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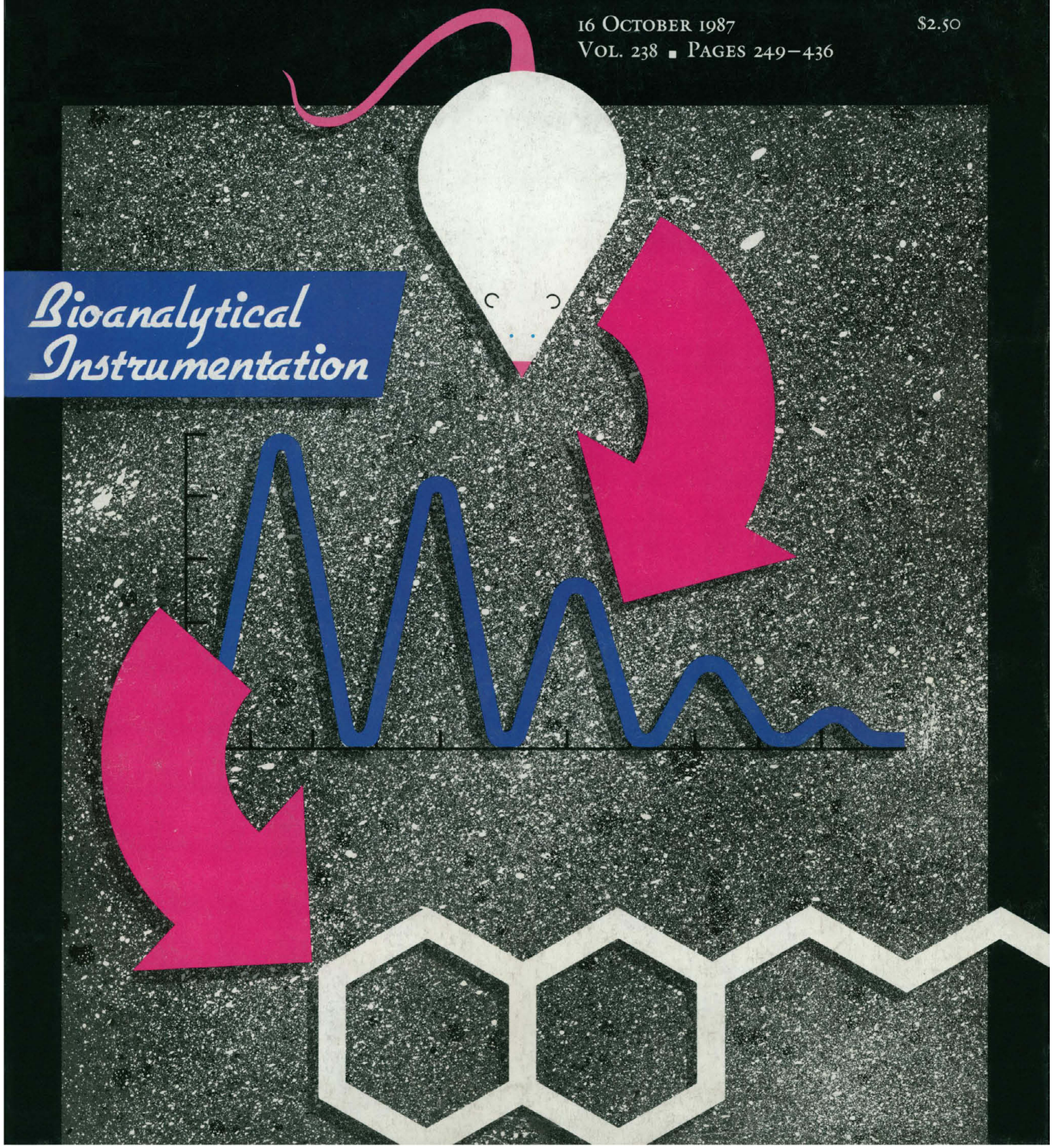

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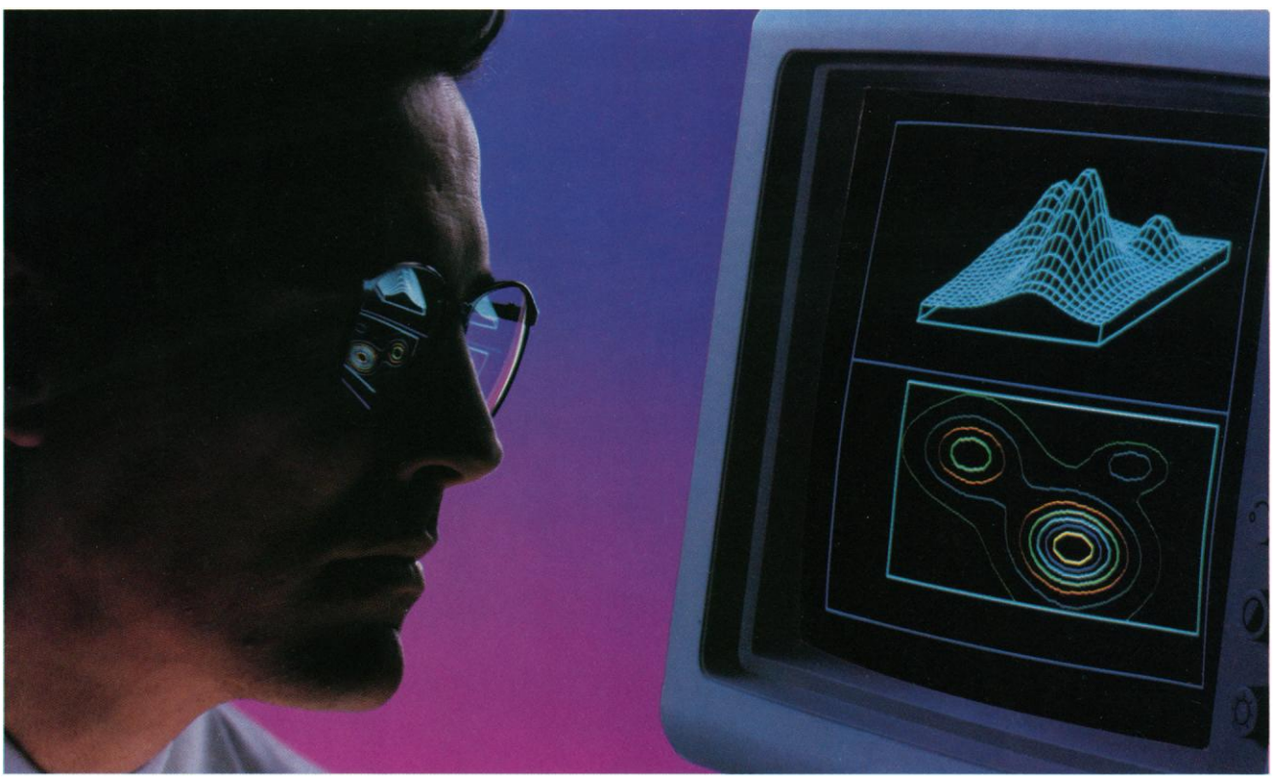

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COVER Molecular structure can be inferred from spectral analysis of biological samples. Our understanding of structure and function has become increasingly fundamental, in part, because of advances in bioanalytical instrumentation. See page 305. [Cover design by Sharon Wolfgang, Washington, D.C.]

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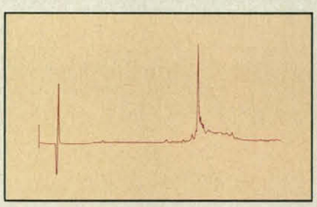

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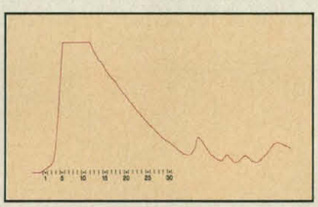

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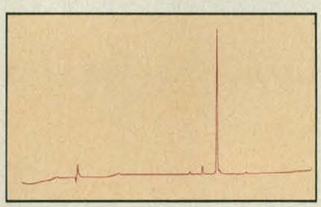

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This Week in
SCIENCE

Mapping the brain's magnetic fields

ABNORMAL electric discharges from neurons in the cortex of the brain accompany seizures in epileptic patients; these discharges generate magnetic fields that can be detected outside the brain (the skull and scalp do not interfere with the fields) by magnetoencephalography (MEG) (page 329). For some (an estimated 50,000 in the United States) patients with epilepsy, surgical removal of epileptogenic subregions could provide freedom from seizures; this requires exact identification of where the unusual neuronal discharges are originating in the brain. Rose *et al.* discuss the components of MEG technology, how environmental magnetic fields are canceled from measurements (brain fields are about one-billionth the size of the earth's magnetic field), how data are collected and projected into three-dimensional maps, how these data both compare and can be coordinated with data from other noninvasive (like MEG) and invasive techniques, and expected improvements in the technology that should make it increasingly useful in the future. Other papers in this special issue on bioanalytical instrumentation appear on pages 305 to 335 and are discussed in Abelson's editorial (page 257) and Roberts' Research News feature (page 271).

Superconductor microstructure

THE appearance at close range of one of the new superconductors—a film of oxides of three metallic substances (yttrium, copper, and barium) deposited on a strontium titanate crystal (the substrate)—is described by Chaudhari *et al.* (page 342). The microstructure of the superconducting film was studied by x-ray diffraction methods and by transmission electron microscopy. The film was aligned with the substrate in a true epitaxy; that is, the crystal structures of film and substrate are the same and the interface between them is nearly flat atomically. Within the system there were many precipitates of yttrium oxides distributed in random orientations and fewer precipitates of copper oxides distributed nonrandomly. The superconducting layer contained numerous twin lattice structures, mirror images of each other. Differences in the microstructure of the superconducting film with that of a polycrystalline film provide clues to the features of the superconductor that contribute to its ability to carry large currents.

Cycling cytotoxicity of T cells

ENVIRONMENTAL signals can affect the ability of cytotoxic T lymphocytes (CTLs) to lyse target cells (page 344). CTLs kill target cells after exposure to target-cell antigens. Shih and Truitt show that exposure of lytic cells to interleukin-2 (IL-2) halts the killing; in its absence, CTLs reexpress their lytic activity. The cells can cycle back and forth many times between their lytic and nonlytic phenotypes. Although IL-2 inhibits lytic activity, it continues to promote clonal proliferation. This in vitro model may illustrate what happens in the body when this subset of cells is alternately and intermittently exposed to antigen, IL-2, and perhaps other up- and down-regulating substances. It may also explain why lytic activity sometimes cannot be demonstrated in vitro for mixed cell populations or for cells grown in the presence of IL-2 producers.

Calcium-independent transmitter release

RELEASE of neurotransmitters from nerve cells often is dependent upon the availability of calcium ions (page 350). However, it is also possible for a neurotransmitter to be released without calcium acting as a mediator. Schwartz shows that release of the neurotransmitter gamma-aminobutyric acid (GABA) from catfish retinal horizontal cells occurs directly in response to depolarization of the cell. The release of GABA in cell cultures was detected by a second cell type, the bipolar cell from the goldfish retina; exposure of this cell to GABA opens chloride ion channels, negative ions flow into the cell, and a large positive outward current is produced. Measurement of the outward currents of the bipolar cell and measurement of the membrane voltage of the horizontal cell showed that the two "communicated" through GABA under calcium-independent conditions. This type of neurotransmitter release may operate in other parts of the brain as well since most synapses in the brain use GABA or glutamate as transmitters.

Humans and African apes

CHIMPANZEES and humans may be more closely related to each other than either is to the gorillas (page 369). Thus, shared attributes of chimpanzees and gorillas (such as their ability to walk on their knuckles) are possibly primitive features lost by humans as they evolved. The phylogenetic relations of these primates were drawn from new sequence data of the psi-eta region of the beta globin gene. To known sequence data of the ψη locus, Miyamoto *et al.* added the sequences of regions flanking this locus, thereby expanding the sequenced stretch to 7.1 kilobase pairs. Overall, there are few differences (1.6 to 2.1%) among all sequences compared for these three primates that are believed to have branched from each other 5 to 10 million years ago. The differences found indicate that nucleotide evolution has not occurred at the same rate in all (the human evolutionary rate has been the slowest), and this further complicates determinations of how long species have been independently evolving. Lewin explains how these and other molecular data lead to a different conclusion than do anatomic data about who is whose closest cousin (page 273).

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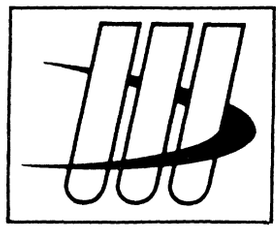

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Instrumentation and Equipment

The scientific enterprise continues to develop new, rewarding frontiers to explore. A key factor is exploitation of opportunities that are created by instrumentation and equipment. This issue of *Science* presents a sample of such opportunities.

Synchrotrons capable of producing ultraviolet radiation and x-rays have been in operation for some years. However, their numbers have increased both here and abroad. In addition their outputs of radiation have been greatly improved by installation of periodic magnetic insertion devices called wigglers and undulators. The flux of energy per unit area of synchrotron radiation exceeds that of older conventional sources by factors of 10^6 to 10^8. An arbitrary portion of the spectrum can be sharply defined and used for particular experiments. An enormous number of studies that previously were impractical can now be performed. Gruner discusses the feasibility of performing time-resolved x-ray diffraction of biological materials. Many biological processes occur on a millisecond time scale, and these are now close to being accessible to investigation.

Prewitt and colleagues list a large number of experiments that have been performed on both inorganic and organic materials. As crystallographers they are pleased with an ability to determine structure of crystals having dimensions on the order of 10 micrometers. They also mention experiments that determine structure of surfaces both of inorganics and organics. In many—or even most—solids the surface structure differs from that of the bulk. Ability to obtain such information is of increasing potential economic importance. Molecular beam epitaxy is now producing a large number of new types of layered materials. Another application is in macromolecular crystallography. The small size of the x-ray beam and its collimation allow possible resolution of reflection maxima from viruses with unit cells as large as 1000 angstroms (mass of about 10,000,000 daltons).

One of the most exciting opportunities of our times is the sequencing of the human genome. It will be an enormous task. But it will be done. Were the techniques of yesteryear employed, the cost would be many billions of dollars, and many years—perhaps decades—would be required. However, human ingenuity is being applied to make the task easier and less costly. In this issue Gray and colleagues describe their work on chromosome purification and, in a research article, Prober and colleagues present a new system for rapid DNA sequencing. Chromosomes can be isolated from cells, stained with a DNA-specific fluorescent dye, classified by flow cytometry, and purified by flow sorting. With newly developed high-speed sorting, microgram quantities of some individual chromosomes having a purity of 90 percent can be isolated in a day or less. The authors suggest that the speed of the separation process might eventually be improved by an order of magnitude.

In the new DNA sequencing method, fluorescent molecules are added to DNA fragments by enzymatic chain extension reactions. The labeled fragments are separated by polyacrylamide gel electrophoresis and identified as they migrate past a fluorescent detection system. The wavelength of the fluorescent radiation differs for each terminal base. Sensitivity of detection is very good. After an initial period of electrophoresis the sequencer is capable of determining 50 bases per hour per lane. Twelve lanes can be used.

