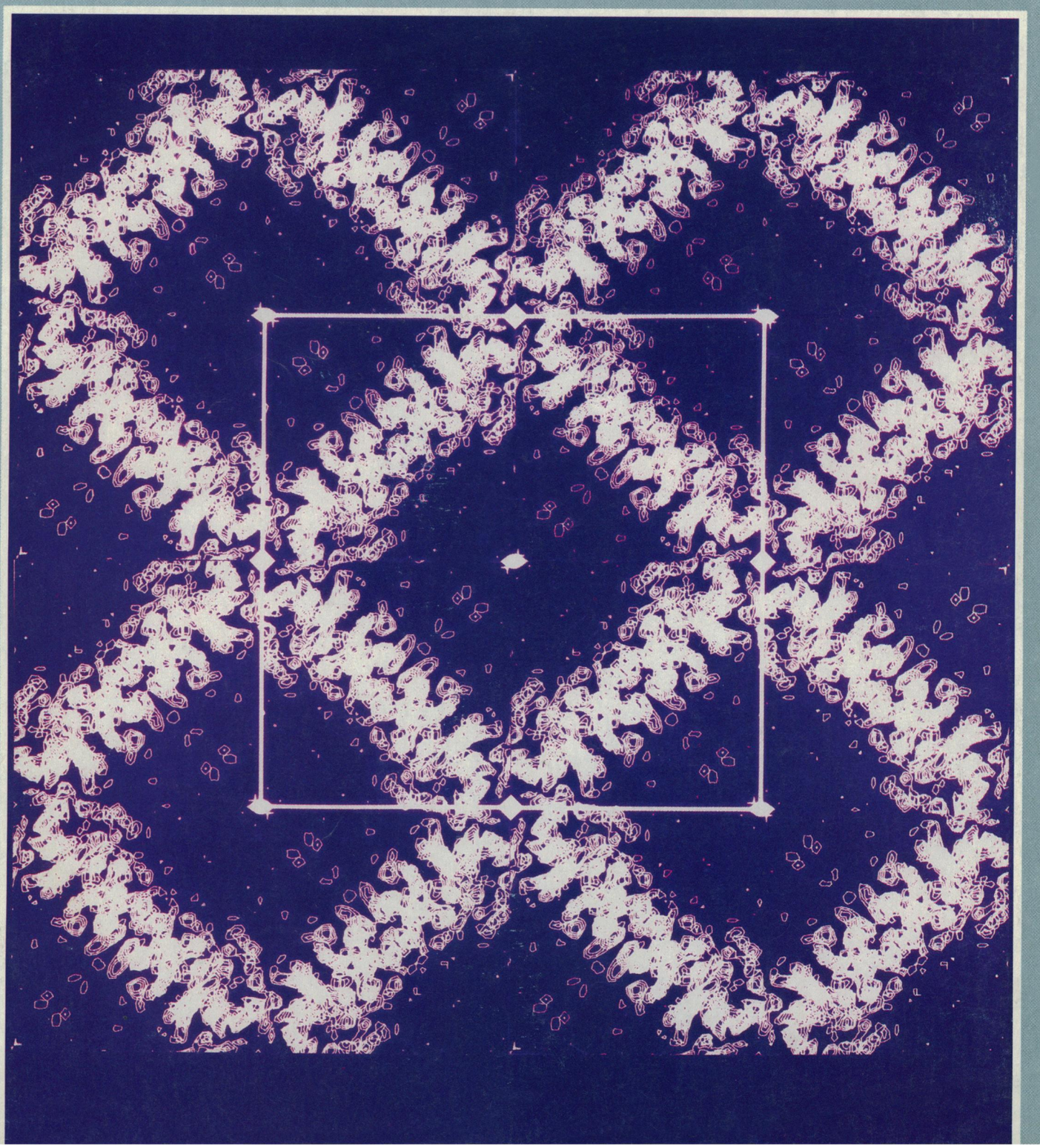

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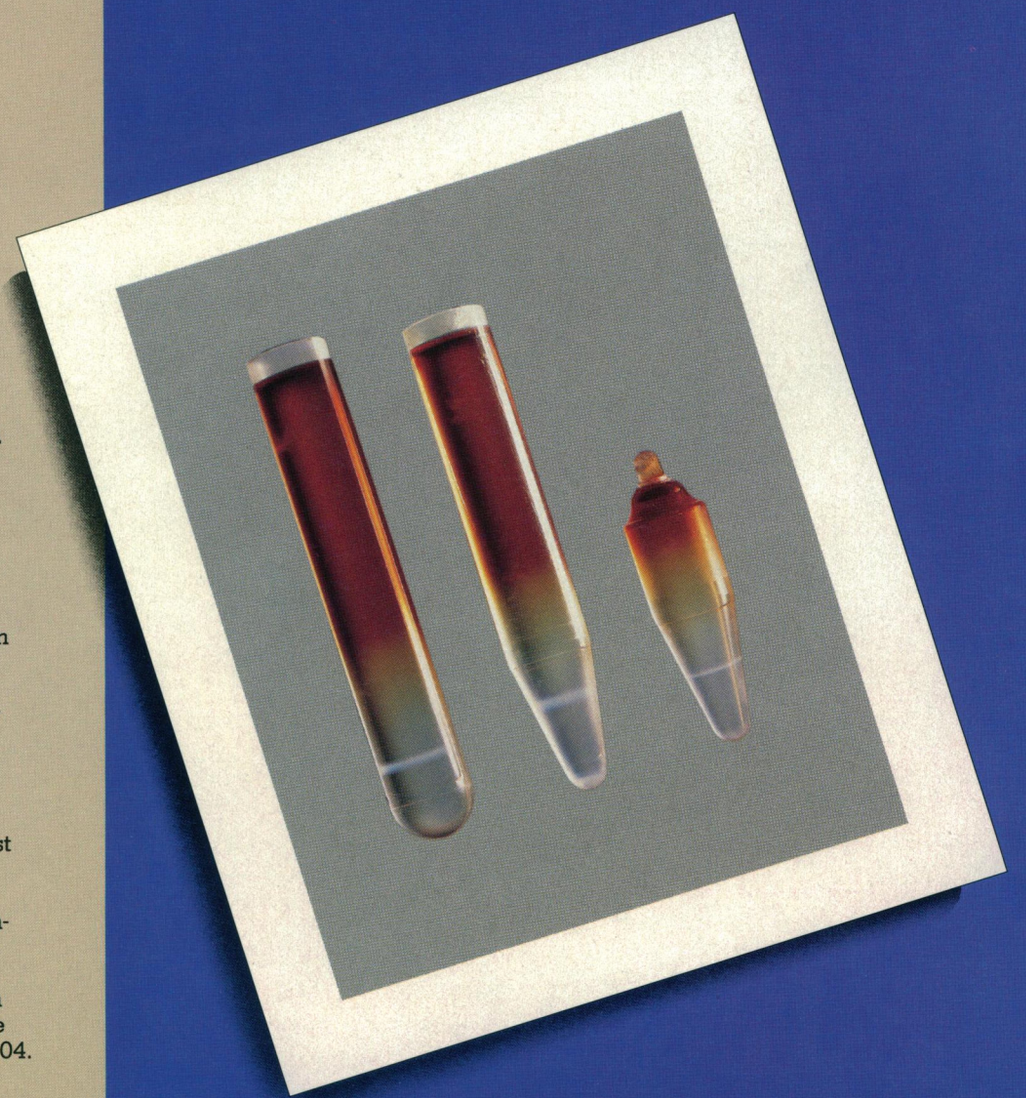

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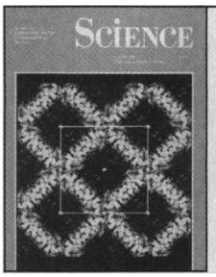

COVER The arrangement of the electron density in a tetragonal crystal of human serum albumin. Prominent features of the molecular packing arrangement are large (90 Å by 90 Å) solvent channels (shown in purple) that pass through the crystal parallel to the crystallographic c-axis. The unit cell and symmetry operations parallel to the c-axis are illustrated. See page 1195. [D. C. Carter *et al.*, NASA, Space Sciences Laboratory, Code ES76, Marshall Space Flight Center, AL 35612]

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California Institute of Technology

Robert Allen
Professor of Pathology
Medical University of South Carolina

Eric Lai
Assistant Professor of Pharmacology
University of North Carolina, Chapel Hill

Norman Anderson
Large Scale Biology Corporation
Rockville, Maryland

Frederick Neidhardt
Professor of Microbiology
University of Michigan Medical School

John McPherson
Director, Protein Chemistry
Integrated Genetics
Framingham, Massachusetts

Donald Hunt
Professor of Chemistry
University of Virginia

James Garrels
Senior Staff Scientist
Cold Spring Harbor Laboratory

Carl Merril
Chief, Laboratory of Biochemical Genetics
NIMH

Denis Hochstrasser
Laboratory Chief, Department of Medicine
Geneva University Hospital, Switzerland

