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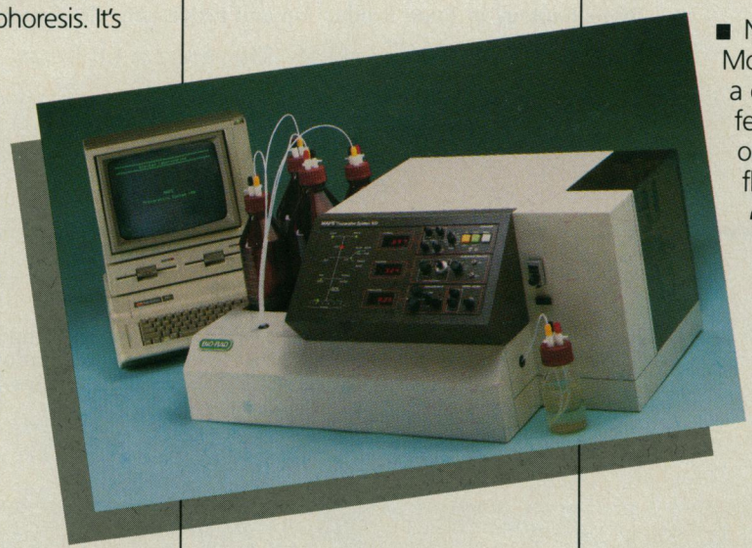

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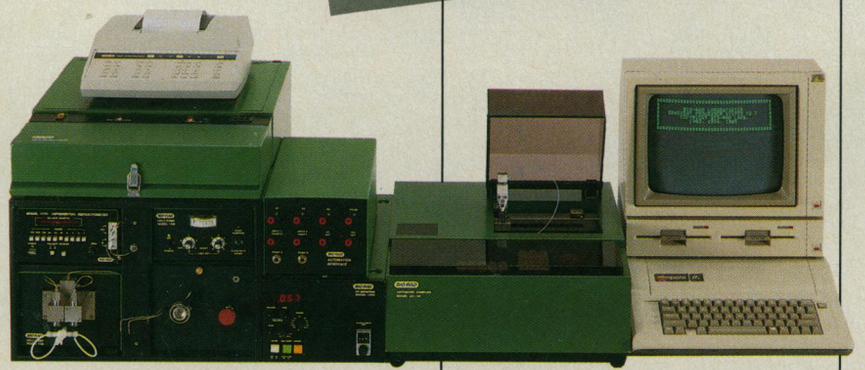

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ISSN 0036-8075
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SCIENCE is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1333 H Street, NW, Washington, D.C. 20005. Second-class postage (publication No. 484460) paid at Washington, D.C., and at an additional entry. Now combined with **The Scientific Monthly**® Domestic individual membership and subscription (51 issues): $60. Domestic institutional subscription (51 issues): $98. Foreign postage extra: Canada $24, other (surface mail) $27, air-surface via Amsterdam $65. First class, airmail, school-year, and student rates on request. Single copies $2.50 ($3 by mail); back issues $3 ($3.50 by mail); Biotechnology issue, $5 ($5.50 by mail); classroom rates on request. **Change of address:** allow 6 weeks, giving old and new addresses and seven-digit account number. **Postmaster:** Send Form 3579 to *Science*, 1333 H Street, NW, Washington, D.C. 20005. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

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COVER

Flowers of *Arabidopsis thaliana*. Although only 2 millimeters in their largest dimension, the flowers of this diminutive member of the mustard family (Brassicaceae) are as structurally complex as the flowers of larger plants. A number of *Arabidopsis* mutations that result in specific alterations of floral morphology have been identified. See page 1214. [Elliott Meyerowitz, Division of Biology, California Institute of Technology, Pasadena 91125]

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Mutation strategies

Recombinant DNA technology is making possible directed mutation of specific genes and mutation of genes for specific purposes; this is a far cry from the older brute force mutagenic approach whereby organisms were subjected to radiation or chemicals and a hunt made for offspring showing altered characteristics (page 1193). Botstein and Shortle describe, in the first of seven articles in this special issue on biotechnology, the range of mutagenic techniques feasible now that cloned genes—homogeneous populations with many copies of a given gene—are available. Methods are described for changing existing genes, inserting newly synthesized pieces of DNA into genes, and assessing effects of mutagenic processes on molecular structure and function.

Antibody chimeras

Genetic engineering techniques bring together within antibodies—the molecules responsible for immune responses to foreign materials (antigens) in the body—desired antigen-binding capabilities with desired "effector functions" (page 1202). In naturally occurring antibodies, binding to foreign material occurs in one region or domain; effector functions, such as the triggering of an allergic response in the host or the stimulation of clearance of the antigen-antibody complex from the circulation, are carried out by other domains. Morrison describes how chimeric antibodies are constructed from two or more antibodies or from an antibody and another type of protein (such as an enzyme) by juggling genes or parts of genes. Through the coupling of antigen-binding capabilities to desired effector functions, desired chimeras can be developed for therapeutic, diagnostic, and research purposes.

Biotechnology in food production

The first use of biotechnology was in the production of food (bread, beer, wine, and cheese); it is still the major use (page 1224). Knorr and Sinskey describe how biotechnology is being used to improve plant crop yields, enhance resistance to disease, and increase or alter the plant's nutritional value. Animals are genetically manipulated to improve reproduction and the quality or quantity of milk and meat; if genetic manipulation does not succeed, enzymes can be used to tenderize meat. New sources of food and nutrients are being generated: vitamin E may be produced through a fermentation process from a precursor found in some bacteria and yeast; chitin, a waste product of the shellfish industry, may be recycled for use as dietary fiber. Increased efficiency of standard processes, such as the fermentation of beer, and creation of new products, such as light beers, are other feats being accomplished through genetic manipulations of microorganisms.

Economics of pharmaceutical production

Pharmaceuticals—insulin, growth factors, interferons—produced by biotechnology have been developed largely at academic laboratories and small companies in the United States; these institutions lack the capital to market products and will share commercial benefits of the industry with large manufacturing companies here, in Japan, and in Europe (page 1230). Genetic engineering facilitates large-scale production of diagnostic reagents, drugs, and vaccines formerly produced only by expensive synthetic or purification processes. Know-how in the United States is strongest in molecular biology; know-how in Japan is strongest in fermentation technology, of key importance to manufacturing. U.S. government funding has gone primarily to basic research; product production has been emphasized in Japan. Dibner recommends that more government support be given to production here, without shortchanging basic research, to ensure future commercial successes and a competitive position in the world market.

Geochemical earthquake warning

Conspicuous changes were observed in gases emitted from a fumarole (volcanic vent) and a mineral spring near the epicenter of an earthquake in central Japan in 1984 (page 1261). Concentrations of helium, methane, hydrogen, sulfur dioxide, hydrochloric acid, and hydrofluoric acid increased sharply 1 week before the earthquake and then dropped precipitously 50 days after the shock. Emitted hydrogen which, unlike other gases, seems to form by reaction of ground water with rock fractured during seismic activity, may have the most value for short-term predictions. Sugisaki and Sigiura suggest that the strain that caused the earthquake and precursor events was the same. Although geochemical changes at this site preceded the earthquake, geophysical measurements (seismic activity and deformations of the earth's crust) yielded no premonitory signals.

Gene activation pattern

Activation of genes for the U1 class of RNA molecules from the cell nucleus is under developmental control in mice (page 1271). Lund *et al.* found that the relative amounts of two types of U1 RNA changed in various tissues in a characteristic pattern. One form was present in all tissues examined; a second form was restricted to embryonic tissue and to those adult tissues (spleen, thymus, testes) in which some cells are able to continue differentiating during development. Since U1 RNA helps in the processing of precursors of the messenger RNA molecules that carry the information from genes to proteins, the availability of two forms of U1 in tissues may offer alternatives for how messenger RNA molecules are assembled during development.

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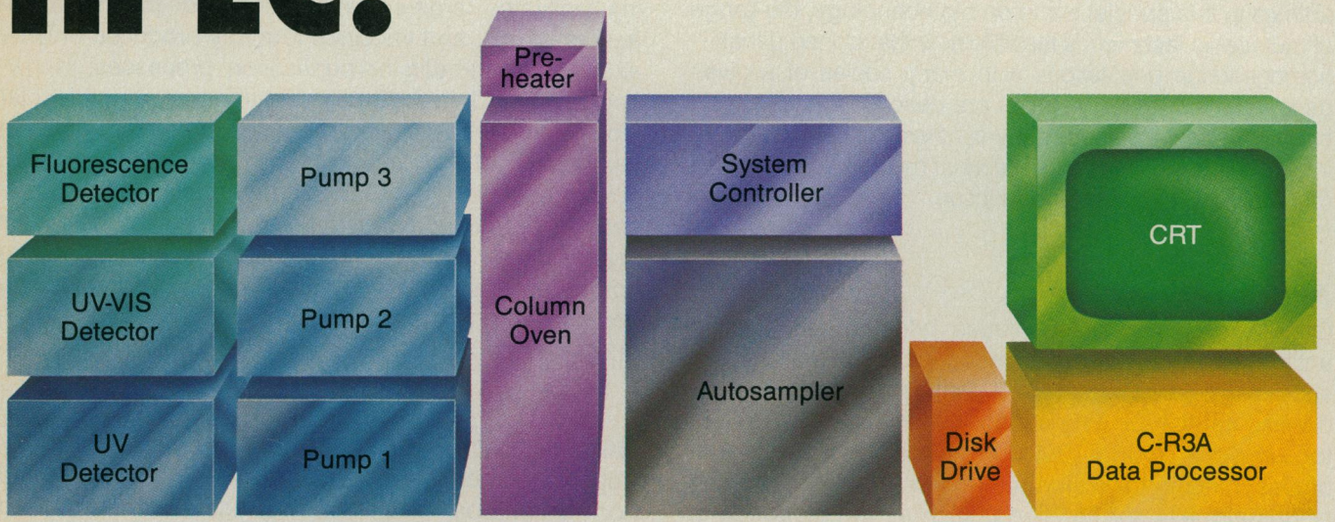

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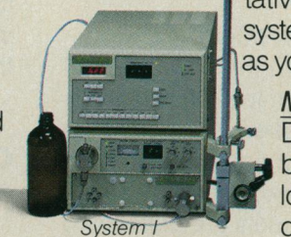

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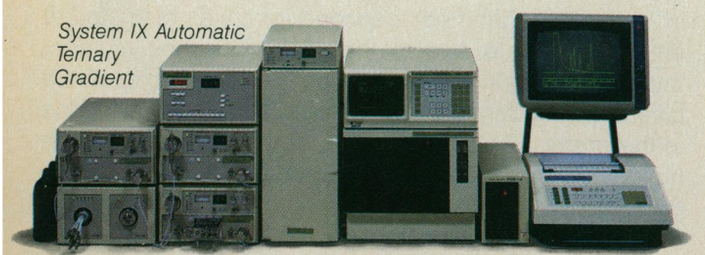

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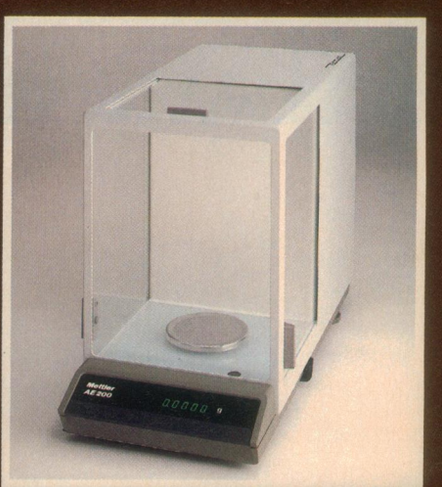

