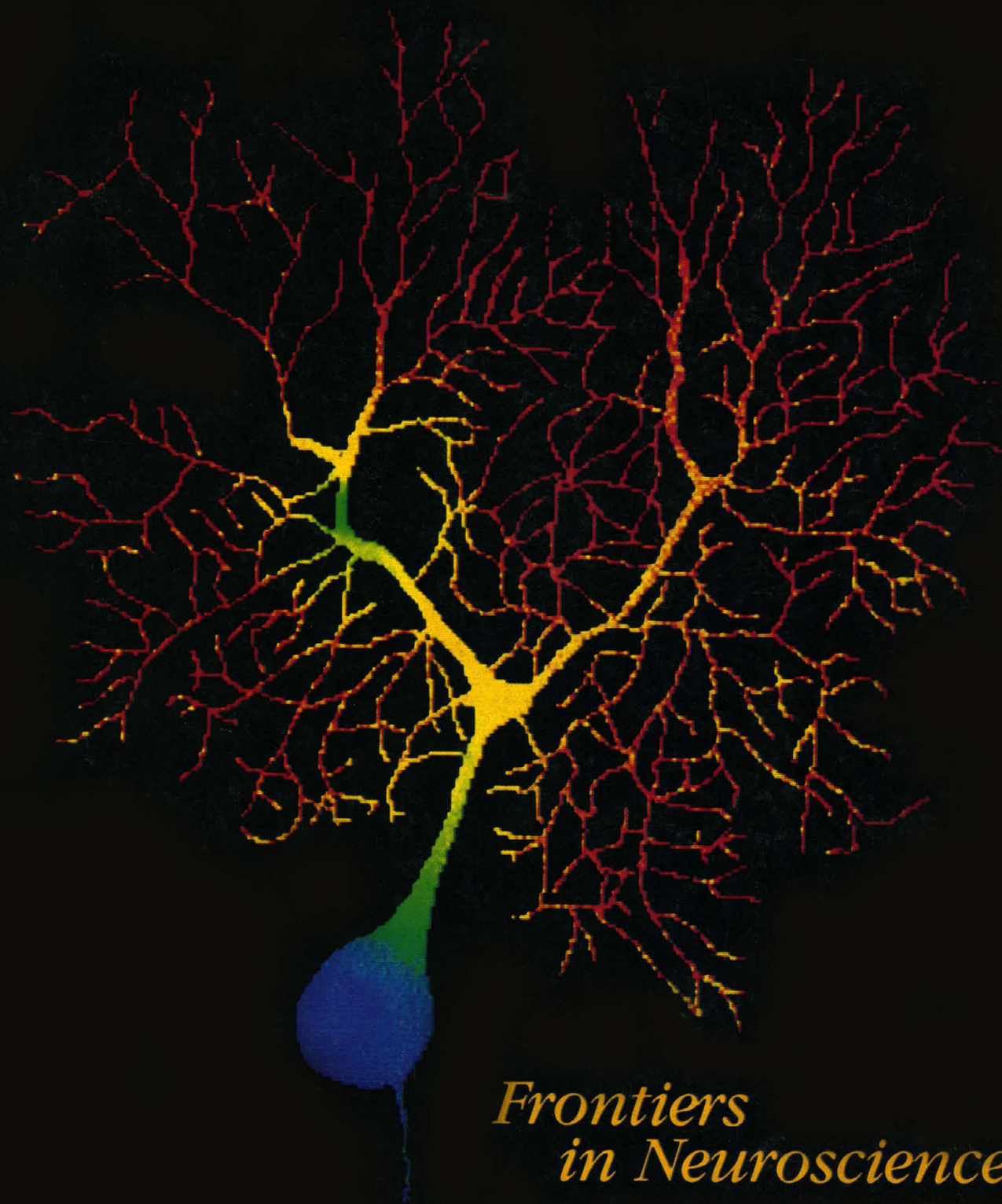


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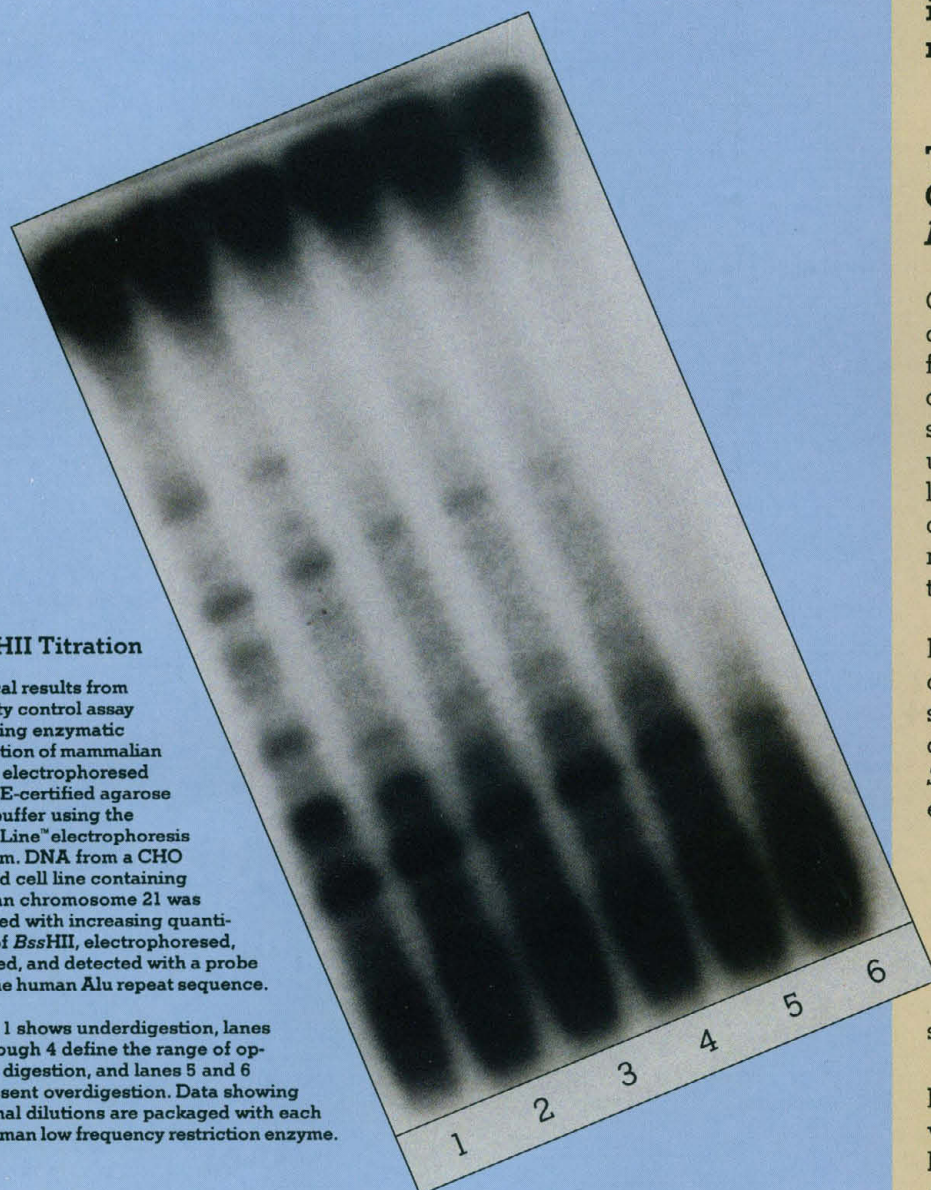
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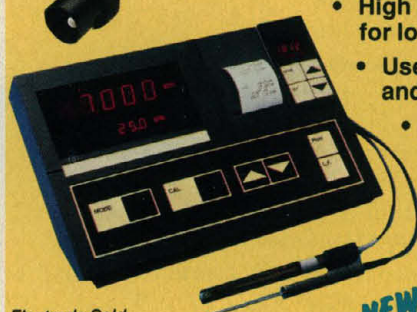
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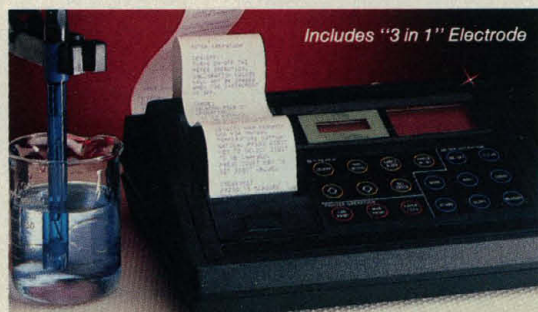
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COVER False color map of intracellular calcium concentration in a guinea pig cerebellar Purkinje cell at the onset of a wave of complex spike activity. A high calcium concentration is observed in the distal dendritic tree. The map was produced from microfluorometric imaging of the fluorescent calcium indicator fura-2. See page 773. [D. W. Tank and J. A. Connor, Molecular Biophysics Research Department, AT&T Bell Laboratories, Murray Hill, NJ 07974; M. Sugimori and R. R. Llinás, Department of Physiology and Biophysics, New York University School of Medicine, New York, NY 10016]