Allan Wilson
Professor of Biochemistry
University of California, Berkeley

Bruce Budowle
Director, FSRTS
FBI Academy, Quantico

Steven Smith
Department of Genetics
University of Washington, Seattle

Gilbert Chu
Division of Oncology
Stanford University School of Medicine

David Patterson
President, Eleanor Roosevelt Institute for
Cancer Research, Inc.
Denver, Colorado

Richard Wilson
Research Fellow
California Institute of Technology

Charles Cantor
Professor of Molecular Biology
University of California, Berkeley
Director, Human Genome Center
Lawrence Berkeley Laboratory

Robert Kelly
Associate Professor of Pathology
University of Pittsburgh School of Medicine

Edward Southern
Whitley Professor of Biochemistry
University of Oxford, United Kingdom

Paul Matsudaira
Associate Member, Whitehead Institute for
Biomedical Research
Massachusetts Institute of Technology

Ronald Davis
Professor of Biochemistry
Stanford University School of Medicine

James Neel
Lee R. Dice Distinguished University
Professor Emeritus of Human Genetics
University of Michigan Medical School

Michael Harrington
Senior Research Fellow in Biology
California Institute of Technology

PARTIAL LIST OF SESSION TOPICS

- New Electrophoretic Technologies for the Human Genome Project
- Opportunities and Applications in DNA Mapping and Sequencing
- Applications and Opportunities in Protein Mapping
- New Technologies: Their Interrelations and the Future
- Gel Imaging and Detection Methodologies in Electrophoresis
- DNA Pulsed Field Technology
- New Forensic and Clinical Applications of Electrophoresis

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ANNUAL MEETING OF THE AMERICAN ELECTROPHORESIS SOCIETY

The accompanying exhibition is open to commercial firms offering or planning to offer equipment appropriate to the content of this meeting. Information about registration, poster submission, and/or exhibits may be obtained from the Society. On-site registration will be available.

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Antibody diversity

INDIVIDUALS inherit multiple genetic elements that get assembled into antibody genes which produce low levels of antibodies before foreign substances (antigens) confront the immune system. It is estimated that 10^8 to 10^{10} antibody genes can be assembled from the gene pieces; exposure to antigens appears to induce mutations that result in the production of even more antibody molecules that have higher binding affinities. Studies of the nature of the changes that occur in antibody molecules have led to inferences about the mechanisms by which the changes are produced (page 1152). However, the mutation process that generates diversity is still largely a mystery. French *et al.* point out that most of the changes are concentrated in certain regions of the antibody genes (called hypervariable regions) where the mutation rate is several orders of magnitude higher than it is for other genes in the same cell, mutation occurs only at certain times during the differentiation of antibody-producing cells and stops by the time cells are secreting large amounts of antibody, and the affinity of the antibodies increases (leading to a more effective immune response) as the mutation-generating process proceeds. Any model for how antibody diversity is generated must account for and is constrained by these and other factors.

Clouds at Neptune

WHEN the Voyager 2 spacecraft arrives at Neptune later this summer—the nearest encounter will occur 24 August—it will get some close-up pictures, at visible wavelengths, of clouds moving in Neptune's atmosphere. Clouds were recently observed from the earth through visible-light filters on the University of Hawaii's 2.24-meter telescope (page 1165); Voyager's wide-angle camera has a similar filter. Hammel describes the earth-based observations that included clouds at Southern Hemisphere mid-latitudes and a hazy layer over the southern pole of the planet. The combination of earth-based observations, which excel in spectral and temporal coverage, and the Voyager images, which will improve spatial resolution a thousandfold, should lead to an enhanced understanding of Neptune's atmospheric rotation period, its atmospheric structure, and its wind systems at different latitudes.

Magmas and ores

THERE are only a few known large deposits of platinum-group elements (platinum, rhodium, ruthenium, palladium, osmium, iridium) on the earth; one of these is a 1- to 3-meter-thick layer that stretches for 45 kilometers in the Stillwater Complex of Montana's Beartooth Mountains (page 1169). An understanding of how the prized ores in the Stillwater Complex were deposited may be helpful in identifying other places where such ores may be found. The Stillwater Complex is 2.7 billion years old and formed when a large body of basaltic magma crystallized in the earth's crust. Lambert *et al.* used two isotope systems—one involving platinum-group elements and the other rare-earth elements—to trace the history of the magmas that contributed to the Stillwater Complex, where these magmas originated in the earth's mantle, and how deposition occurred. Two different magmas were apparently involved in the formation of the Complex. Platinum-group elements, abundant in one magma, appear to have crystallized out when this magma mixed with the second magma in the Stillwater magma chamber.

