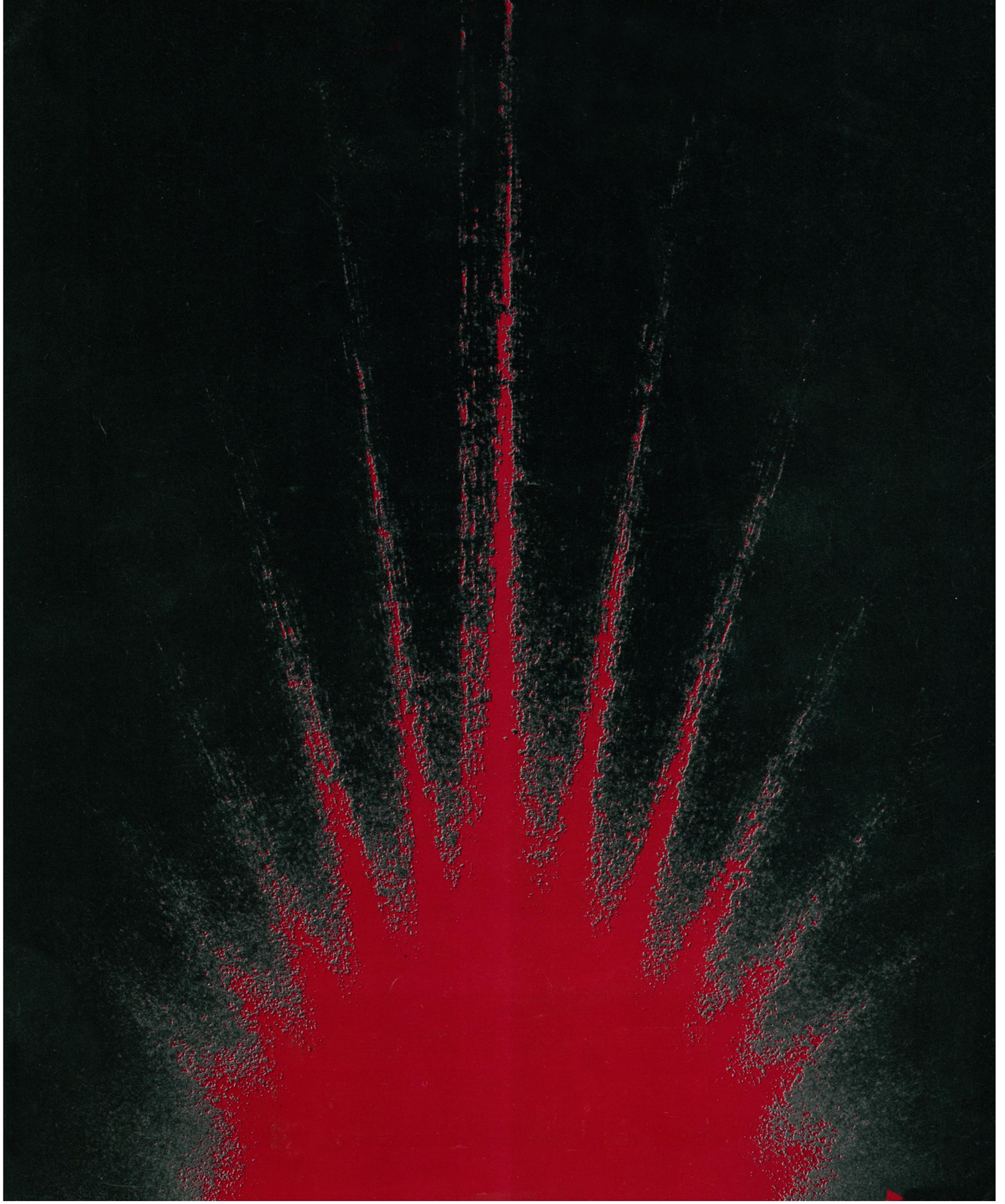
13 DECEMBER 1985 · VOL. 230 · NO. 4731 · $2.50

SCIENCE

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



New System 7300 Amino Acid Analyzer Plots, Labels, Calculates, Prints, Remembers

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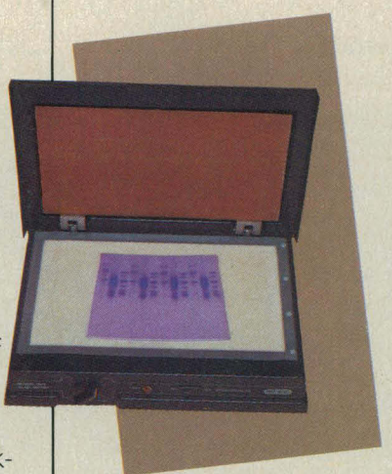

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COVER

Diffraction pattern, obtained with a He-Ne laser ($\lambda = 0.633$ μm), from intact skeletal muscle of frog. To detect the diffracted rays directly, an opaque screen was placed parallel to the incident laser beam. Generally, the diffracted rays are intercepted by a perpendicular screen, yielding the more familiar pattern of fringes. Six orders of diffraction are visible. This muscle has been stretched to sarcomere length 4.54 μm, at which length non-overlap of thick and thin filaments would be reproduced. See page 1280. [Alan Magid and Douglas J. Law, Duke University, Durham, North Carolina 27710]