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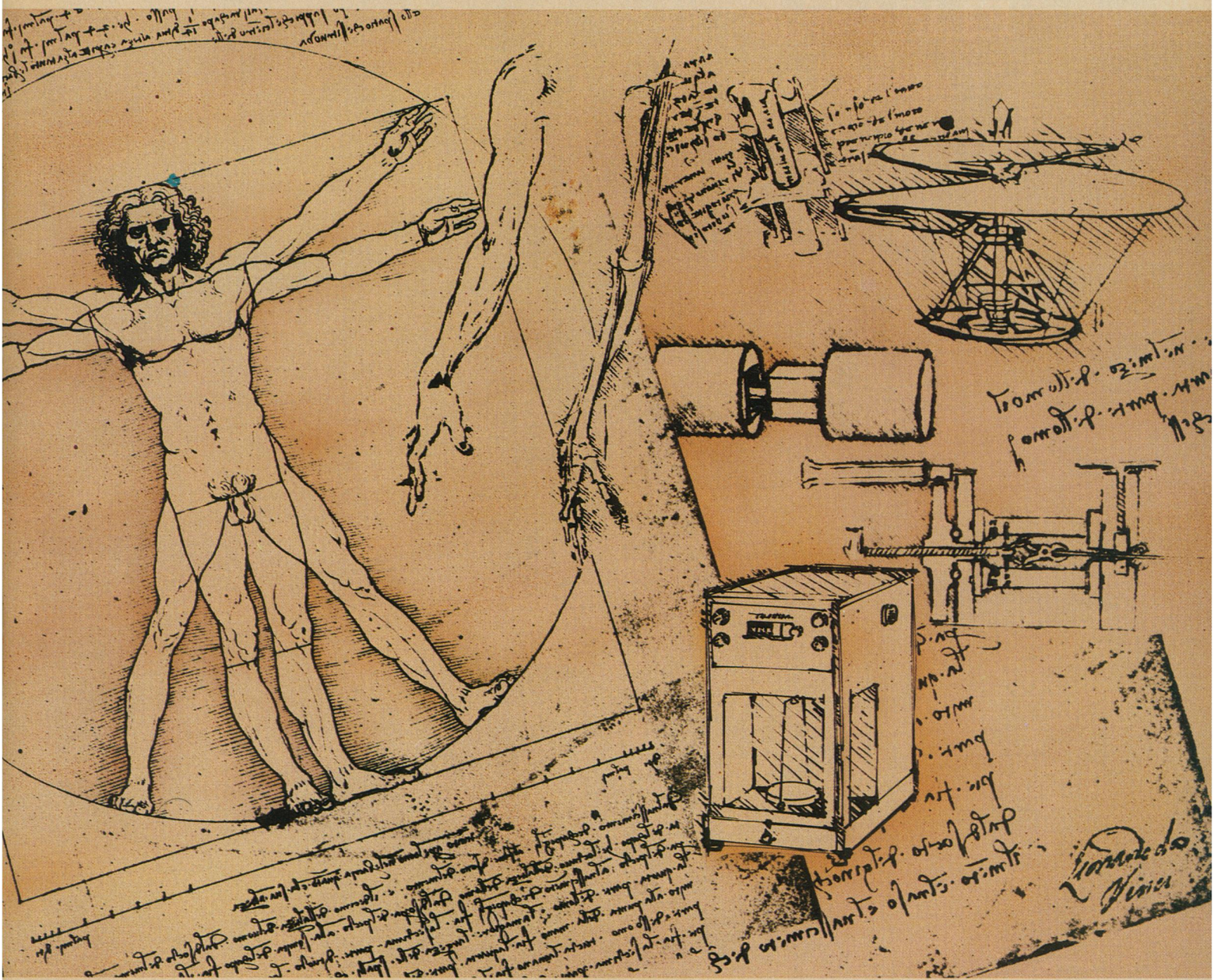

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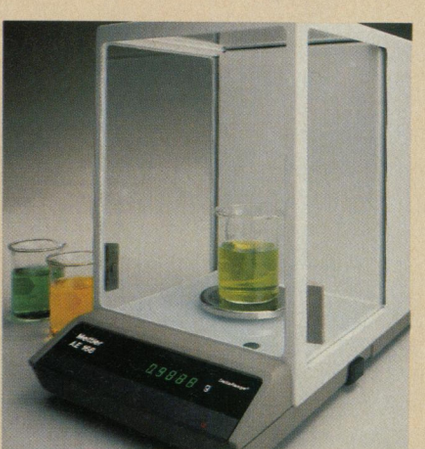

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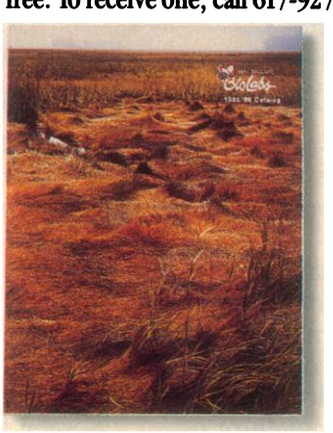

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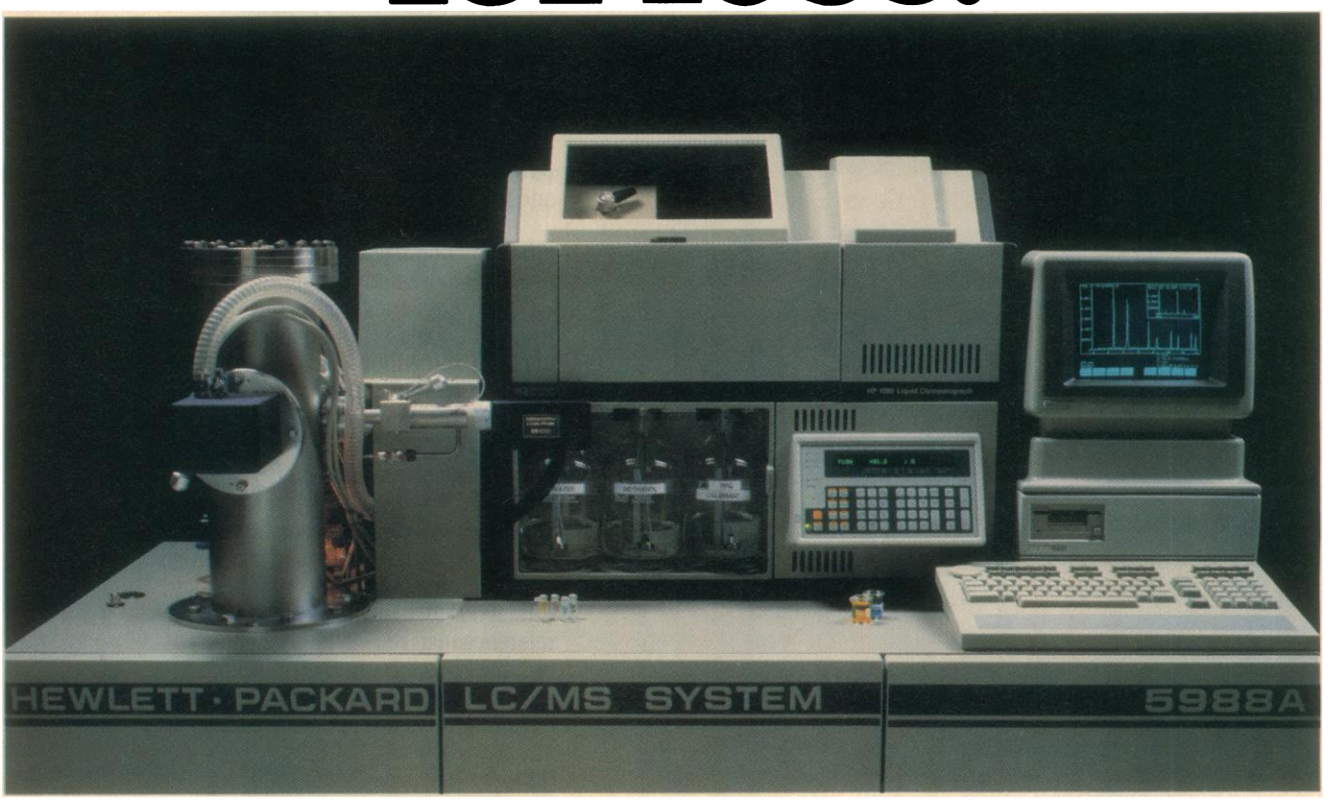

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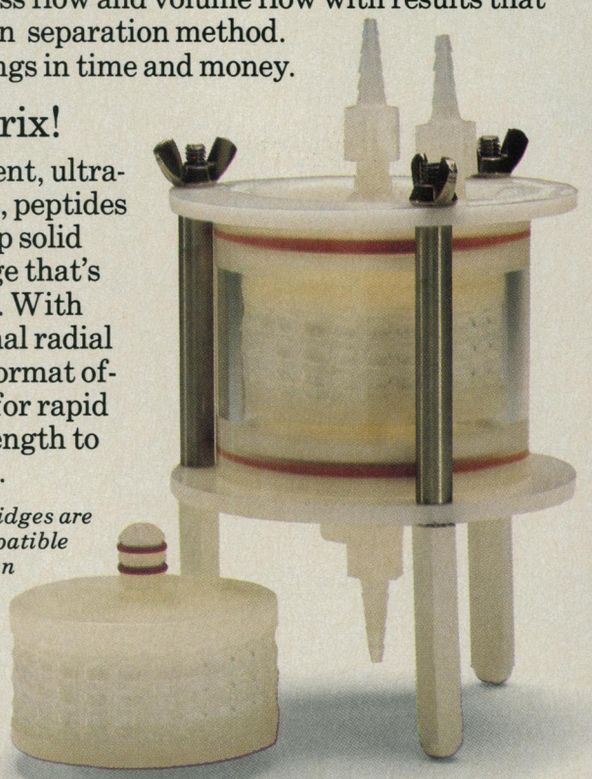

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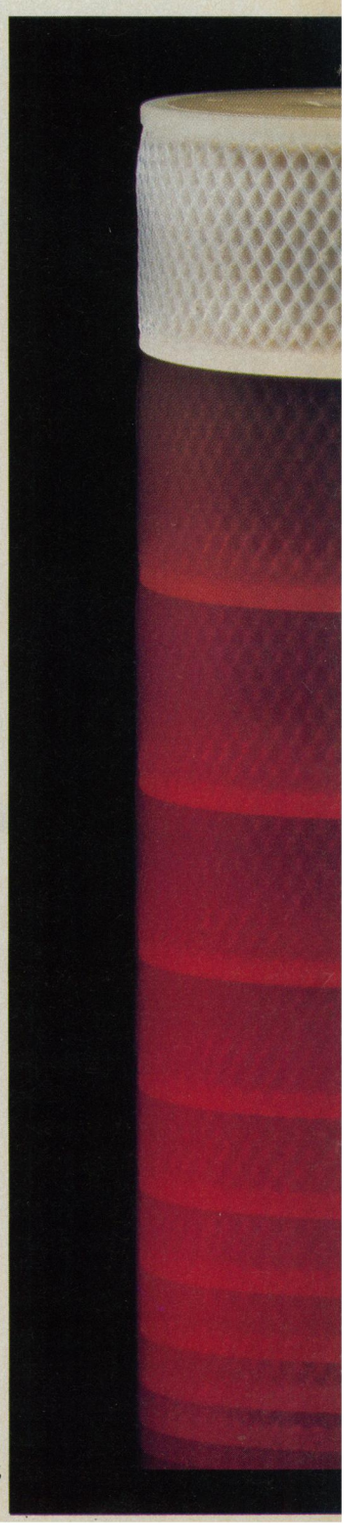

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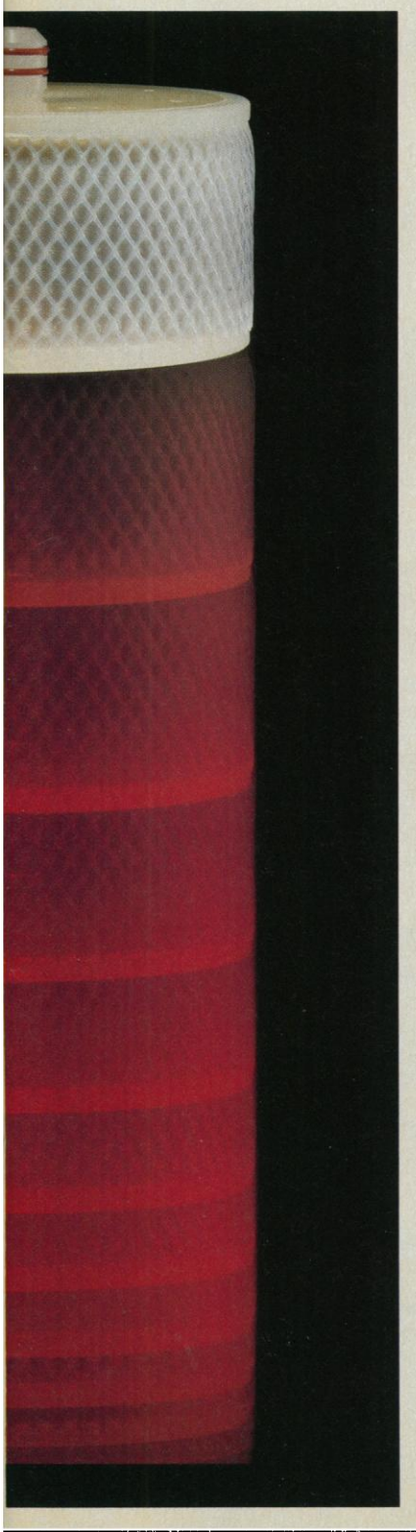

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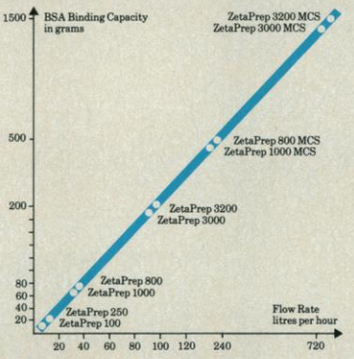

