

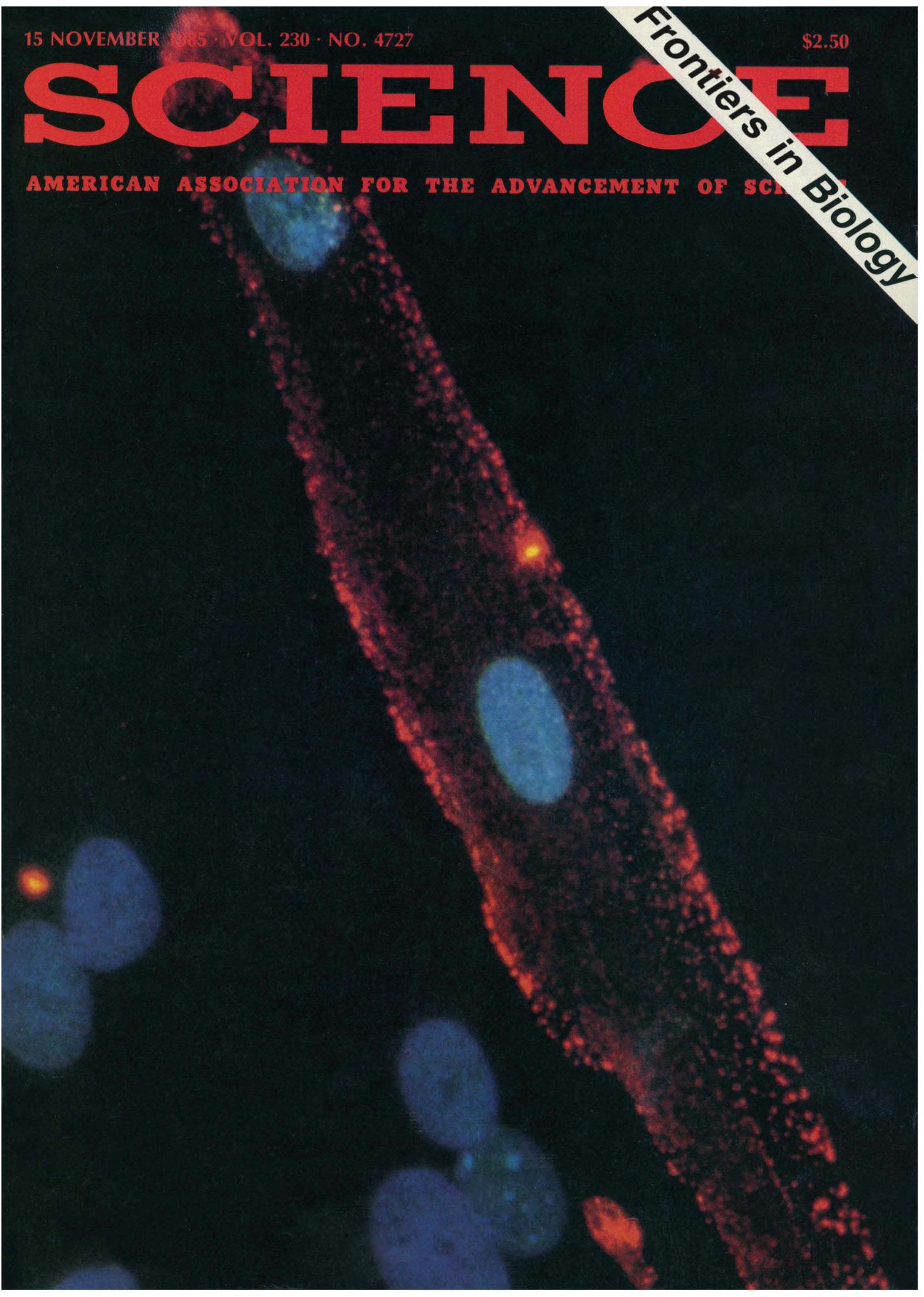
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AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