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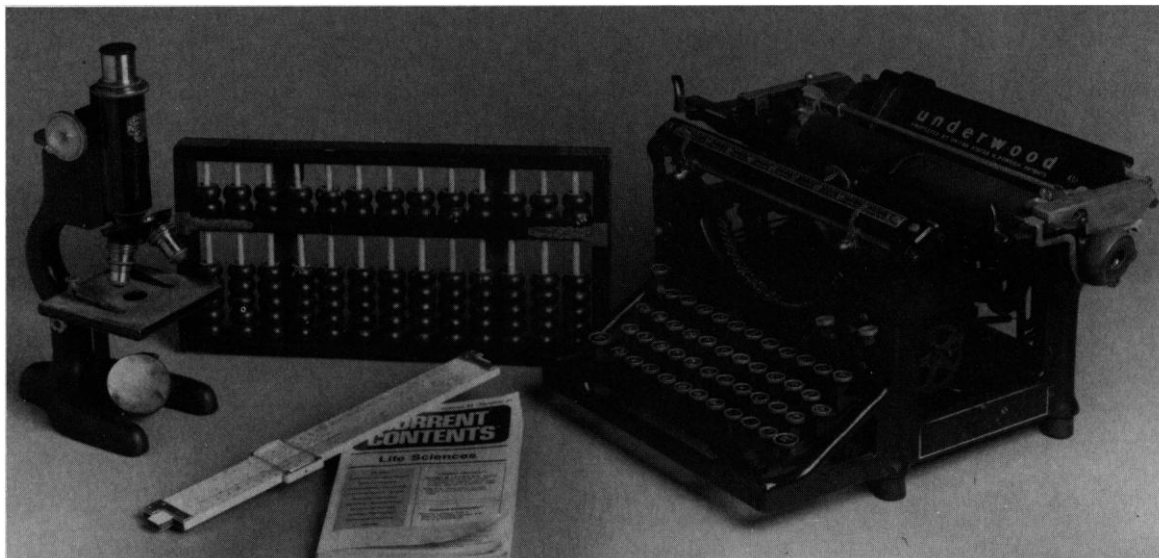
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This Week in SCIENCE

Mountain building thermodynamics

THE thermodynamic efficiency of brittle frictional mountain building on Taiwan is about three or four times less than that of a nuclear power plant (page 749). This comparison, made by Barr and Dahlen, is based on energy balance equations that describe what fraction of the mechanical and heat energy supplied from external sources is expended in the performance of useful work—the uplift of rocks against gravity—so that the mountain topography is maintained despite erosion. Taiwan was chosen as a prototype for calculating mountain building thermodynamic efficiency because the geometry of the region of deformation is well known and there is abundant geophysical data on heat flow, pore fluid pressure, and plate velocities; the island is situated where the Eurasian and Philippine Sea plates collide. Most of the mechanical energy that drives deformation and mountain uplift comes from the sinking Eurasian slab, although minor contributions are made by heat from the heat of accreting rocks and from radioactive decay; much of this energy is lost out of the boundaries as heat. This and other fold-and-thrust belts provide insights into thermal convection processes in the earth's interior.

Gene abnormalities in muscular dystrophies

MUTATIONS in the X chromosome gene BMD/DMD produce muscular dystrophies that range from the mildest forms (Becker) to the most severe (Duchenne). The classification for any patient reflects the rapidity with which muscle deterioration proceeds and the age at which he—usually males are affected—becomes wheelchair-bound. Over 50% of all muscular dystrophy patients have deletions in BMD/DMD, and characteristics of such deletions have now been studied. Boundaries of the first ten exons (the nucleic acid segments that get translated) on BMD/DMD with intervening nontranslated

sequences (introns) were determined (page 755). Deletions occurred in exons 3 to 7 in patients diagnosed with mild, intermediate, and severe Becker; thus, a simple correspondence of disease severity with the size or location of the deletion was not found. Malhotra *et al.* therefore propose that what may distinguish those patients with mild clinical profiles from those with severe disease may be the ability of their cellular machinery to restore translation with a “start” signal downstream from the deletion so that a partially functional dystrophin protein can be produced from BMD/DMD and disease will be mild.

Fetal tissue transplants

IT might be possible, through the transplantation of fetal neural tissues, to restore neurologic function to people who have neurodegenerative disorders such as Parkinson's disease; in monkeys, signs of parkinsonism have been reversed with neural tissue transplants. However, for such transplants to be safe, it is necessary to characterize the tissues—to type them, assess their viability, and evaluate them for contaminating microorganisms—and, while these procedures are being carried out, the tissues must be stored. Redmond *et al.* report that neural tissue fragments from human fetuses can be preserved in liquid nitrogen for many weeks; the tissues survived freezing and thawing and transplantation into the brains of immunosuppressed monkeys (page 768). At 10 weeks post grafting, good growth of neural cells with dopamine receptors was observed in the recipient animals. These banking and testing procedures will be assets to both clinical and basic research.

Purkinje cell studies

EVIDENCE of the electric activity of Purkinje cells, the large branching nerve cells in the brain, can be seen in dramatic fluorescent microscopic images (cover). Calcium ions flow into neurons through channels in conjunction with spontane-

ous and evoked electric activities; the locations of ion influxes were mapped in single cells by Tank *et al.* with the fluorescent indicator fura-2 (page 773). At the beginning of excitation, intracellular calcium was associated with the more distal (tertiary) branches of the dendritic tree; later, secondary and primary regions of the tree that are close to the cell body filled with calcium. The imaging results are in accord with electrophysiological studies and strengthen the notion that electric conductance in neurons is fine tuned in time and space by calcium ions.

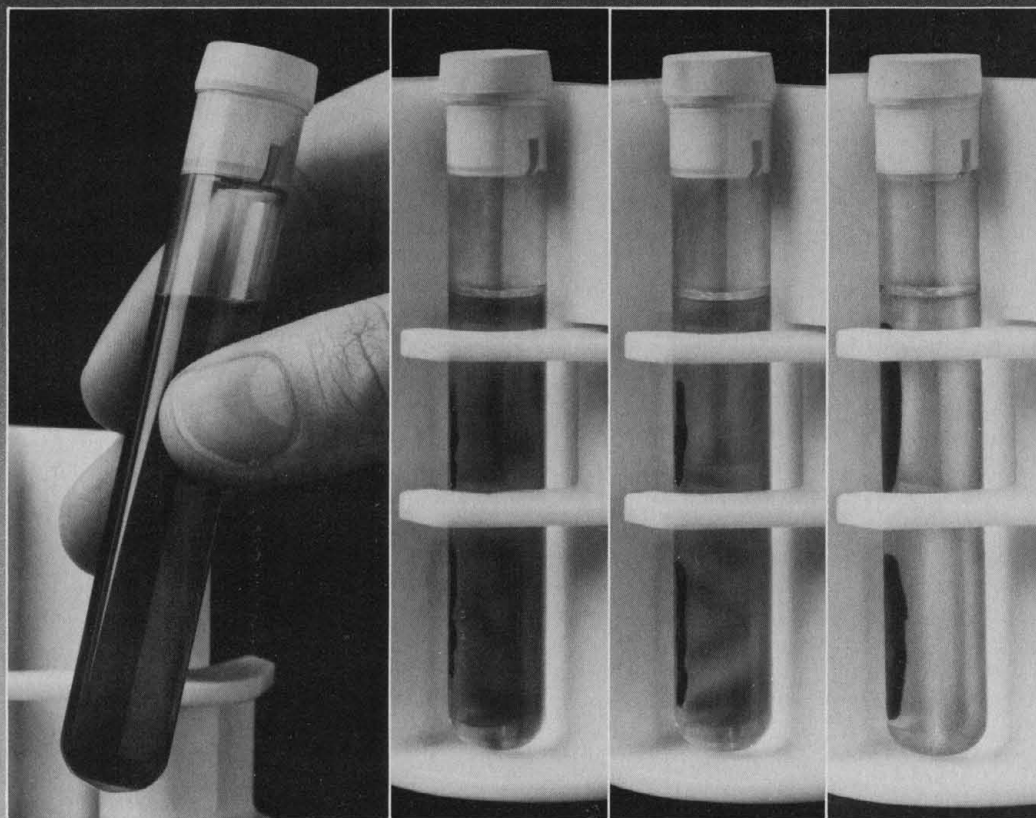
Lens development

THE normal lens is a transparent refractile optical element that lacks blood vessels and nerves and is rich in protein. Lens development in the body proceeds in an uneven (oscillatory) rather than steady fashion. Brewitt and Clark have developed an organ culture system in which the effects of various growth factors on lens growth and development can be assessed (page 777). The lenses of 3-day-old rats developed normally in culture when they were exposed to pulses of platelet-derived growth factor (PDGF); this factor, which has been observed as a component of the aqueous humor that normally bathes the lens in vivo, stimulated growth and increased the soluble protein content of the lens. When lens tissue was continuously exposed to PDGF or exposed only to culture medium, cataracts formed, soluble proteins were lost, and lenses stopped growing; similar changes accompany in vivo cataract development.