Proteins for therapeutic applications are major crude products of recombinant DNA technology. To be safe for human use, the proteins must be highly purified. A major means of achieving this is the use of liquid chromatography. The crucial factors in such separations are interactions between the proteins and the column packing. Regnier has analyzed the interactions that occur when various types of packing are used. He points out that only a fraction of those amino acid residues at or near the exterior surface of a three-dimensional protein can interact with a particular type of chromatographic matrix.

Electroencephalography is now being supplemented by an increasingly useful magnetoencephalography (MEG). Rose, Smith, and Sato describe use of MEG in determining the location of epileptic discharges. Sensitive superconducting quantum interference device (SQUID) sensors can detect the tiny magnetic fields that are produced when the electric discharges occur. With information derived from a number of detectors the location of the source of the discharge can be determined. The procedure holds promise of becoming a valuable noninvasive diagnostic aid.—PHILIP H. ABELSON

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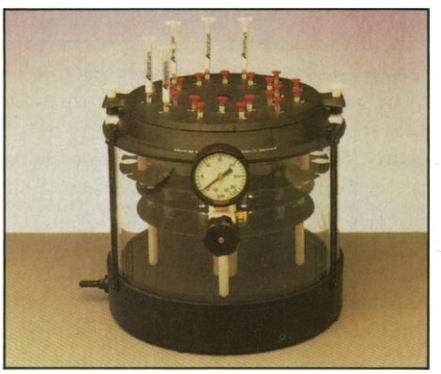

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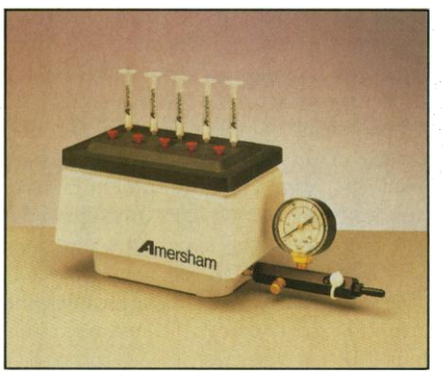

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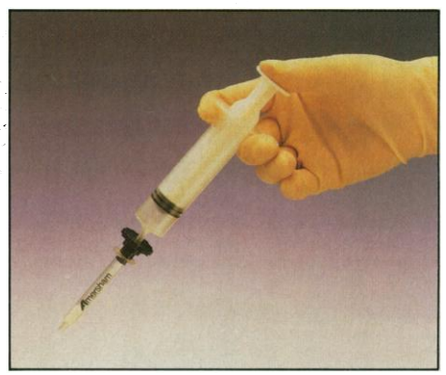

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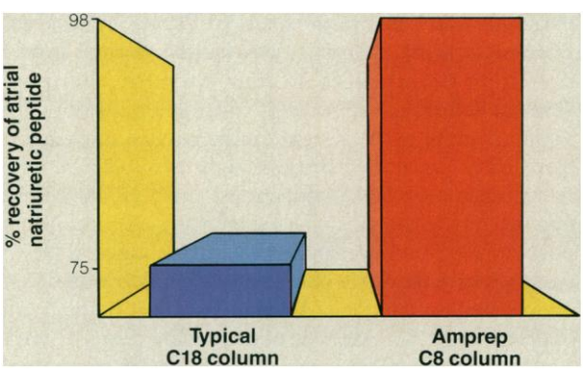

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Response: Shapiro, Evans, and Shapiro point out complexity in the construct of control, correctly noting that there are different types of control, and they argue for conceptual and empirical rigor. While there is undoubtedly need for clarity, I am not confident that the several distinctions among types of control that Shapiro *et al.* propose have been shown to have significant heuristic value in generating research questions. One must be careful not to overemphasize the importance of differentiation of terms and concepts when indeed there may be fewer, rather than more, underlying constructs in this area. This remains an empirical question, however, and one that most urgently needs to be addressed.

Shapiro *et al.* comment on the distinction between control-enhancing interventions offered by the environment and *self*-control strategies. They discuss impairment of self control as an essential feature of many clinical problems, for example, obesity, bulimia, and alcoholism, and cite weak results from the use of self-management strategies in these areas. These data are then used to imply that self-control interventions may not work. One must be careful, however, to separate studies of clinical populations from studies of normative samples, for example, the aged or children, who may suffer an impairment in control because of developmental stage and environmental change. In addition, many clinical disorders have been intractable after self-control interventions, not because of problems with self-management as an intervention strategy, but because they often have a large genetic contribution and involve a heavy burden of biological change once the disorder is initiated (*1*). Control-relevant intervention may not work where biological and genetic factors influence the disorder. Indeed, I have argued that teaching self-management strategies in these domains can convey an implicit message of personal blame for the cause of the disorder, leading to feelings of shame and reduced ability to exercise control (*2*).

The study of control in human populations is an exciting and timely one, especially with increasing demonstrations of potential health significance. Like Shapiro *et al.*, I believe strongly that the time has come to understand the underlying similarities and dissimilarities among the various constructs that have been used in the control literature. These are not context-free evaluations, however; setting accounts for a substantial portion of the variance when studying the construct of control. As Bandura (*3*) has suggested, individuals with a high degree of self-efficacy still can recognize when there are no response-outcome contingencies, that is when events in the environment are uncontrollable by anyone, despite the individual's own sense of personal mastery.

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Comparison of High Schools

Luther B. Otto's review (11 Sept., p. 1357) of *Public and Private High Schools: The Impact of Communities* by James S. Coleman and Thomas Hoffer does not stress a problem presented by overall comparisons of public with private and Roman Catholic high schools. It is easy to make a case for private and Roman Catholic schools if one does not take into consideration the superb records of selected public schools.

The public high schools welcome students of all sorts to the extent that the students can meet current standards of admission. Public schools are required to be as inclusive as possible. The students in public high schools in such choice areas as Short Hills or Madison, New Jersey, however, have records of accomplishment that go well beyond those of students in the local Roman Catholic schools.

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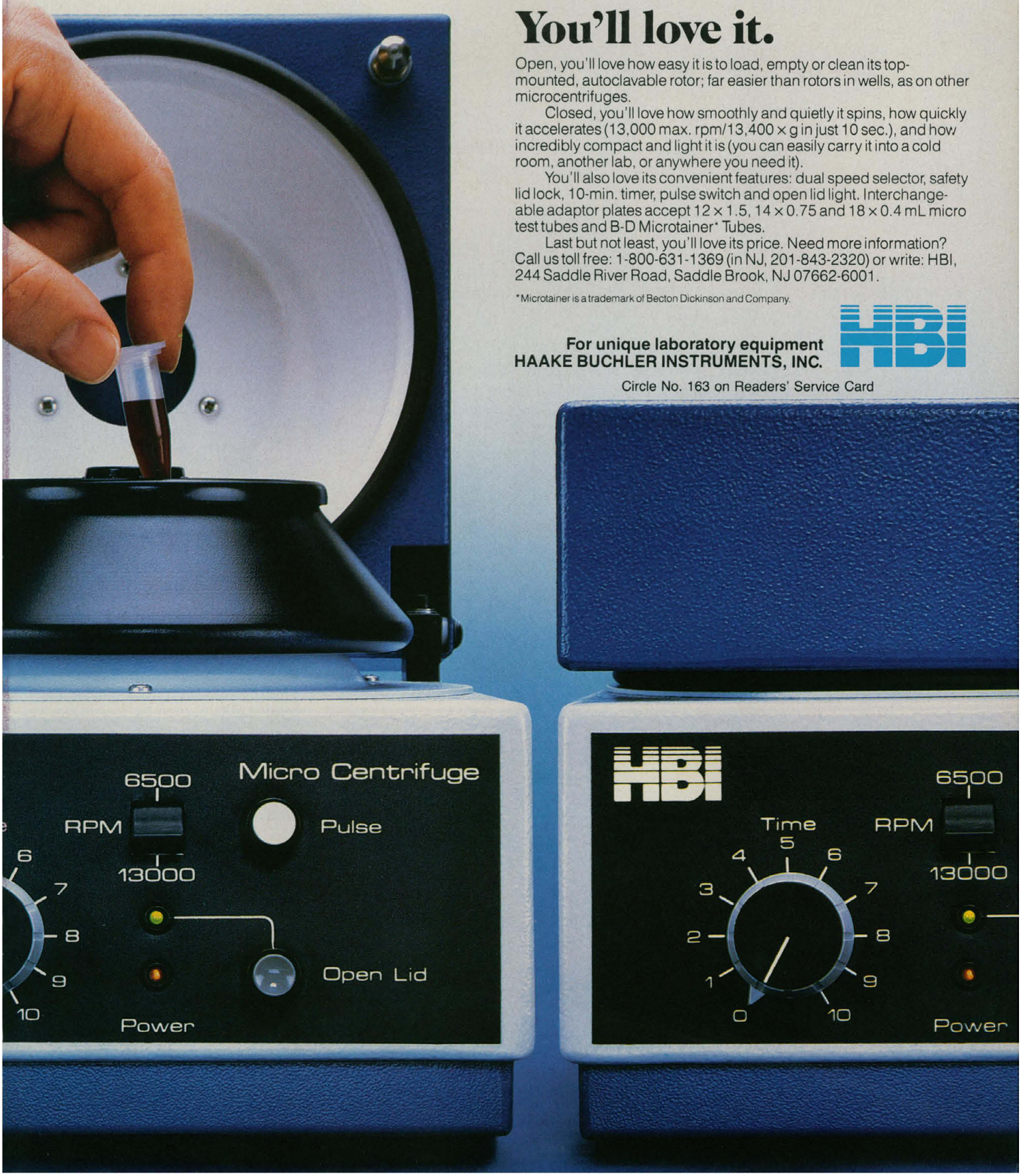

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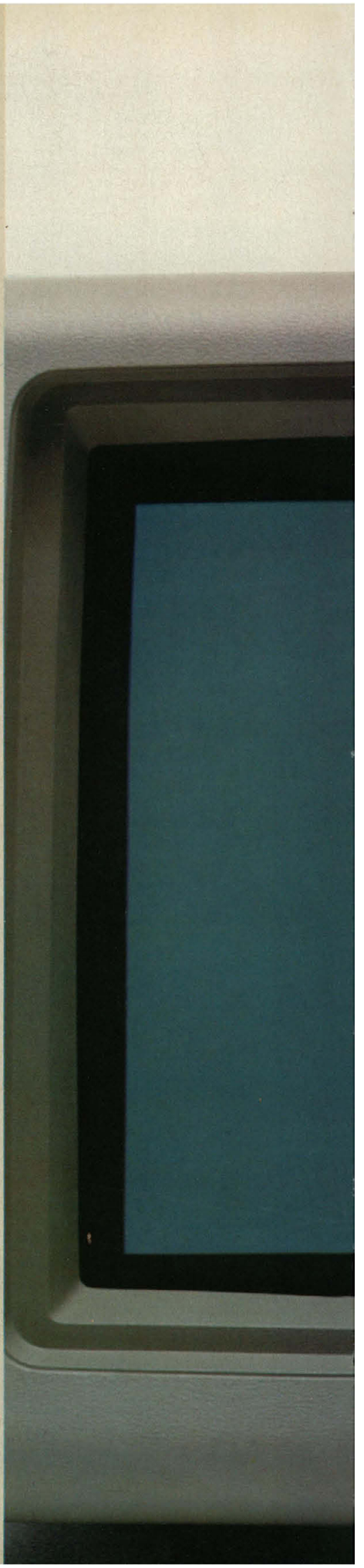

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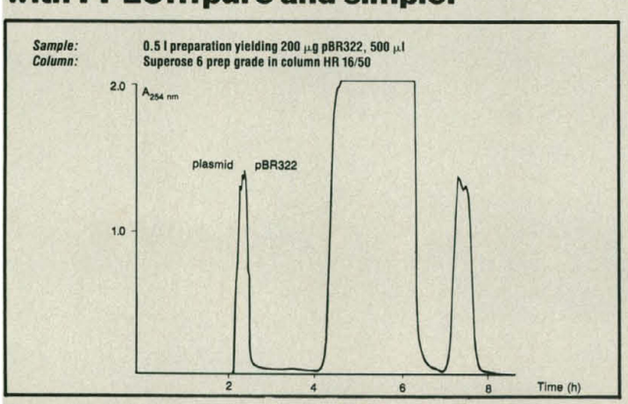

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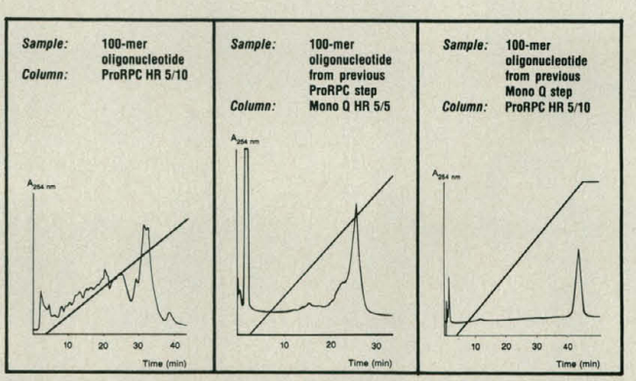

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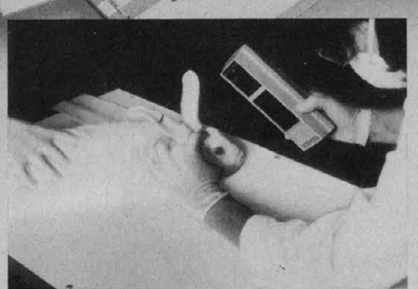