Frontiers in Biology



SCIENCE

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COVER

Expression of a human muscle gene by a human hepatocyte nucleus. Mouse muscle cells (blue punctate nuclei) and human nonmuscle cells (blue uniformly stained nuclei) are fused to form heterokaryons. Upon exposure to muscle cytoplasm, cells specialized for different tissues can be induced to express gene products characteristic of muscle (red immunofluorescence). See page 758. [S. C. Miller in collaboration with H. M. Blau, Department of Pharmacology, Stanford University, School of Medicine, Stanford, California 94305]

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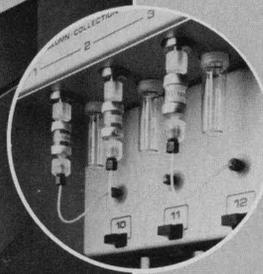
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Hypertensive rats and salt

"Salt sensitive" rats, first bred some 20 years ago for use in studying the ability of salt to induce hypertension, have high blood pressure even when fed a salt-deficient diet (page 808). Kurtz and Morris, using an indwelling catheter, made repeated measurements of the high blood pressure in resting, alert rats during the first 3 months of the rats' lives. A possible biologic consequence of the innate high blood pressure was obvious from early life: the hearts of newly weaned rats were heavier than those of related "salt resistant" control rats of equal body weight. Although initiation and maintenance of high blood pressure appear to be largely independent of salt intake, heavy salt loading may exaggerate the predisposition to hypertension.

Resolving mirror images

Naturally occurring mixtures of amino acids can be resolved at femtomole (10^{-15} mole) levels into right-handed and left-handed isomeric forms by high-voltage zone electrophoresis coupled to laser-fluorescence detection (page 813). Amino acids derivatized with a fluorescent agent were separated on a column containing an optically active support electrolyte to which the isomers attached and dissociated at different rates during migration in an electric field. The more strongly bound isomer traveled faster but gave a lower fluorescence signal. The technique of Gassman *et al.* will have diverse applications, from use in monitoring the extent of racemization in peptide syntheses, to use in dating geologic events and diagnosing genetic, metabolic, and other types of diseases.

Steps toward malaria control

A synthetic or genetically engineered vaccine for the vivax form of malaria common in Asia and Central America is one step closer: structures of the major immunologically recognizable region of the parasite and of the gene that carries information for its synthesis have been determined (page 815). Although there is less mortality associated with vivax than with other forms of malaria, great suffering occurs, with crises roughly every third day. Protective immunity has been achieved experimentally by immunization with irradiated sporozoites (the parasite's infective form); most host antibody is directed against the circumsporozoite (CS) protein on the sporozoite's surface. Arnot *et al.* cloned the gene for the vivax CS protein, deduced the amino acid sequence of CS, and synthesized a peptide that matched a repeating portion of CS. The peptide reacted with antibody to CS. The repeating region of CS is the major candidate for inclusion in a malaria vaccine both because it contains the primary immunogen of the parasite and because it has so far been invariant in all isolates of *Plasmodium vivax*.

New food source for livestock

The competition between livestock and the expanding human population for cereal grains, an obstacle to increasing worldwide production of livestock, may be surmountable (page 820). Agricultural residues such as wheat straw, corncobs, and cornstalks can be converted into useful nutrients for sheep and other ruminants by a simple chemical treatment. Kerley *et al.* found that alkaline hydrogen peroxide converts the fibrous lignocellulose of these by-products to more digestible materials. Scanning electron micrographs of wheat straw removed from rumens showed that digestive bacteria (which must attach to the straw in order to degrade it) completely covered treated straw but colonized the untreated straw only where raw ends were exposed. Because the food energy in crude roughage is equivalent to that of starch in cereal grains, the large-scale conversion of by-products to useful nutrients would constitute a significant step toward expanding the global food supply.

Synthesis of cellulose

Cellulose, a naturally occurring matrix material of plants, algae, fungi, and some bacteria and the primary component of wood, cotton, and paper, has been produced outside the living cell (page 822). When an enzyme from a cellulose-producing bacterium, *Acetobacter xylinum*, was incubated with a glucose substrate, microfibrils of cellulose were assembled. Lin *et al.* characterized the product and found that its morphology and later degradation by a cellulose-specific enzyme were like those of authentic cellulose. As cellulose is the most abundant biopolymer on Earth, there is great interest in studying features of its synthesis, assembly, and degradation.

