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SCIENCE

7 July 1989
Vol. 245 ■ Pages 1–100

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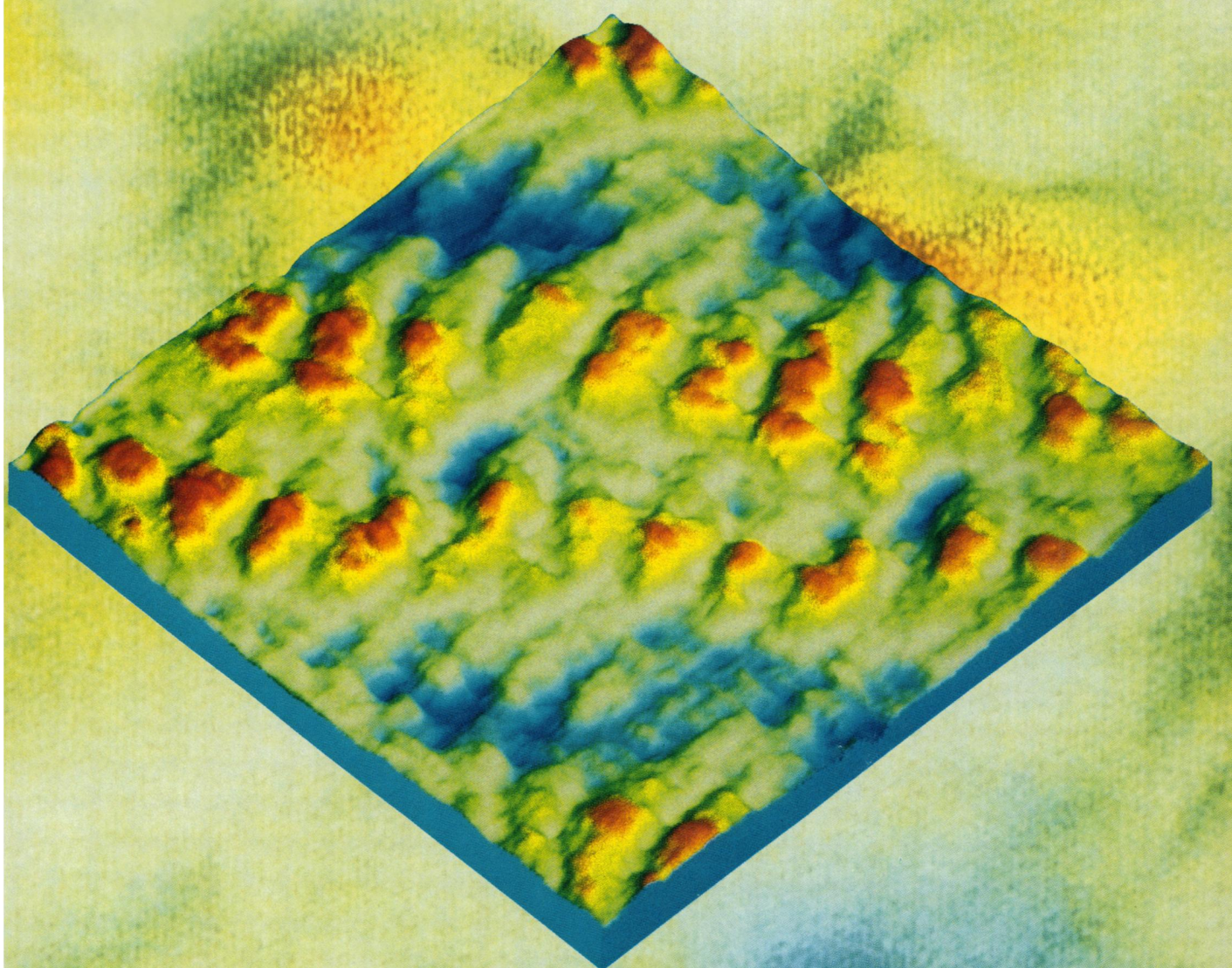