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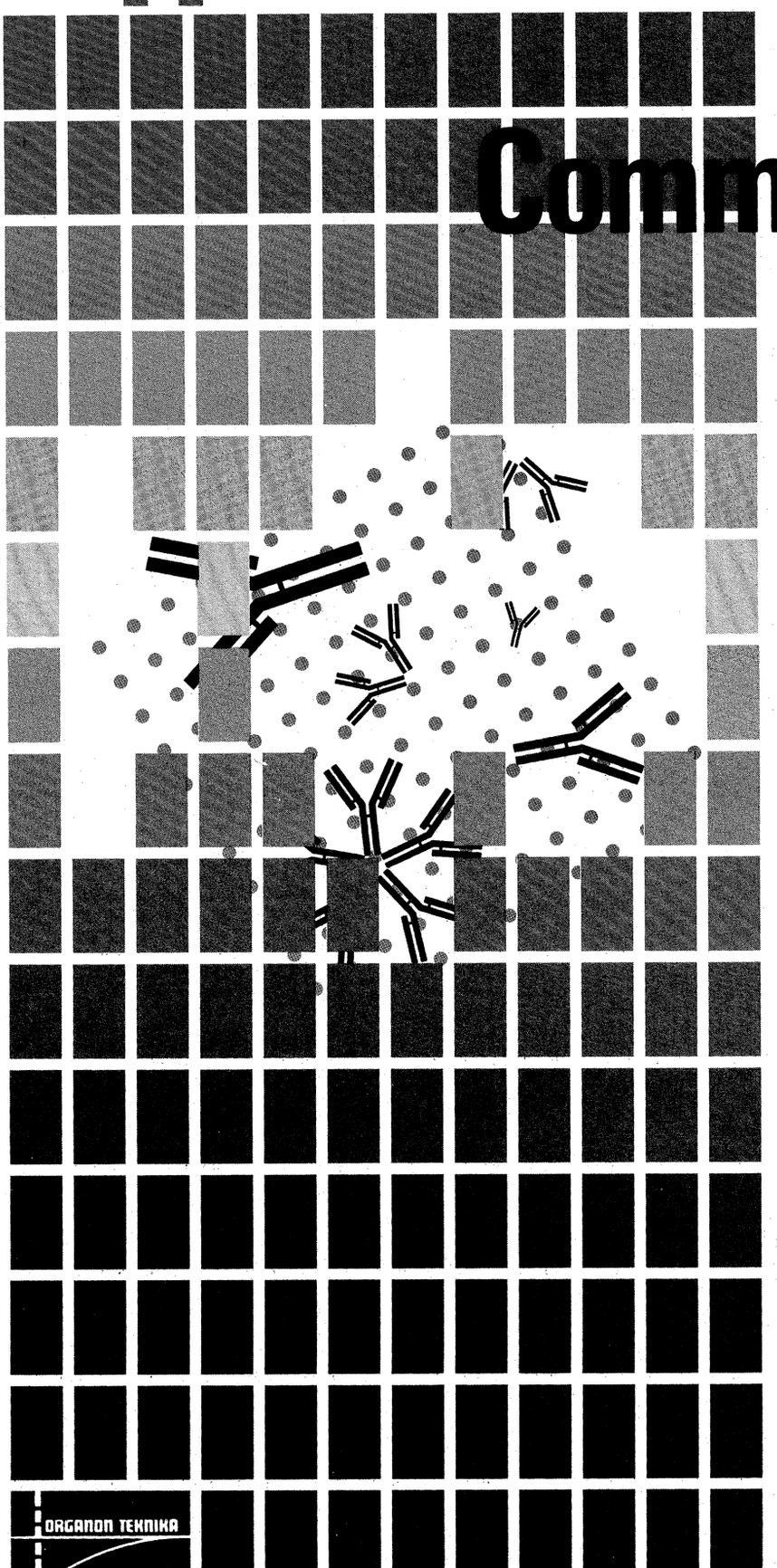

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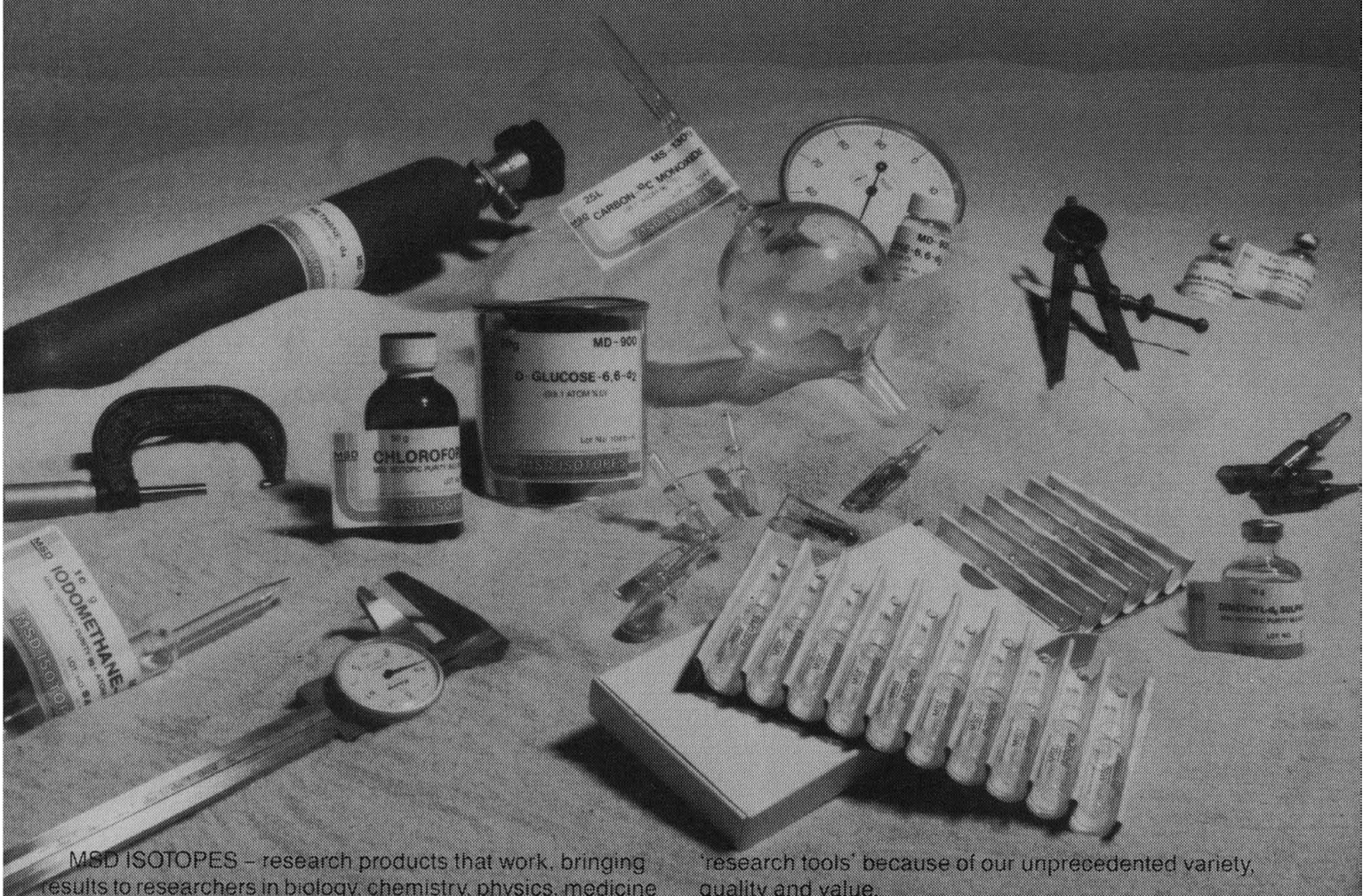

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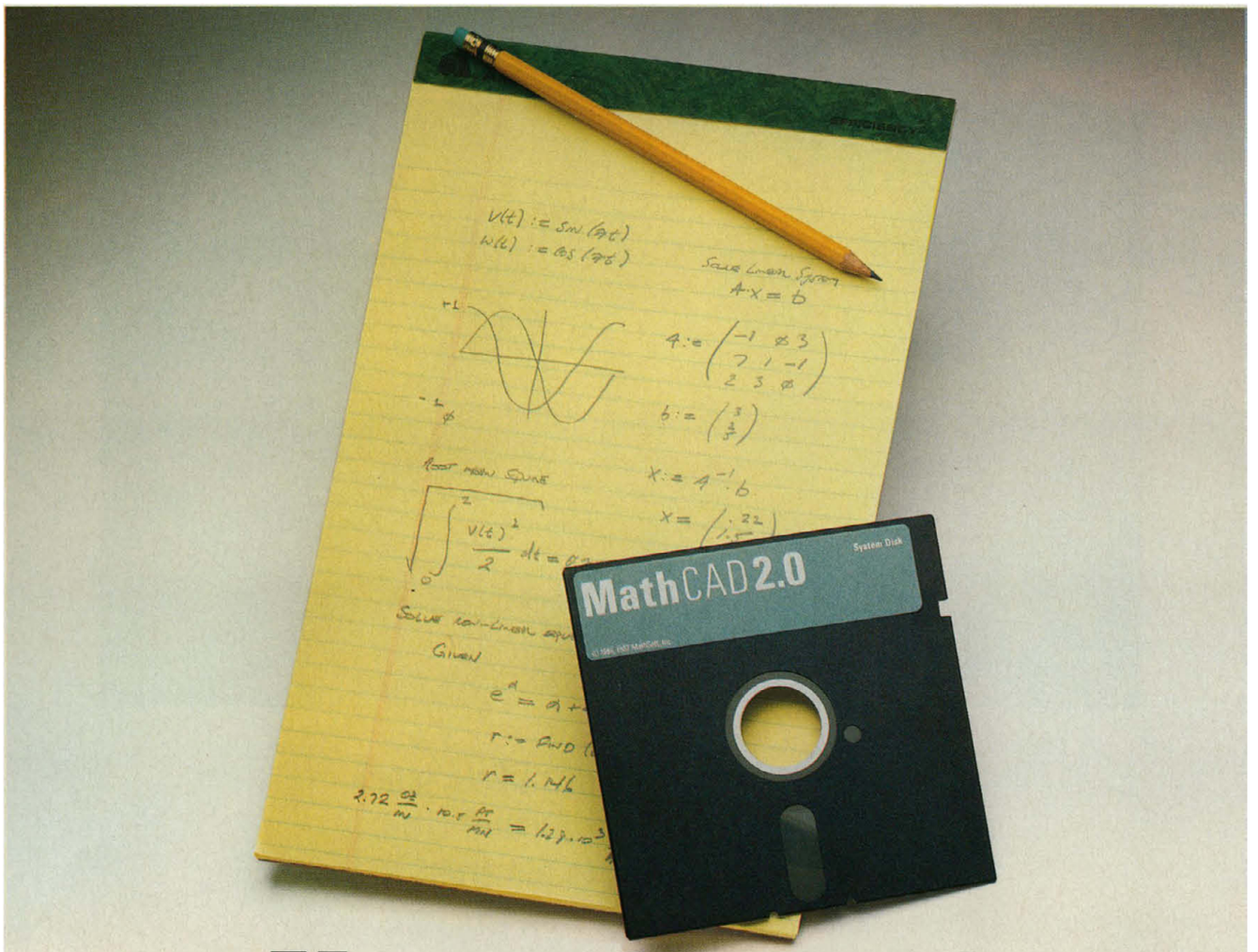

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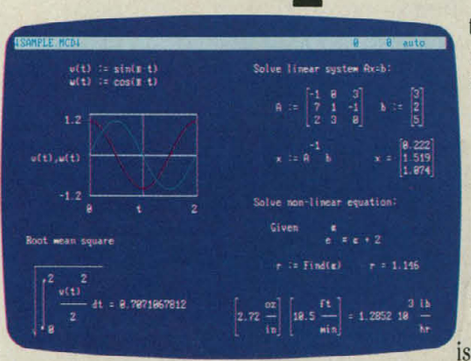

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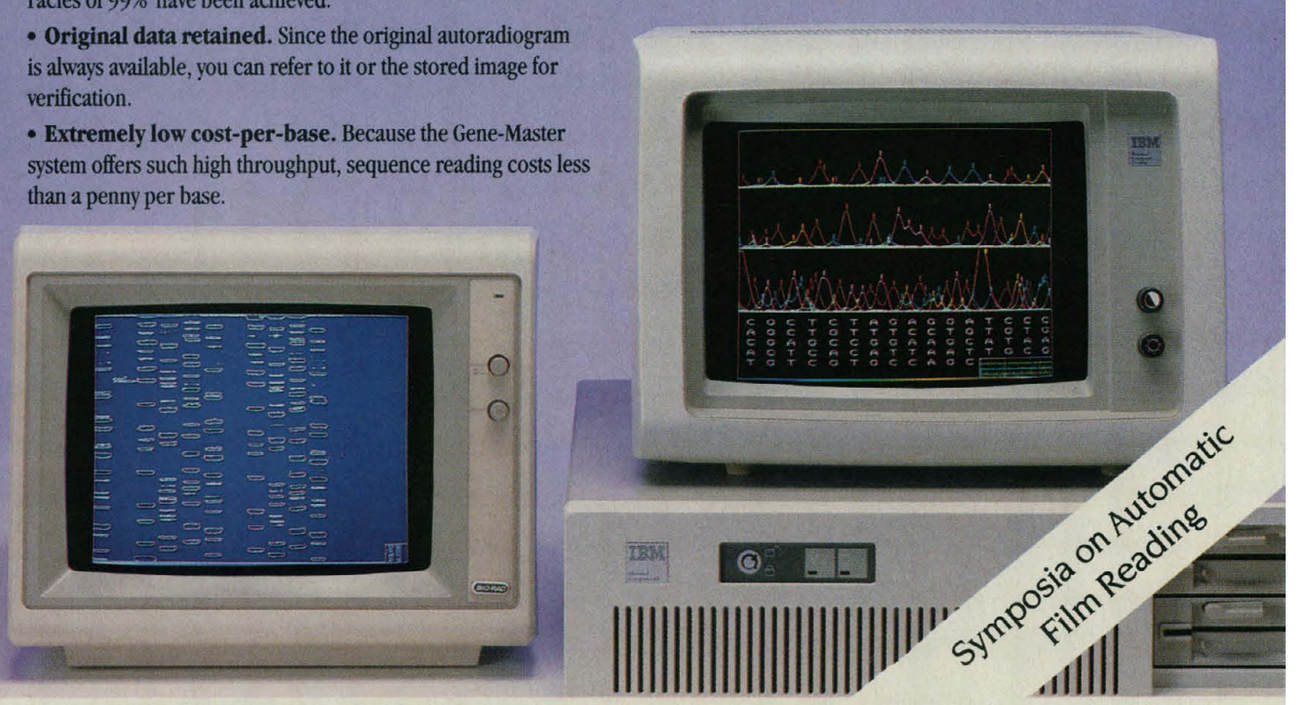
1. Elder, J.K., Green, D.K., and Southern, E.M. (1986). *Nuc. Acids Res.* **14**:417-424.