Neuroscience

The lead articles and a number of the reports in this issue address the structure, development, activities, and relations of the brain and other tissues of nervous systems (pages 641, 692 to 745, 762, 768, 771, and 773).

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Frontiers in Neuroscience

The human brain contains about 10^{12} neurons, many of which have more than 10,000 connections with other neurons. This incredibly sophisticated supercomputer presents an enormous intellectual challenge. Elucidating its function will be of great importance to the understanding of human behavior and the support of mental health. In this issue, assembled with the expertise of Katrina Kelner, eight articles cover selected aspects of modern neurobiology and illustrate the power of new concepts and new experimental tools.

Memory is of course one of the most intriguing areas of study in the brain, and describing the physiological changes in neurons that generate long-term memory is a first step in understanding all subsequent learning processes. Major developments in this area are discussed by Brown and co-workers, who have used the technique of long-term potentiation, that is, a long-lasting change in a neuron as a result of repetitive stimulation. Indications of Hebbian feedback behavior in these stimulated neurons combine modern molecular biology with classical postulates of psychology.

Learning also involves complex motor patterns such as hitting a baseball moving at 150 kilometers per hour. This action requires the training of motor skills so that a rudimentary native ability is converted to a more precise learned ability, as described by Lisberger. Moreover, as discussed by Wise and Desimone, correlation of movements with visual stimuli requires groups of neurons that can select objects and also constantly adjust to the fact that limbs grow, muscle mass changes, and visual experience accumulates.

How neurons make connections to develop the complex wiring diagram of the brain is discussed in three papers. To the dismay of some who may like to think that humans are appreciably more worthy than insects, the development of neuronal interconnections in a grasshopper is not so different from that of so-called higher species. It appears that neurons making distant connections follow predetermined pathways by groping along structural elements that contain molecular signposts in the form of proteins on the surface of cells. They also may use chemical gradients that attract or repel the advancing tip of the neuron, the growth cone. Moreover, these extensions have feedback mechanisms that allow them to withdraw from incorrect surfaces and fasten tightly to the correct ones. Dodd and Jessell focus on vertebrate glycoproteins that provide a guidance system in nonspecific parts of the developing neuron and discuss axon guidance by contact inhibition. Harrelson and Goodman discuss the same subject with emphasis on fasciculation in invertebrates, particularly as mediated by fasciclin II, a member of the immunoglobulin superfamily. These immunoglobulin-like molecules are structurally homologous to guidance molecules in the vertebrate neural system. Finally, Smith discusses the mechanics of cell motility during neuron development and identifies actin polymerization as the force behind the protrusion of the growth cone while the actin-myosin system, fueled by adenosine triphosphate, appears to drive growth cone retraction.

Koob and Bloom discuss the currently prominent issue of drug dependence from the molecular point of view. The drug problem will not be solved solely by elucidating the biochemical mechanisms, but understanding the molecular basis of tolerance and withdrawal will help. Such findings may also help explain why people become addicted to drugs and lead to the development of better procedures for detoxification.

Churchland and Sejnowski consider some aspects of theoretical computer programs that show computation patterns analogous to those of the brain. Some experimenters regard such theoretical programming as too esoteric to be of much practical use in understanding brain function. Nevertheless, there are principles applied in algorithms that are functionally similar to mechanisms in the human brain. In fact, insight into new types of information processing is leading to an entire industry in which the simulation of neuronal activity in an algorithm is being used to attract venture capital. The brain is becoming big business, as well as a big intellectual challenge.

Sometimes intellectual challenges are fascinating but of debatable value such as the design of new weapons or the breaking of secret codes. Understanding the brain is a monumental puzzle, the solution of which can provide great humanitarian advances. This issue presents some beginnings at unraveling that Gordian knot.