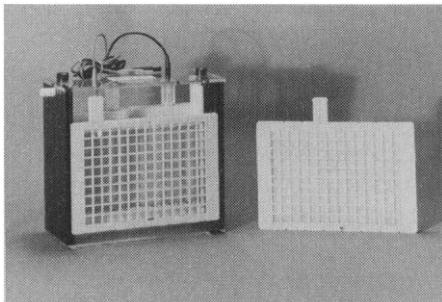
Culture for spiroplasmas

Conditions have been found for growing a spiroplasma—a wall-less microorganism—outside its insect host; the growth characteristics, behavior, and physiology of the spiroplasma can now be studied in detail (page 825). Spiroplasmas live in many insects, some in harmony with the host, others as pathogens. The latter are of particular interest because they may be of use as biological control agents for specific pests. Hackett and Lynn designed a culture system that is conducive to the growth of a spiroplasma that lives in the gut of the Colorado potato beetle, which has devastated potato crops in the United States and Europe. Embryonic insect cells were added to a complex tissue culture medium and apparently provided essential growth factors not supplied by other culture components. The microorganisms flourished and retained infectivity for beetles. This or a similar cell-enriched medium may support growth of other species of spiroplasmas that have not previously been grown successfully outside insects.

How to get the most out of your Transphors.

Whether for nucleic acid hybridization, immunostaining or autoradiography, your transfers must be fast and uniform. The current must be high and homogeneous throughout the transfer chamber, and the temperature must be controlled. We took these factors into consideration when we developed our transfer systems, and as a result produced electrode panels, heat exchangers and power supplies to give you the best transfers possible.

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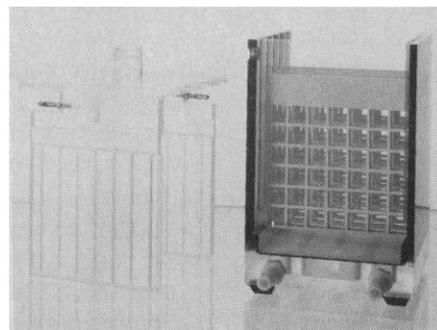
- The **PS 250 Power Supply** is ideal for transfer electrophoresis, which requires high current flow at relatively low voltage. It produces 0-250V, 0-2.5A, adjustable in both constant current and voltage modes. We recommend running transfers in constant current to eliminate any possibility of overheating. The PS 250 provides ample current for several small or 2 large Hoefer



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a magnetic stirrer and cooling, the unit will show no more than a 5°C heat rise over the length of the run.

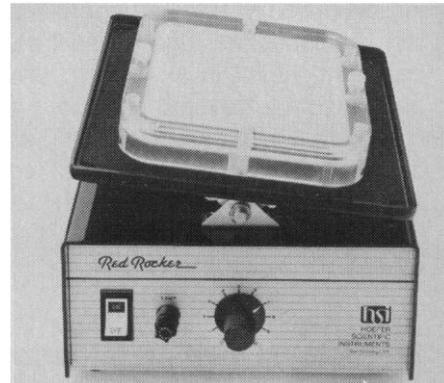
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- Hoefer sells **Transfer Membranes** to use with its Transphor (TE 42) and Mighty Small Transphor (TE 22). A pure grade of Transphor Nitrocellulose Membranes free from admixtures of other cellulose esters insures faithful replicas, maximal binding and minimal background staining. The