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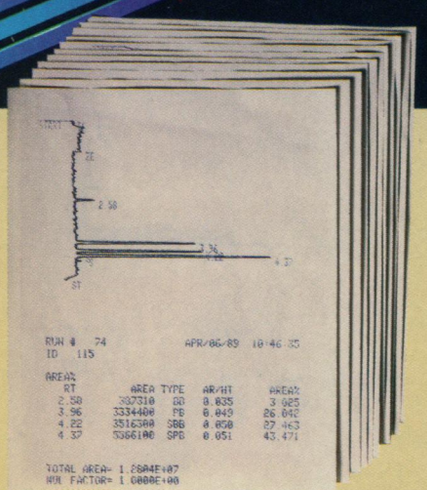

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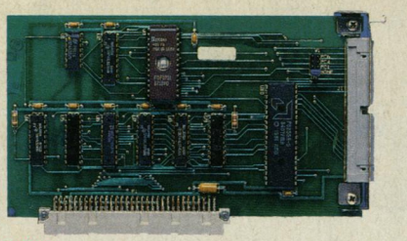

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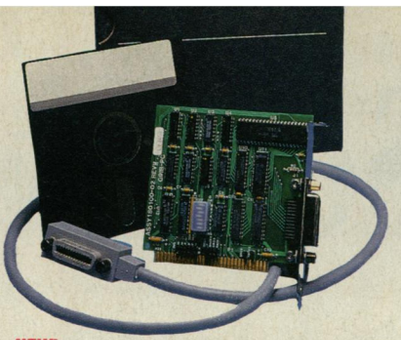

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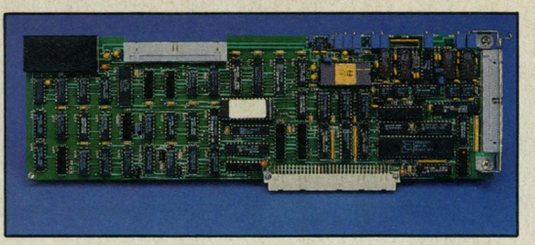

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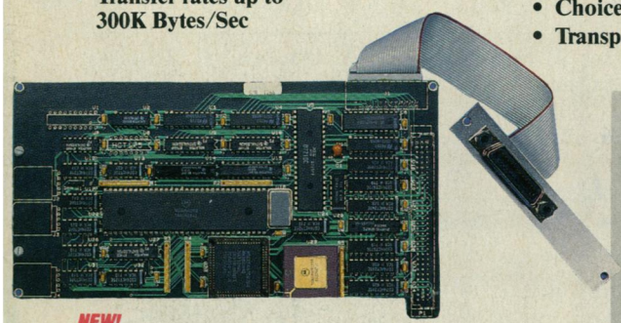

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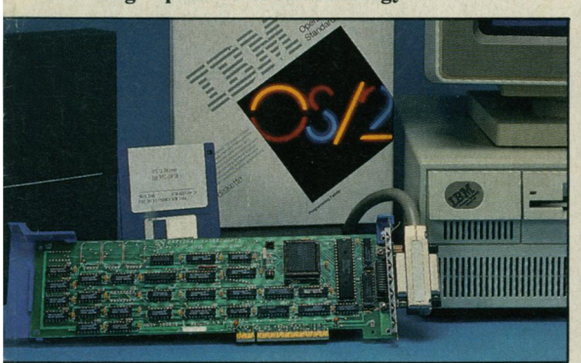

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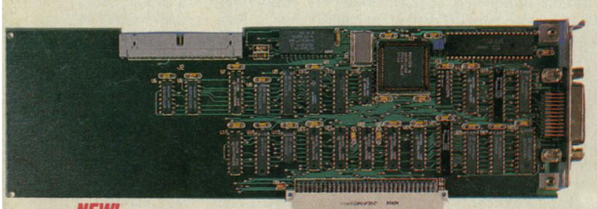