BIOSYSTEMS UPDATE

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Halley's comet

A swarm of spacecraft is speeding toward Halley's comet for close encounters (one set to approach within 500 km of the comet's nucleus) in March (page 1229). Humans recorded seeing this comet as far back as 240 B.C. Halley stands out among the roughly 10^{12} extant comets, having both a relatively short return period and the full range of cometary features (atmospheric jets, halos, and dust and ion tails). Belton describes what has been learned so far and what is being sought concerning Halley's water-ice constituents, dust, and carbonaceous materials, sounds, colors, and interactions with the solar wind. Since comets are thought to be remnants of materials from which the solar system formed cometary study is expected to provide information about the evolution of the earth and other planets. Look for Halley's comet in the sky now in the Northern Hemisphere and in spring in the Southern Hemisphere. Next chance will be in the year 2061.

High resolution three-dimensional images

Although the naked eye readily sees three-dimensional (3D) details, such details are difficult to see in a microscope and are even harder to record (page 1270). A major breakthrough in high resolution 3D analysis has been made by Boyde using a tandem scanning optical microscope. The details of the technologic feat of recording 3D pictures at the limits of resolution of the light microscope, the history behind the development, and future applications of this technology are explained in Lewin's Research News article (page 1258).

Improving memory

The drug clonidine helps forgetful, aging monkeys remember the location of objects; it may have a clinical use as well for improving certain types of memory losses that afflict aging humans (page 1273). Arnsten and Goldman-Rakic tested the ability of monkeys to perform a delayed-response task—to find food that the monkeys earlier had watched being placed in one of two identical wells. This task, which requires working memory, depends on the proper functioning of the prefrontal cortex surrounding the principal sulcus of the brain, an area in which age-related lesions develop. Evaluation of the effects of clonidine, similar drugs, and drugs that oppose the functioning of various brain receptors showed that clonidine acted at the α_2-adrenergic receptors, perhaps facilitating transmission of neurosignals to the prefrontal cortex. These results link a specific cognitive process to a specific receptor. Clonidine has been reported to improve memory in one age-associated memory disorder, Korsakoff's syndrome; it may provide a new option for treating memory dysfunctions in Alzheimer's disease, a disease that so far has not been treated with drugs that act on adrenergic receptors.

Muscle mechanics

The tension that a muscle (cover) at rest exerts against being stretched, its passive tension, depends on the tension in its component fibers (page 1280). Passive tension had long been attributed to elastic forces in the connective tissues around and within a muscle rather than to forces in the fibers themselves. Magid and Law measured equal passive tensions in intact frog muscle and in mechanically skinned, single muscle fibers. Resistance to stretching can be accounted for by the passive tension in individual fibers, at least for stretch distances that occur during natural muscle movements. Over greater stretch lengths, forces in connective tissues may play more of a role in the resistance found in resting muscle.

Preleukemic chromosomal aberrations

Clues to what causes the preleukemic state, $5q^-$ syndrome, may be at hand (page 1282). This syndrome is most common in older women; some types of blood cells are depleted, others are increased in number, and acute leukemias eventually develop. The name $5q^-$ derives from the gene deletions in the q region of chromosome 5 that characterize the syndrome; similar chromosomal anomalies occur as well in acute myelogenous leukemia. Huebner *et al.* found that the gene encoding a growth factor—granulocyte-macrophage colony-stimulating factor (GM-CSF)—was situated in this same chromosomal region and thus was deleted or rearranged in affected individuals. A human leukemia cell line growing in culture was also found to carry one rearranged, partially deleted gene for GM-CSF. This factor is important in helping to maintain normal growth of just those blood cells affected in $5q^-$ syndrome. Chromosomal anomalies in $5q^-$ at the site of the GM-CSF gene may explain the aberrant growth of cells in $5q^-$ syndrome and even how the preleukemic state is initiated.

Ion regulation by kidney cells

The distribution of band 3 protein in the membranes of rat kidney cells (the intercalated cells) may clarify how distal tubules and collecting ducts of the kidney regulate the ionic balance of body fluids (page 1287). In red blood cells, band 3 is the anion channel protein; it spans the membrane and is linked with membrane-skeletal proteins (spectrin and ankyrin) in a fixed orientation. Drenckhahn *et al.* found, with immunostaining techniques, that kidney cells contain band 3 only at their basolateral surfaces. This restriction and localized concentration of band 3 may account for the observed polarity of ion reabsorption by the kidney. Earlier observations that the number of intercalated cells can increase by 200 percent in rats subjected to bicarbonate loading are in accord with a major role for these cells in ion regulation.