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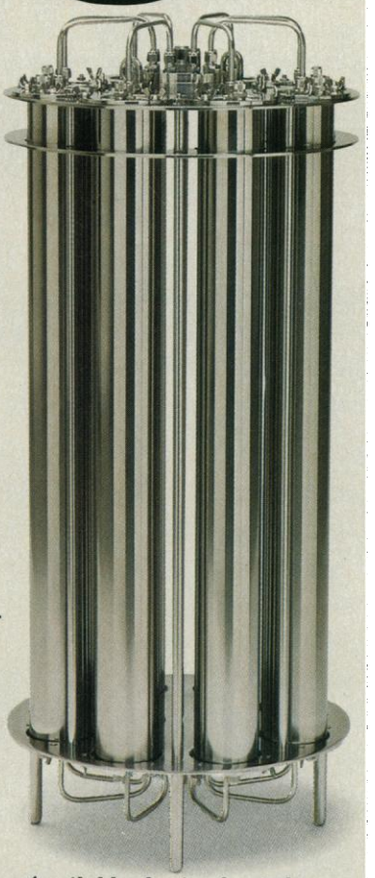

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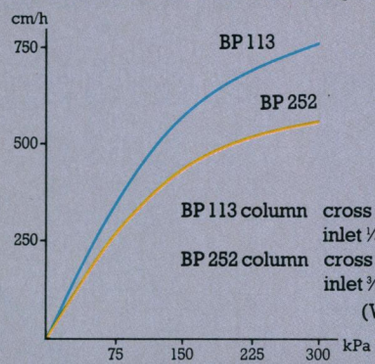

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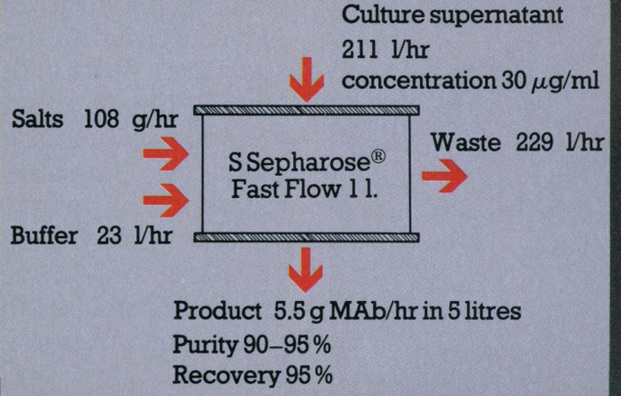

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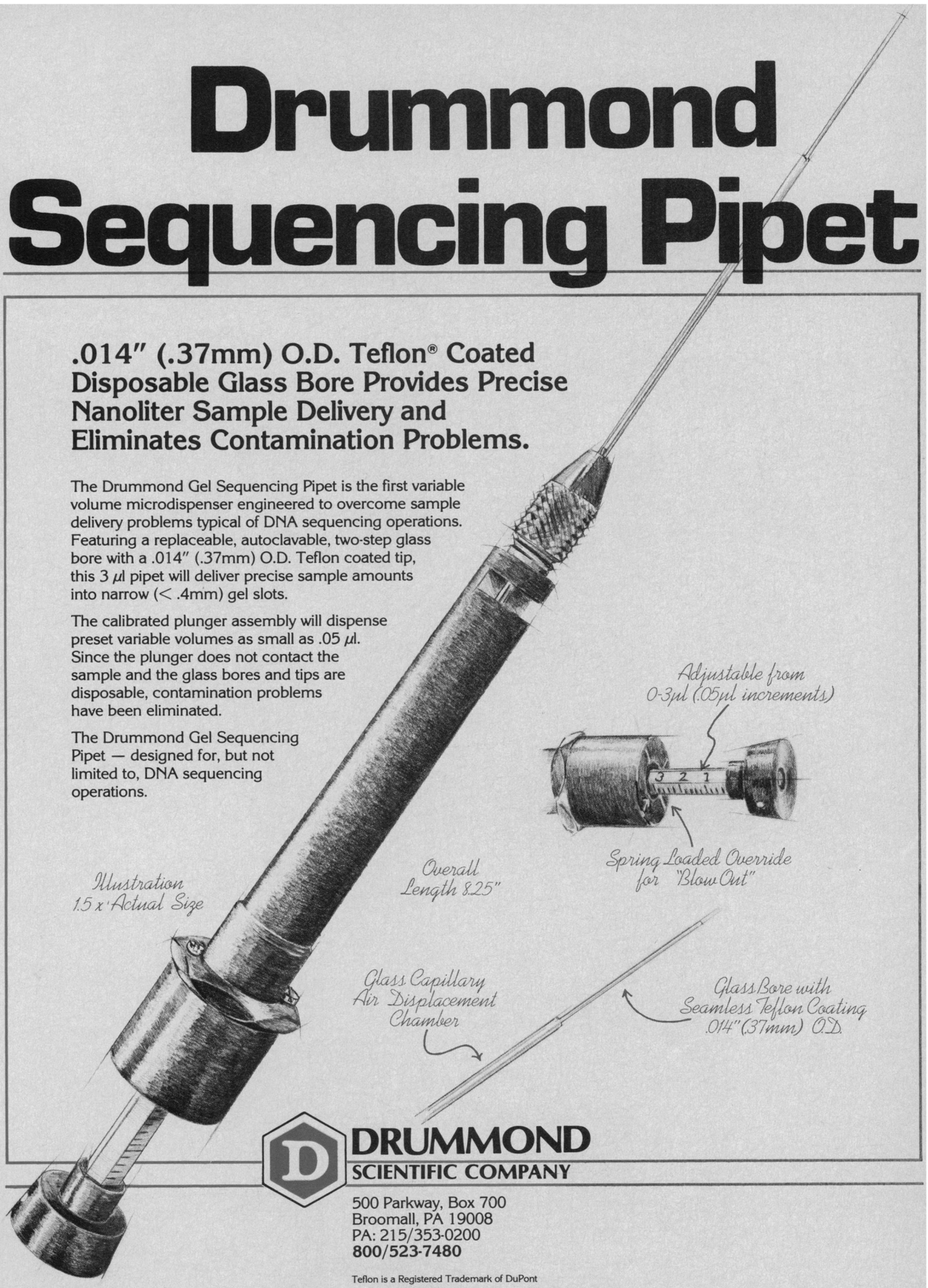

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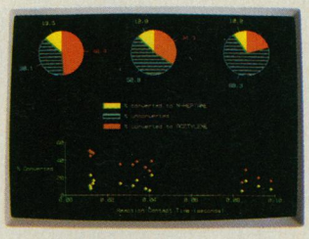

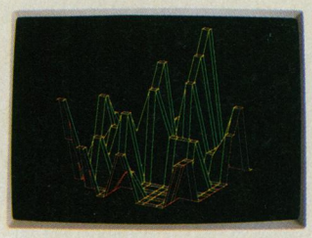

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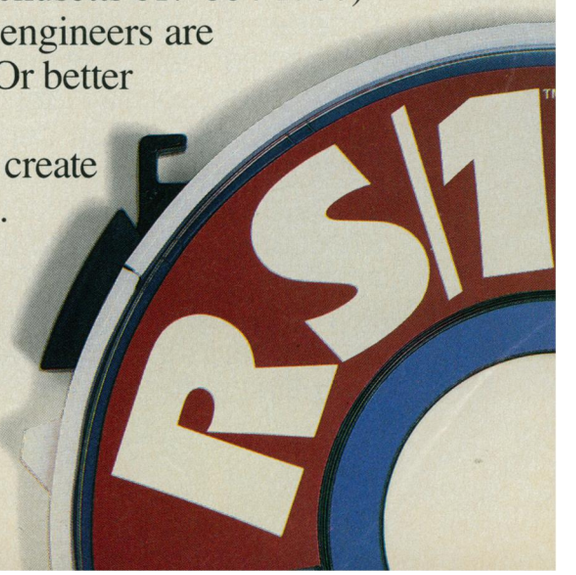

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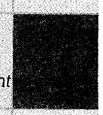

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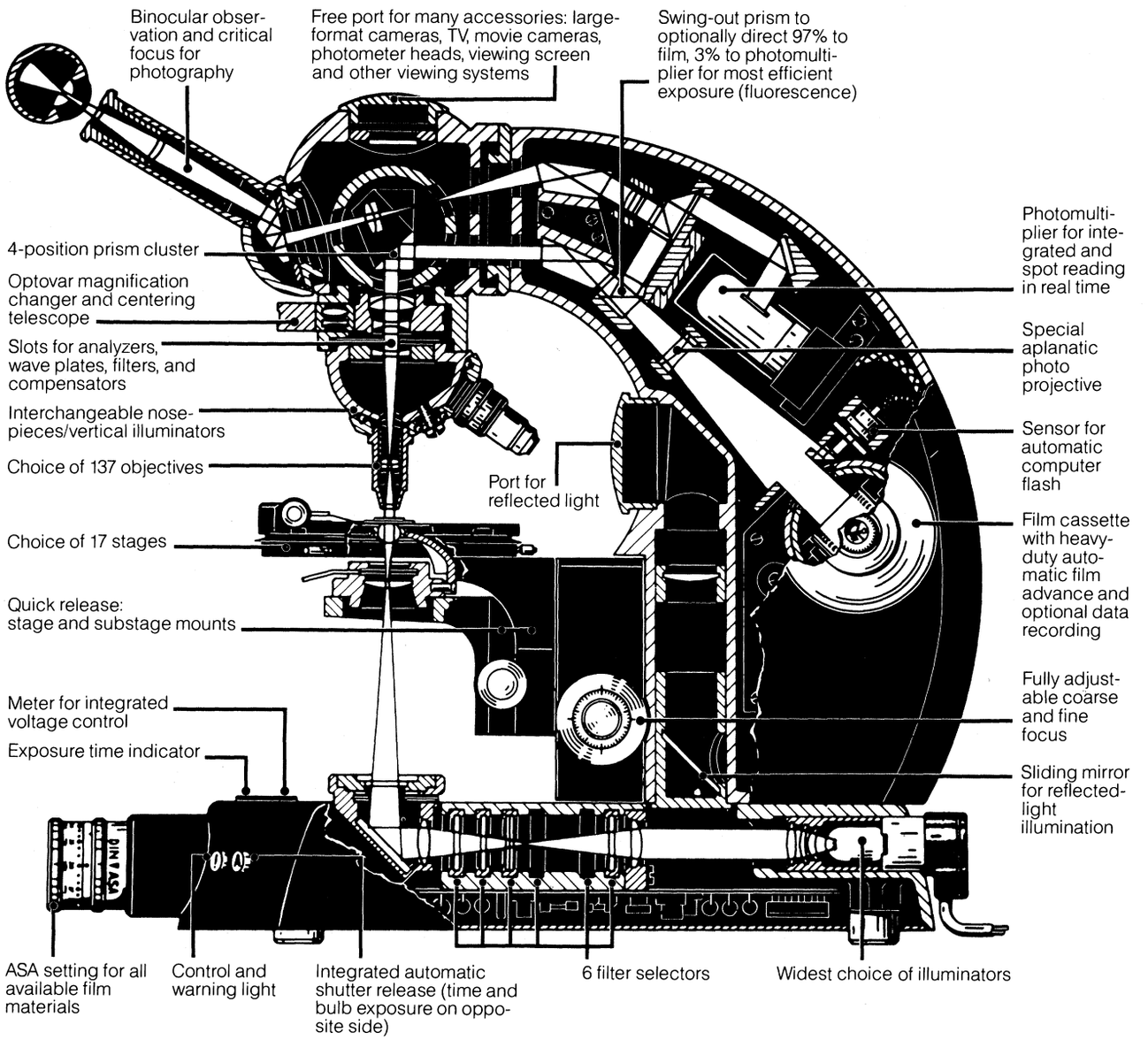

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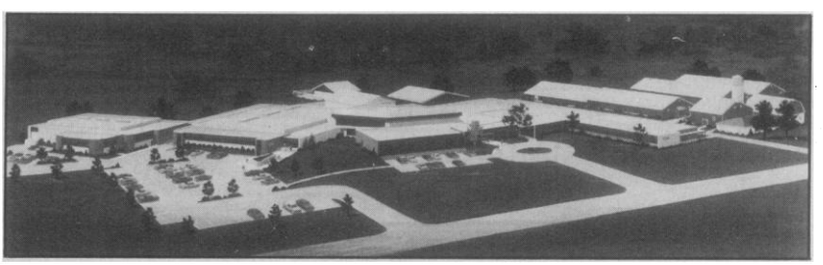