Arachidonic acid and channels

A NEW class of membrane channels has been identified: these channels, which transport potassium ions across cell membranes, are activated directly by arachidonic acid and other fatty acids that are constituents of the membrane's lipid bilayer. Previously, only the breakdown products of fatty acids had been implicated in channel activation, and thus the role of fatty acids was considered indirect. However, direct activation of individual channels has been demonstrated in smooth muscle cells of the hearts of newborn rats (Kim and Clapham on page 1174) and the stomachs of toads (Ordway *et al.* on page 1176). These fatty acids may play the part of "second messengers" (responding to external signals) in many types of cells. In heart cells, arachidonic acid is released from membrane phospholipids when blood flow is impaired; it may be that, during a heart attack, it is these channels that help rescue oxygen-deprived cardiac cells from death.

Albumin structure

THE most abundant soluble protein in the bloodstream is albumin. Although its exact function is not known, albumin is believed to contribute to the stabilization of salts and blood pressure, and diverse substances in the blood bind to it and get transported through the circulation. Serum albumin has been found to block actions of a number of pharmaceutical drugs, and, therefore, a better understanding of its structure could contribute to the design of more effective, nonbinding drugs. Human serum albumin has been fully sequenced (as have other albumins), many of its biologic properties have been identified, and much has been determined and inferred about its structure. It is a large protein (585 amino acids) with 17 disulfide bonds; it has a high α-helical content and three major domains. When albumins from different species are compared, they are very similar; the three domains within a given molecule are also homologous. Carter *et al.* have now evaluated human serum albumin in three dimensions (page 1195); they prepared a tetragonal crystal and resolved its structure at 6.0 angstroms (cover). Despite this relatively low resolution, the folding of the molecule, the domain structure, the location of binding sites within specific subdomains, and other details of the molecule's conformation were confirmed and further defined.

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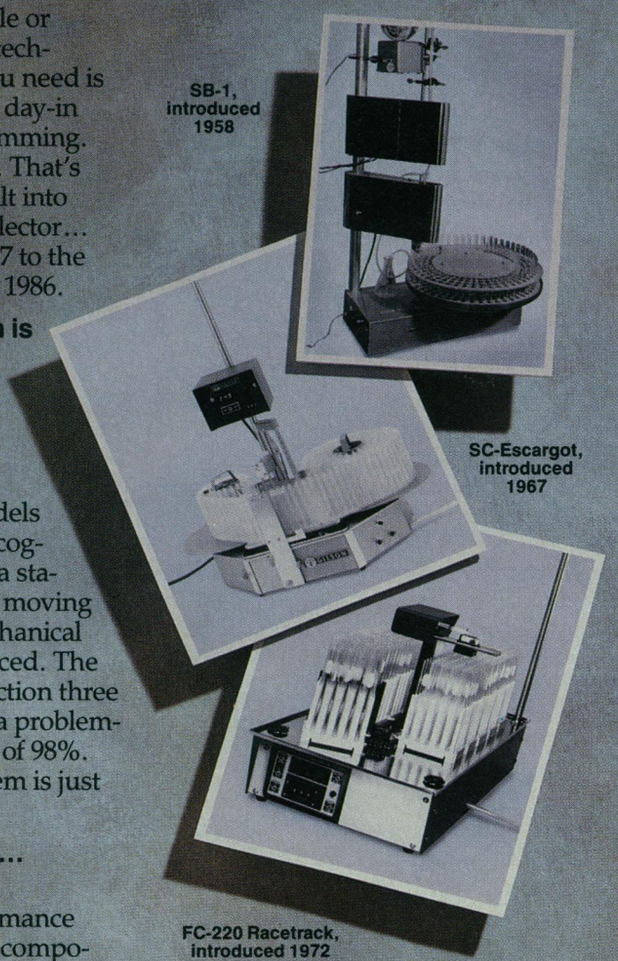

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Combating High Journal Costs

The number of journals devoted to science and medicine continues to expand, and their cost to libraries has escalated. Librarians have complained for many years about the phenomenon and have found it necessary to make painful curtailments of expenditures for other periodicals, books, salaries, and equipment. In their travail they earlier had few allies and were not well organized to deal with the mounting problems.

But librarians are now more effectively united and are finding allies among scientists and among chancellors of universities. Perhaps most important, they have identified major contributors to their financial problems—the international commercial publishers. These companies now print much of the scientific literature and in many specialties hold monopolistic positions. A series of recent studies concluded that the companies have exploited their business opportunities to raise prices much faster than inflation.