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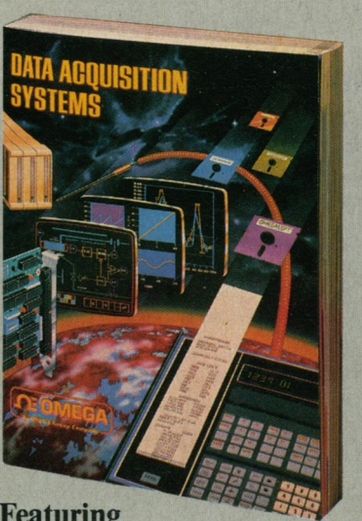

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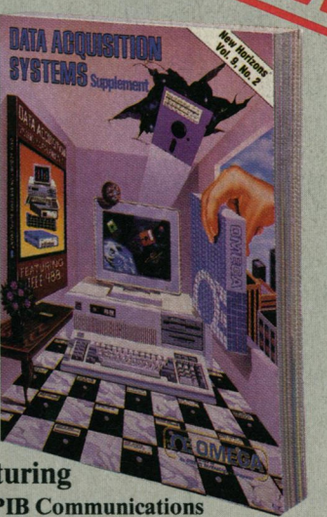

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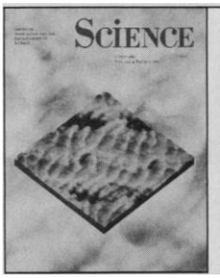

COVER Molecules of 10-alkylcyanobiphenyl condensed onto the surface of graphite are imaged with the scanning tunneling microscope (STM). The image is seen over an enlargement. The 56 by 56 Å^2 image has a height range of 1 Å, where red is highest and blue is lowest. The STM is sensitive to the different functional groups of the molecule; the biphenyl groups appear in the image as red ovals and the alkyl groups as green tails. See page 43. [Photograph by Douglas P. E. Smith; computer graphics by Michael Niksch and Lloyd LaComb, Jr., using a silicon Graphics Iris computer]

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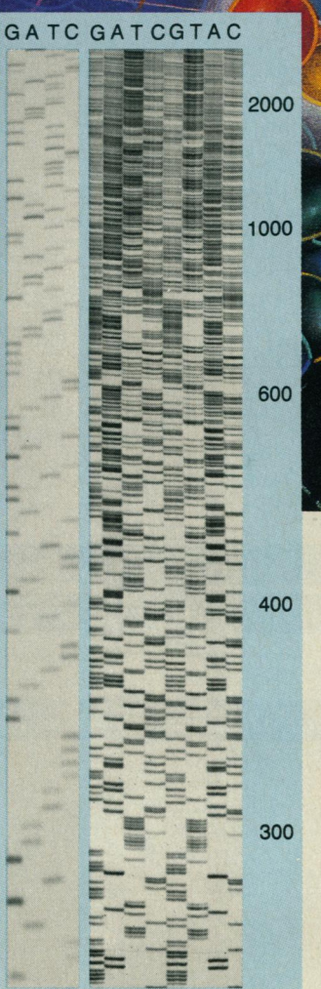

FIGURE 1. FIGURE 2.

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

Figure 2.
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This Week in
SCIENCE

Scanning and tunneling through liquid crystals

THE structures of ordered arrays of molecules, such as liquid crystals, can be perturbed by the presence of a surface like graphite. With scanning tunneling microscopy, it has been possible to study changes in the structures of a series of molecules—the *n*-alkylcyanobiphenyls in which *n* is 8 to 12—adsorbed onto graphite (cover) (page 43). In bulk form, the *n*-alkylcyanobiphenyls are smectic liquid crystals: they flow like liquids but have some order, and their molecular axes are perpendicular to the plane of the repeating layers. The contact layer on the graphite surface, which is the layer that is scanned, assumes even more order than the bulk material and resembles a two-dimensional molecular crystal. Smith *et al.* present a model for the adsorbed liquid crystal lattice structure that depicts how the cyanobiphenyl head groups and alkyl tails are packed, how molecules are paired in layers, and how the lattice is ordered in space.