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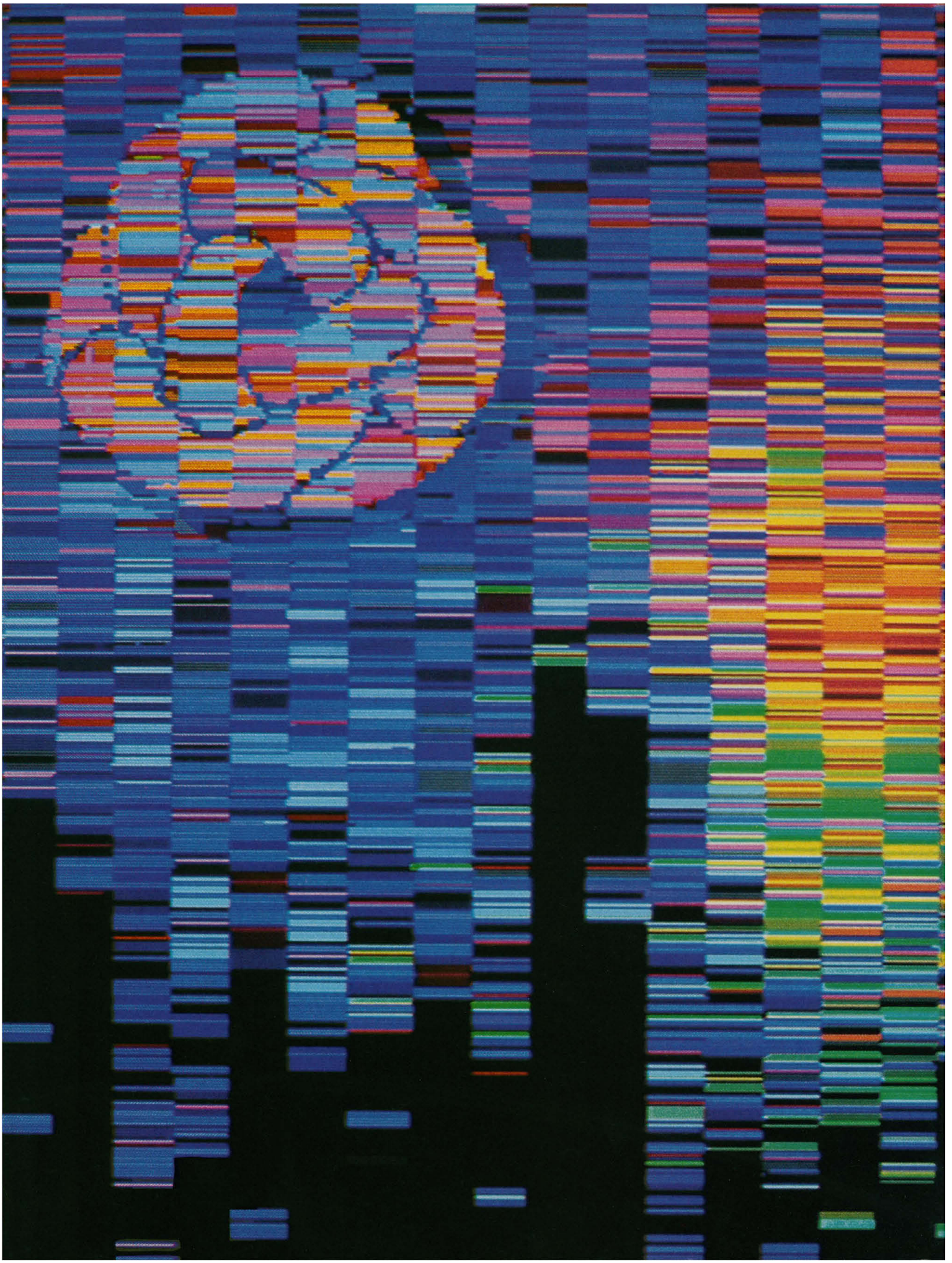

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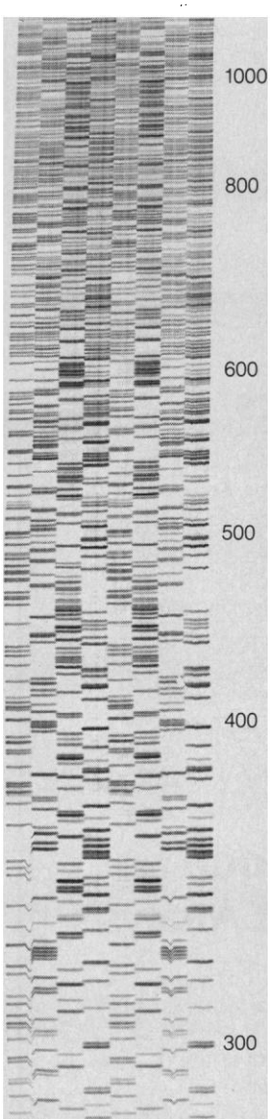

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1. Tabor, S. and Richardson, C.C., *Proc. Nat. Acad. Sci., USA* **84, No. 14,** 4767-4771 (1987).

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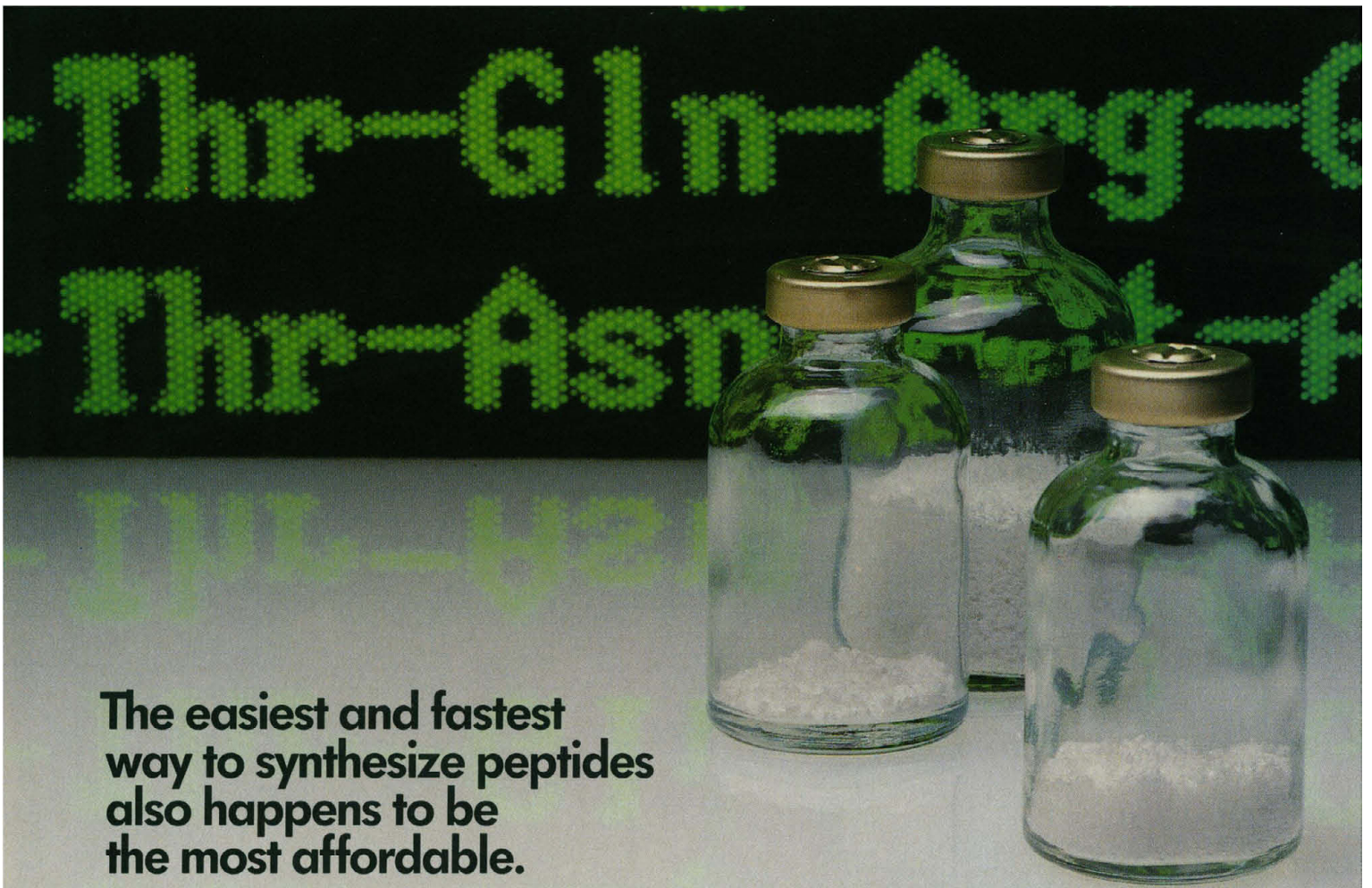

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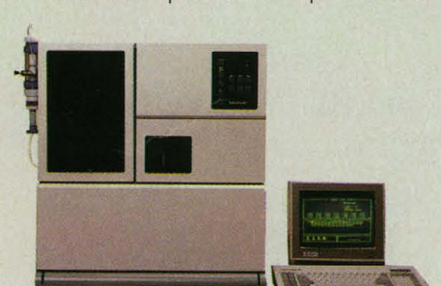

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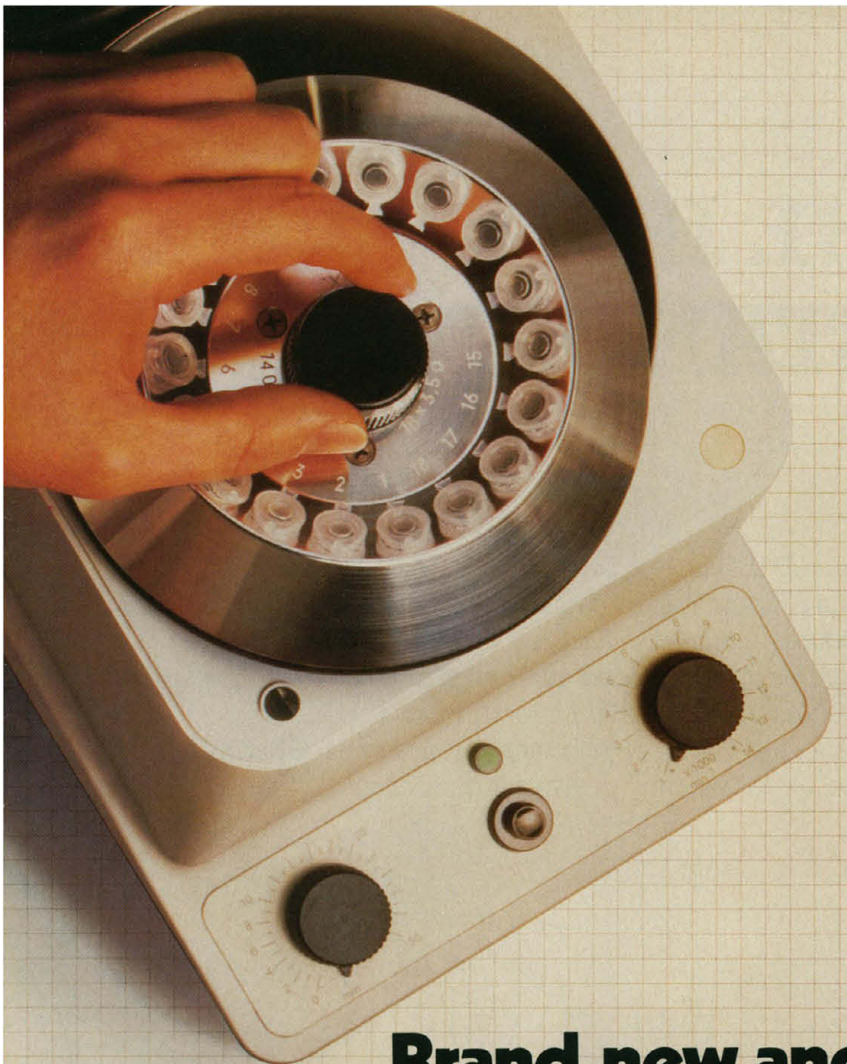

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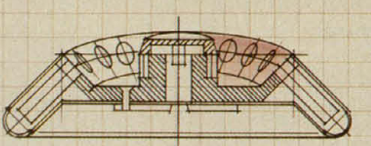

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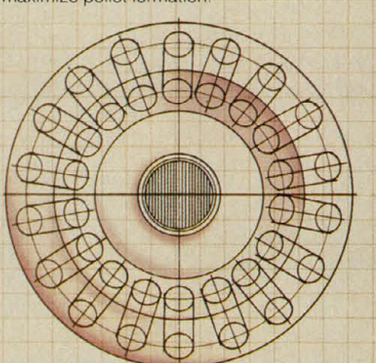

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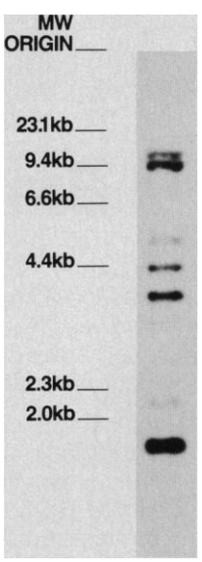

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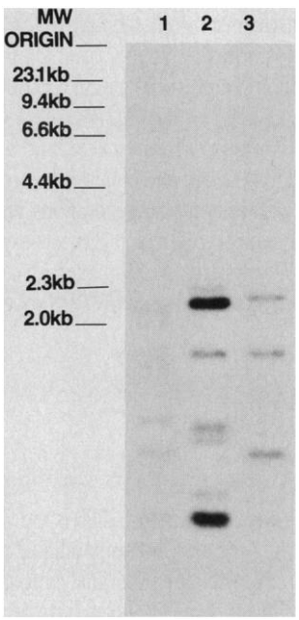

DNA was prepared from three different cultured β-lymphoblastoid cell lines, digested to completion with *Rsa* I (Genomic Grade) and transferred to a nylon filter membrane. A DRβ clone contained in the plasmid pBR322 was then nick-translated and used as the probe. DRβ was employed because of its highly polymorphic nature. As is evident in the autoradiogram, no signals are present in the molecular weight range >2.3 Kb, where one would expect to detect plasmid contamination.

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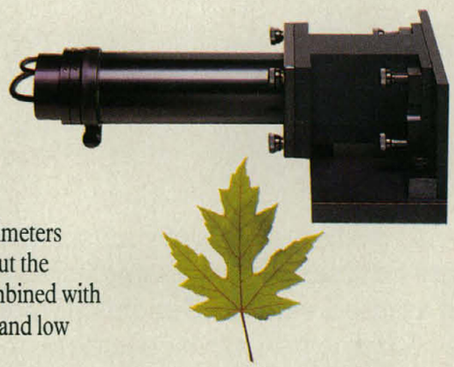

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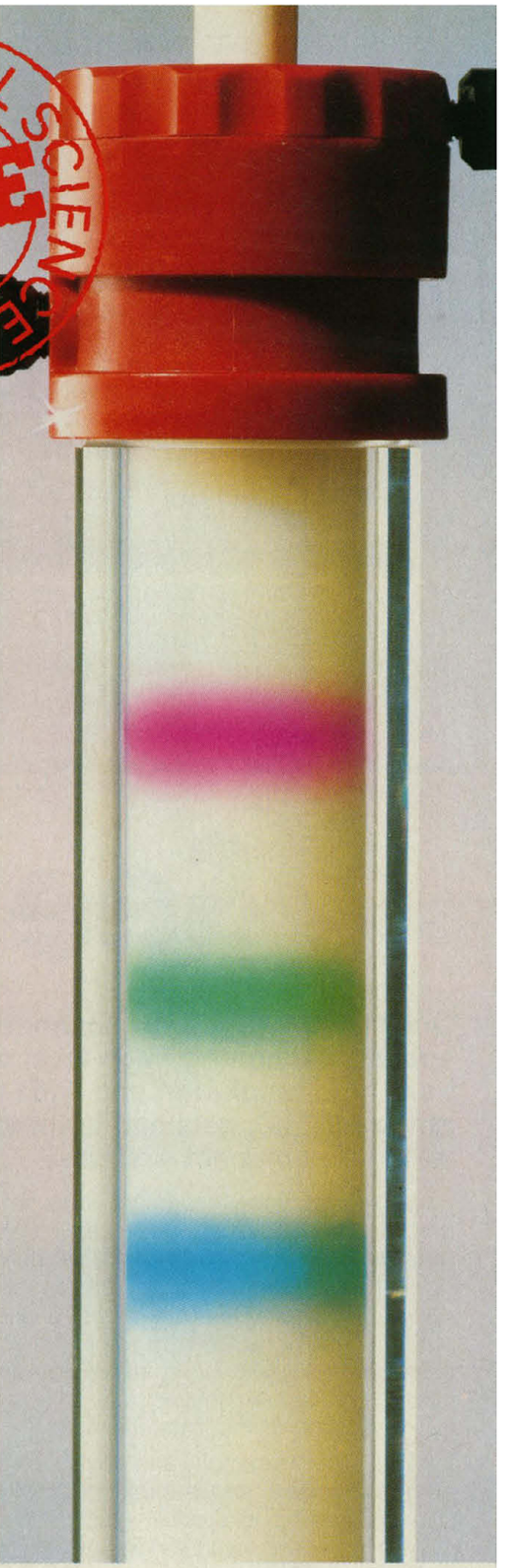