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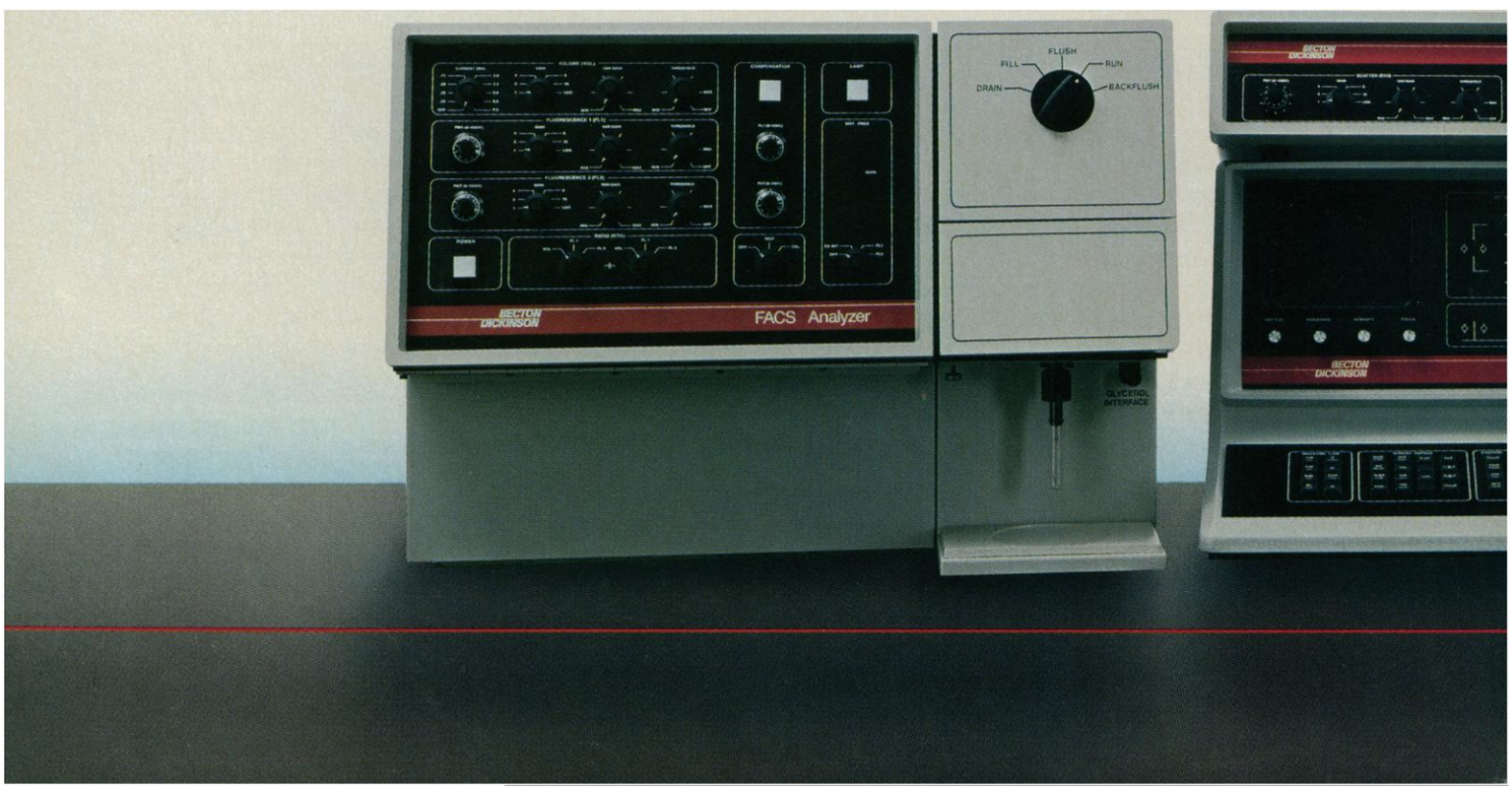

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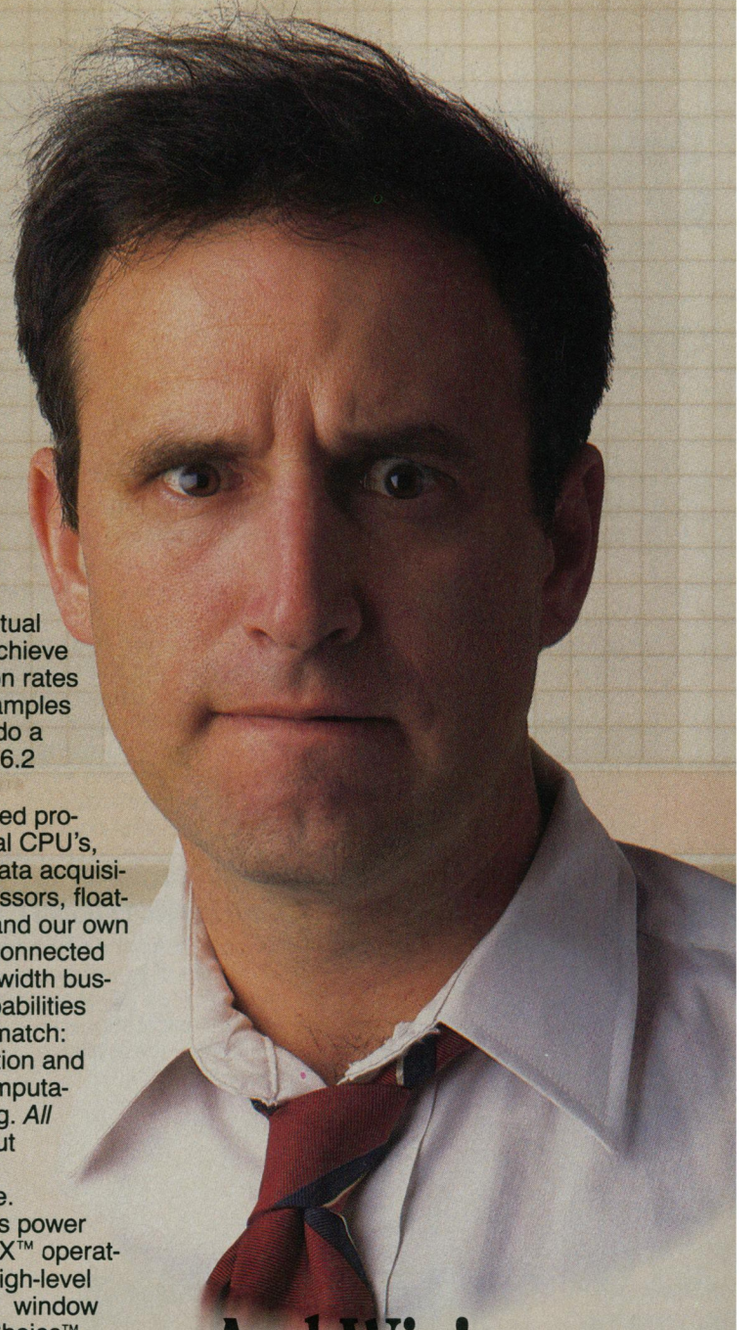

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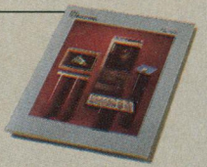

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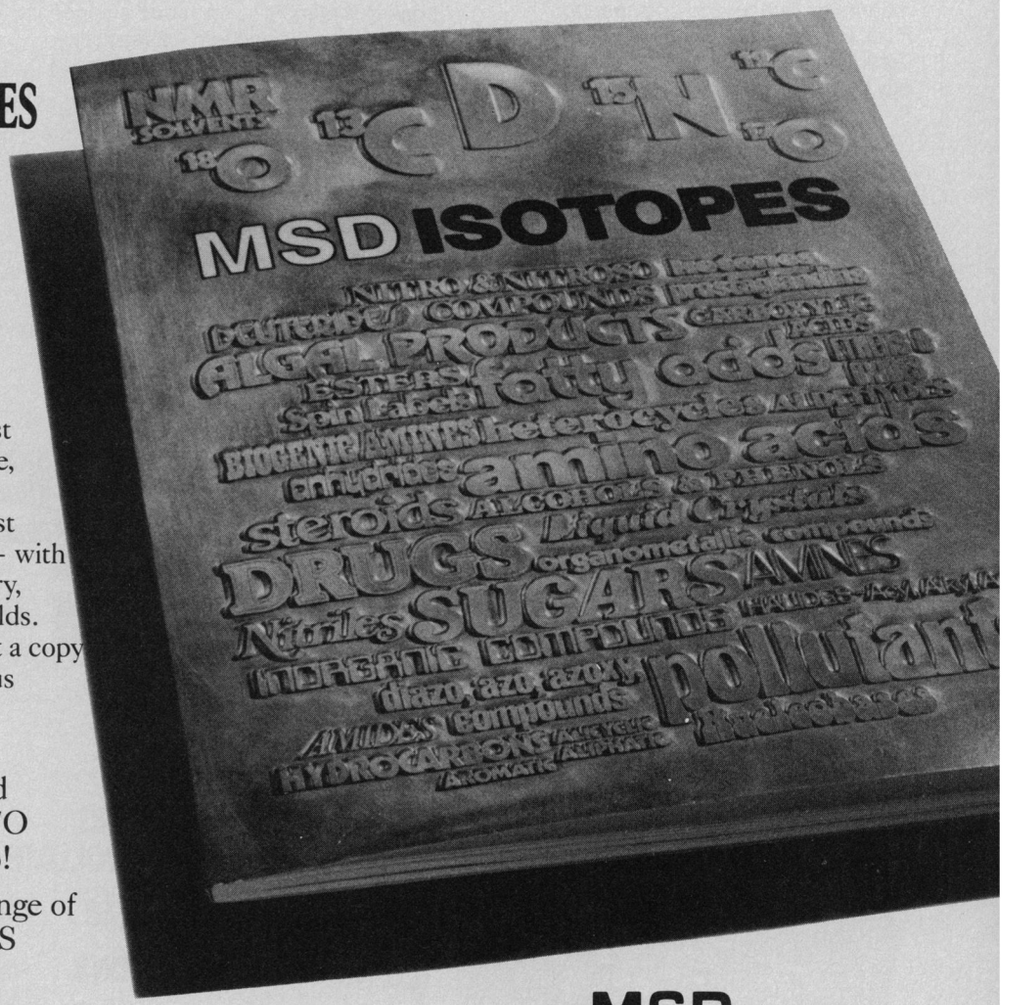

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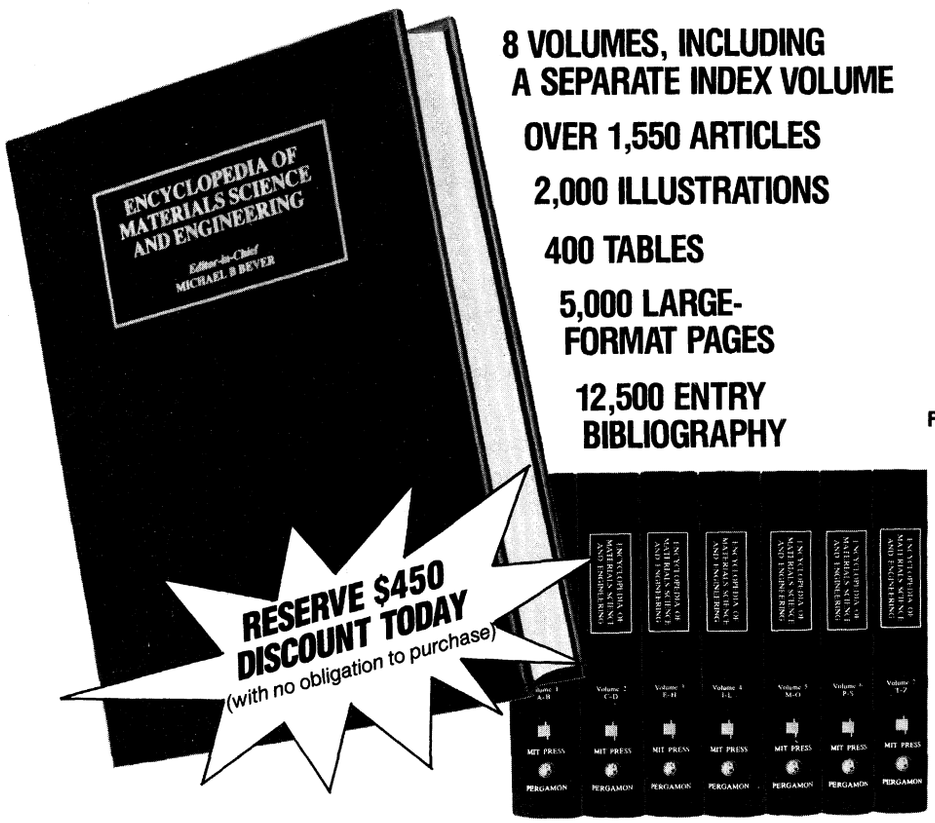