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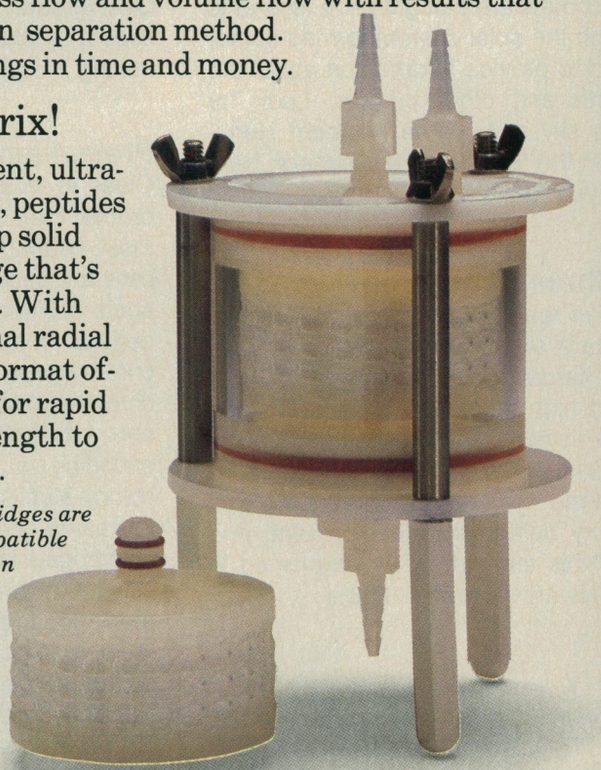

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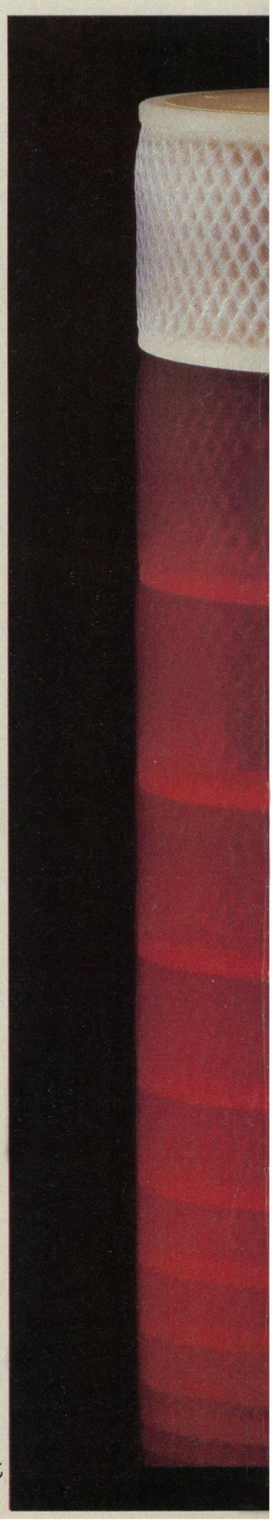

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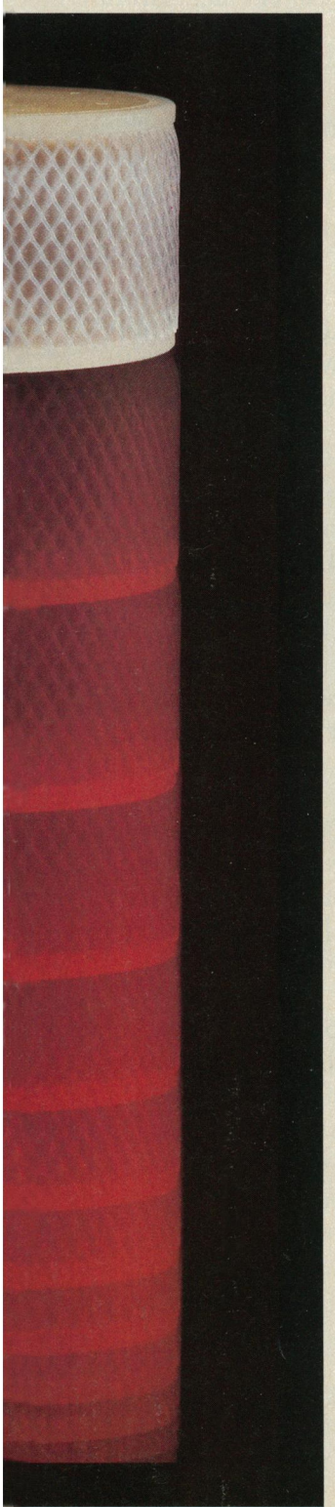

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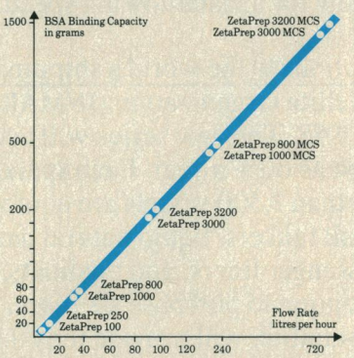