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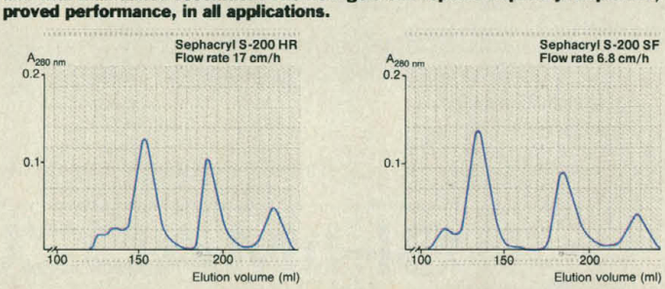

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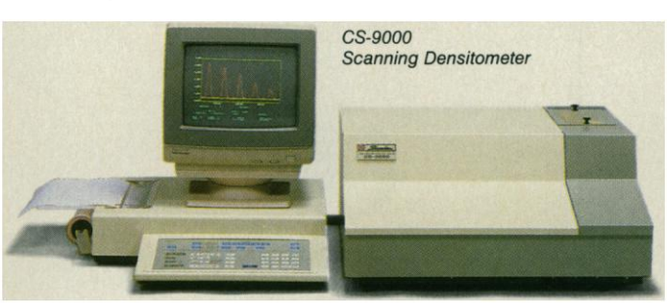

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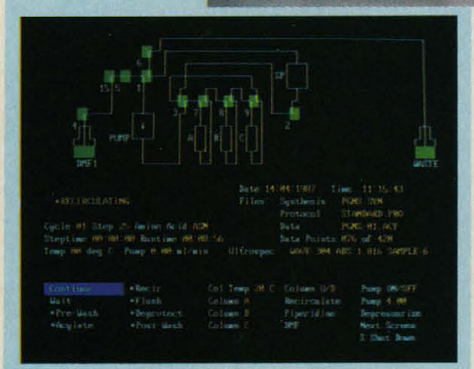

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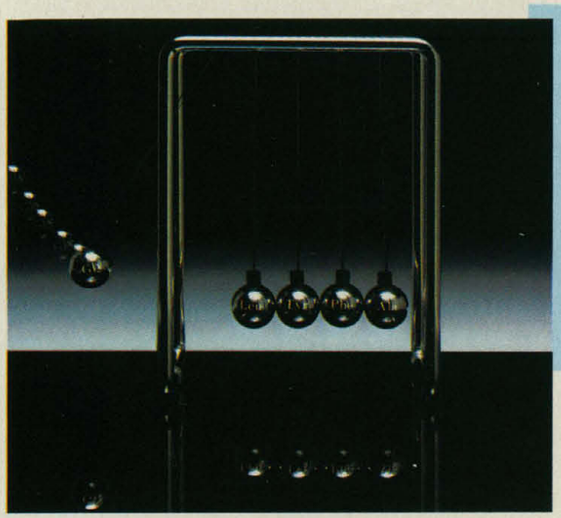

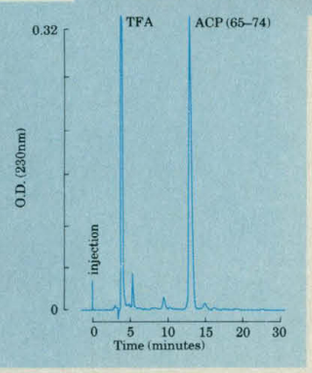

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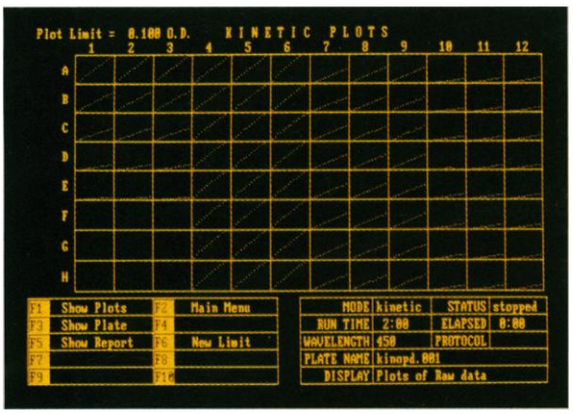

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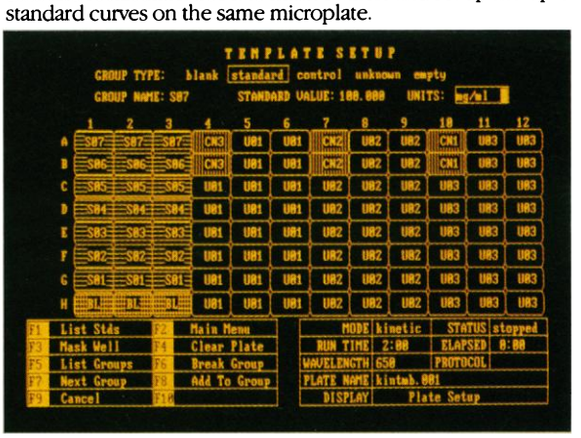

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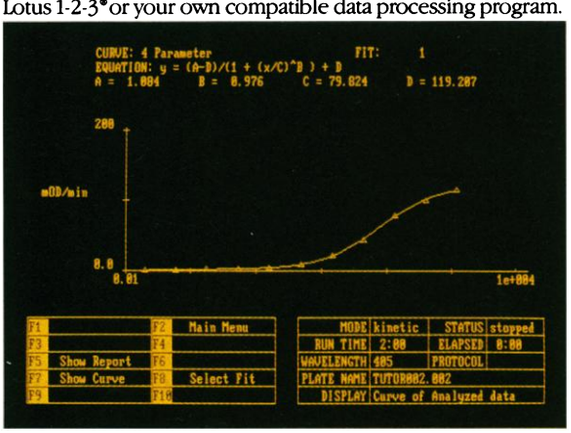

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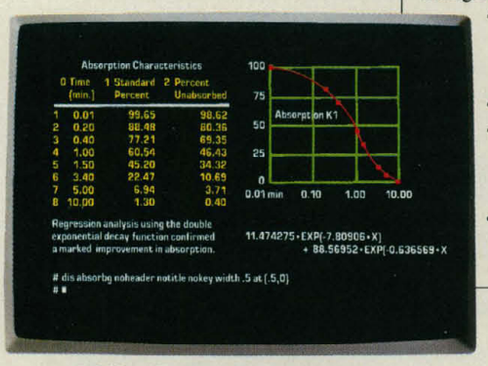

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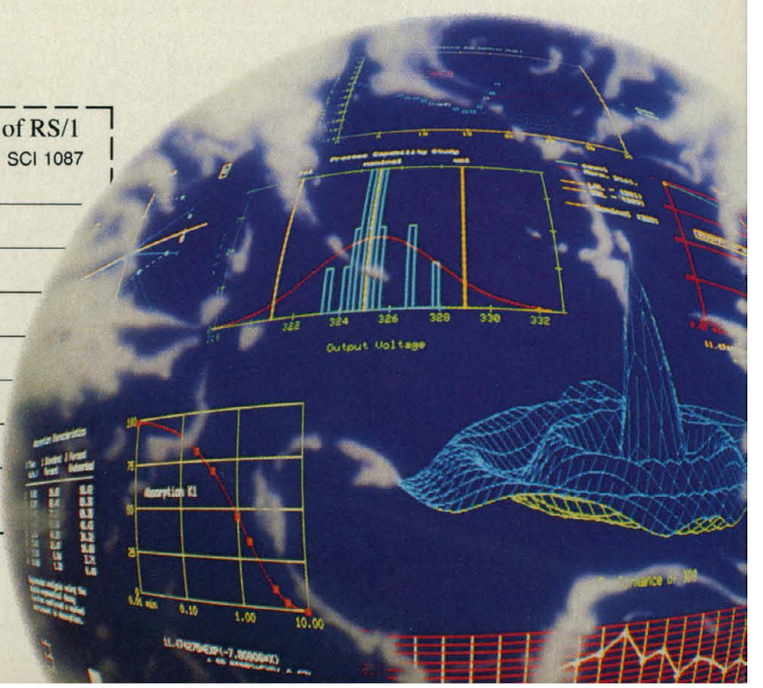
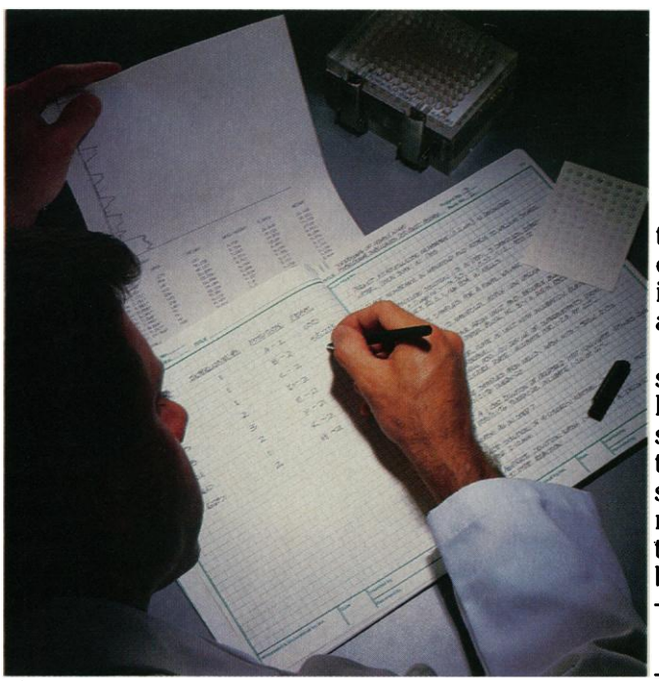


Membrane vs. polystyrene based assays?

S&S asked proteins to decide.



We at S&S had a head start in developing an efficient and economic alternative to standard ELISA testing.

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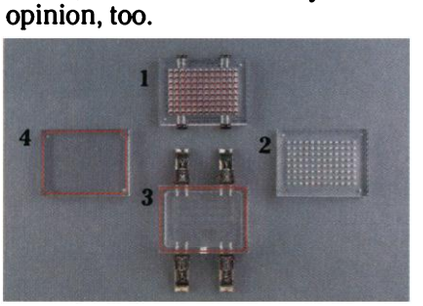

The Minifold I consists of (1) the 96-well sample plate, (2) the filter support plate and (3) the vacuum plenum. The accessory incubation plate (4) replaces the filter support during incubation.

An EC910 Transmission Densitometer from the EC Apparatus Corporation was used for the dot-blot reading.

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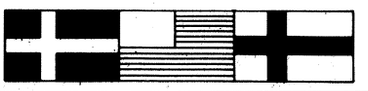

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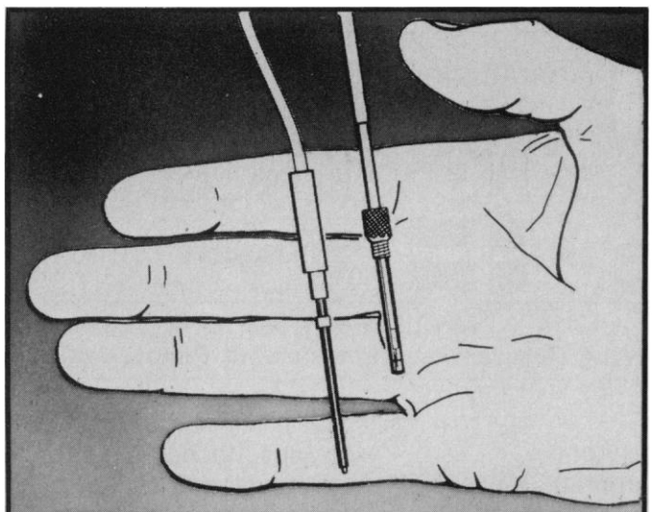

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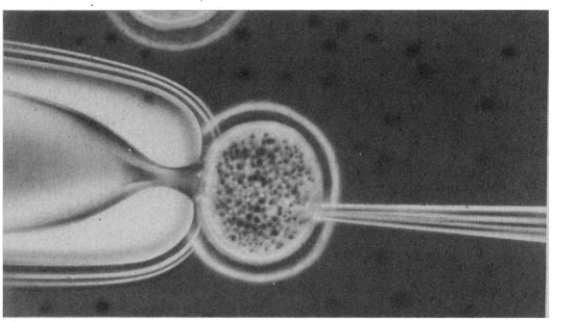

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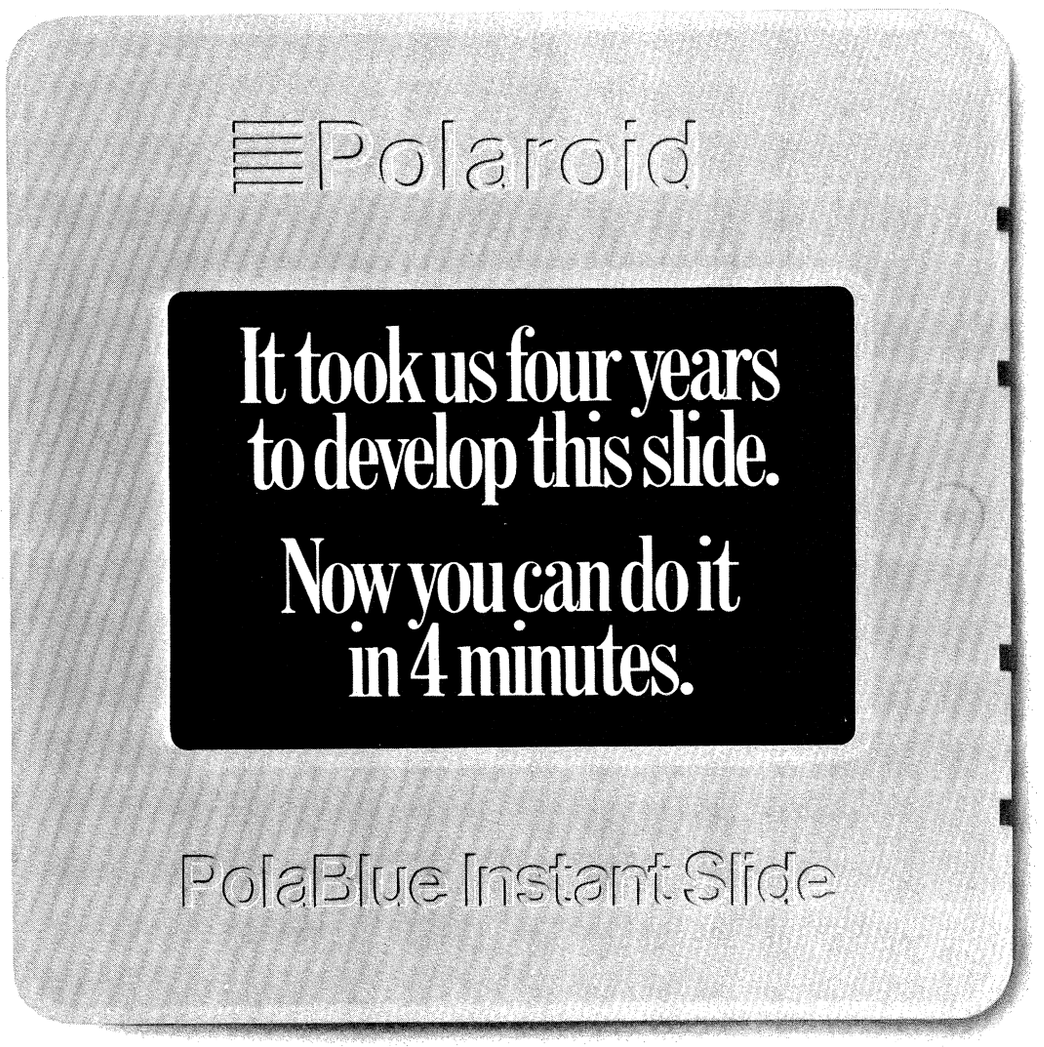