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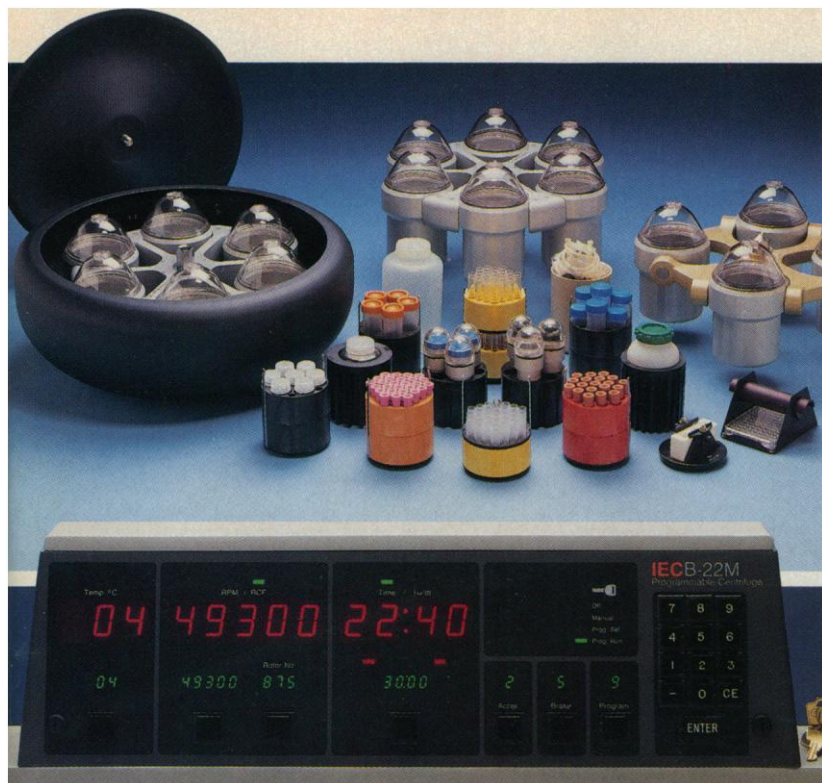
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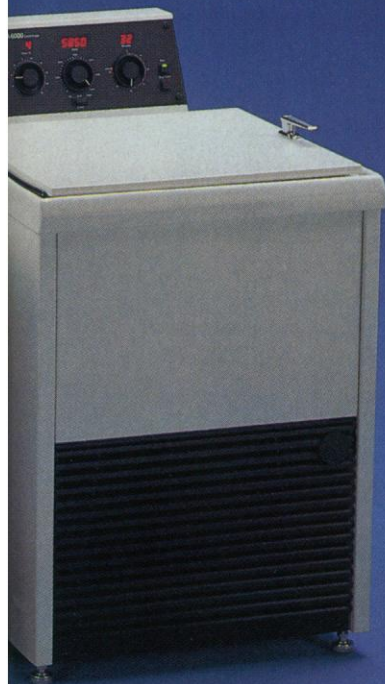
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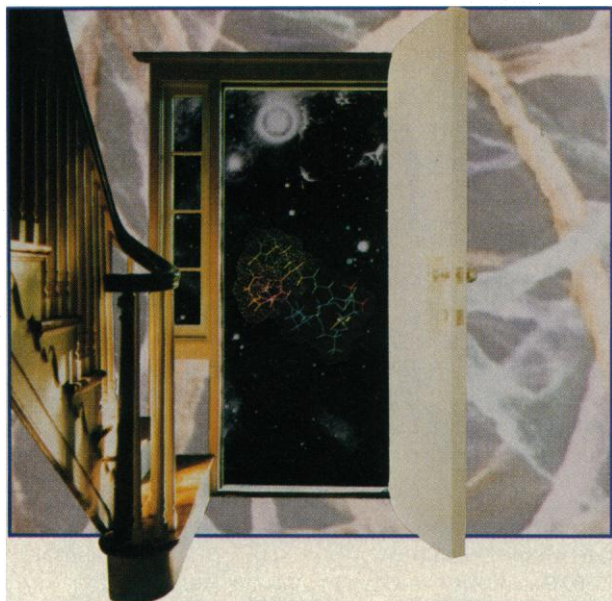
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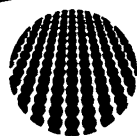
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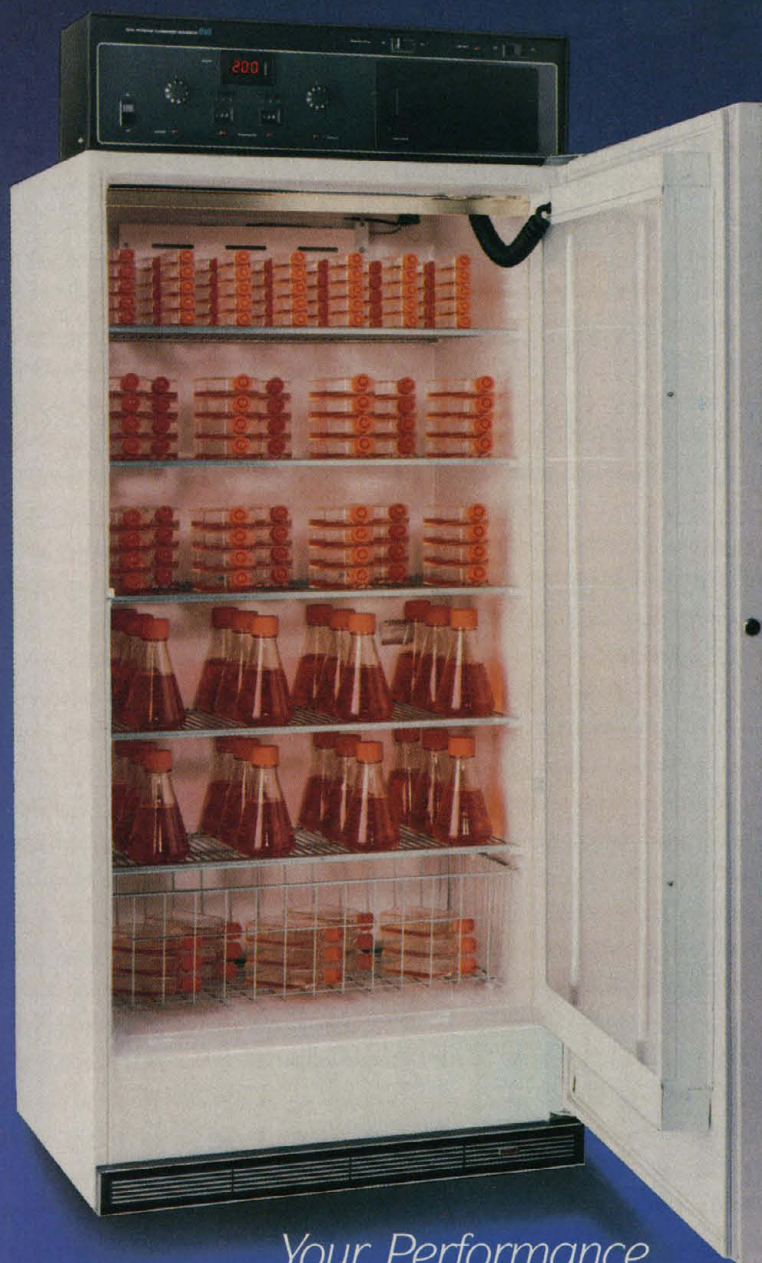
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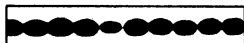
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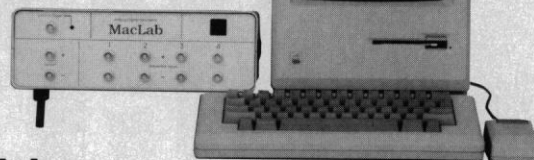
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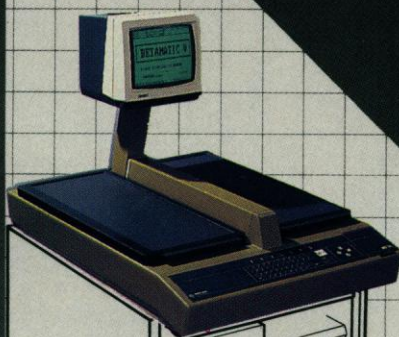
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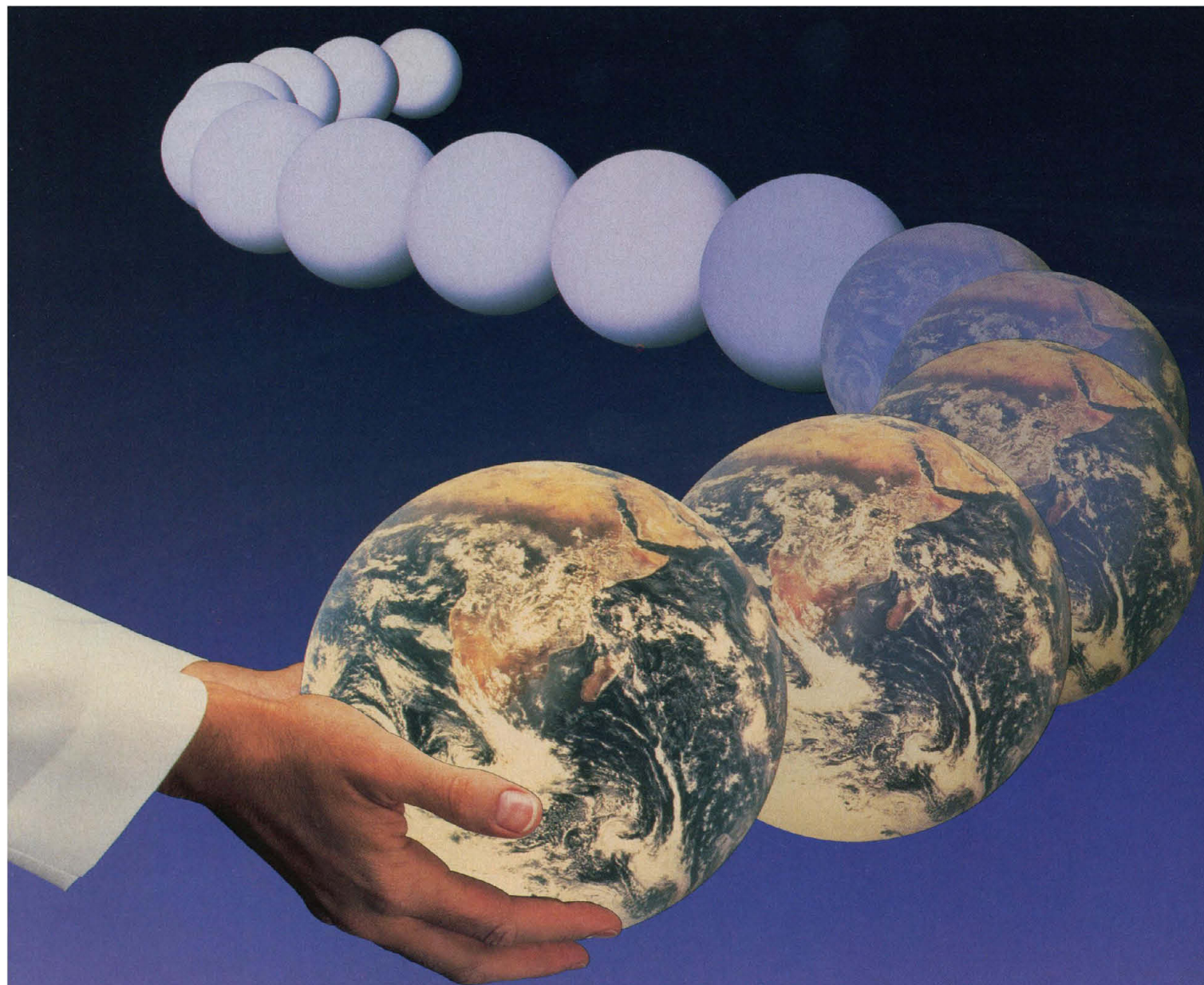
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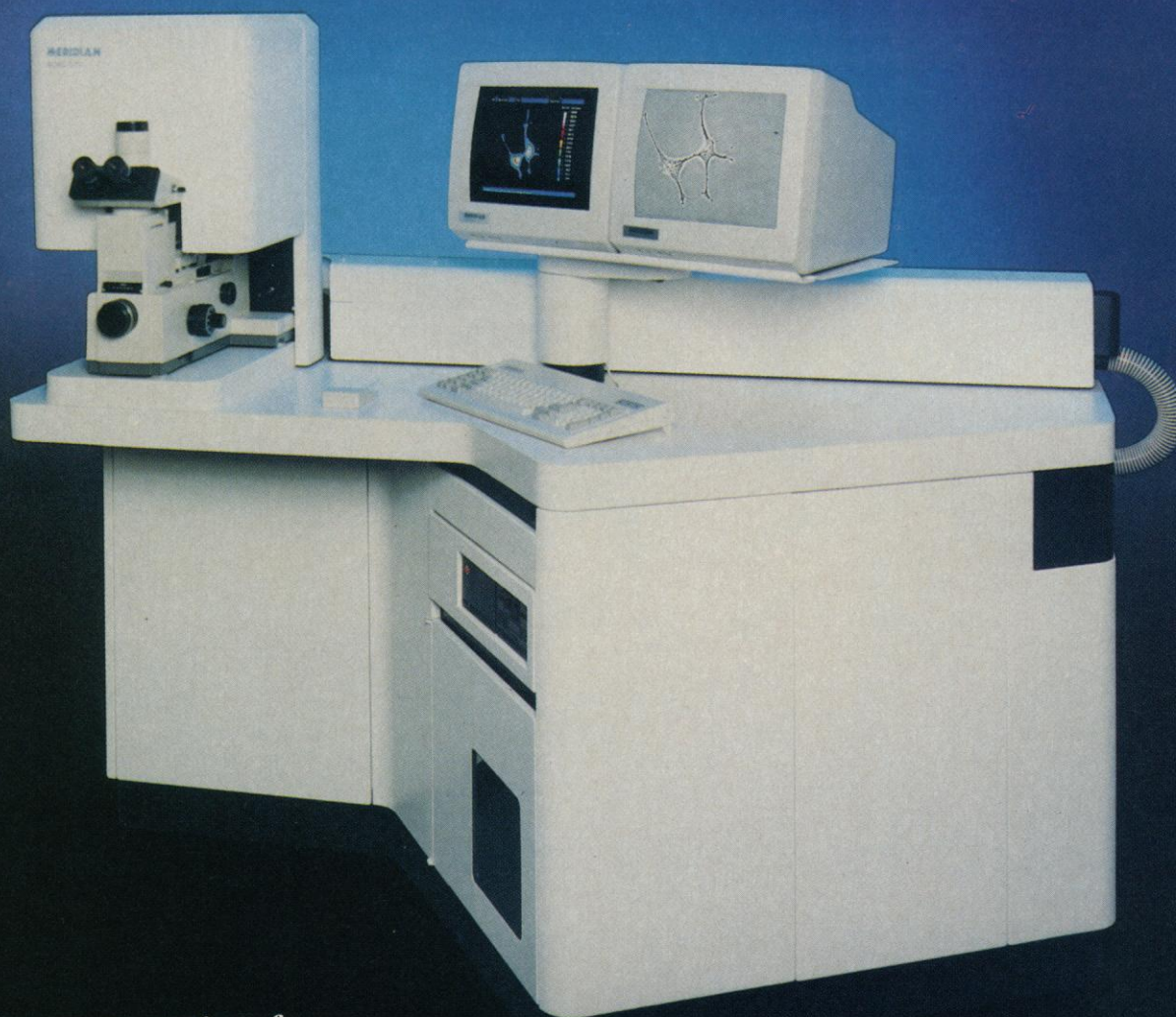