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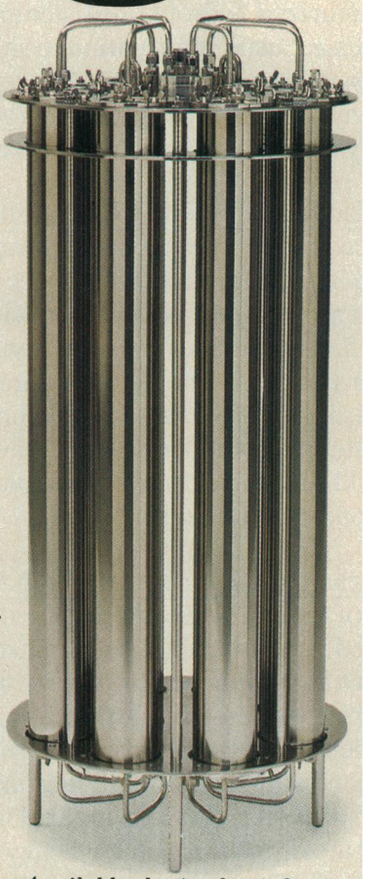

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Advanced satellites will provide communications to the world's shipping and offshore industries later this decade. The International Maritime Satellite Organization (INMARSAT), a group of 43 countries, plans to launch the first of the spacecraft in 1988. The new series will accommodate the increasing demand for services, which is growing as fast as 60% a year. Each spacecraft will be able to carry at least 125 simultaneous transmissions. More than 3,300 vessels are equipped to use the INMARSAT satellite system. Users include operators of oil tankers, liquid natural gas carriers, off-shore drilling rigs, seismic survey ships, fishing boats, passenger liners, and tug boats. British Aerospace will build three satellites, with INMARSAT having an option to purchase six more. Hughes, which in 1976 built the world's first maritime communications satellite, will provide the communications electronics for the second-generation spacecraft.

An Amraam missile bored through radar clutter to intercept a drone aircraft target in the second guided launch of the full-scale development program. The test firing was the third consecutive launch of the advanced medium-range air-to-air missile, under development by Hughes for the U.S. Air Force and Navy. An F-15 launched the missile in a "look-down, shoot-down" tail-aspect attack while flying at Mach 0.9 approximately 16,000 feet above the desert floor at White Sands Missile Range. The QF-100 target flew at Mach 0.7 only 1,000 feet above the ground. The Amraam flew the first part of its flight under control of its on-board inertial reference unit, using target coordinates provided in prelaunch by the F-15's Hughes APG-63 radar. The missile then switched to its own active radar for guidance and tracked the drone through the heavy ground clutter to intercept.

Controller-thrust aircraft engines will be tested at NASA's Lewis Research Center with three heat monitors. Three Probeye® thermal video systems will monitor, measure, and analyze heat from the engines while they are operated within the environmental test chamber at the research center. Each Probeye system consists of an infrared imager, image processor, and TV display, all of which interface with a computer. Hughes designed and produces the Probeye system.

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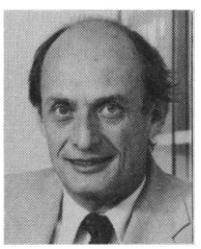
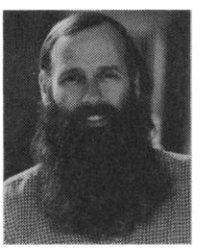
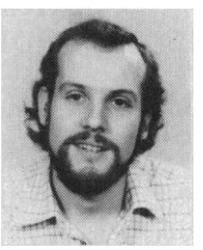


Paul Greengard
Neuronal Phosphoproteins and Their Physiological Significance



Tony Hunter
Protein Phosphorylation: A Connection Between Growth Control and Viral Transformation



Chris J. Kirk
Inositol Lipids and Cellular Signaling Mechanisms

Yasutomi Nishizuka
Phospholipid Turnover and Protein Phosphorylation in Stimulus-Response Coupling

CONVENER'S OF SESSIONS-IN-DEPTH

Susumu Tonegawa, "Growth and Differentiation of Immunologic/Hematopoetic Cells"

James Rheinwald and ***Elaine Fuchs,*** "Intermediate Filaments"
Speakers: ***James Rheinwald, Elaine Fuchs, Tung-Tien Sun, Victor E. Gould,*** and ***Michael Klymkowsky***

Ann Fallon, "Molecular Biology of Invertebrates"
Speakers: ***Ann Fallon, Russell Durbin, Virginia Walker, Edward Berger, Gregory Guild,*** and ***Henry Hagedorn***

Howard Rasmussen, "Calcium Metabolism and Cell Function"
Speakers: ***Howard Rasmussen, Joel Brown, James Putney,*** and ***Maurice Feinstein***

Donald Steiner and ***Howard Green,*** "Molecular Control of Cell Differentiation"
Speakers: ***Donald Steiner*** and ***Howard Green***

Daniel Acosta, "Mechanisms of Cell-Toxicant Interaction"
Speakers: ***Joe W. Grisham, Gary J. Smith, Benjamin Trump, Brooke T. Mossman,*** and ***Elsie M. B. Sorensen***