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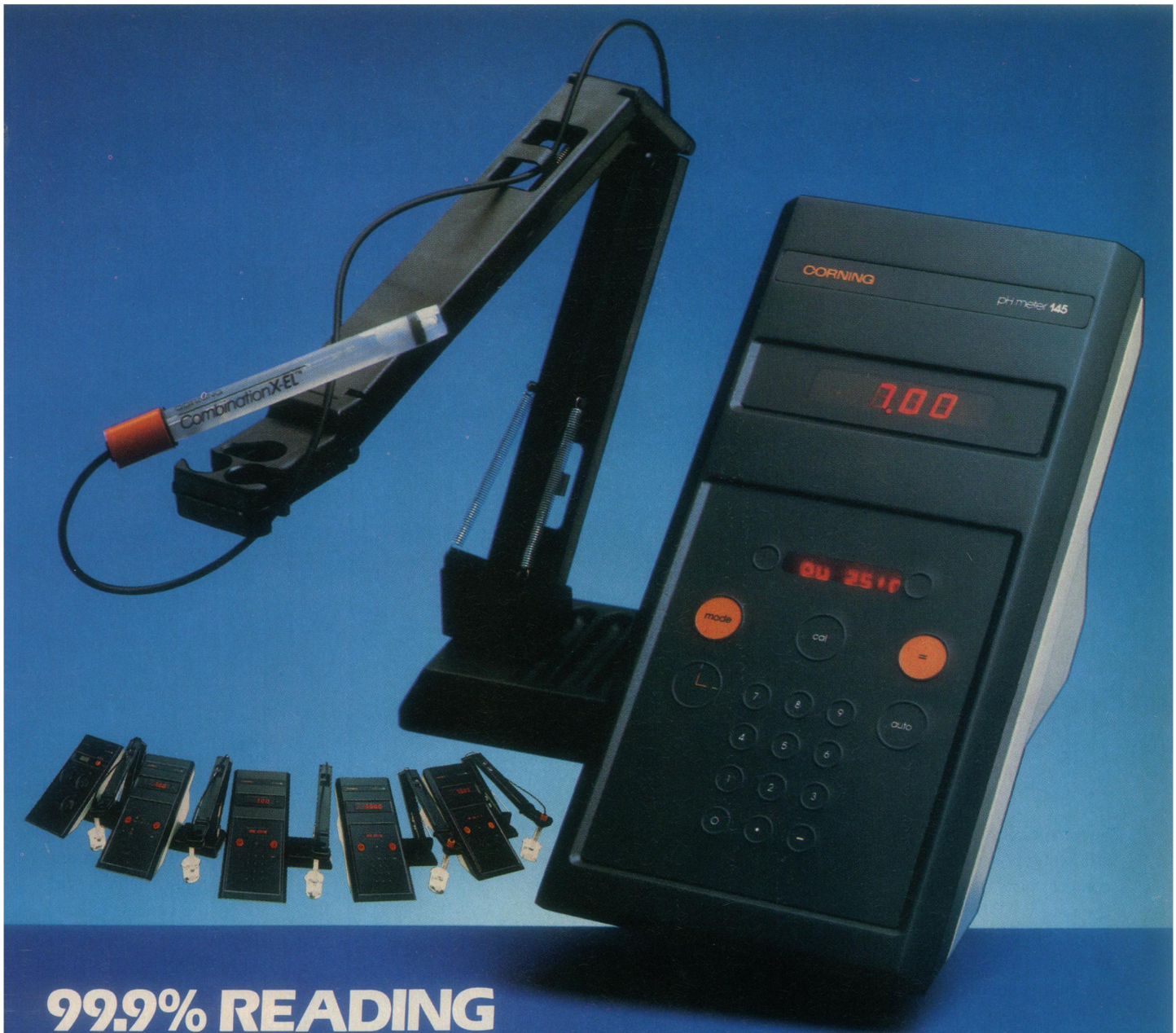

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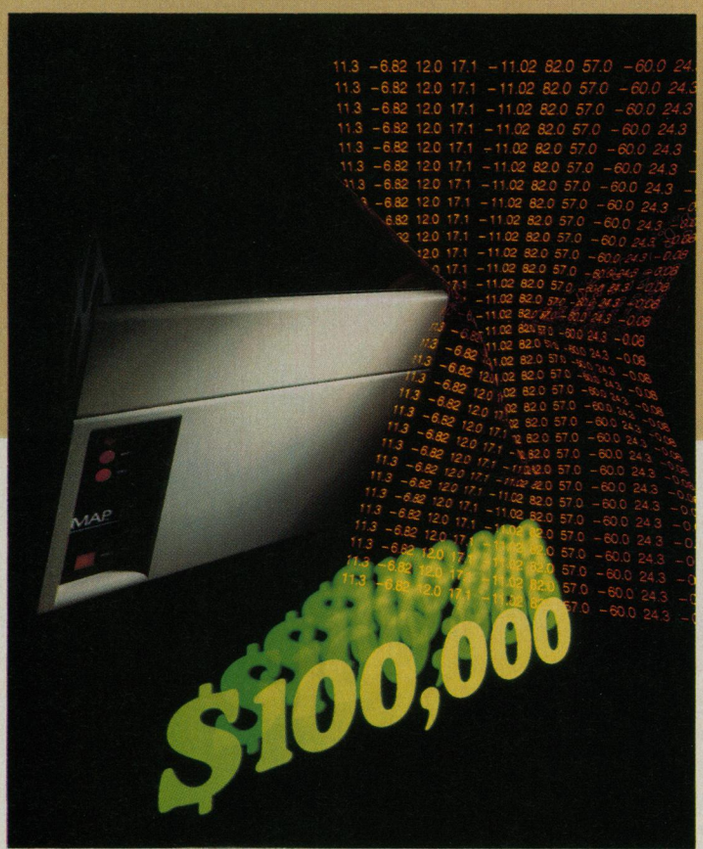

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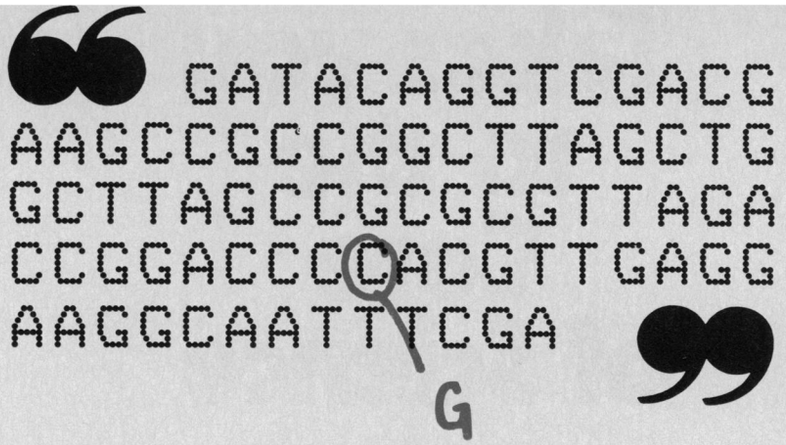

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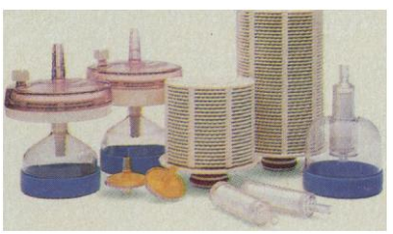

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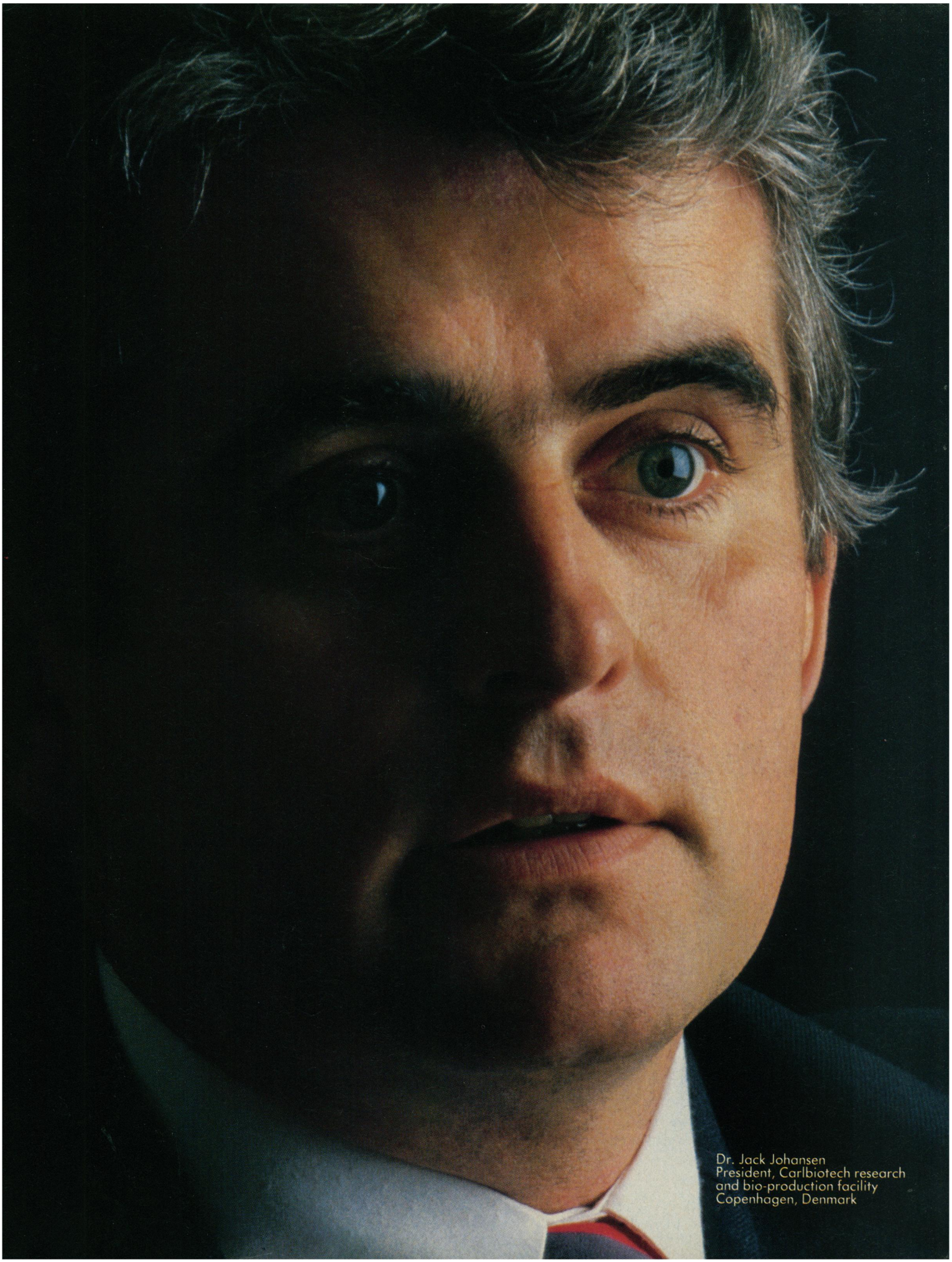

Dr. Jack Johansen
President, Carlbiotech research
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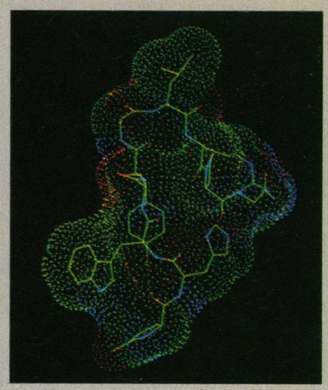
"It could be a new weapon in the fight against cancer, if we can just make enough."

Scientists like Dr. Jack Johansen of Carlbiotech believe that analogs of LHRH peptide, an elusive brain hormone, could play an important role in cancer therapy, particularly prostate cancer. LHRH (Luteinizing Hormone-Releasing Hormone) works with the body's own endocrine system, cutting off the production of testosterone, which prostate cancer thrives on.



Computer Model of LHRH peptide.

Isolating and identifying LHRH helped win a Nobel Prize in 1977. But synthesizing it with high enough purity has been a challenge all its own. And though chemical means have been used to produce analogs of LHRH, success has been varied. Now Carlbiotech has pioneered a biological method of synthesis; an enzyme-based method, which is more precise and less costly than traditional techniques.

The heart of the enzymatic method is the purity of the reaction mixture in combination with the resolution power of Millipore's High Performance Liquid Chromatography (HPLC) technology, pioneered by its Waters Chromatography Division. HPLC is used by Carlbiotech throughout the painstaking process of building the peptide structure, first for isolating peptide fragments that are linked to form LHRH, then for isolating and purifying the final product. HPLC is also built into quality control procedures. Other crucial steps use membrane filters to harvest the enzymes from yeast cells, purify water and sterilize therapeutic doses.

Lab and pilot scale quantities of LHRH are synthesized and purified using Millipore instrumentation and membrane devices.