Binding sites for tomato juices

AUXINS are powerful hormones that promote plant growth. Although they were first identified some 50 years ago, little is known about how they work. Like other hormones, a compulsory and key first step is their binding to cellular receptors; therefore, one approach to understanding their activity is to determine where and how they bind. Hicks *et al.* have been studying mutant tomato plants that produce but are unable to respond to auxins and in which both functional and structural abnormalities occur as a result of the (likely) receptor defect (page 52). In stems and roots of parent plants, a pair of auxin-binding proteins can be detected; in mutant plants, the roots contain normally functioning auxin-binding proteins but the stems do not. If the defective expression of the auxin-binding proteins is shown to be causally related to the known mutations in *dgt* genes of the mutant plants, an elusive auxin receptor gene could be cloned and studied at last. The tomato mutants serve as an excellent system in which features of auxin binding and the molecular bases of auxin actions can be further evaluated.

Fibroblast growth factor receptor

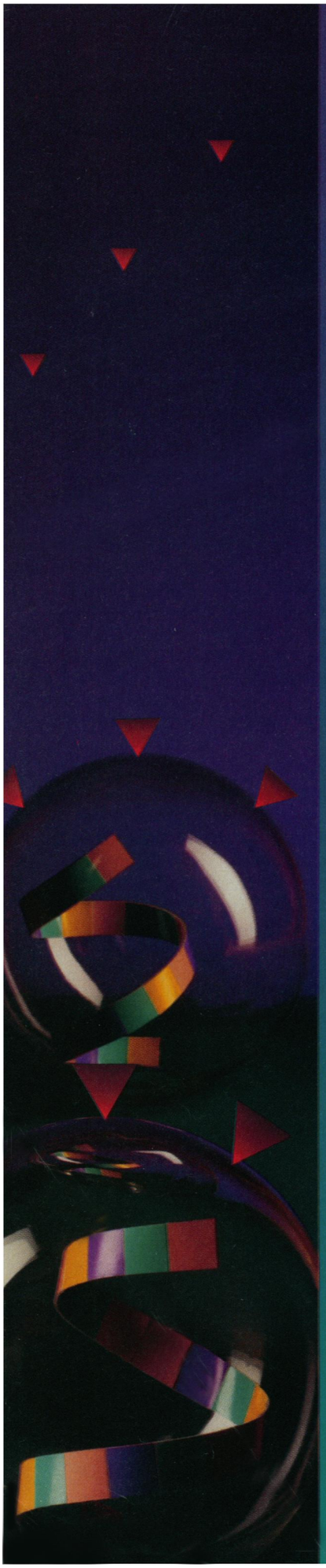
THE fibroblast growth factors are important proteins. After binding to receptors on the surfaces of cells, they induce a variety of helpful and pathologic effects in a range of cell types. For example, they participate in wound healing and in the formation of new blood vessels, they promote certain developmental steps, but they also can enhance tumor growth. The family of fibroblast growth factors includes both acidic and basic proteins. Lee *et al.* have now purified and cloned the receptor to which basic fibroblast growth factor binds and report on its sequence and structure (page 57). The receptor is a large protein that consists of discrete domains: the intracellular domain contains sequences for the enzyme tyrosine kinase; the extracellular portion includes an uncommon, small, and very acidic domain and three immunoglobulin-like domains; there is a membrane-spanning region that is linked to the intracellular tyrosine kinase domain by an unusually long juxtamembrane region. The corresponding domains from chicken and human fibroblast growth factor receptors were compared and found to have significant homologies with each other.