Bruce Freeman, "Oxygen Free Radicals: Aging, Cell Damage and Carcinogenesis"
Speakers: ***Bruce Freeman, Steve Weiss, A. Keith Tanswell,*** and ***Sigmund Weitzman***

George Martin, "The Mitotic Cell Cycle and Chromosomal Aberrations"
Speakers: ***George Martin, Doug Koshland, Adelaide T. C. Carpenter, Robert T. Schimke,*** and ***Ram Parshad***

Mina Bissell and ***Gerald Cunha,*** "Endocrine Sensitive Tissues: The Role of Cell-Cell and Cell-ECM Interactions in Regulation of Tissue-Specific Functions"
Speakers: ***Mina Bissell, Gerald Cunha,*** and ***Robert Isaacs***

Joanne Emerman and ***June Biedler,*** "Mechanisms of Drug Interaction and Resistance in Human Cells in Culture"
Speakers: ***Joanne Emerman, June Biedler, Robert Kerbel, Branimir Sikic,*** and ***Gregory Curt***

ROUNDTABLES

Interfacing Cytotoxicity and Genotoxicity in Cell Culture Systems
Cell Transformation Assays (State-of-the-Art)
Toxicity Investigations with Insect Cells
Cell and Organ Cultures Derived from Respiratory Tract
Hybridoma Technology
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CHAIRMAN: Gerald L. Hawk, PhD, Zymark Corporation

PROGRAM

MORNING SESSIONS – Thursday, January 30, 1986

The Role of People in High Technology Automation: R.G. Miller, Ortho Pharmaceutical Canada, Ontario, Canada.

Development and Evolution of Perfusion Culture Systems and Static Maintenance Systems for Large Scale Production of Mammalian Cell Derived Products: W. Tolbert and C.V. Benton, Invitron, Clayton, MO.

Multiple Approaches to Protein Purification Using Solid Phase Interaction on Silica Based Bonded Phases: L.J. Crane, J.T. Baker Company, Phillipsburg, NJ.

POSTER SESSIONS – EXHIBITS

Synthetic DNA: Application of Robotics to the Purification of Oligonucleotides: S.S. Jones, J.E. Brown, D. Stone and E.L. Brown, Genetics Institute, Cambridge, MA.

Preparative High Performance Liquid Chromatography of Proteins: L. Beadling, C. Mason and G. Sofer. Pharmacia, Inc., Piscataway, NJ.

Ultrafiltration Processes for the Purification of the Enzyme Alkaline Phosphatase: C.S. Slater, H.C. Hollein, T.G. Hugguns, Jr., and C.A. Brooks III, Manhattan College, Riverdale, NY.

AFTERNOON SESSIONS – Thursday, January 30, 1986

Cell Culture on Porous Microcarrier Particles: A.F. Steuer and F. Cahn, Biotech Research Laboratories, Inc., Rockville, MD. I.V. Yannas, Massachusetts Institute of Technology, Cambridge, MA.

L-Asparaginase from "Erwinia Cartovara": An Improved Recovery and Purification Process Using Affinity Chromatography: S. Lee, M.H. Wroble, J.T. Ross, G.M. Muschik and W.B. Lebherz III, National Cancer Institute – Frederick Cancer Research Facility, Frederick, MD.

Proteolytic Enzyme Removal by Zeta-Affinity Cartridge: K.C. Hou, AMF Specialty materials group, Meriden, CT.

Optimal Control of Temperature and Enzyme Feed Rate in Simultaneous Batch Saccharification and Fermentation: J.L. Spencer, W.H. Sun and J.A. Assenjo, Columbia University, New York, NY.

MORNING SESSIONS – Friday, January 31, 1986

Factors Influencing Monoclonal Antibody Production in Mouse Ascites Fluid: J.P. Chandler, Charles River Biotechnical Services, Inc., Wilmington, MA.

Study of High Immunoglobulin Productivity in Immobilized Hybridoma Cultures: N.G. Ray, Verax Corporation, Hanover, NH.

Hybridoma Data Bank: A New Resource: L. Blaine, American Type Culture Collection, Rockville, MD.

Buying and Selling Biotechnology Equipment, Supplies and Chemicals: W.J. Carik, The Salk Institute, San Diego, CA.

Optimization Strategies for Increasing Production of Monoclonal Antibodies in Hollow-Fiber Bioreactors: M. Tyo and M. Gruenberg, Endotronics, Inc., Coon Rapids, MN.

Production and Concentration of Monoclonal Antibodies Using the Opticell™ Culture System: J.E. Putnam, G.G. Pugh and L.A. Noll, KC Biological, Lenexa, KS.

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justify. No such large planetary probes are known to us to be on the drawing boards, and operations such as fueling could be accomplished by rendezvous at the most desirable altitude for the mission rather than at a fixed altitude for all missions. The suggestion of an inspection in orbit ignores the fact that engineers have developed a successful program of testing and inspection on the ground. It is not clear why a space crew would be instructed to open a carefully prepared spacecraft for inspection.