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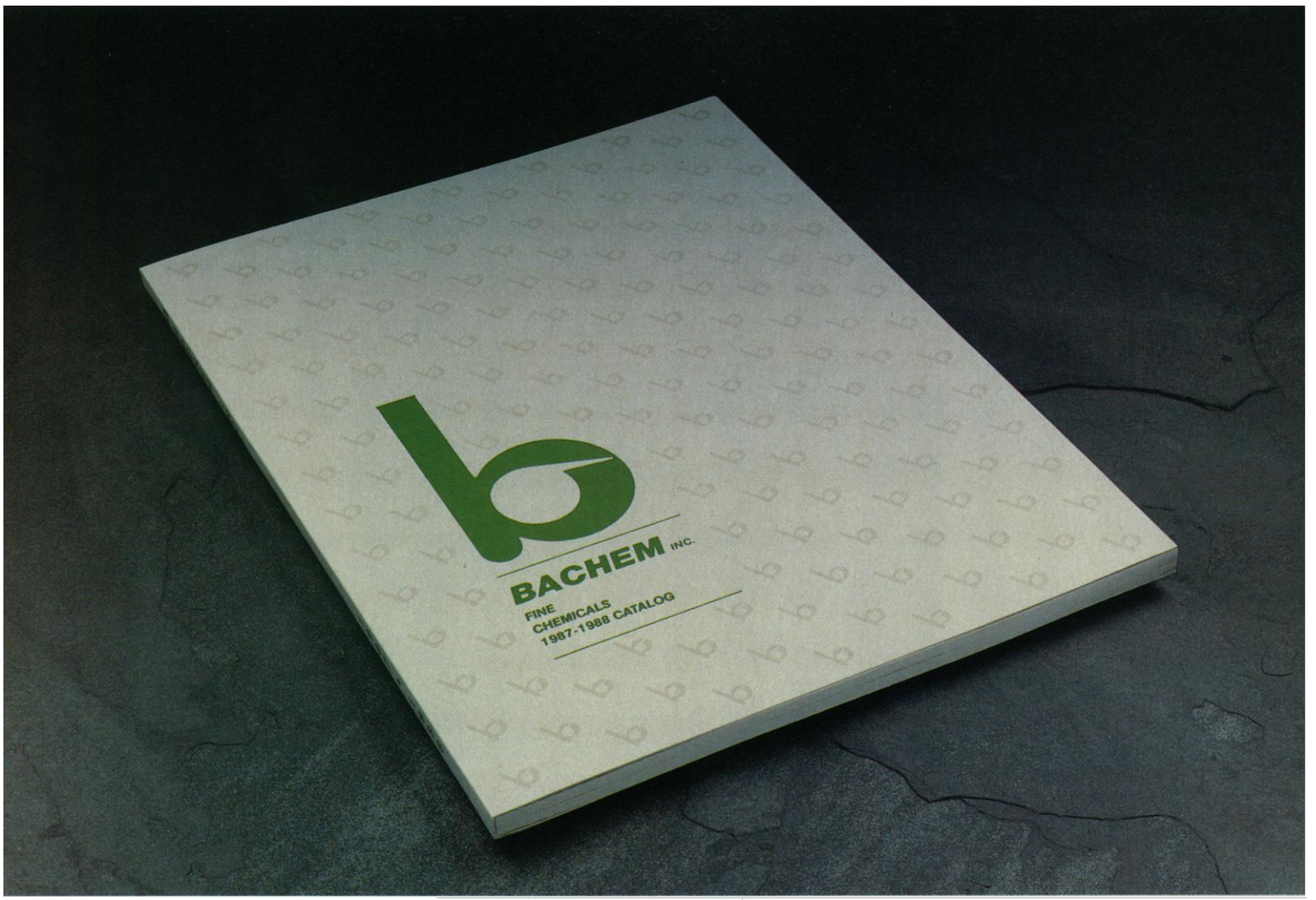

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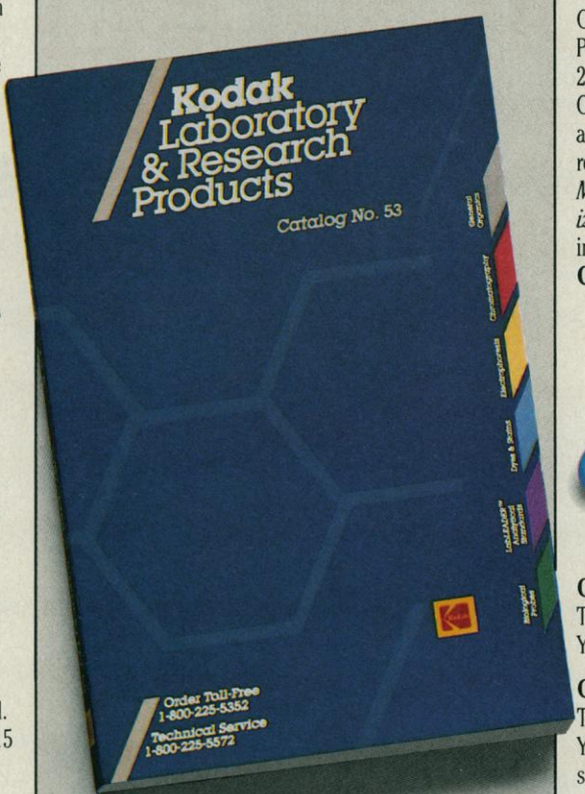

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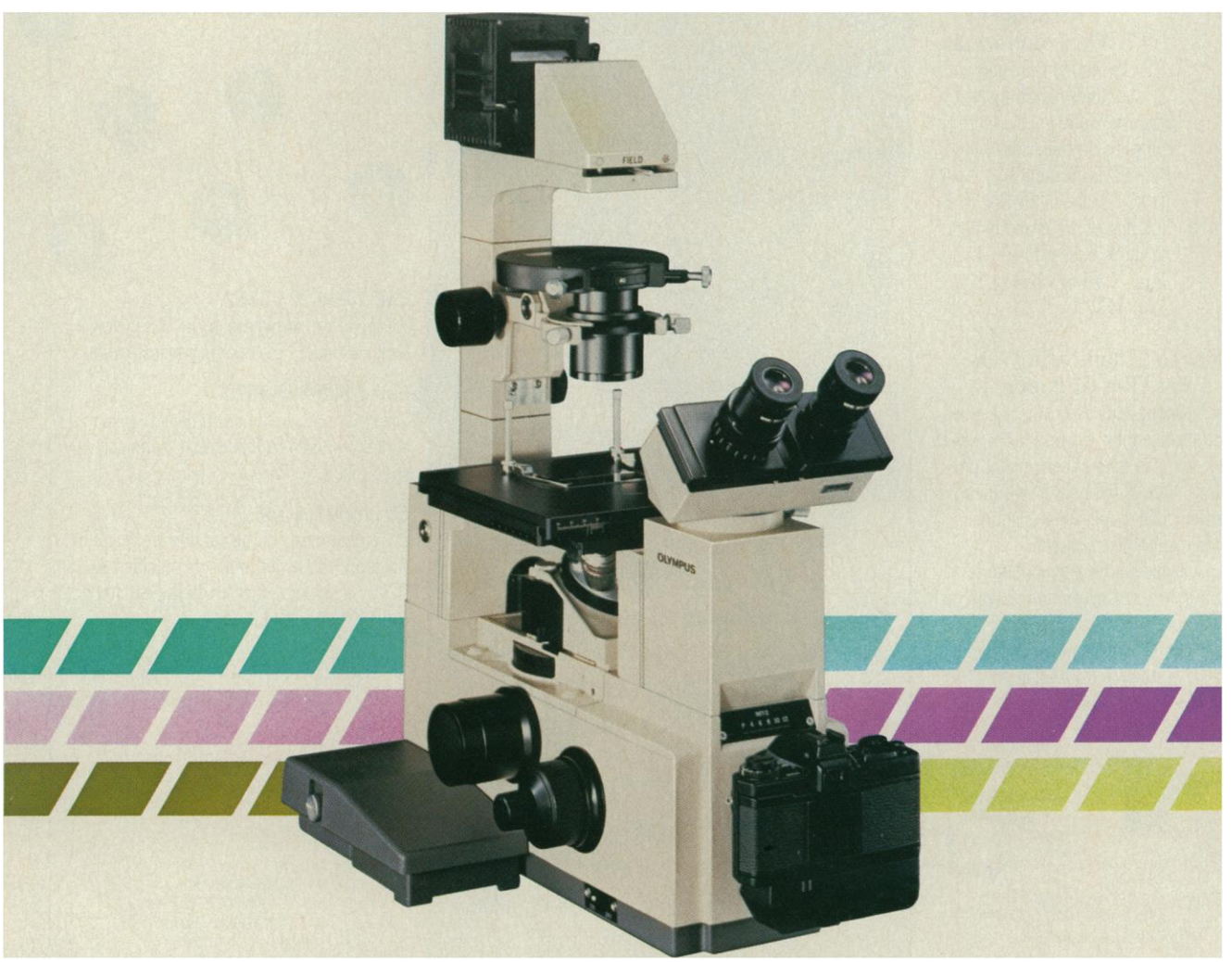

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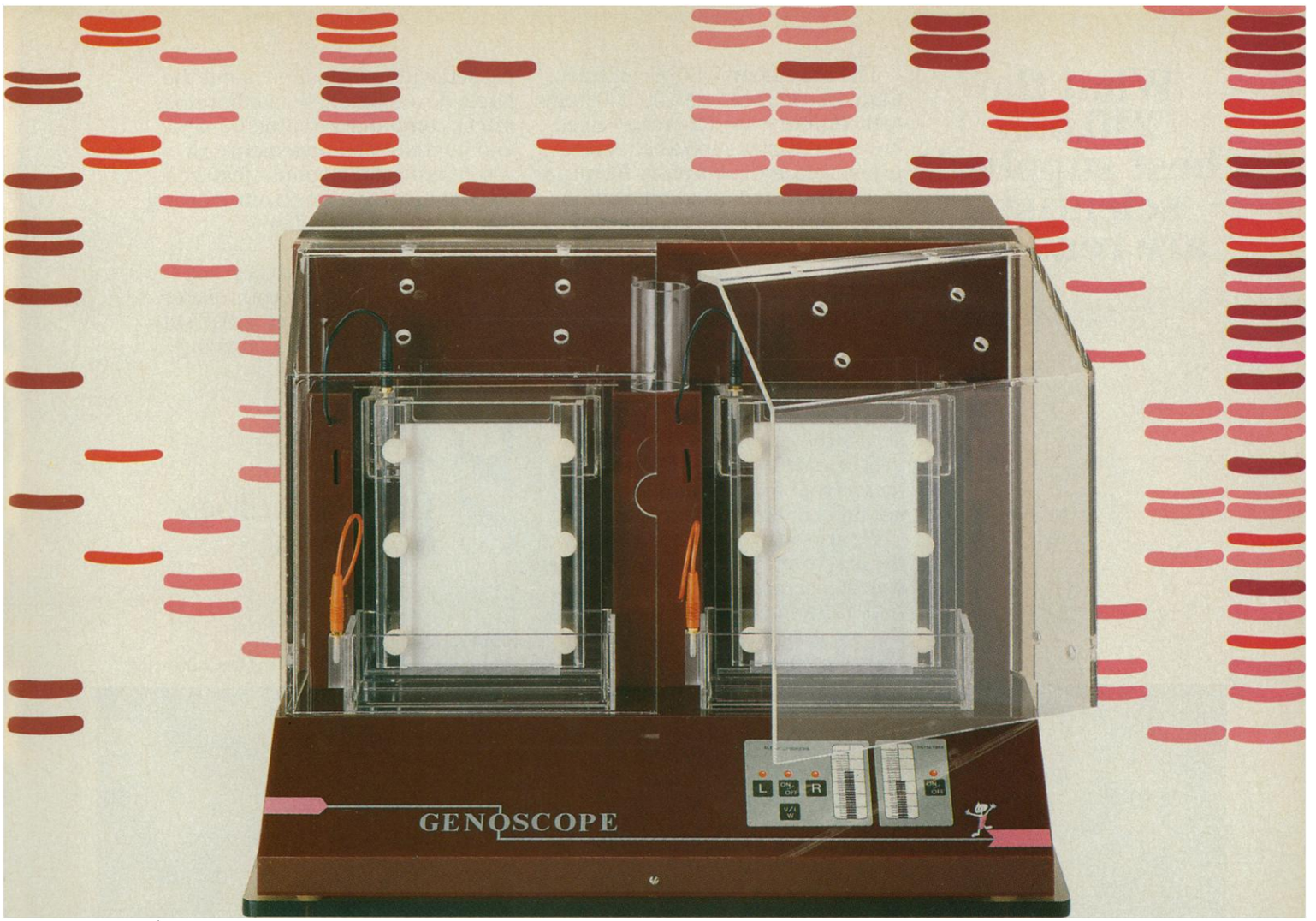