Understanding diabetes

DIABETES is not a cut-and-dried condition; a predisposition to diabetes may be inherited, but compounding events, such as obesity or accumulating gene mutations, may be needed to tip the balance toward disease. Therefore, a number of molecular and genetic defects are probably associated with and may underlie diabetes. In normal individuals, the binding of insulin to its receptor initiates a chain of events that includes tyrosine kinase activation, triggering of biologic responses inside cells, and transport of glucose into target tissues. Taira *et al.* have studied a young Japanese woman (page 63) and Odawara *et al.* describe a young Japanese man (page 66) whose insulin receptors are defective in tyrosine kinase activity; the faulty tyrosine kinases—one resulting from a gene mutation and the other from a gene deletion—greatly diminish receptor effectiveness. Garvey *et al.* assess how aberrant levels of glucose transport proteins contribute to the diabetic state in animals with a chemically induced form of diabetes (page 60). Kahn and Goldstein review characteristics and distinguishing features of the different diabetic states and explain how the new findings will help clarify the nature of diabetes (page 13).

Desktop mining

PREDICTING the locations of gold mines in Nova Scotia, copper deposits in Canada, and other hidden mineral deposits around the world requires sifting through mountains of data; the task has been made easier for geologists with the advent of computer programs that are dedicated to mineral exploration. How this software has evolved, the types of information that go into mineral exploration databases (they range from remote-sensing data to regional and worldwide geochemical information to theories of how orebodies form), the computational strategies that are used, the different means of handling certain and uncertain information, and the strengths and limitations of the computer methods are described in Agterberg's Software Review (page 76). The application of computer programs to prospecting began in the early 1970s, but the intellectual roots of the logical approach to locating buried minerals date back at least to the 1500s when the German mineralogist Georgius Agricola proposed that signs at the earth's surface might provide clues to where mineral deposits are hidden.



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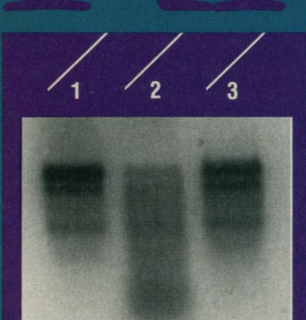

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References:

1. Schneider, R., *et al.* (1988) *EMBO Journal* **7**, 4151-4156.
2. Cask, D. (1988) *Lancet*.

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Retrieval of Scientific and Technical Data

At one time it was possible for an individual to become knowledgeable about new developments impinging on his or her field by simply scanning a few publications. But with the continuing proliferation of new journals and of interdisciplinary work, this is no longer feasible. Electronic equipment is creating an enormous flood of data. At the same time, computers and electronics are providing means of storing and retrieving new and old information so that in many instances an individual can tap information even more effectively than did predecessors a generation ago. Procedures for making information more readily available to the user are evolving.

Starting in the early 1970s, a few bibliographic databases became accessible on-line. Since that time, the number of publicly accessible databases has increased to about 4200 and their character has changed. Full text is available in some instances. Numerical databases have come to constitute a substantial fraction of the total. A majority of the bases are devoted to legal or business matters, but about 30% are related to medicine, science, or engineering.

The National Library of Medicine draws on the world's medical literature and that of related fields to create 20 important databases, including Medline. The Chemical Abstract Service of the American Chemical Society has joined with associates in Germany and Japan in a network (STN) that provides 85 databases. Their resources include 8 million chemical abstracts dating back to 1965 and information concerning the properties of 9.5 million substances. The consortium is expanding its coverage of biology, physics, mathematics, engineering, and materials science.