Enzymatic technique for synthesizing LHRH is scaled-up in large Millipore processing systems.

Millipore worked closely with Carlbiotech in the development of its process: from the lab, through pilot production, and into full-scale manufacturing. Together they overcame the complex problems encountered in scaling up production from milligrams to kilograms.

Carlbiotech is now using its new enzymatic process to produce kilogram quantities of LHRH with high recoveries and high purities. And it is only by producing quantities like this, that scientists can determine whether or not they have a new weapon in the ongoing fight against cancer.

Millipore is working with a variety of scientists who, like those at Carlbiotech, are expanding the limits of applied technology. For more information, write: Corporate Communications, Millipore, Bedford, MA 01730.

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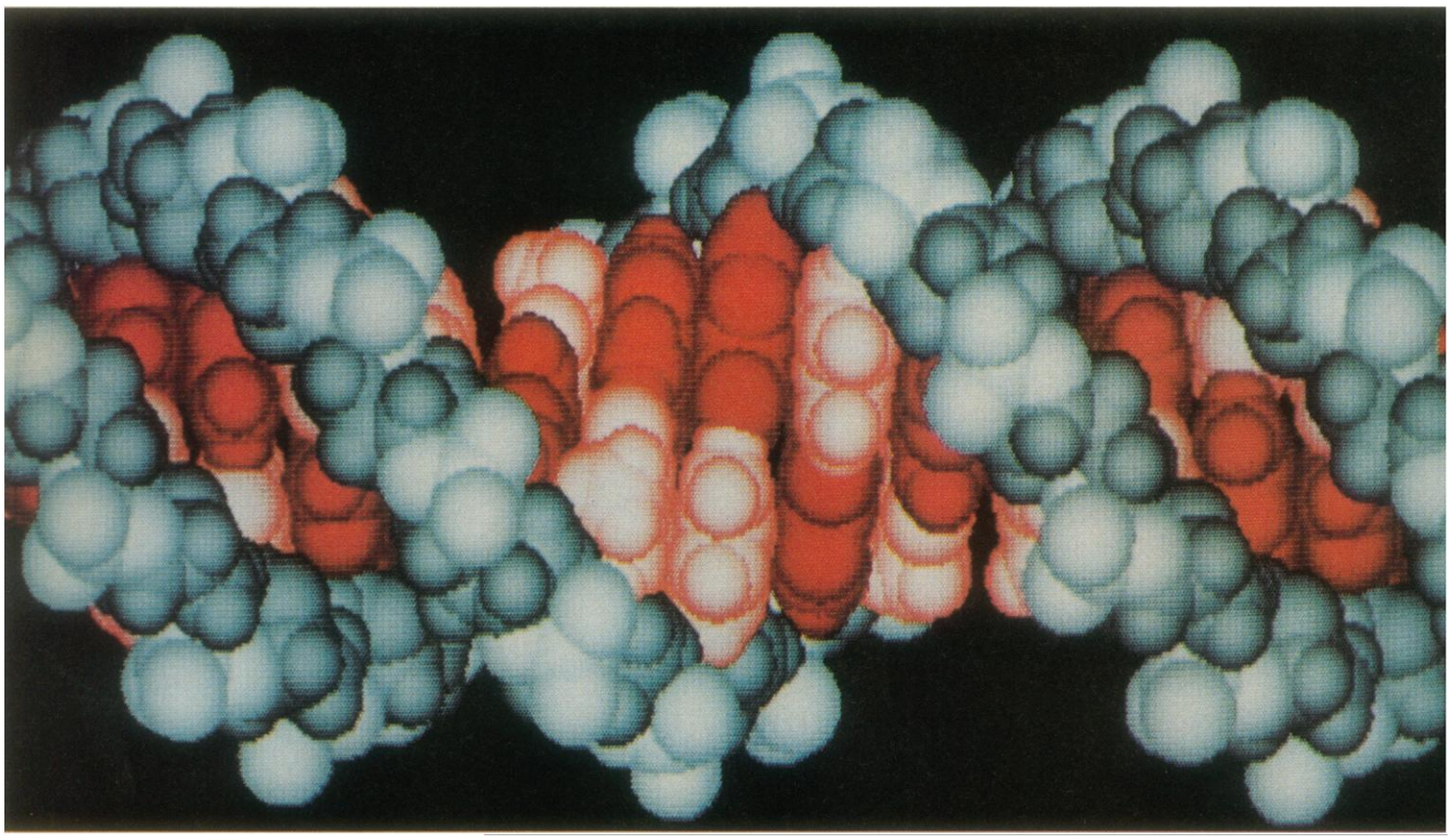

Computer visualization of B-DNA courtesy of Richard J. Feldmann, National Institutes of Health, Bethesda, MD.

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Session Topics

POLICY ISSUES – Jerrold Roschwalb, National Assoc. of State Univ. & Land Grant Colleges
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SYSTEMS and RESOURCES – Lewis Gevantman, National Bureau of Standards
This session will present examples of computer systems and developments related to and supporting biotechnology. Speakers will include Professor Carver Mead (CalTech), Professor David Mount (Arizona State), Richard Feldmann (NIH), Dr. Kevin Ulmer (CARB), Dr. Charlotte Hollister (BBN), and Dr. Dennis Smith (Intellicorp).

APPLICATIONS IN AGRICULTURAL BIOTECHNOLOGY – Joseph Modelevsky, International Minerals and Chemicals, Northbrook, Ill.
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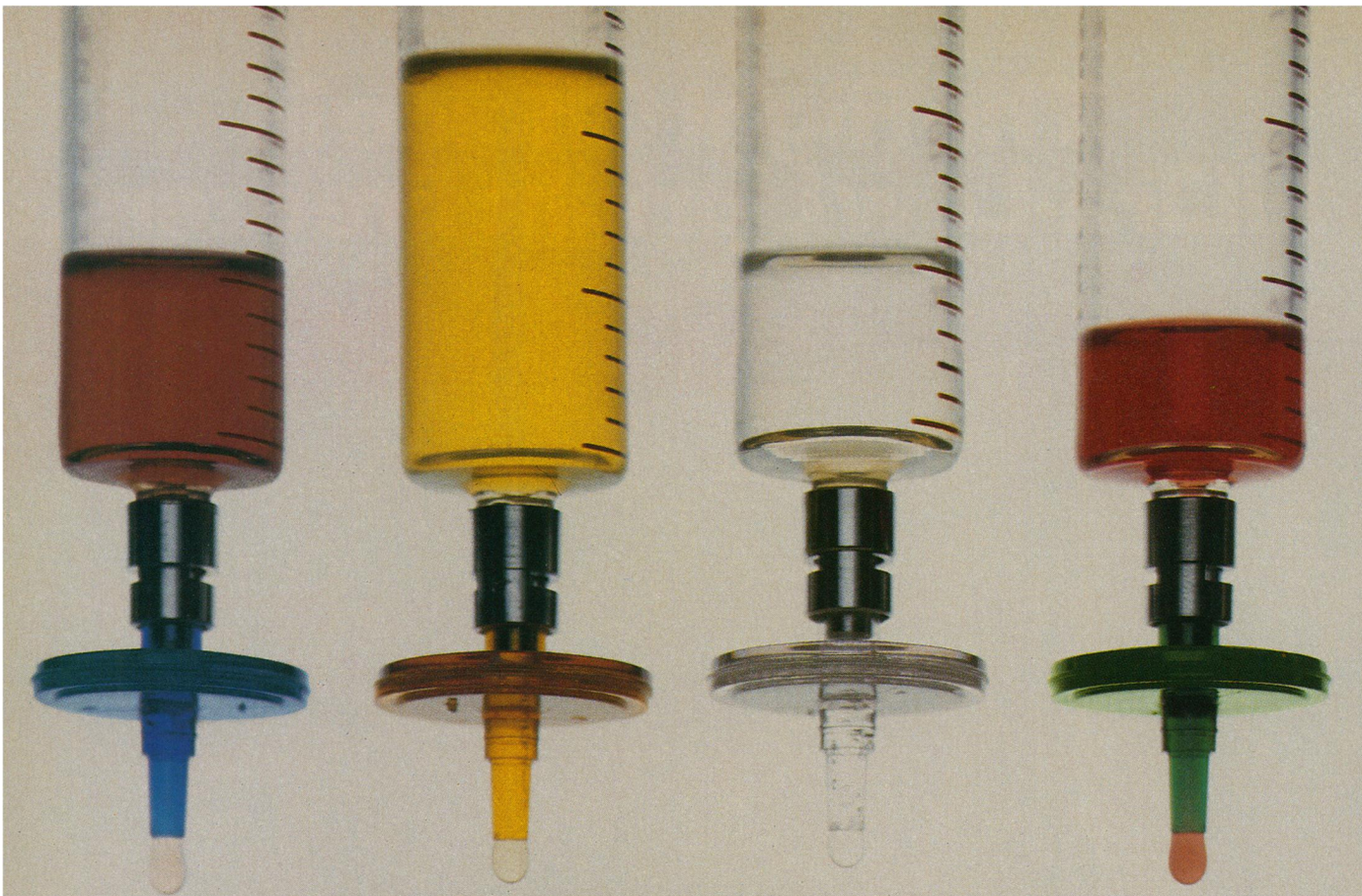

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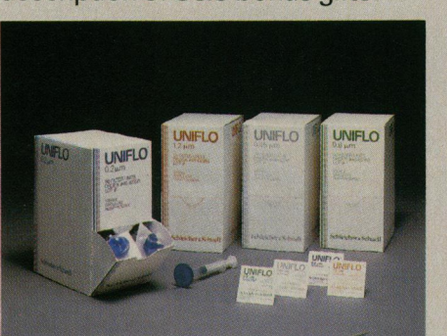

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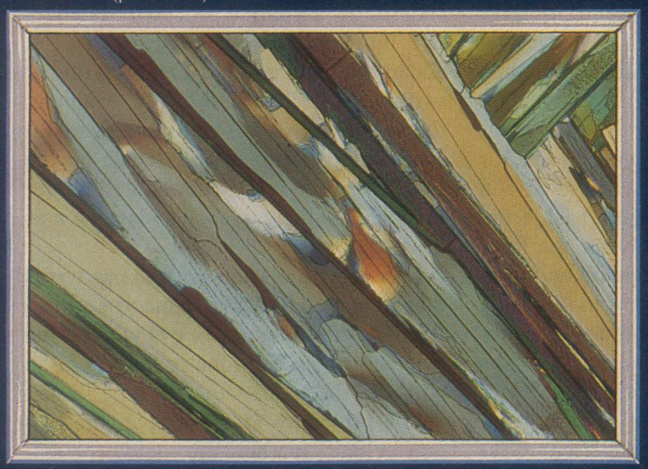

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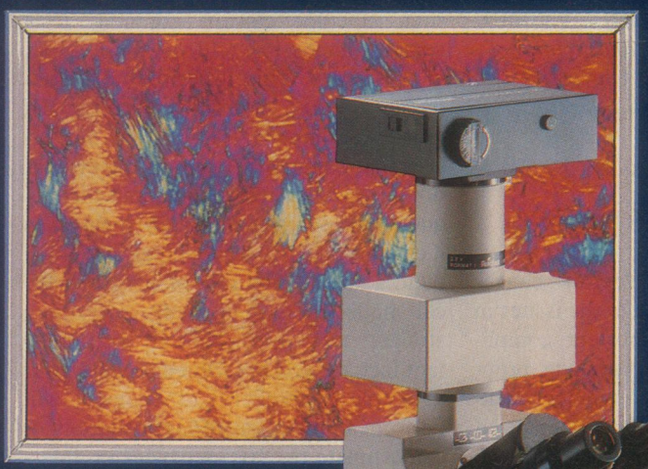

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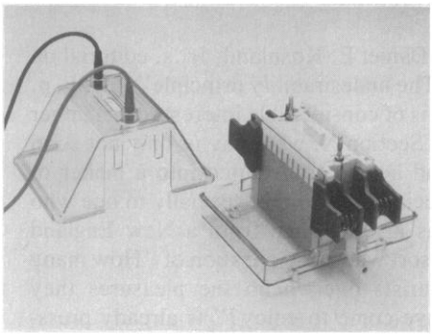
Hoefer's Mighty Small I has become the laboratory standard for doing electrophoresis in the small gel format. Now Hoefer is introducing Mighty Small II, and to complete the system, Mighty Small Transphor, Casting Stand, and Power Supplies.