In summary, the *scientific* justifications for a manned space station are manifestly inadequate. There may be other justifications, such as a first step of a manned mission to Mars or desire to show the world that we can operate a manned space station, but those reasons should not be confused with scientific reasons. I agree with T. M. Donahue, chairman of the Space Science Board, who wrote: "We have not been able yet to identify missions that would be enabled by the space station, except possibly in the field of space medicine" (*1*).

When one considers the obvious economic necessity of maintaining careful control of the federal budget, it is clear that the need for a space station should be most thoroughly investigated before such a program is authorized and funds for its planning are appropriated.

GEORGE WALLERSTEIN
Department of Astronomy, University of Washington, Seattle 98195

References

1. T. M. Donahue, paper presented at the AIAA/NASA Symposium on the Space Station, Arlington, Va., 18 to 20 July 1983.

In his thoughtful letter, Wallerstein stresses what appear to be some of the constraints associated with astrophysical observatories on platforms that co-orbit with the space station along with several other questions about the station. In my view, he underestimates the scientific impact of the "great observatories"—the Hubble Space Telescope, the Gamma-Ray Observatory (GRO), the Advanced X-Ray Astrophysical Facility (AXAF), and the Space Infrared Telescope Facility (SIRTF)—and the necessity to maintain these over a period of 10 to 15 years. Detailed studies concerning AXAF and SIRTF have shown that these missions are compatible with orbits that can be serviced from the space station. The Space Telescope and the GRO will also be accessible from the station. In our view the more complex servicing of these missions will extend significantly beyond what could be supported from the space shuttle. The Orbital Maneuvering Vehicle is planned as part of the station's initial operating capability and will provide the means for bringing the spacecraft to the station.

The position of the Space Science Board was somewhat different from what is implied in Wallerstein's statement. The Board's view can be summarized as follows: A space station is not needed to carry out the NASA science missions planned for the immediate future. "In the longer term, the Space Science Board sees the possibility that a suitably designed Space Station could serve as a very useful facility in support of future space science activities" (*1*).

Over the last 18 months, the scientific community has participated extensively in helping to define the Space Station's capabilities. In particular, the Task Force on Scientific Uses of the Space Station, under the chairmanship of Peter M. Banks at Stanford University, has had a significant impact. The task force has concluded that the space station can be of great value to the advancement of space research. Many other smaller-scale studies and working groups are also providing scientific support and guidance.

Frost and I tried to stress the point that our present limits on putting experiments in space are both technological and managerial in nature. The space station is an opportunity to move those limits with creativity and imagination. In the future we hope to get samples from Mars, Venus, and comets; fly large astronomical interferometers and gravity wave detectors; study collective phenomena in various forms; and do experiments in life sciences in particular, on cardiovascular problems and on calcium loss from bones, and, in general, on understanding the role that gravity played in shaping life on Earth. The space station as a laboratory, as a place for assembly and integration of new experiments and spacecraft, and as a center for maintenance and refurbishment provides us with a new capability that can be of invaluable service to science. It is important that we in the space science community make sure that this potential is realized.

FRANK B. MCDONALD
National Aeronautics and Space Administration, Washington, D.C. 20546

References

1. *Space Science Board Assessment of the Scientific Value of a Space Station* (National Research Council, Washington, D.C., 9 September 1983).