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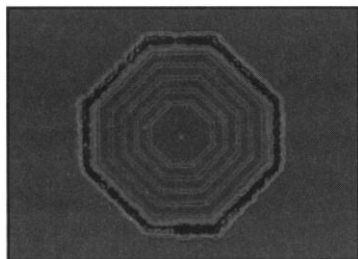
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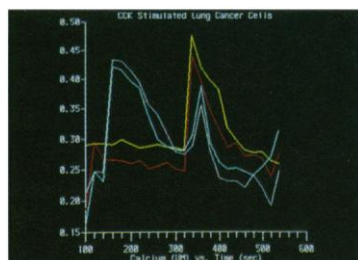
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When you want to make quantitative fluorescence measurements you need the ACAS 570 Interactive Laser Cytometer.

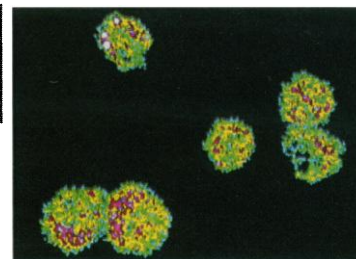


Cholecystokinin induced increase in intracellular calcium levels in human small cell lung cancer cells. Only 2 cells responded to cholecystokinin, whereas all 4 cells responded to carbachol as evidenced by the later peaks. (Courtesy of Dr. Ronald Barrett, Abbott Laboratories.)

Reason #3 Sensitive Fluorescence Measurements

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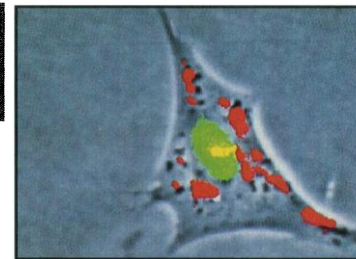


Detection of 30-60 copies of ABL mRNA by in situ hybridization in the leukemia cell line, K562. (Courtesy of Dr. Joel Bresser, M.D. Anderson Hospital.)

Reason #4 Versatile Integrated Instrumentation

From cloning cells, to fluorescence imaging, and measuring rapid calcium fluxes, the ACAS Interactive Laser Cytometer is the only instrument that provides you with such a broad range of cell and molecular biology applications. The model 570 with advanced computer and detection systems offers you even more power and versatility with new options such as confocal fluorescence imaging and video processing.

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Overlay of phase contrast and two fluorescence images of a 3T3 cell labeled with acridine orange (Green: nucleus; Red: lysosomes). (Courtesy of Dr. Margaret Wade, Meridian Instruments.)

Reason #5 Exceptional Technical Support

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Nucleotide sequence of
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Autoradiograph showing the products of sequencing MI3mp7 with the TaqTrack™ Sequencing System. The figures show the sequence of the multiple cloning site region, which contains a GC-rich, perfectly inverted repeat of 24 base pairs. A reaction temperature of 70°C simplifies polymerization through highly structured templates. The DNA polymerase isolated from *Thermus aquaticus* exhibits a consistent band intensity and a high degree of accuracy when used for sequencing. This thermostable enzyme lacks intrinsic exonuclease activity, which results in a low gel background. In addition, the analogue 7-deaza dGTP can be used to resolve gel artifacts associated with GC-rich regions, as shown.