• **Mighty Small II** is Cool and Fast: It can run two mini-gels, 8 x 10 cm, in 45 minutes. Two mini-gels are produced in two gel sandwiches, held back to back, in a



double-sided pod. The pod consists of two discretely separate upper buffer chambers and a serpentine coolant chamber between. *Cooling is the key feature of the Mighty Small design.* The back plate of each gel sandwich is in contact with the upper buffer and is made of sturdy alumina. Alumina is an excellent heat conductor, 40 times faster than a comparable thickness of glass. It rapidly conducts joule heat away from the gel sandwich into the buffer. A serpentine coolant chamber, permanently sealed between the two buffer chambers, assures further heat dissipation. This excellent cooling system means you can get flat, side by side sample lanes with no smile in 45 minutes.
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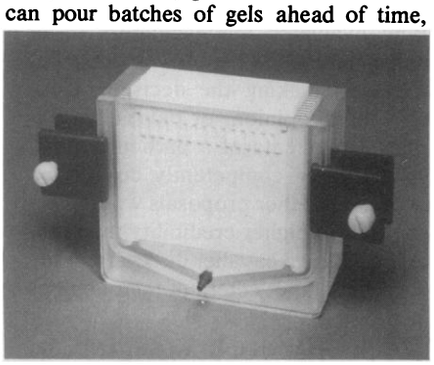
• **The Mighty Small Multiple Gel Caster** enables you to cast 10 gels at a time, 8 x 10 cm, gradient or native. You can pour batches of gels ahead of time, probably a week's supply.



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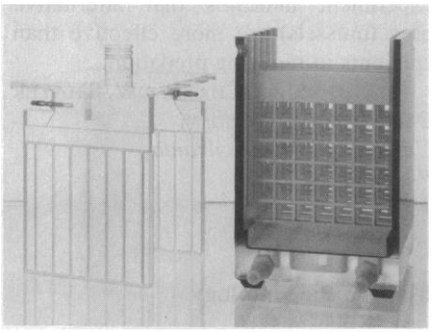

glass-filled polycarbonate cassettes. A serpentine cooling channel milled into the base and covered with alumina assures *excellent cooling.* Under standard transfer conditions the temperature variation will be less than 5°C. Platinum wire, 155 cm of it, strung in 14 opposing strands 1½ cm apart establishes a *uniform electrical field.* Because of its small size, it is possible to use a standard electrophoresis power supply — we recommend the Hoefer PS 500X. Mighty Small Transphor requires only a small amount of buffer, about one liter, another important cost-saving factor.
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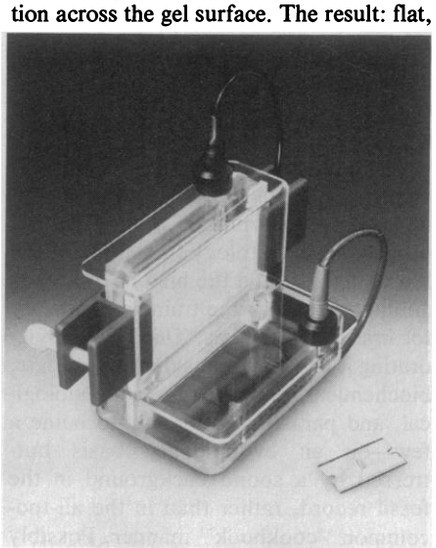

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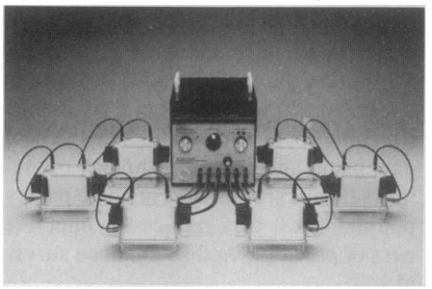

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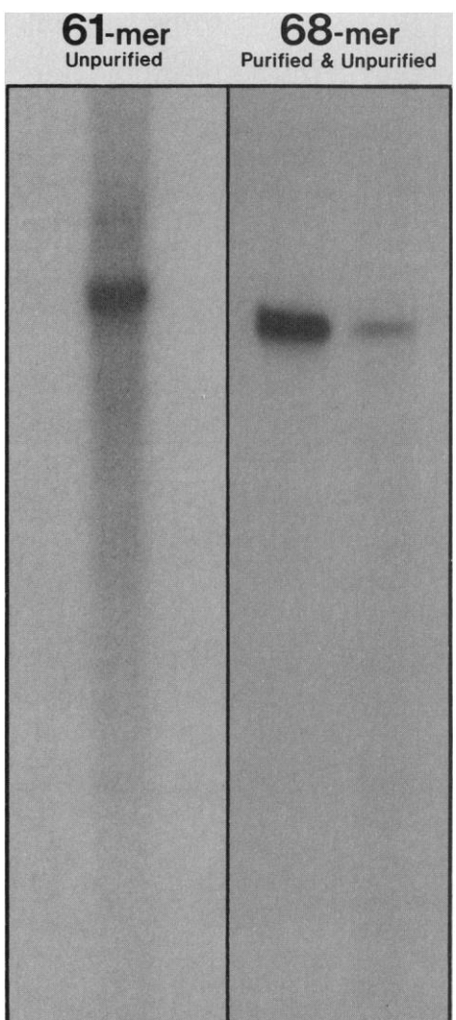

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20 September 1985, Volume 229, Number 4719 SCIENCE

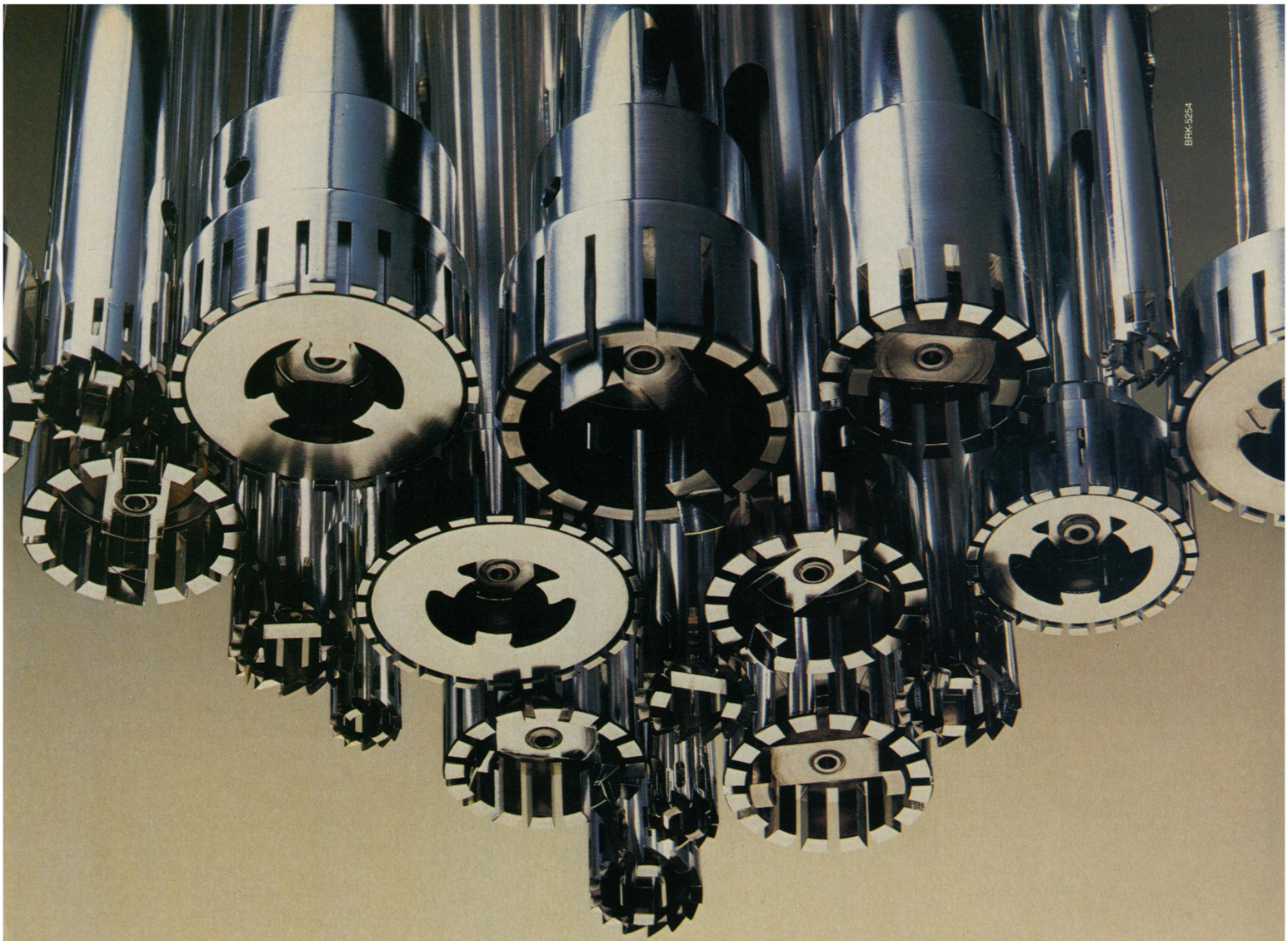
Excursions in Biotechnology

Today's recombinant DNA biotechnology has brought with it the usual concomitants of basic research, applied research, and happy accidents. Some individuals worry that science has blurred the lines of demarcation between universities and industry. Their concern is probably justified. Others worry that many biotechnology companies are in financially shaky condition. They are accurate observers. Still others are euphoric about biotechnology; they await a grand flowering after a rather anemic beginning. Their expectations may also be justified. For the accomplishments of the still infant biotechnology industry, its promises of new procedures and new products, to say nothing of its ever more efficient production of goods, are awesome.

Biotechnology already permeates too many fields to describe them in a definitive fashion; only a few samples can be included in this issue of *Science*. Some of these deal with new areas of research that have great promise but are not yet ready for industrial application. Meyerowitz and Pruitt, for instance, describe studies of the plant *Arabidopsis thaliana*, which may become the *Escherichia coli* of the plant kingdom. Because of its small genome and small amounts of repetitious DNA, the ease of manipulation of this species suggests a future as a favorite experimental material for basic studies in plant development, and indeed of differentiation in general. Morrison describes new approaches to the production of novel antibody molecules, part mouse and part human. Her procedures are giving us insights into basic immunology and are also laying the groundwork for medical applications to autoimmune diseases. Some methods that are useful with small viruses, such as adenoviruses (35 kilobase pairs), are not applicable to large viruses, such as herpesvirus (150 to 250 kilobase pairs). Roizman and Jenkins describe advances in the manipulation of these inconveniently large structures. The procedures will be helpful not only in work with these specific viruses but also in using the viruses as carriers for additional vaccines.

Inasmuch as we wish to improve on nature, mutagenesis is employed with increasing frequency and potency. Botstein and Shortle summarize strategies for producing an enormous range of mutations: localized and random, in context and out of context. Other articles deal with processes closer to the chemical assembly line. Knorr and Sinskey discuss additives, safety, and quality control in food production and the structure-function relation of food materials. Smith, Duncan, and Moir describe procedures to produce the enzyme chymosin (also known as rennin); they used secretion from engineered yeast cells, a procedure in which a fully activable protein is formed in contrast to the insoluble inactivable protein that is formed if the enzyme is made in the cytoplasm. Thus, appropriate "ticketing" of a protein is crucial to its successful production. Perhaps the most interesting feature of each of these papers is the demonstration that the line between basic and applied research is almost impossible to draw. A basic finding leads to a new industrial procedure; a difficulty in applied technology requires a reevaluation of basic understanding.

Finally Dibner discusses the Japanese challenge, perhaps a necessary comparison for any technology article these days. The efficiency of the Japanese in organizing industry for the exploitation of fundamental research can elicit only admiration. Let me cite just one figure: the Japanese biotechnology industry introduced six times as many drugs per dollar spent on research and development as did comparable U.S. companies. Those in the United States who read this and the recent news items describing increasingly bureaucratic procedures for control of recombinant DNA in this country (News and Comment, 23 August, p. 736) may find it hard to hold back tears. We hope they do so, because the scientific frontiers that are being explored are so fascinating that making money may become incidental.—DANIEL E. KOSHLAND, JR.



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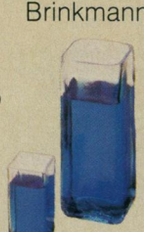

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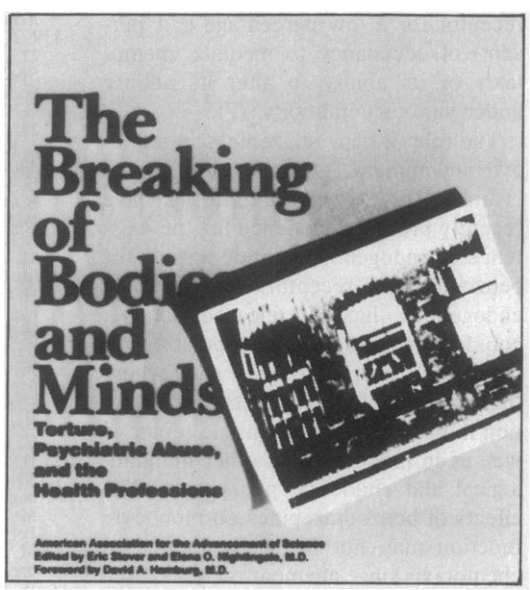
The Breaking of Bodies and Minds

Torture, Psychiatric Abuse, and the Health Professions

A documentation of systematic use and effects of physical and mental torture throughout the world

Edited by Eric Stover and Elena O. Nightingale

With a Foreword by David A. Hamburg



This eye-opening book brings together for the first time writings on the role of medical personnel in cases of torture and psychiatric abuse. Through analyses and case histories, psychiatrists and other health care professionals, political scientists, ethicists, and other writers discuss the systematic use and effects of physical and mental torture in the Soviet Union, Latin America, and other parts of the world.