Another factor influencing a revolt against monopolistic pricing is growing recognition that some high-priced journals have little impact. That is, the average number of citations listed in the *Science Citation Index* to past articles may be small.

Henry Barschall, a retired professor of physics at the University of Wisconsin, has surveyed the "cost effectiveness" of about 200 journals related to his discipline.* He found that the cost per 1000 characters varied from 0.39 cents to 31 cents. The ratio of cost to impact varied from 0.63 to 54, that is, by a factor of 850. Articles in some of the high-priced journals each received, on average, less than one citation. The group of journals published by the American Physical Society had on average a "cost effectiveness" more than 12 times that of the best group averages for any of several major publishing houses

The present situation has developed during more than 35 years, and scientists have been partly responsible. In the earlier days, most scientific publishing was conducted by the scientific societies. But some of the societies and their editors were slow to recognize new developing fields, thus creating an opportunity for private enterprise. Many of the societies in effect levied page charges. The companies did not, and they quickly came to have an important role in publishing exciting new material. The scientists also demanded that libraries subscribe to the new journals. Thus a monopolistic position was established, and librarians later found they were paying huge prices for the subscriptions.

A study commissioned by the Association of Research Libraries (ARL) and recently released† has noted that the phenomenon of escalating costs has created a crisis for its members. The study also points to the "key role of commercial, profit-seeking publishers, especially the international publishers." The study makes a number of recommendations for action. One is for the development of publisher- and subject-specific cost indexes for critical serial titles and for a mechanism to maintain and distribute such indexes.

Another recommendation is that the ARL should strongly advocate the transfer of publication of research results from serials produced by commercial publishers to existing noncommercial channels. The study also recommended that ARL should encourage the creation of innovative nonprofit alternatives to traditional commercial publishers. The study points out that most research that is published is supported by public funds, but that a large proportion of the research results must be purchased from commercial channels. As a step toward remedying this anomaly, it was recommended that ARL urge university and granting agencies to explore the feasibility of making publication through a noncommercial channel the preferred means for reporting the results of publicly funded research. The study also urged ARL to present its position to the House and Senate committees specifically involved in the funding of the federal granting agencies.

The study also recommends a major effort to minimize pressures for excessive publication. This goal could be achieved only slowly. However, the proposal to give publicity to the poor "cost effectiveness" and lack of impact of some of the international journals could have substantial effects, and soon. Libraries would have a basis for choice of serials to cancel. Scientists would become more aware of the obscurity that their papers might encounter. Granting agencies and universities would have a yardstick for measuring and discounting the likely impact of grantees' publications.—PHILIP H. ABELSON

*H. H. Barschall, *Physics Today* **41**, 56 (1988). † Association of Research Libraries, "Report of the Association of Research Libraries Project on Serial Prices" (Washington, DC, June 1989).