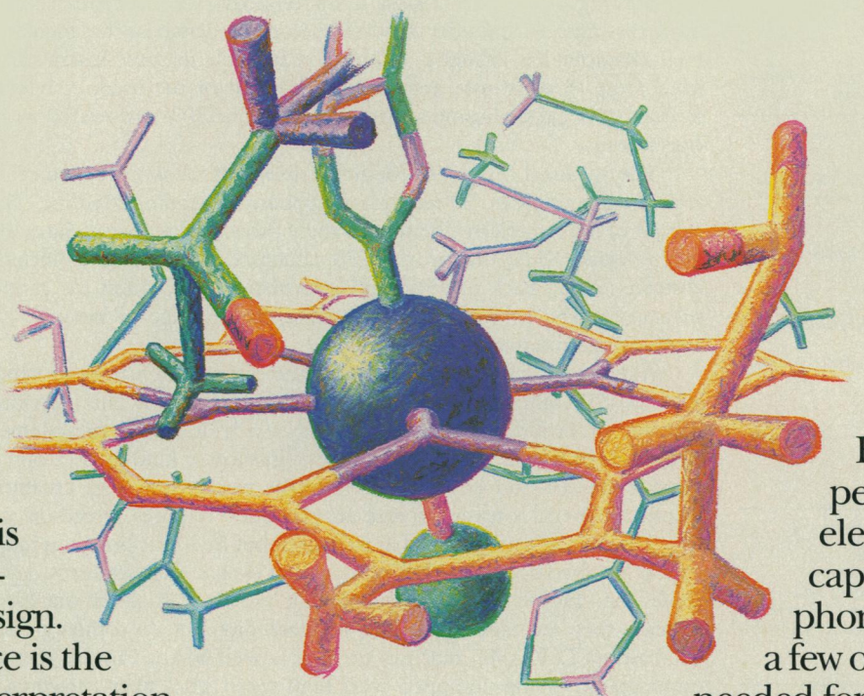
Although a few organizations are the dominant creators or vendors of databases, as many as 1700 different entities maintain at least one base. This individual initiative, coupled with the procedures of vendors, has led to a wide variety of systems, services, command languages, protocols, and terminologies—in short, a kind of electronic chaos that limits the value of the vast store of information for the average user. The situation demands more and helpful front-end software to ease access. It also requires agreed-on standards.

The costs of on-line searches average about $120 per hour and range from about $26 to several hundred dollars per hour. Such costs do not seem to discourage business or the legal profession. However, universities find it necessary to limit the use of on-line vendors. Instead, they are tending to buy or lease diskettes or compact disc read-only memory databases (CD-ROMs) that can then be tapped by the campus computer network. Some campuses are being equipped with high-speed glass fiber networks, and professors and students have their own personal computers.

The CD-ROM is already having an increasing role in data storage and retrieval. A disc only 12 centimeters in diameter can contain the equivalent of 200,000 pages of book text. For databases that do not change rapidly or at all, the disc is an ideal repository. Currently the commercially available CD-ROMs are priced at about $6000 each. This covers the cost of creating the master from which the discs are produced as well as a profit. Once the master is paid for, the cost of producing additional CD-ROMs is only a few dollars per copy. The cost of a CD-ROM reader is only a few hundred dollars. When demand for the discs becomes substantial, their price will fall. Already competition has become evident. There are now nine producers of CD-ROMs containing the information available on Medline. Price ranges from about $1000 to $1500. Special beneficiaries of cheaper CD-ROMs would be physicians, scientists, and engineers in Third World countries. They would need some simple equipment, but the cost of the information provided would be a tiny fraction of what it has been. Already CD-ROMs containing vast amounts of geophysical data are being supplied for a few dollars.

In the United States, computer networks are playing an increasing role in the research and education communities. More than 600 networks with over 100,000 computers and workstations are currently linked by INTERNET. NSFNET, one of the key components of INTERNET, links 250 institutions and major laboratories. Its traffic has been increasing rapidly. During April 1989 it carried 800 million packets. A larger, faster, federally sponsored network is being advocated. This would facilitate enhanced exchange of complex numerical data and transmission of figures and images.—PHILIP H. ABELSON

Is protein chemistry an art or a science?



The art of protein chemistry is the experimental design. The science is the correct interpretation of results. Just as the protein chemist integrates art with science, Applied Biosystems integrates chemistry and instrument design with application expertise to become partners with you in developing solutions to your problems.