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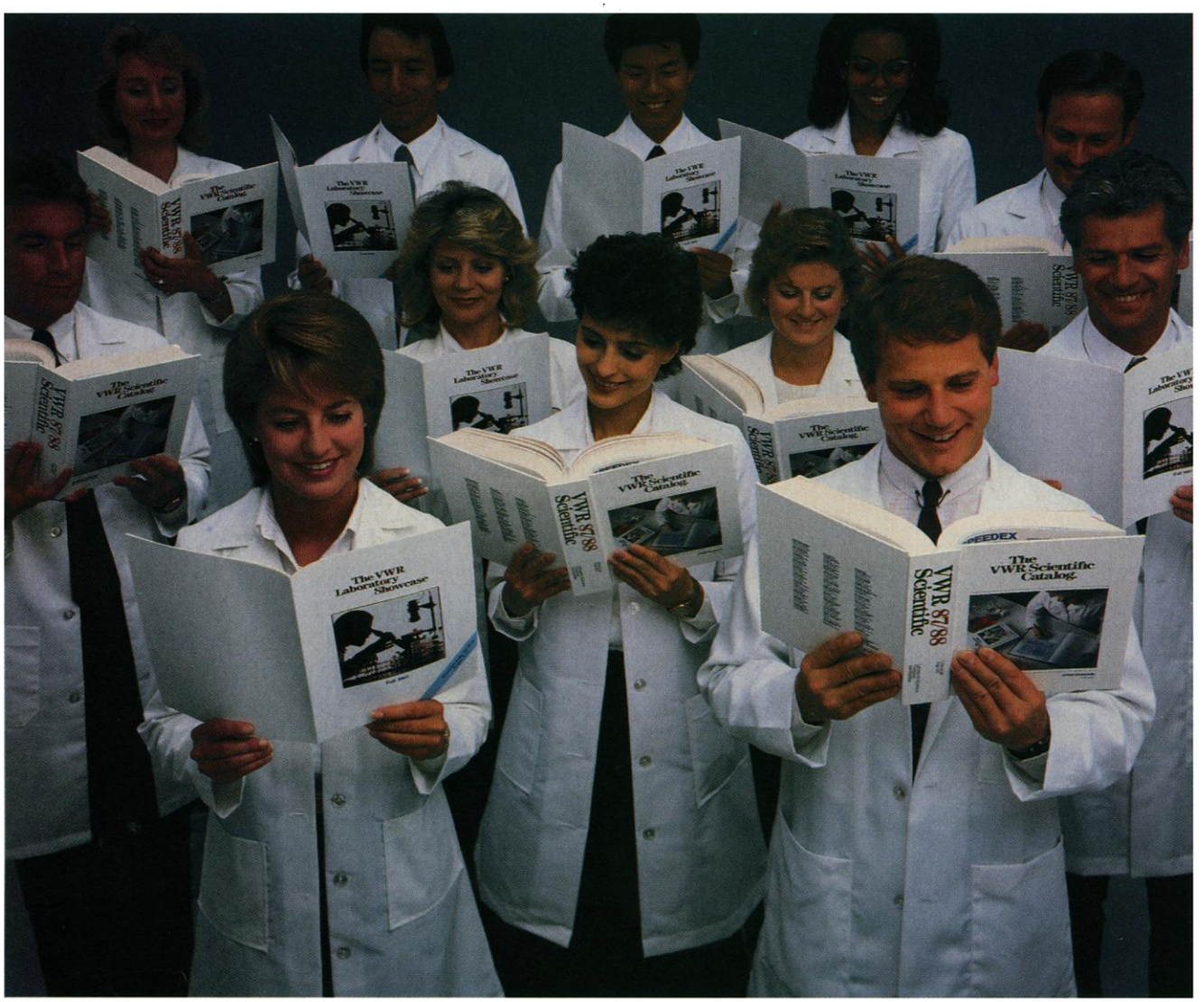

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Scientific Organization: M. Maggi (I) and C.J. Johnston (USA)

Platelets and Vascular Occlusion
Rome, Italy / June 1-3
Scientific Organization: G.A. FitzGerald (USA) and C. Patrono (I)

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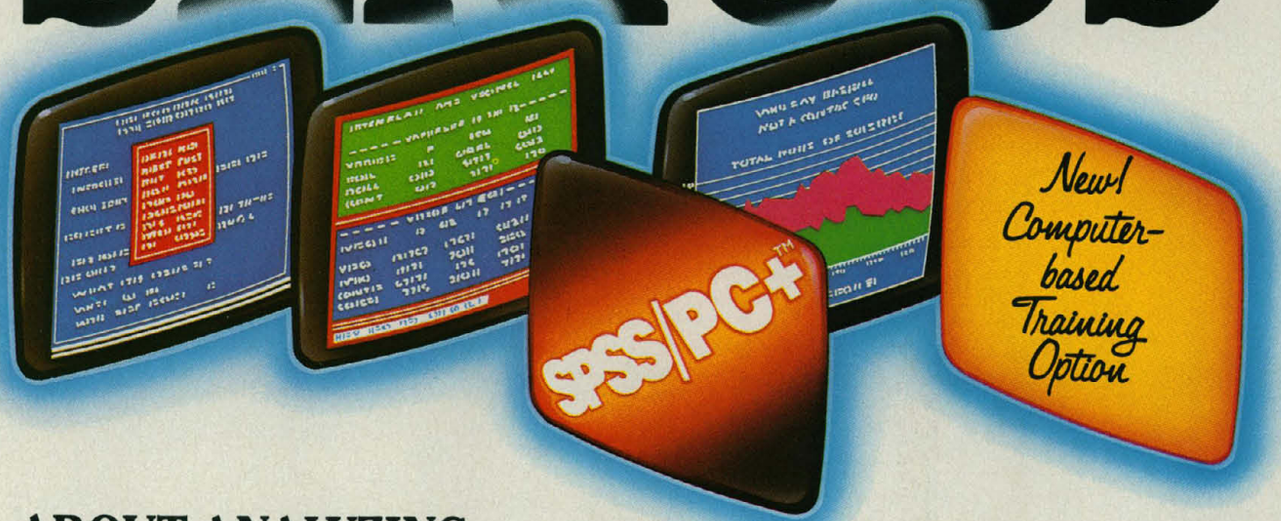

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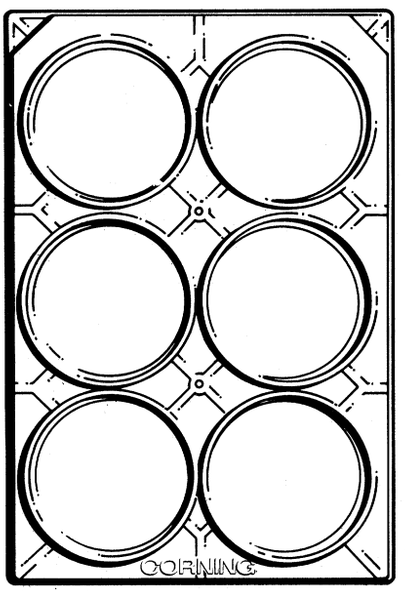
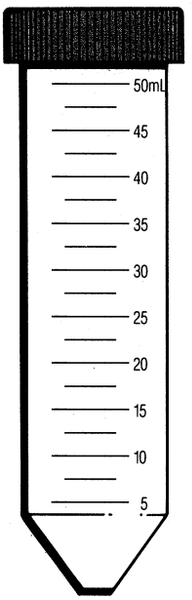
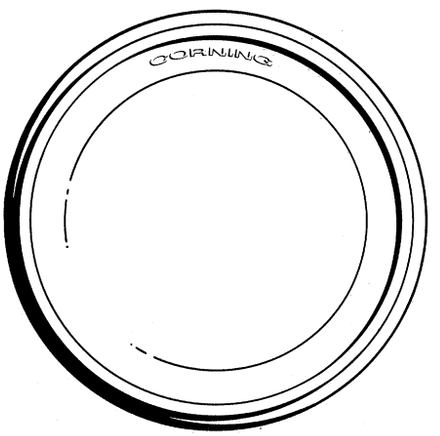


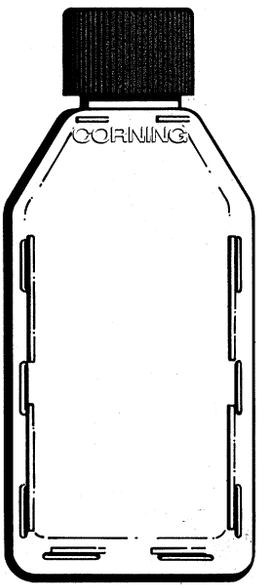
6, 12, 24 wells. 96 well TC & ELISA



15, 50, 250 mL



35, 60, 60 (w/grid), 100 mm



25, 75, 150 cm²

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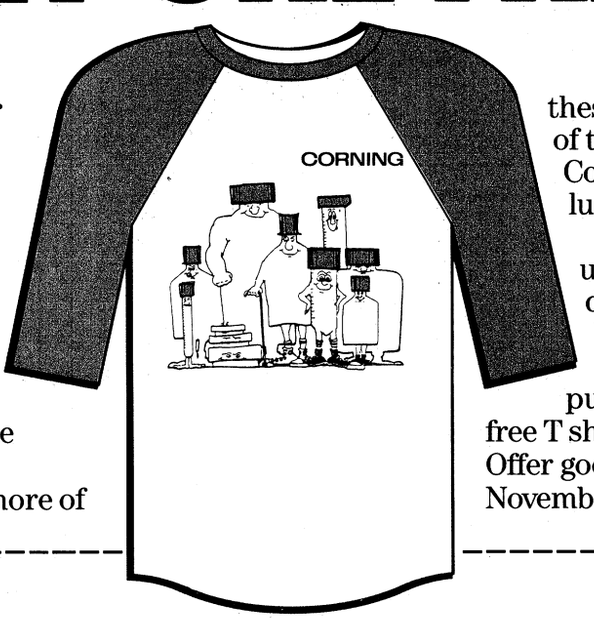

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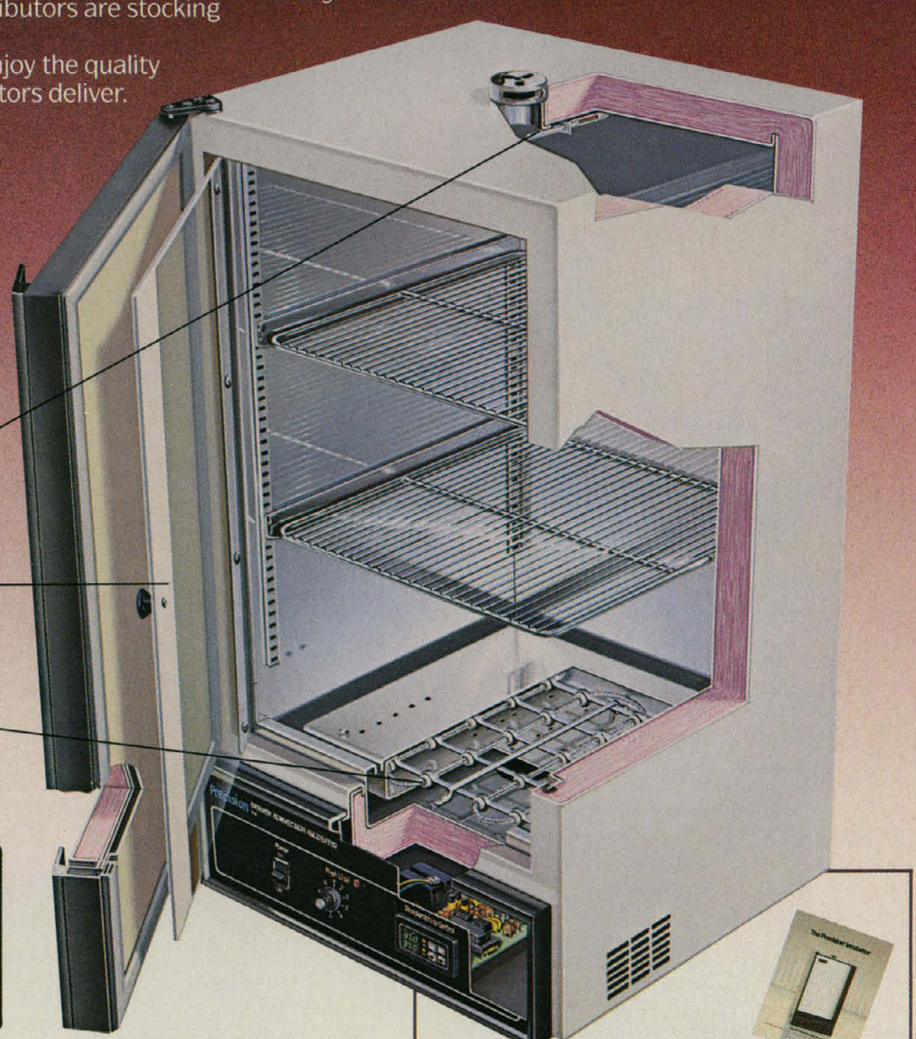

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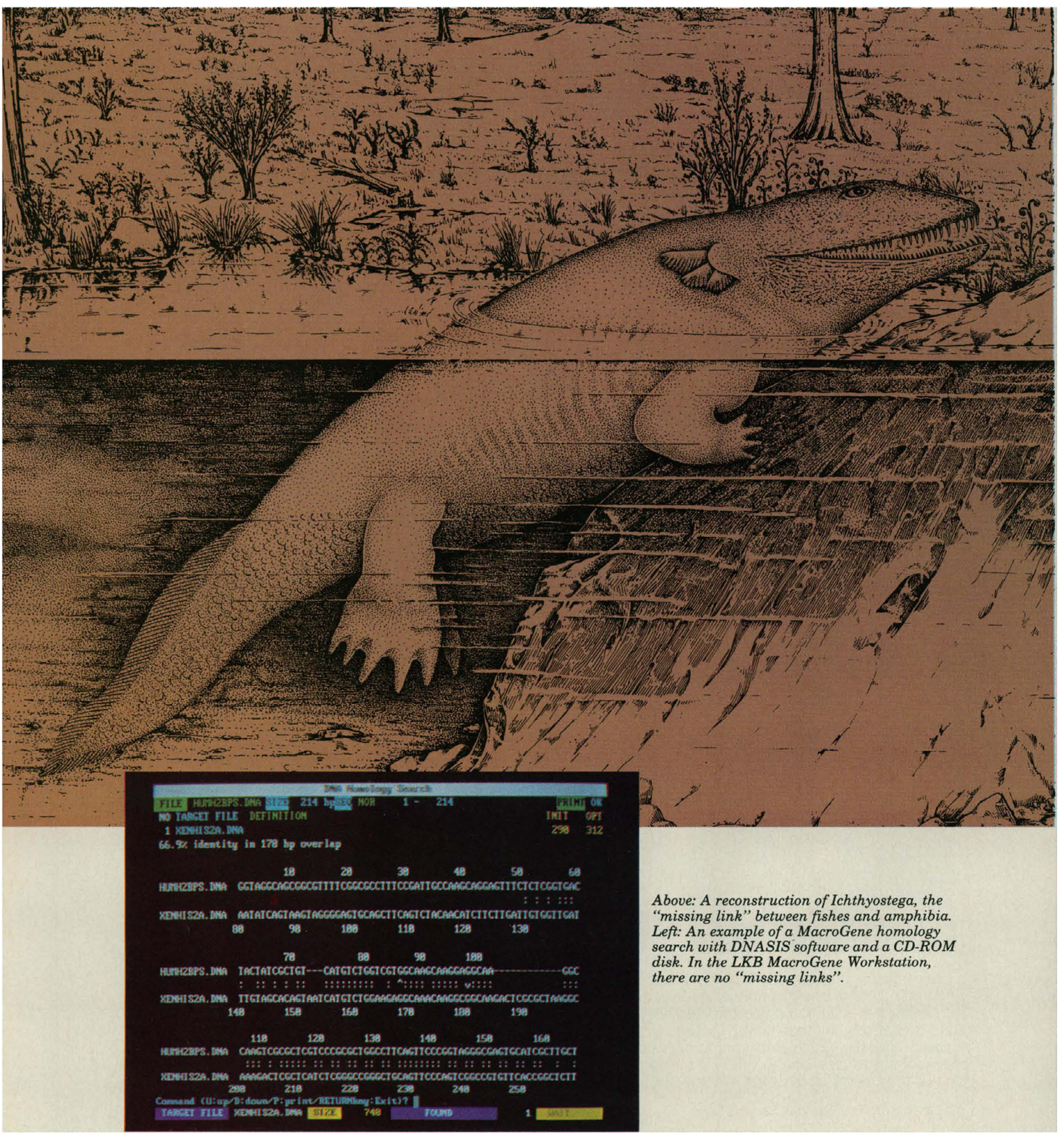

Above: A reconstruction of Ichthyostega, the "missing link" between fishes and amphibia. Left: An example of a MacroGene homology search with DNASIS software and a CD-ROM disk. In the LKB MacroGene Workstation, there are no "missing links".