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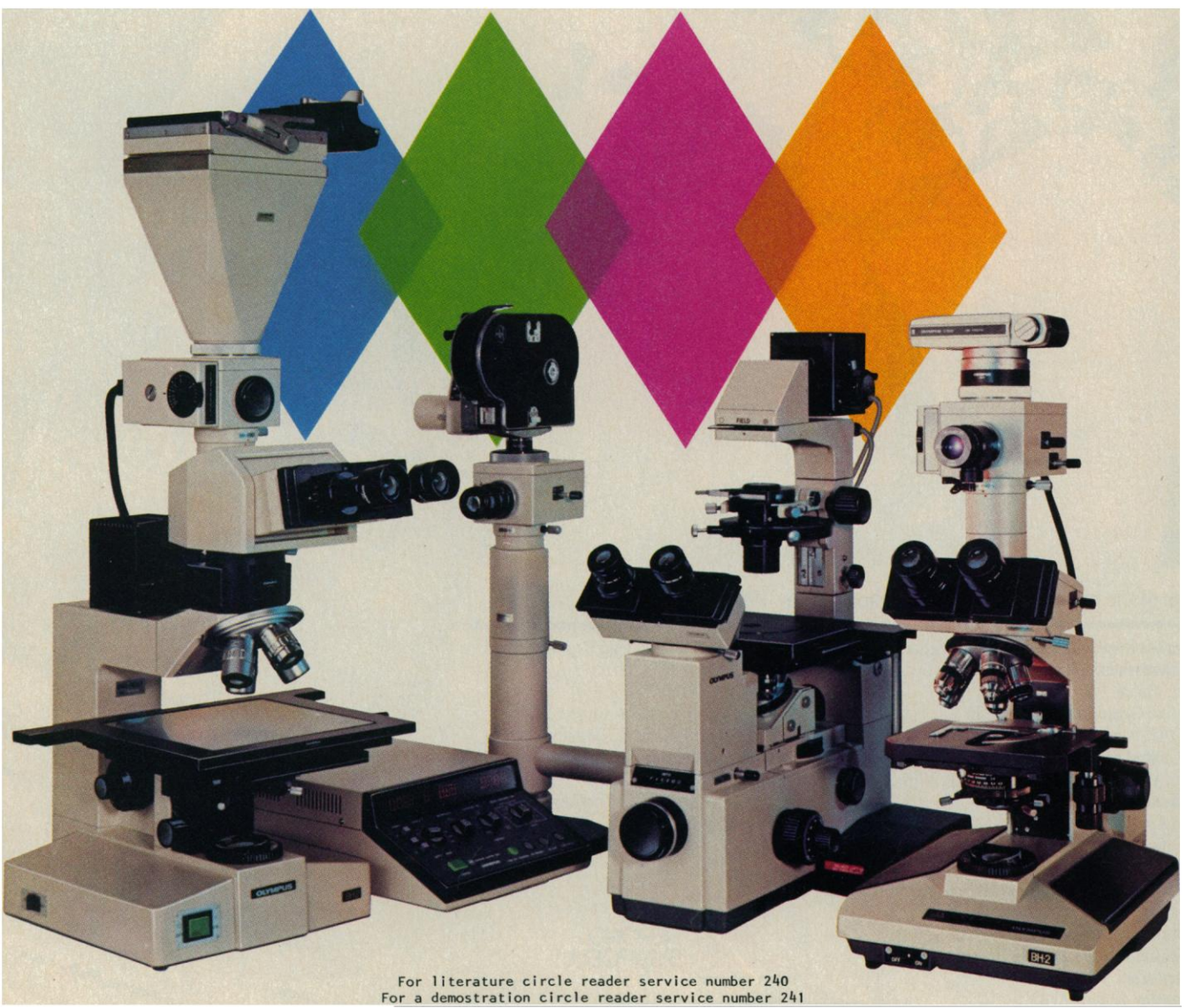

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13 December 1985, Volume 230, Number 4731 SCIENCE

Time to Revive Systematics

Systematics, the study of biological diversity, is sometimes portrayed as the mere classification of organisms, but in fact its range and challenge are among the greatest in biology. At the present time we do not even know, to the nearest order of magnitude, how many species there are in the world. Approximately 1.7 million have been described since Linnaeus, including about 250,000 flowering plants, 47,000 vertebrates, and according to one meticulous estimate published earlier this year, 751,012 insects. But these numbers are far below the actual diversity. Recent studies in rain forests and other major habitats indicate the presence of as many as 30 million kinds of insects alone.