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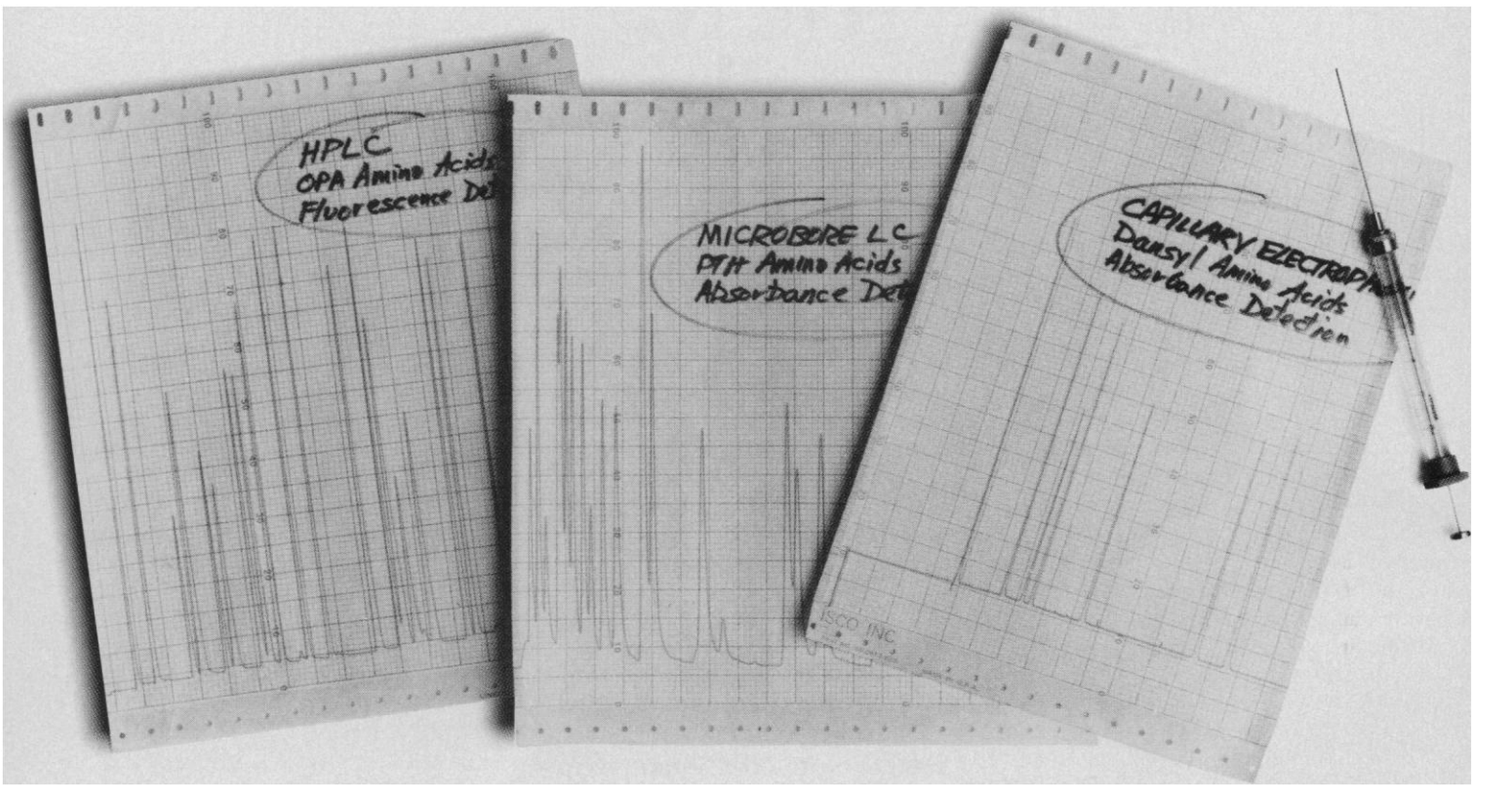

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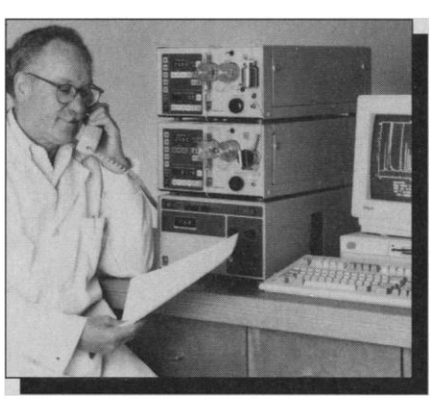

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Richard Atkinson, President, American Association for the Advancement of Science.
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Charles Cantor, Director, Human Genome Center, Lawrence Berkeley Laboratory.