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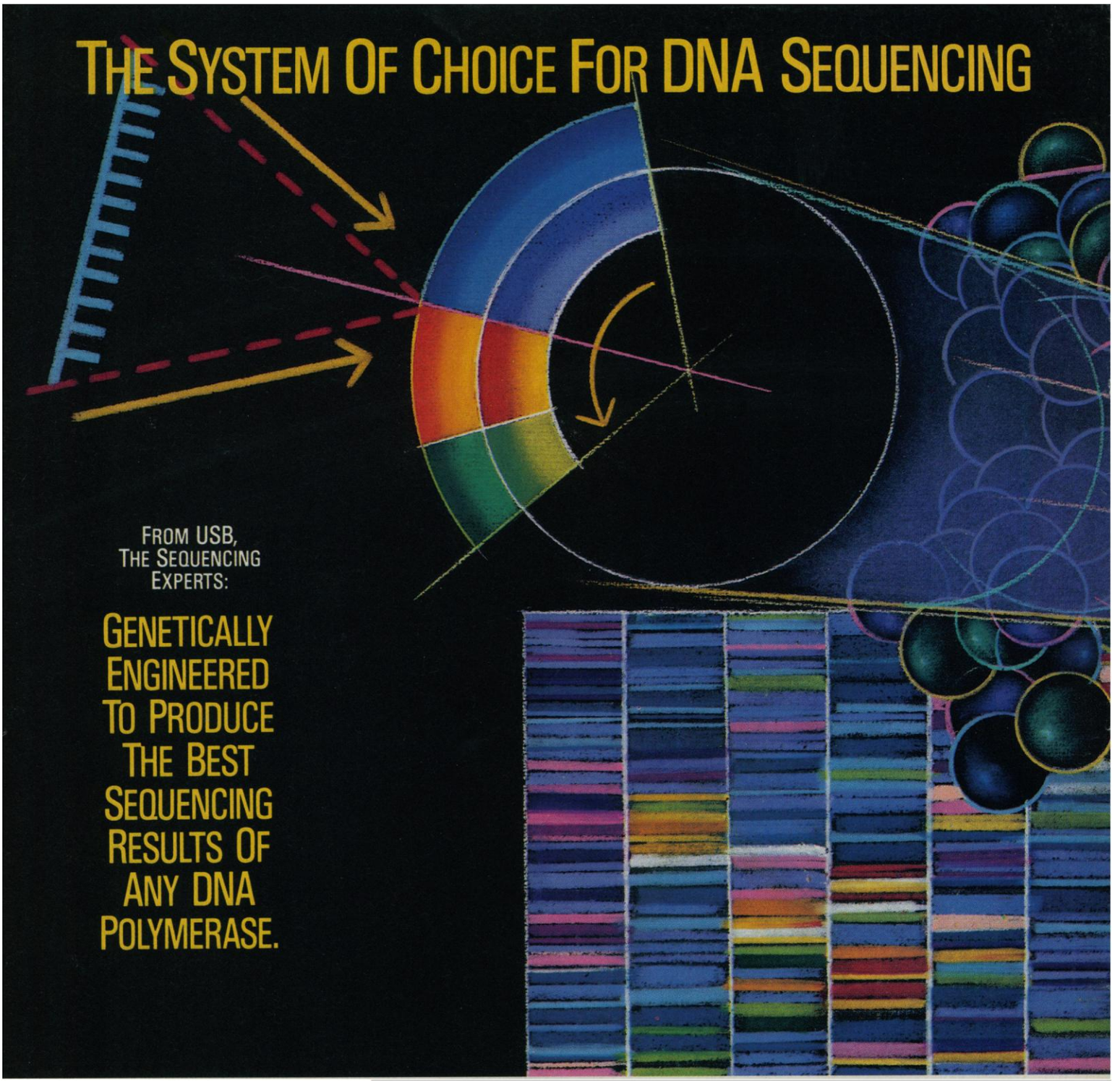

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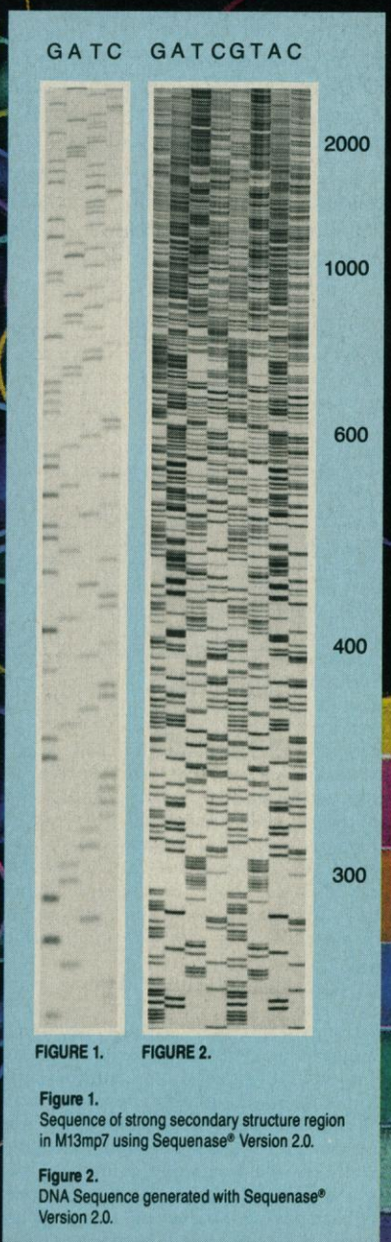

FIGURE 1. FIGURE 2.

Figure 1.
Sequence of strong secondary structure region in M13mp7 using Sequenase® Version 2.0.

Figure 2.
DNA Sequence generated with Sequenase® Version 2.0.

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human history than the genetic relationships." They do not specify, however, any basis for their belief. Our data provide the first evidence that "much later" translates on average into a factor of 5 or 10. Genetic data indicate that most human linguistic phyla known today must have arisen approximately 25,000 to 8,000 years ago, while Khoisan, Indopacific, and Australian arose perhaps 30,000 to 50,000 years ago. In contrast, modern humans are more than 100,000 years old. While our dates for the origin of linguistic phyla seem more convincing than the few statements in the linguistic literature, they do not necessarily disagree with them.