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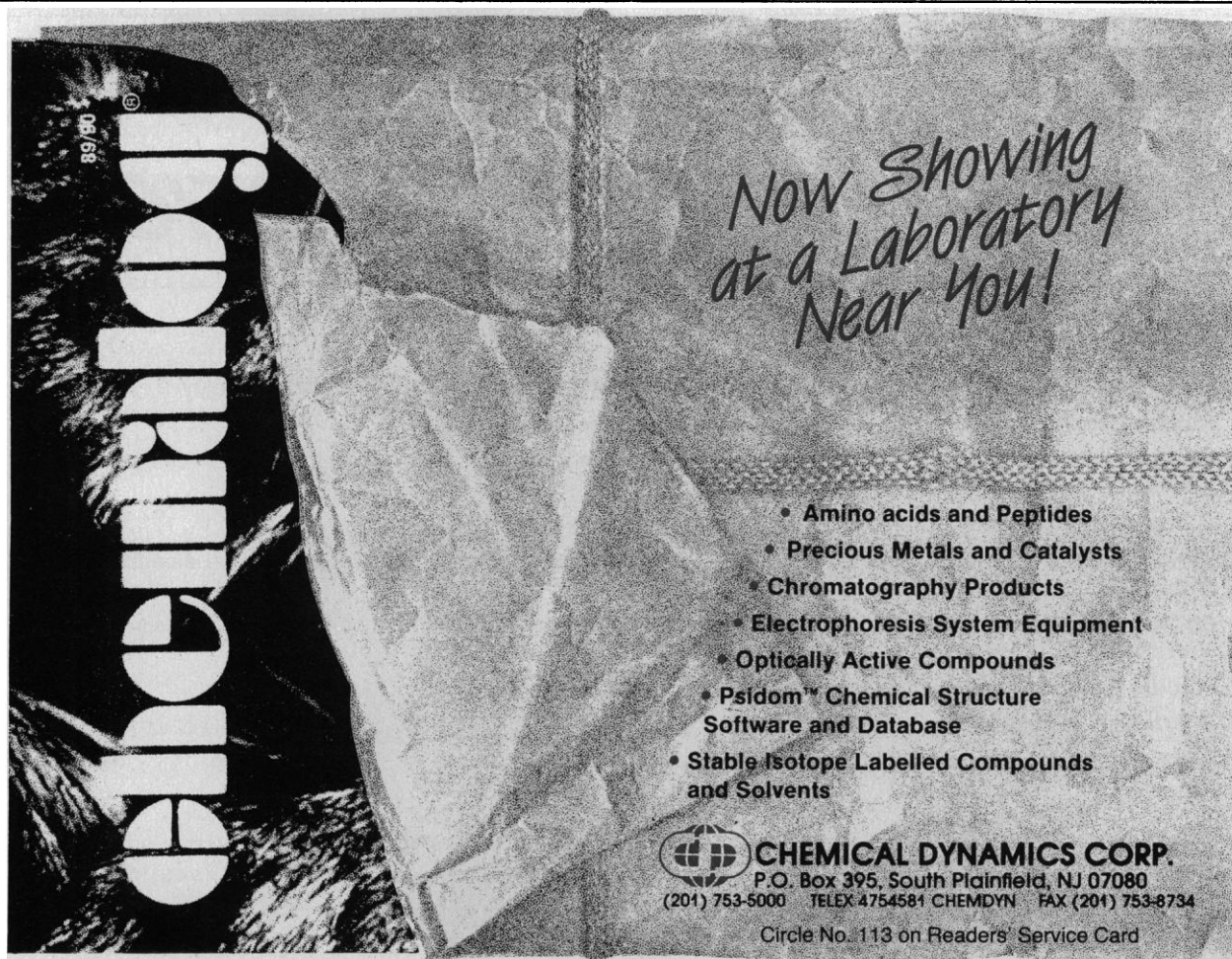
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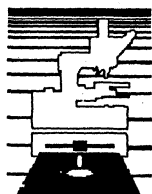
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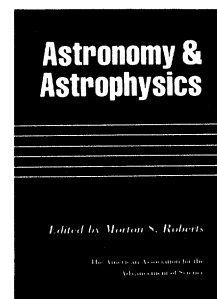
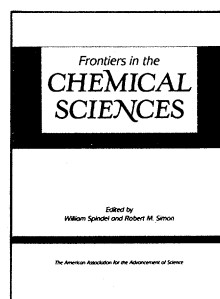
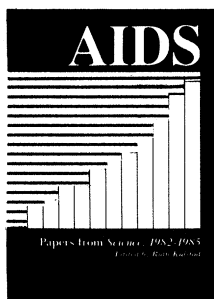
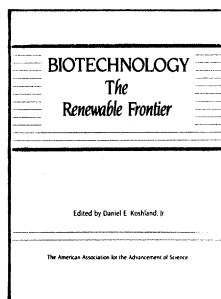
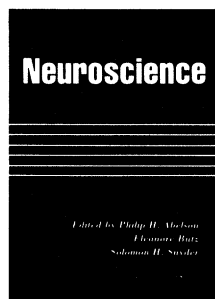
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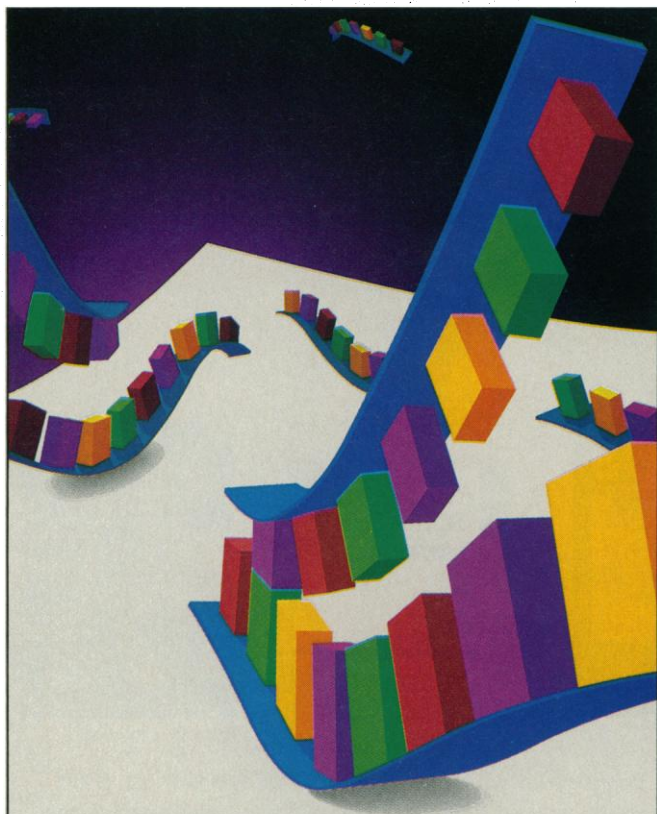
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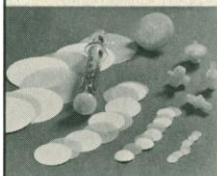
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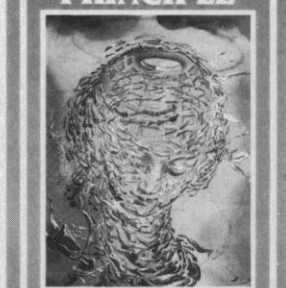
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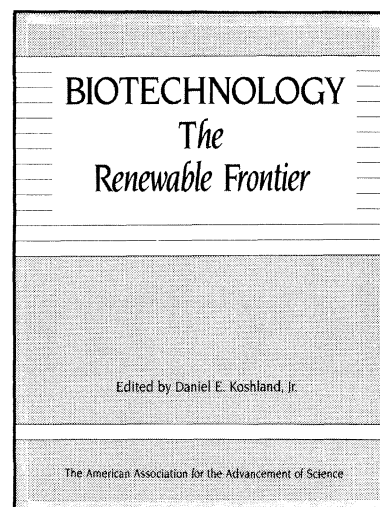
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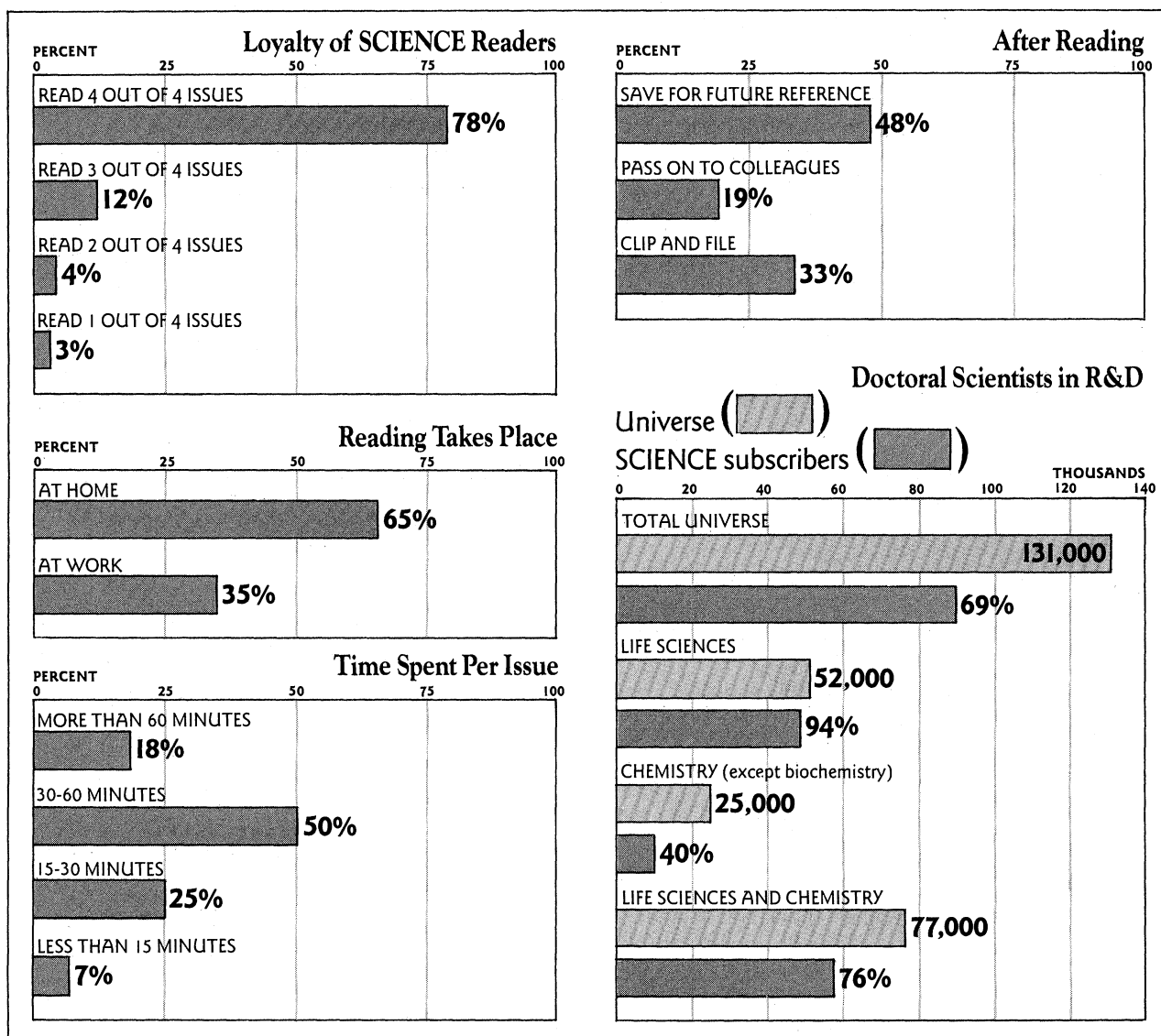
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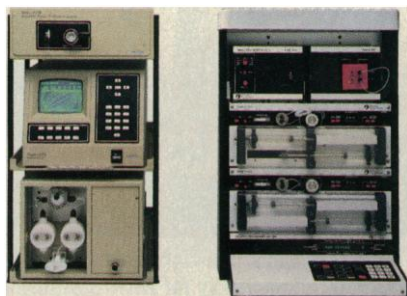
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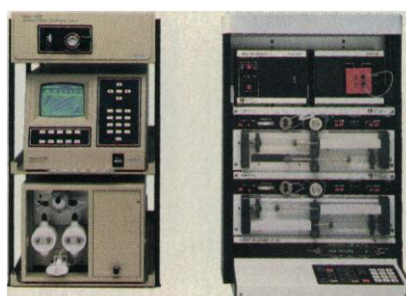
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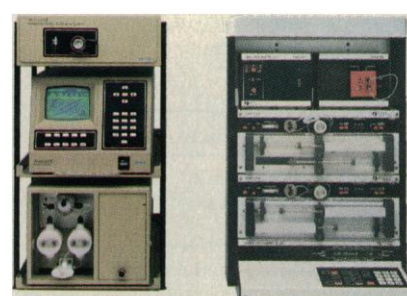
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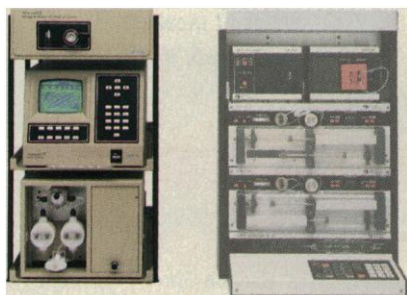
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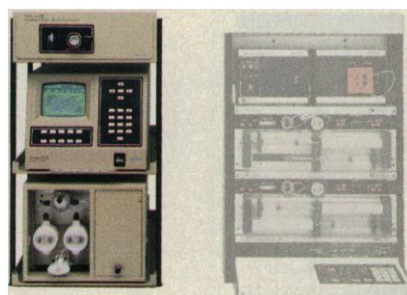
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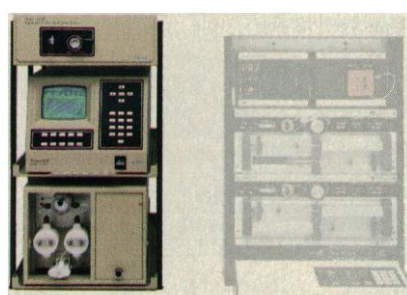
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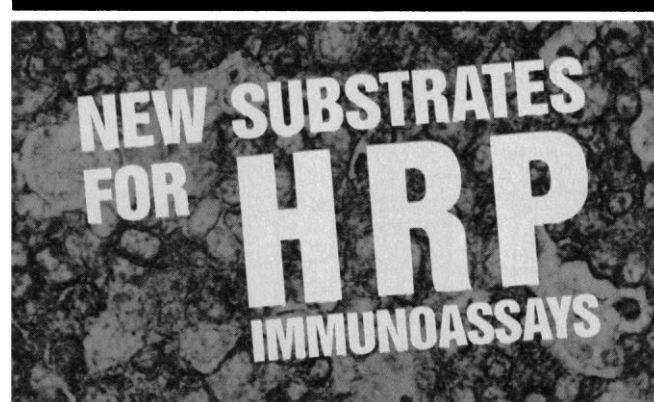
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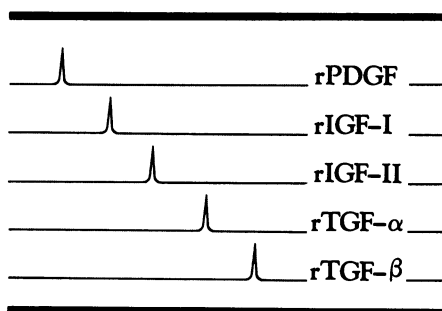
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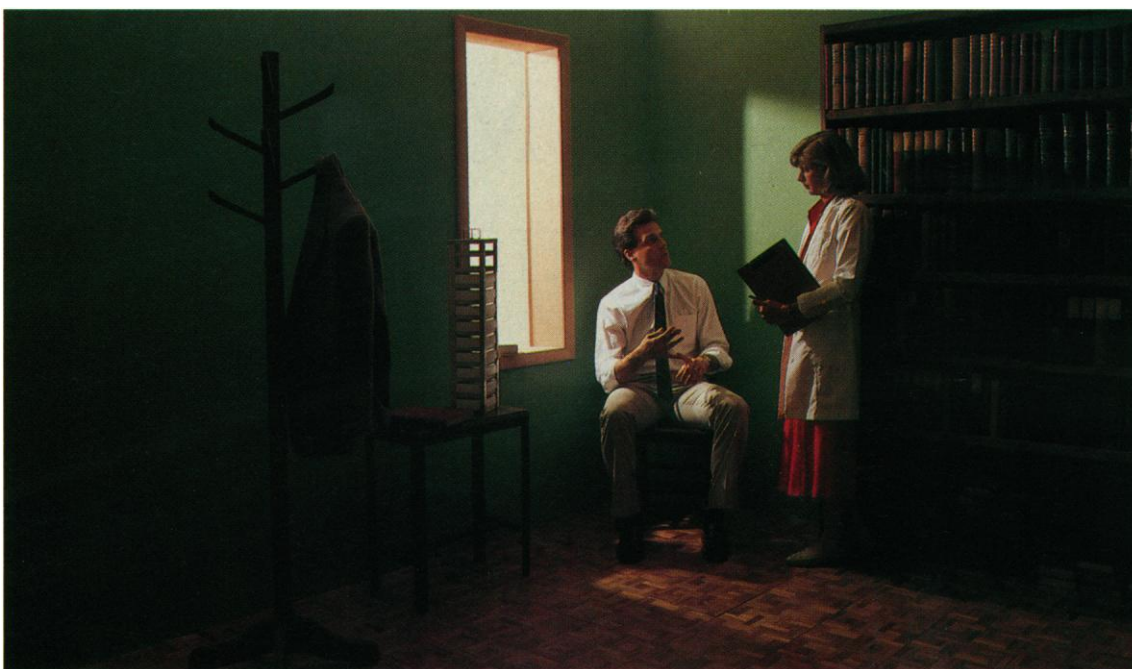
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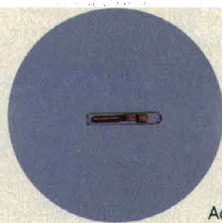