CURRENT STATUS OF THE GENOME PROJECT

THE GENETIC MAP: Raymond White, Howard Hughes Medical Institute, University of Utah.
RESTRICTION MAPS: Cassandra Smith, University of California, Berkeley.
CLONING: Ronald Davis, Stanford University School of Medicine.
ORDERED LIBRARIES: Sydney Brenner, MRC Molecular Genetics Unit, Cambridge, England.
APPLICATIONS: Thomas Caskey, Howard Hughes Medical Institute, Baylor College of Medicine.
SOCIETAL IMPLICATIONS: Daniel Koshland, University of California, Berkeley.

TECHNIQUE INNOVATIONS

PCR OF SINGLE SPERM: Norman Arnheim, Ahmanson Center for Biological Research, University of Southern California.
SEQUENCING METHODS: George Church, Harvard Medical School.
DNA CLEAVAGE: Peter Dervan, California Institute of Technology.
RADIATION HYBRIDS: David Cox, University of California, San Francisco.
IN SITU HIBRIDIZATION: Jeanne Lawrence, University of Massachusetts Medical Center.
RAPID MAPPING: Glen Evans, Salk Institute.

INTERESTING REGIONS

CYSTIC FIBROSIS: Francis Collins, Howard Hughes Medical Institute, University of Michigan Medical Center.
TELOMERES: Robert Moyzis, Los Alamos National Laboratory.
IMMUNOGLOBULINS: Tasuku Honjo, Kyoto University Faculty of Medicine.
IMMUNOGLOBULINS: Hans Zachau, Institute for Physiological Chemistry, University of Munich.
T-CELL RECEPTORS: Leroy Hood, NSF Science and Technology Center for Biotechnology, California Institute of Technology.
FRAGILE X: Jean-Louis Mandel, Institut de Chimie Biologique, Strasbourg.

APPLICATIONS

HUMAN EVOLUTION: Allen Wilson, University of California, Berkeley.
MULTIGENE DISEASES: Eric Lander, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts.
HUMAN DIVERSITY: Jean Dausset, Human Polymorphism Study Center (CEPH).
SEX DETERMINATION: David Page, Whitehead Institute for Biomedical Research.
UNSTABLE SEQUENCES: Michio Oishi, University of Tokyo.
INTERPRETING SEQUENCE: Russell Doolittle, University of California, San Diego.

ORGANIZATION – DIFFERENT VIEWS OF CURRENT AND FUTURE SCIENCE AND PROCEDURES

HUGO: Victor McKusick, Johns Hopkins University School of Medicine; President, The Human Genome Organisation (HUGO).
NIH: James Watson, Cold Spring Harbor Laboratory; NIH Human Genome Project.
DOE: Charles Cantor, Human Genome Center, Lawrence Berkeley Laboratory.
EEC: Peter Pearson, Johns Hopkins University School of Medicine.
JAPAN: Nobuyoshi Shimizu, Keio University School of Medicine.
INFOMATICS: David Lipman, National Library of Medicine.
OVERVIEW: Renato Dulbecco, Salk Institute.

POSTER SESSIONS AND EXHIBITS

Registrants of the meeting may submit abstracts for poster sessions by requesting abstract forms on the registration tear off below. Exhibits will be open to all attendees and interested researchers Monday, Tuesday and Wednesday.

REGISTRATION FEES: Make checks payable to: **Scherago Assoc., Inc.,/Human Genome**
$250 ON-SITE REGISTRATION – Includes Abstract Booklet.
$200 ADVANCED REGISTRATION – (Received by Sept. 1, 1989) Includes Abstract Booklet.
$ 75 STUDENT REGISTRATION – Student status must be confirmed in writing by department chairman.

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