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Erratum: In Eliot Marshall's article "Bomb factories of the 21st century" (News & Comment, 20 Jan., p. 305), it was erroneously reported that the Department of Energy proposed to close down the Mound Facility in Miamisburg, Ohio. In fact the department suggested shifting all radiation-related work (amounting to 30% of the total) to other sites.

Erratum: In figure 3B (p. 699) of the report "Calicheamicin γ_1^I and DNA: Molecular recognition process responsible for site-specificity" by N. Zein *et al.* (12 May, p. 697), the stereo pair was incorrectly printed and inverted. The correct representation is a mirror image of what was shown.

Agency for International Development

Announcement of
Malaria Vaccine Research & Development
Request for Applications
[RFA-ST/H-89-001]

Background. For more than 20 years, the United States Agency for International Development (A.I.D.) has supported a program of applied research in malaria vaccine development. Currently, the primary research foci of the Malaria Vaccine Research & Development Project include:

—the identification and characterization of malaria parasite antigens, with emphasis on asexual, sporozoite, and liver stages of the parasite by immunochemical and/ or molecular biological methods, for development of vaccine candidates;

—the elucidation of the importance of identified antigens and B-cell and T-cell epitopes in providing a protective immune response in naturally acquired human malaria and in relevant animal models, including appraisals of strain specificity of protective immunity;

—the elucidation of humoral and cellular effector mechanisms of protective immunity to malaria and the development of *in vitro* correlates of protective immunity;

—the modification of the structure and/or mode of presentation of antigens, which have been shown to have a role in protection, in an attempt to increase their ability to induce a protective immune response;

—the testing of vaccine candidates for immunogenicity, safety, and efficacy in appropriate animal models, including non-human primates.

Proposals. A.I.D. is soliciting proposals for Cooperative Agreements describing a program for malaria vaccine research. In general, the range of activities requested in the RFA is as outlined above. However, there is a special interest in proposals whose major emphasis is on development of vaccines that induce responses mimicking natural immunity (*i.e.*, a state characterized by protection from disease but not necessarily from infection) thus allowing restimulation of immunity through natural exposure to parasites. It is the intent of A.I.D. to support 3-year research programs. **Only U.S. institutions are eligible for these grant awards.**

Applications. The American Institute of Biological Sciences (AIBS) will process all applications. **Proposals must be received by September 1, 1989.** The complete RFA and detailed information on the application process may be obtained from:

American Institute of Biological Sciences
1800 North Kent Street (Suite 930)
Arlington, Virginia 22209
fax: 703-527-4404

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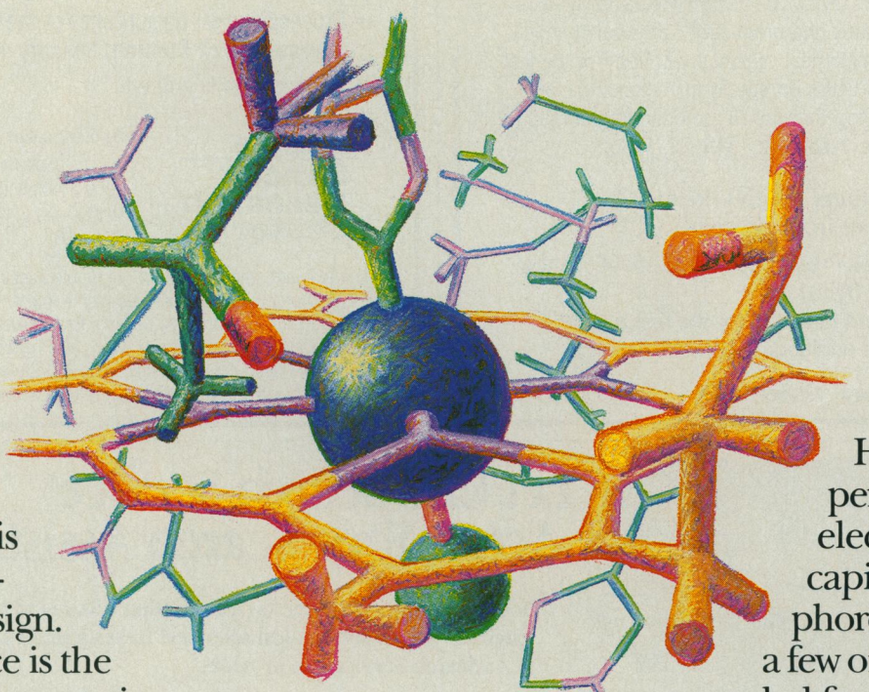