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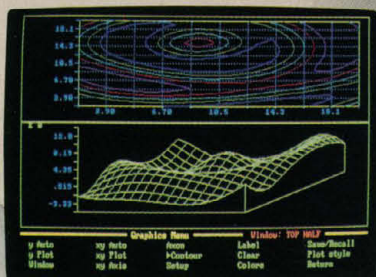
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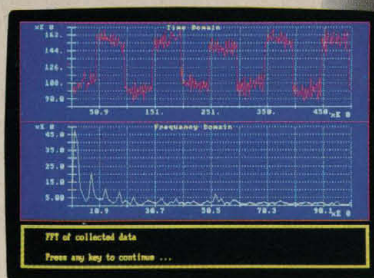
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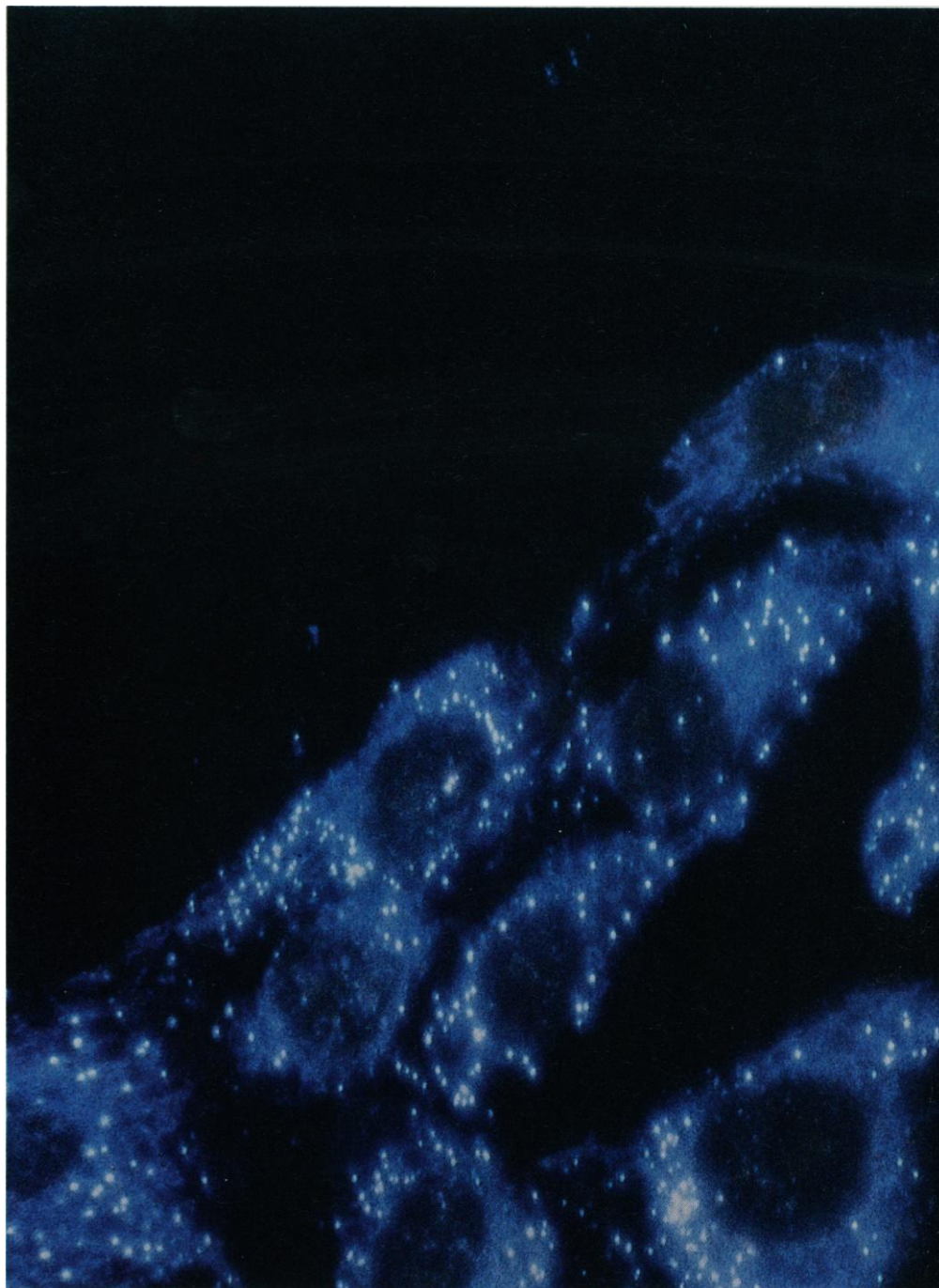
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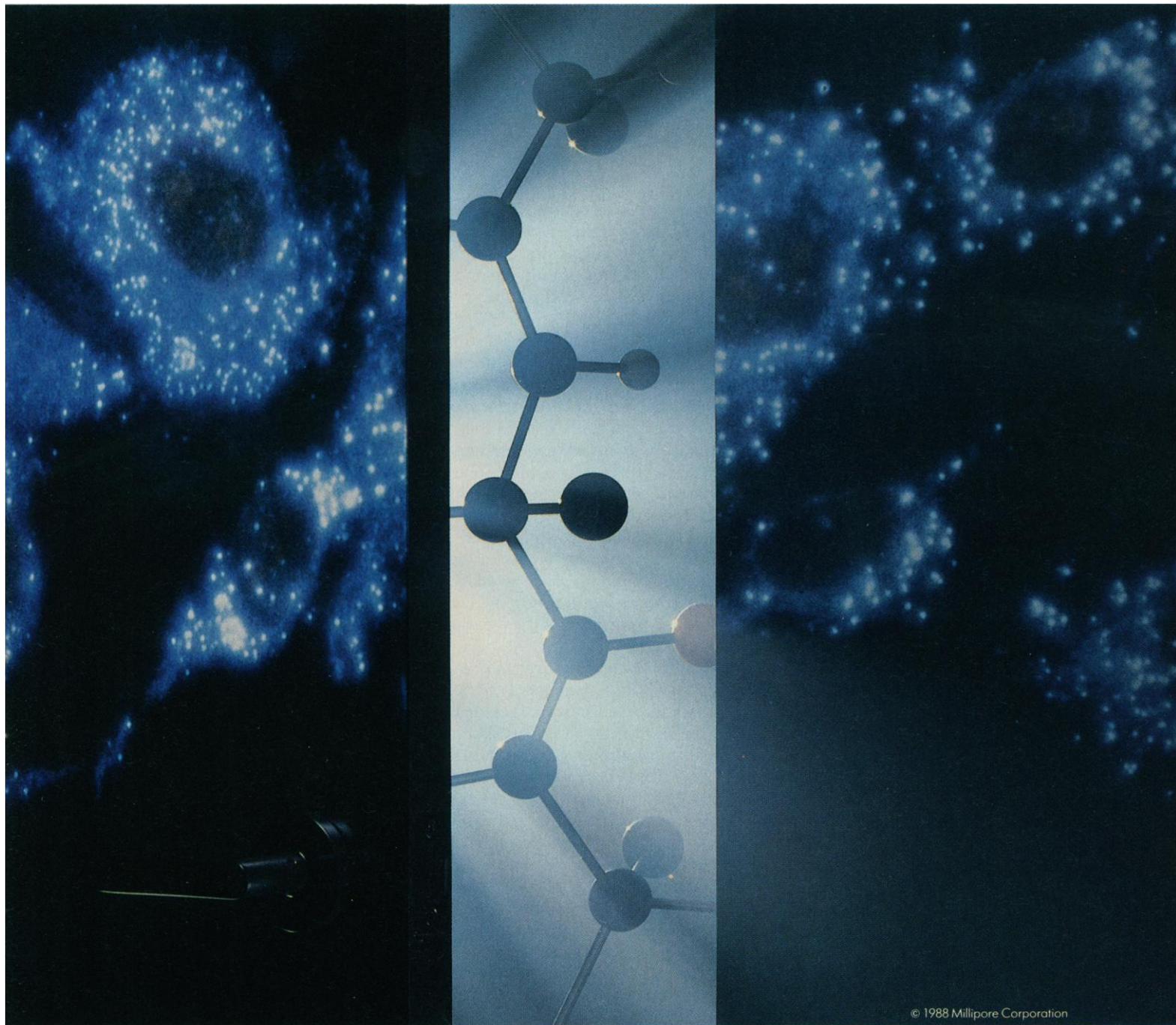