The short-legged fish on the facing page is Ichthyostega, the oldest known four-footed animal. Until fossils of this meter-long creature were found, he was one of evolution's missing links. Too bad there's none of his DNA to analyze! On LKB's new MacroGene Workstation, his evolutionary relationships could be evaluated quickly with the sequence information on the unique CD-ROM Laser Reference Disk.

Not only does the LKB MacroGene Workstation let you study intergenic relationships easily — it fully equips you to achieve optimum results at every step in DNA sequencing. From start to finish.

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You can also read a longer DNA sequence rapidly and transfer it directly into your personal computer for analysis with user-friendly DNASIS* software.

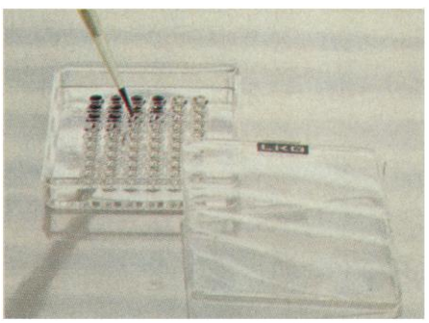
DNASIS has all the functions needed to manipulate and evaluate large amounts of data in little time at all. It enables maximum matching, auto-connection of shotgun sequence fragments, control element search, automatic generation of restriction maps from gel data, reformatting of external files, and scores of other routines. And DNASIS alone offers you instantaneous access to the complete GenBank and NBRF databases, both on one laser disk.

MacroGene is the only DNA sequencing system you can buy which has no missing links. See for yourself! Ask your nearest LKB representative today for a MacroGene brochure and a DNASIS demonstration disk.

** DNASIS is a trademark of Hitachi Software Engineering Systems, Ltd. GenBank is a registered trademark of NIH.*

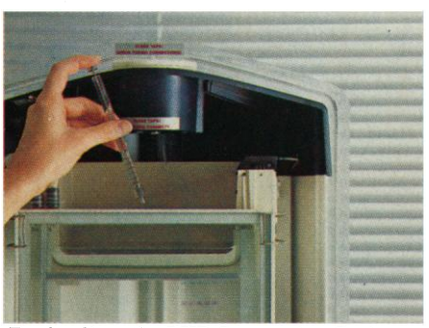
*** MacroMould is based on an invention of Dr. W. Ansorge. Rights are held by The European Molecular Biology Laboratory, Heidelberg, FRG.*

There are no missing links in a MacroGene Workstation

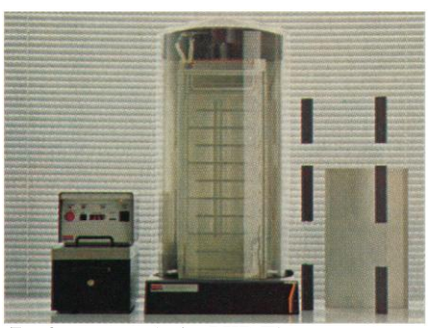


For sequencing reactions: the 60-well LKB MicroSample Plate.

*For casting and moulding sequencing gels: the LKB MacroMould™ System.***



For loading: the LKB Sequencing Syringe, with unbreakable, exchangeable needle.



For heat control: the LKB Thermostatic Plate or Isothermal Plate.

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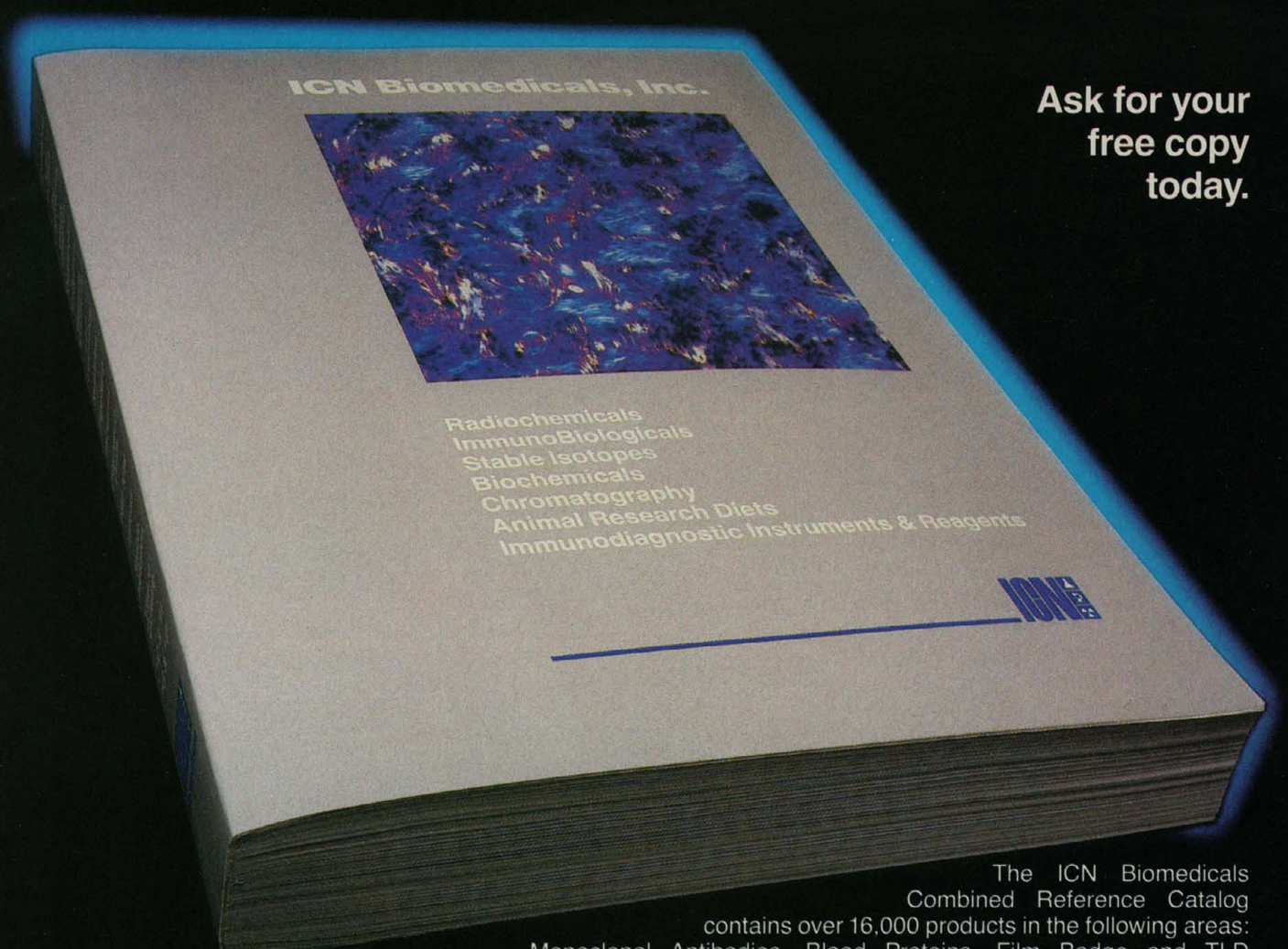

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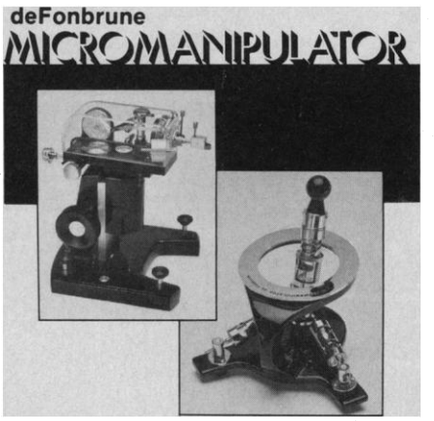

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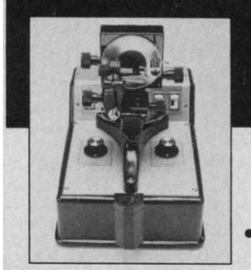

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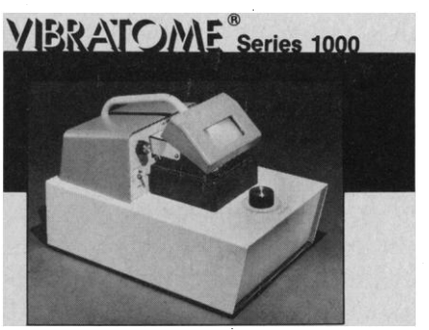

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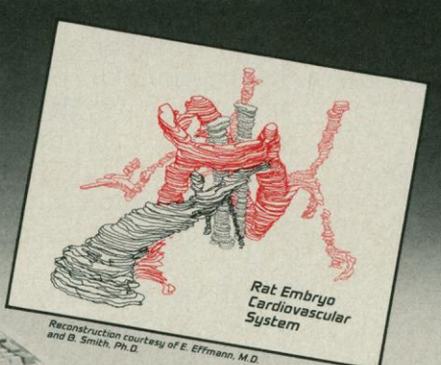

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Hyatt Regency Crystal City
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The **National Forum for School Science** provides an annual opportunity for teachers, scientists, science educators, and other individuals to analyze and discuss key issues, and to focus attention on the most enduring concerns and most promising new directions in science education.

Forum '87 Program

OPENING ADDRESS: **What Do We Want Students to Learn?**

PANEL: **Perspectives on Science Learners** — The speakers in this session will present some of the different ways of thinking about learners: as constructors of knowledge, as processors of information, and as products of social and cultural influences. How these different perspectives affect science education policy and practice will be the topic of the ensuing discussion.

LUNCHEON ADDRESS: **Diversity Among Learners**

PANEL: **Information Needed to Develop Practice and Policy** — Following a brief analysis by educators and policymakers, Forum participants will break into groups to discuss the types of information they need about students and learning. The focus will be on identifying research (such as demographic data, science aptitude, attitudes toward science, etc.) that will enable them to make informed policy and practice decisions.

PANEL: **Environments and Strategies for Effective Science Learning** — The environments and strategies for science learning can be based on our conceptions of science, or on our knowledge about how people learn. This panel will explore the differences and similarities between these designs, and ask if there are optimal systems. Particular attention will be paid to the practical considerations imposed by school structures.

SUMMARY DISCUSSION: **Developing Practice and Policy That Adapt to Science Learning Goals**

Register today by completing and returning the form on the next page. *For more information*, contact the AAAS Office of Science and Technology Education, 1333 H Street, NW, Washington, DC 20005; (202) 326-6620.

American Association for the Advancement of Science

Advance Registration Form

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AAAS Forum '87: Students and Science Learning

20 – 21 November 1987 ✦ Hyatt Regency Crystal City, Arlington, VA

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$ 20 Lunch, Saturday (21 Nov.) _____

TOTAL AMOUNT: $ _____

All registrants will receive a program, registration badge, and *This Year in School Science 1987: Students and Science Learning*. Registration is limited; preregistration form and payment **must be received by 30 October** to ensure receipt of advance materials. Registrations received after 30 October will be held at the AAAS registration desk in the Hyatt Regency. **Refund Policy:** If cancellations are received by 30 October, advance registration and meal ticket fees will be refunded after the Forum. ***No refunds will be made on cancellations received after 30 October.***

Mail top half (registration form) to: AAAS, Forum '87 Registration, Room 830
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AAAS Forum '87 ✦ 20 – 21 November 1987

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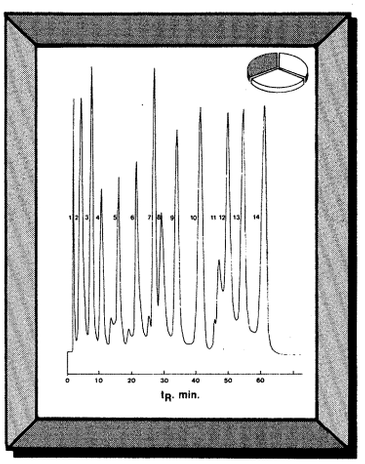
PORTRAITS IN CHROMATOGRAPHY

Protein Separation Ion Exchange Preparative HPLC



Protein Standards on BAKERBOND WP-PEI+

(weak anion exchange)

Analytical Conditions:

Column: 10 mm x 250mm. 15-μm BAKERBOND WP-PEI (Cat. #7278-0)
Mobile Phase: A = 25mM Tris, pH 7.5; B = 3 M NH_4OAc, pH 5.8
Gradient: 0% B to 100% B in 1.5 hours
Flow Rate: 8 ml/min
Pressure: 50 psi
Detection: UV at 280 nm; 2 AUFS
Sample: 48 mg total protein
Peaks:

1. Cytochrome c (Horse heart type VI)
2. α-Chymotrypsinogen
3. Carbonic anhydrase (Bovine erythrocyte)
4. Impurity (?)
5. Impurity (?)
6. Conalbumin (Bovine milk)
7. α-lactalbumin (Bovine milk)
8. α_1-acid glycoprotein (Human)
9. β-Lactoglobulin B (Bovine milk)
10. β-Lactoglobulin A (Bovine milk)
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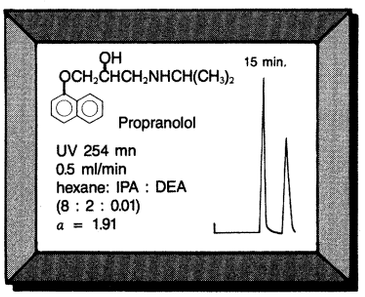
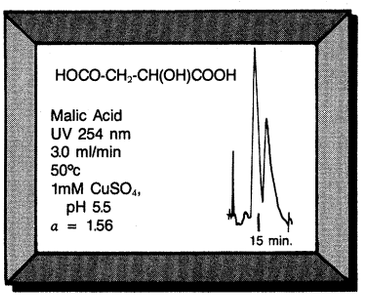


Racemic propranolol separation on Chiralcel® OD



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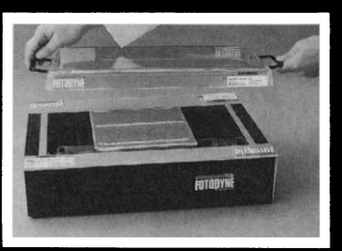

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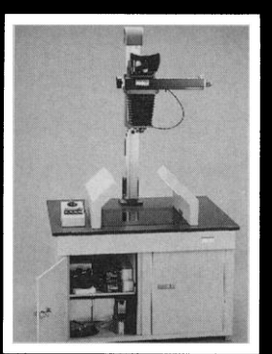

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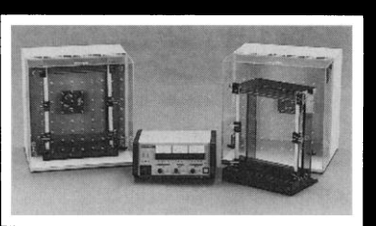

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