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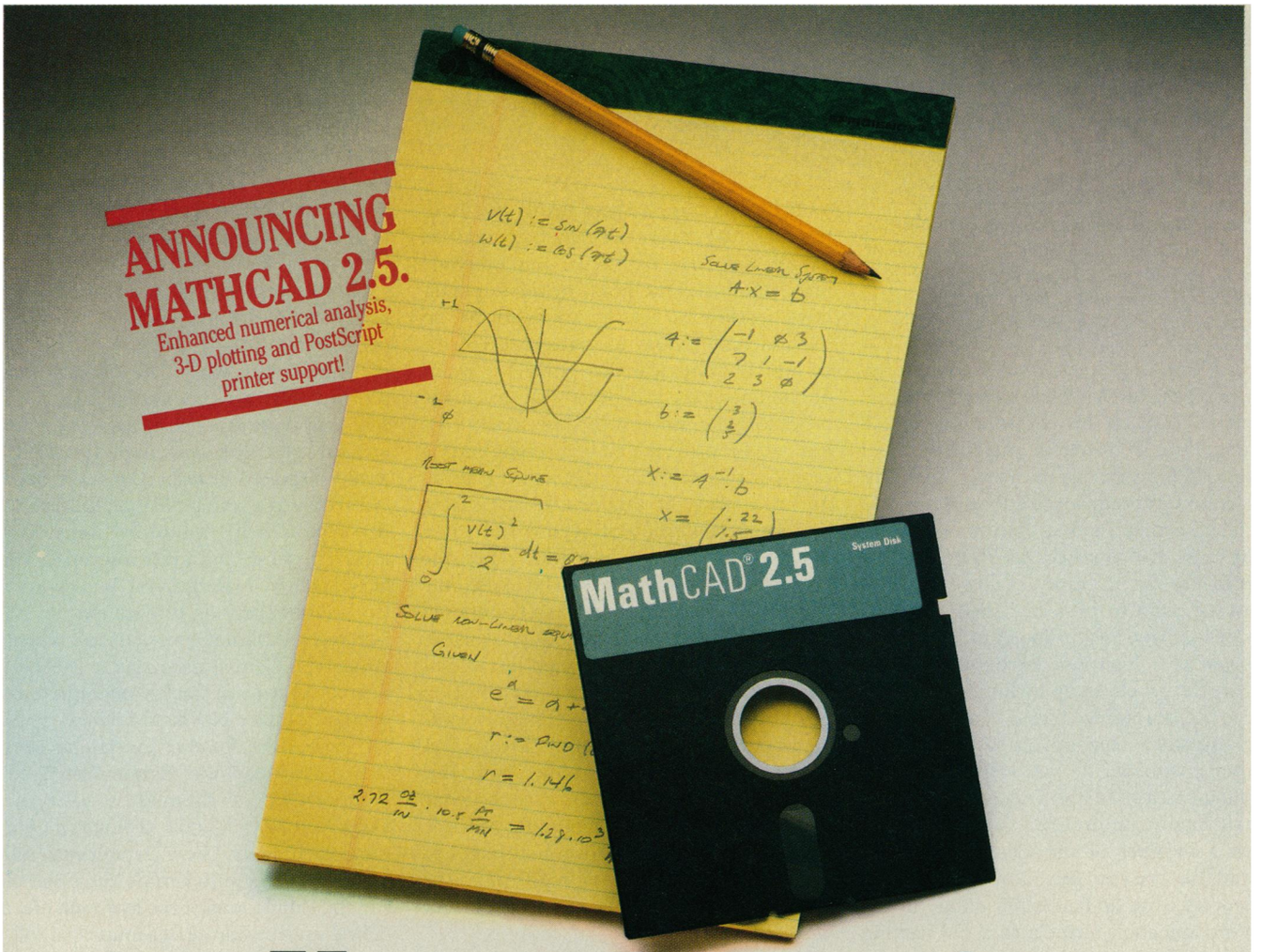

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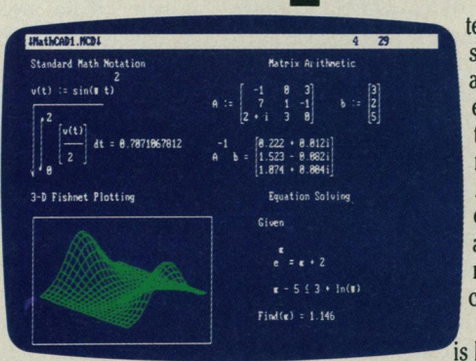

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