The book also details the complicity of an alarming number of medical personnel in torture and psychiatric abuse and examines the ways in which governments use a medical rationale to seek legitimacy for human destruction. Finally, it describes efforts by medical and other associations both to combat offensive practices and treat victims.

Contents

Part I Torture

Torture and the Ethics of Medicine
Albert R. Jonsen and Leonard Sagan

Victims of Torture: Two Testimonies
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The World of Soviet Psychiatry
Walter Reich

A Response to Psychiatric Abuse
Paul Chodoff and Ellen Mercer

Toward the Prevention of Torture and Psychiatric Abuse
Elena O. Nightingale and Eric Stover

The Breaking of Bodies and Minds is important reading for anyone concerned with the preservation of basic human rights.

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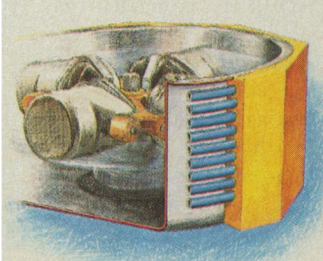

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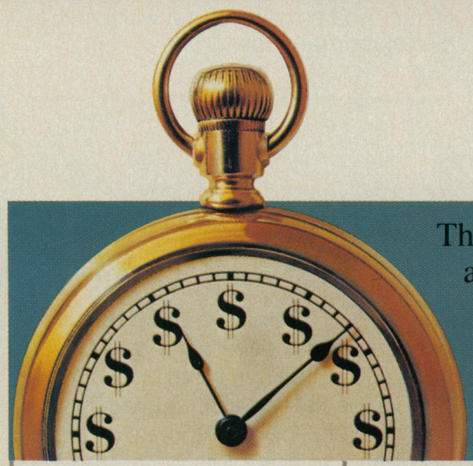

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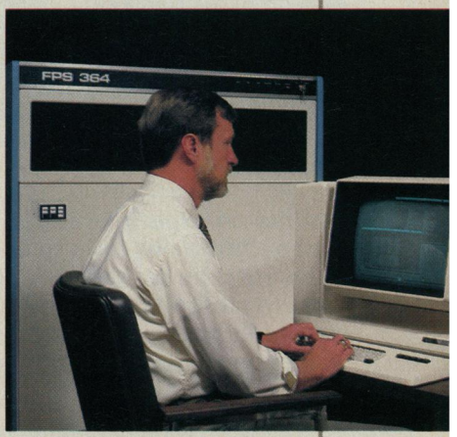

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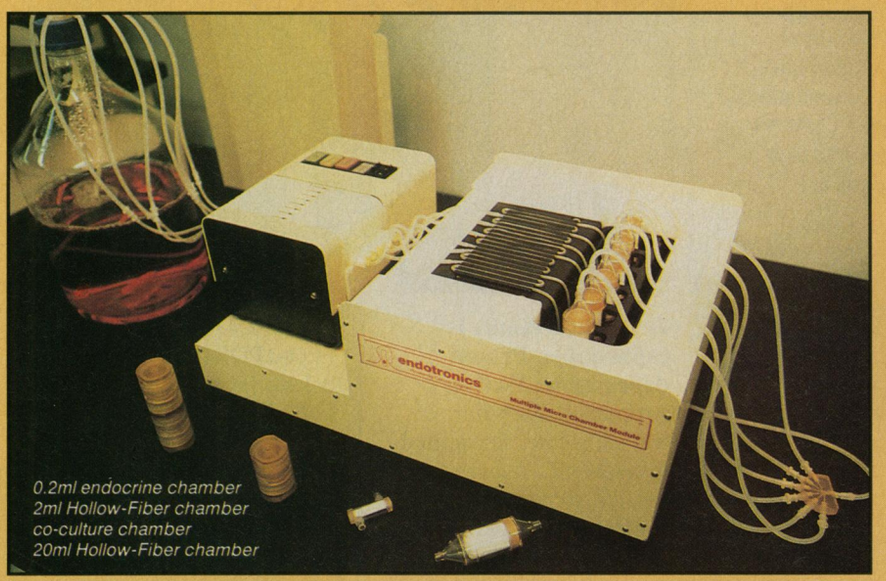

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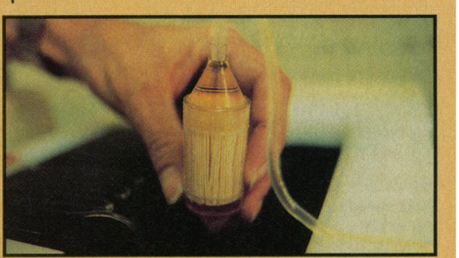

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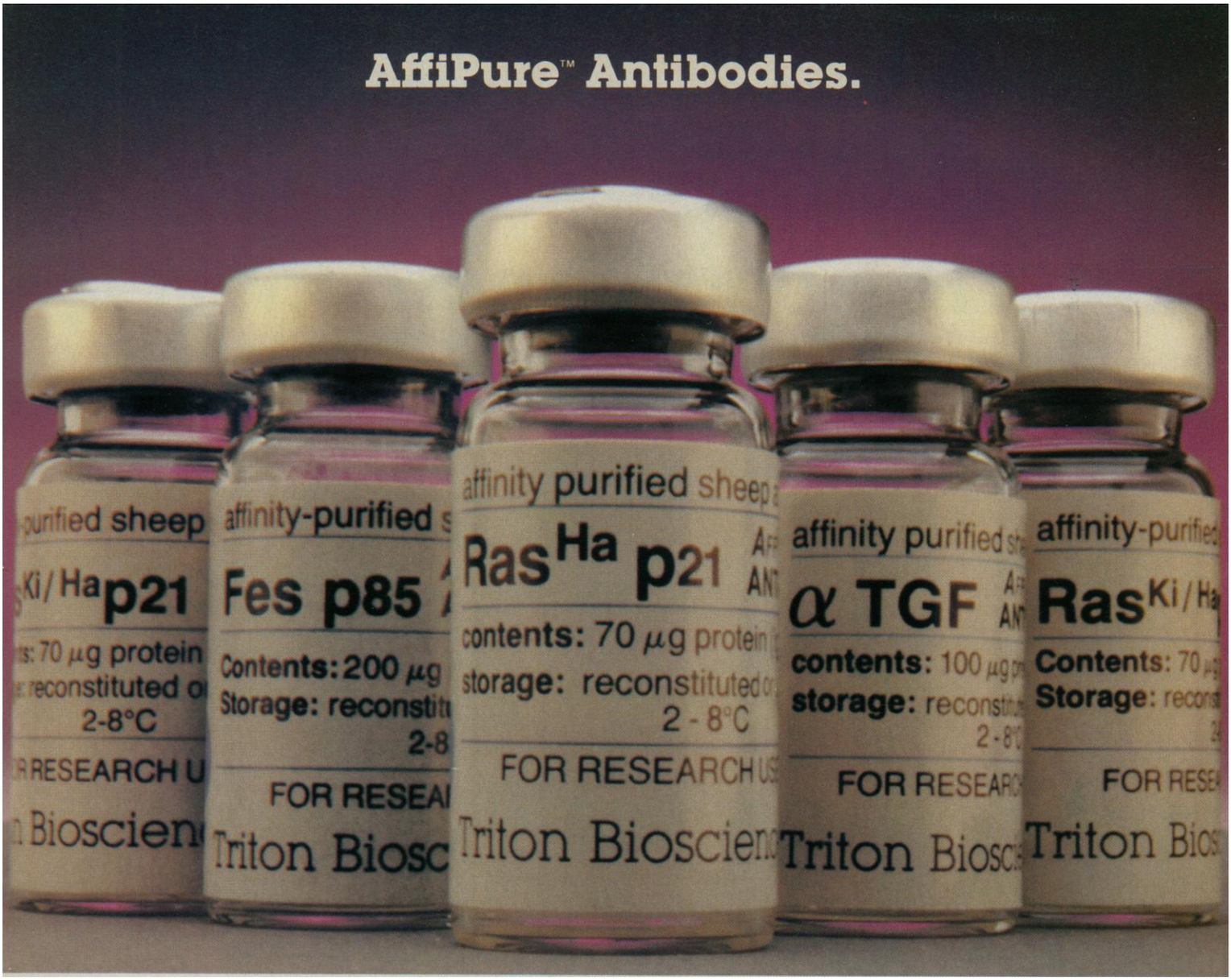

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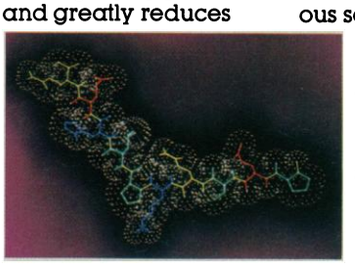

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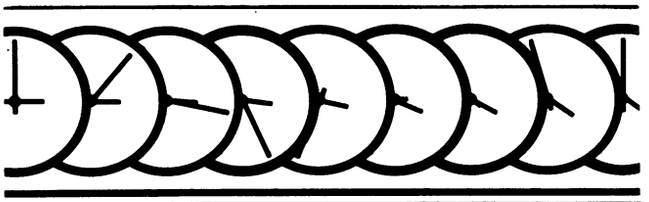

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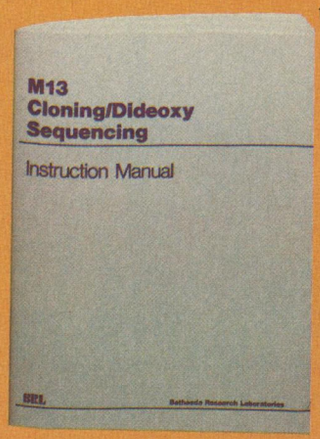

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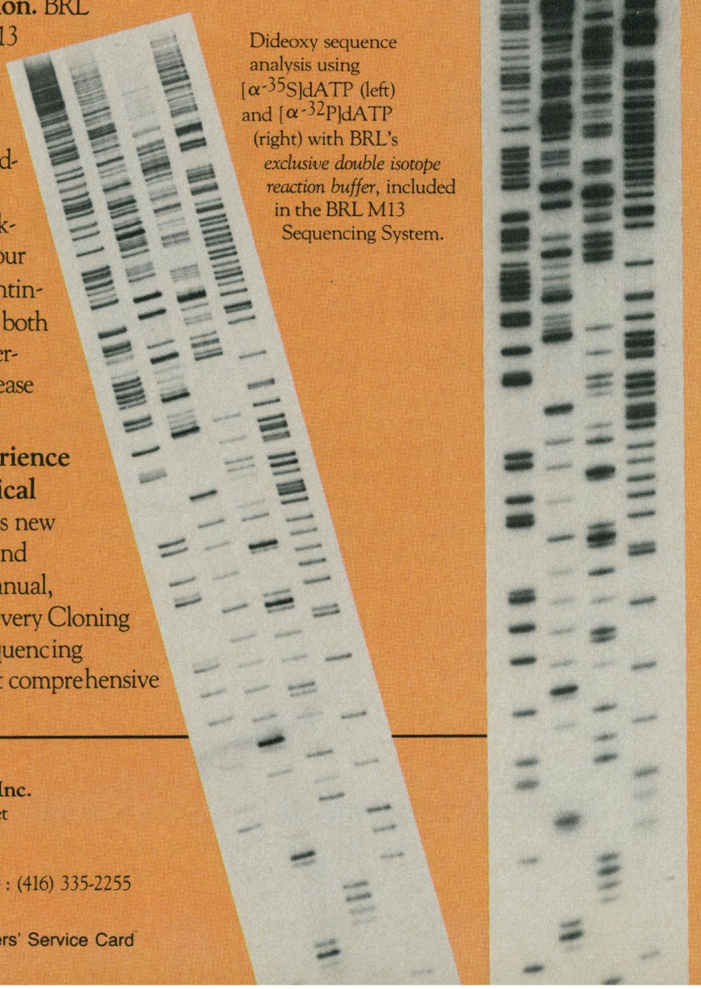

Dideoxy sequence analysis using [α-^{35}S]dATP (left) and [α-^{32}P]dATP (right) with BRL's *exclusive double isotope reaction buffer*, included in the BRL M13 Sequencing System.

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