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gists with their subject matter was manifested during a symposium on population dynamics that focused heavily on Scottish seals and salmon. Students of salmon biology tended to neat tweeds, conservative politics, and pipe smoking whereas students of seals were kilted, bearded, and reddish. Out of intellect and passion there has developed a British, and generally Old World, tradition of painstaking, long-term, field investigation, which, though it may not have high prestige among the hot sciences of the universities, has enormous value.

At a deeper level, ecology is intractable in contrast with, say, traditional branches of physics, the epitome of intellectual tractability. Physics is free to decide what is or is not within its own domain. Meteorology and most nonlinear hydrodynamics were banished as non-physics for most of this century and permitted in only when a promising theoretical methodology became available. Sciences whose domains are defined by their capacities are tractable in a way that is impossible for sciences defined by a domain of subject matter. Ecology, geology, medicine, and other intractable sciences must wrestle with a preassigned subject matter as best they can, often by focusing on expensive test cases. But their subjects are ones of enormous importance. Major advances in intractable sciences can only be expected from new technologies, adequate funding, and intelligent administration, with constant reexamination of current state and pattern of progress. We cannot rely on rigid administration, proclamations, low funding, and the hope that somehow the problems will solve themselves.

We know that current applied ecology is mired in litigation and suffers a shortage of relevant data, at every scale from local water supplies to global wood supplies. We are not doing the obvious things that need doing. We know, for example, that satellites can provide ecologically important observations if their eyes are turned toward Earth and the resultant data are made generally available. This ought to be considered while NASA gropes for a post-shuttle mission. We know that ecotoxicology requires doing and isn't being done; and so on. Certainly scientific societies ought to be facing these various problems, and perhaps this volume can provide suggestions of how scientific societies can and cannot function. We must show better progress in the next 75 years, lest the problem becomes moot in the 75 years after that.

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Uses of Biology

Racial Hygiene. Medicine under the Nazis. ROBERT PROCTOR. Harvard University Press, Cambridge, MA, 1988. xii, 414 pp., illus. \$34.95.

Since the Nazi period there have been a variety of books concerned with the so-called "roots," or at least background, of National Socialism. Proctor's intensively researched work is the most thoroughgoing yet with regard to the so-called scientific background of a movement that often declared itself to be "scientific" in the application of what it liked to call the "laws of life" to human affairs. It is a deeply disturbing book, concerned as it is with how fine scientific minds, many of which were at least formally committed to the practice of healing, not only "sold themselves to the devil" but, through their own theoretical musings and prejudice-tinted social concerns, anticipated his arrival. It is an at times passionate exegesis on how "value-free" science is a disingenuous contradiction in terms and, more important, on how people who believe in so chimerical an enterprise could and can contribute to social pathology.

Proctor does not view the emergence of

"racial hygiene" as an aberration. Indeed, one of the most valuable aspects of his work is his placement of this notion within the context of Western scientific traditions, the most important of which was that concerned with racial betterment. Here, Proctor points out that eugenics, not necessarily racist in nature or application, was a crucial concern not only of individuals who could be identified as "right-wing" in nature but of a panoply of left-wing or "progressive" thinkers as well as social reformers, including, among others, Margaret Sanger. Indeed, during the early years of the 20th century, individuals such as Alfred Ploetz, Wilhelm Schallmayer, and Ludwig Woltmann, who would later be seen as ground-breakers for the application of the Nazi scientific vision to human affairs, were "cautious advocates of certain forms of progressive social reform" (pp. 21-22). The application of presumably well-established biological laws (in part resulting from the overthrow of Lamarckian hypotheses by genetics) to social issues was part of the ideational environmental of Western civilization. Eugenics, and radical articulations of it such as forced sterilization of "defective" or "criminal" types, had found legal expres-

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