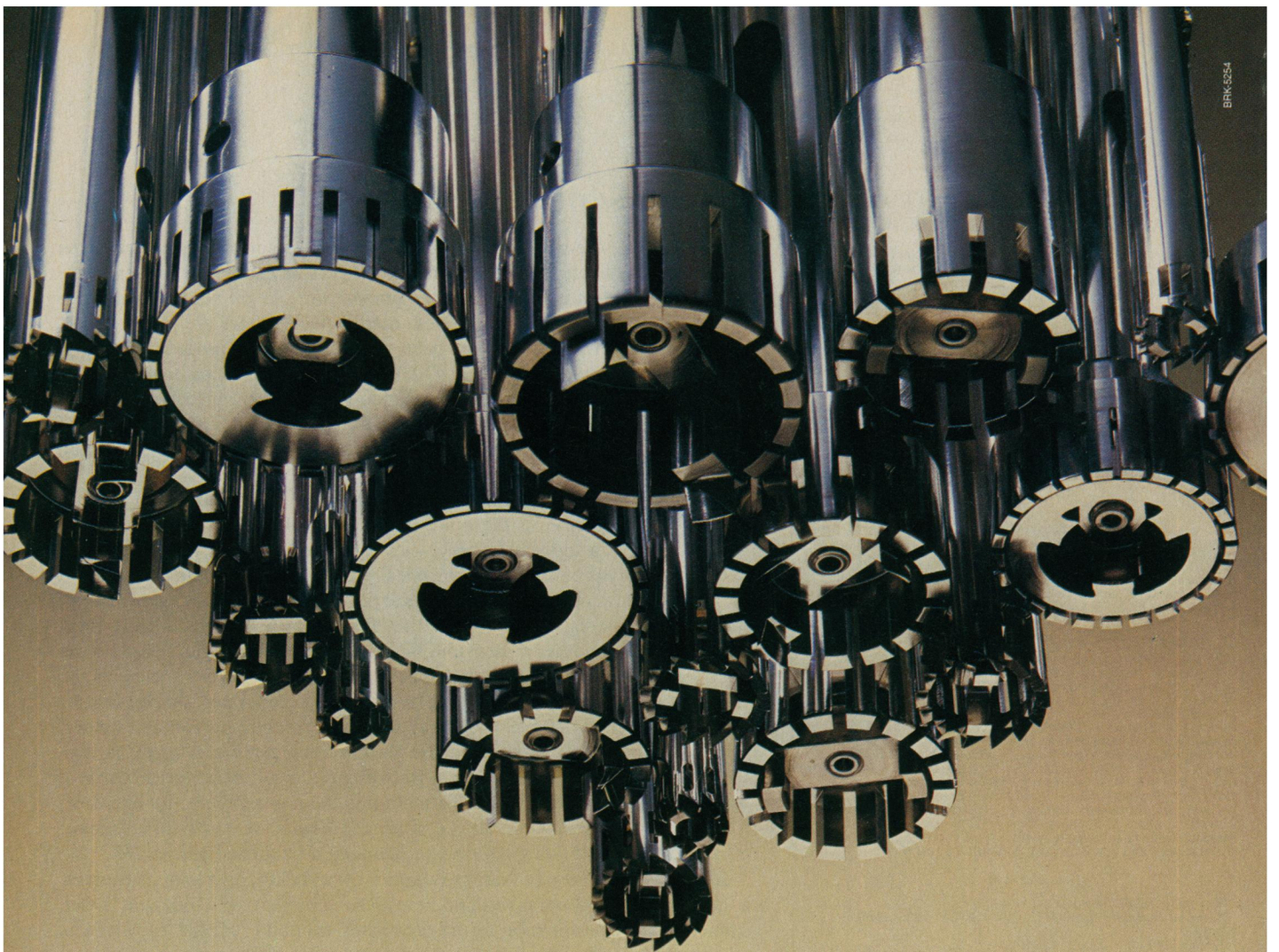
The magnitude of biological diversity has many ramifications of general interest. For example, if there are really 30 or 40 million animal species, why didn't just a thousand evolve—or a billion? It is not known to what extent diversity is controlled by physical properties of the planet as opposed to the mechanics of evolution itself. Nor do we know to what degree species numbers can be raised or lowered artificially without destabilizing local ecosystems. In another dimension, biologists have only begun to assess the complexity and potential of each species individually. Every species is the terminus of an ancient lineage that has been hammered and shaped into its present form by a complex interplay of genetic recombination and natural selection. In a purely technical sense the resulting genome is richer in content than a Caravaggio painting, a Bach fugue, or any other great work of art. The billion bits of genetic information in the house mouse, for example, if transformed into an equivalence of printed English text, would just about fill all editions of the *Encyclopaedia Britannica* published since 1768.

Because of the largely unknown nature of diversity, systematics remains a fountainhead of discoveries and new ideas in biology. If a biologist is well trained in the classification of the organisms encountered, the known facts of natural history are an open book, and new phenomena come more quickly into focus. The irony of the situation is that successful research then gets labeled as ecology, physiology, or almost anything else but its true source, the study of diversity.

Much of the research also has economic and medical importance. The discovery of new sources of biomass energy, lumber, pharmaceuticals, and pollination complexes depend ultimately on taxonomic exploration. Also, the design of natural reserves, critical to the preservation of diversity in tropical countries, cannot be performed reliably without a thorough knowledge of local faunas and floras. The problem is intensified by the accelerating destruction of natural habitats and extinction of species.

At present the community of systematists is sadly inadequate to the immense task before it. In North America about 4000 specialists, most part-time, work on 3900 collections. Probably no more than 1500 trained professional systematists in the world are competent to deal with tropical organisms. To cite one striking example, there are exactly two such persons qualified to deal with termites, which are among the principal insect pests and soil movers of the world. In fiscal 1985, the National Museum of Natural History, our largest institution of basic research, spent $12.8 million to support the activities of 85 scientists engaged partly or wholly in systematics. The Program in Systematic Biology of the National Science Foundation, the principal funder of independent projects, granted $12 million. Other programs in the NSF and Department of Interior provided $13.8 million for support of museum services and other activities related to systematics. At this level, which reflects a low priority worldwide, less than 1 percent of the species of organisms are under active investigation.

Systematics deserves more cultivation and the attention of our brightest minds. It is in a position to yield increasing returns to scale, with a variety of benefits for both science and society.—EDWARD O. WILSON, *Museum of Comparative Zoology, Harvard University, Cambridge, Massachusetts 02138*



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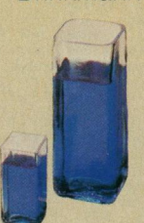

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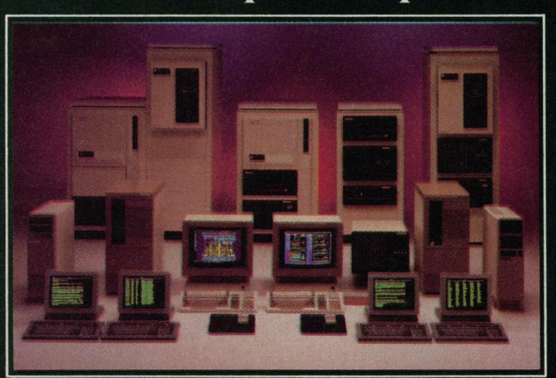

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