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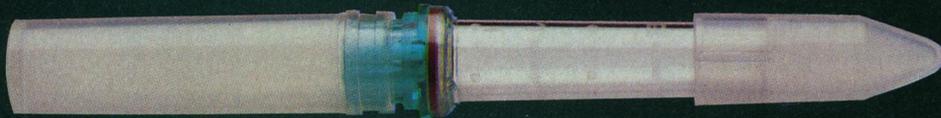
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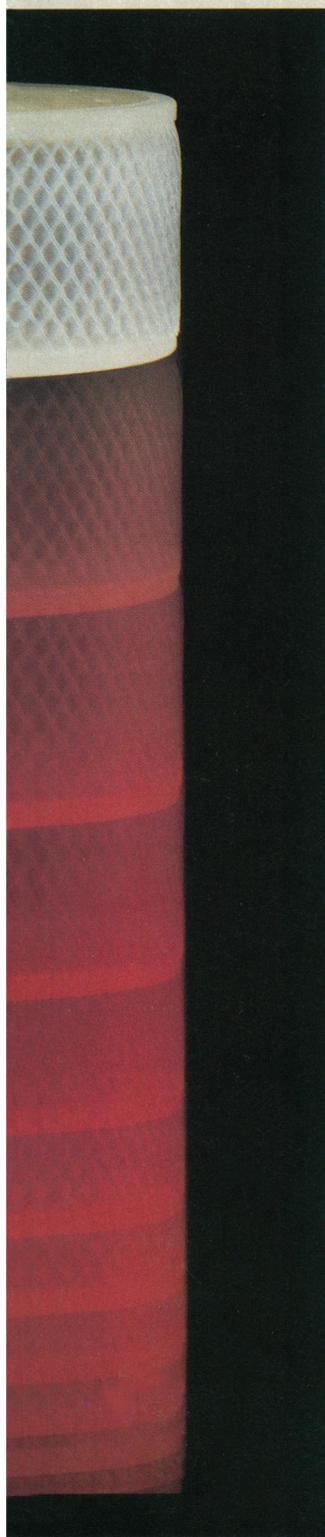
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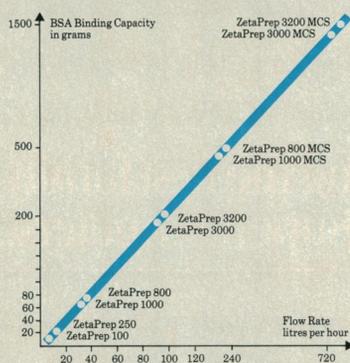
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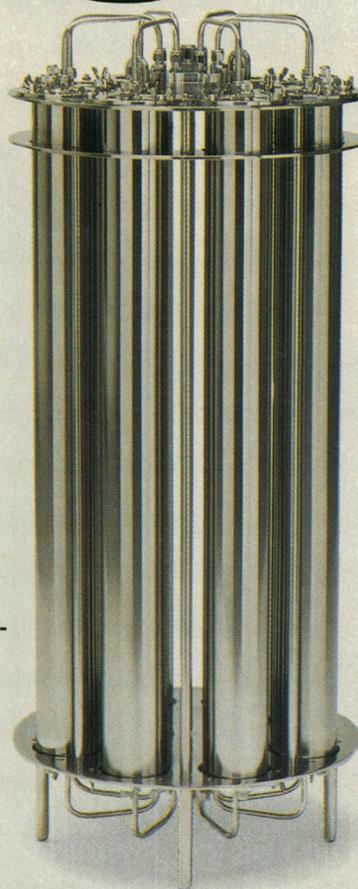


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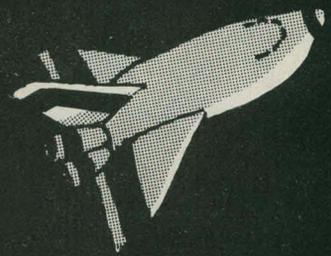
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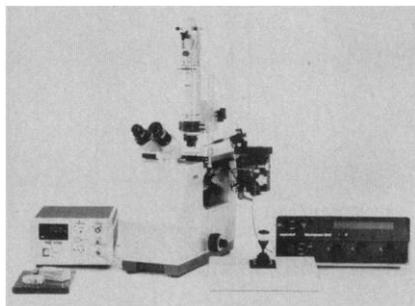
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Equipped with DC motor controls, the **Micromanipulator** offers exceptionally smooth, responsive and vibration-free X, Y, and Z movement at speeds ranging from 0 to 0.1 mm/sec. For positioning of X-Y movements parallel to the stage plate a special holder permits precise mounting of the micromanipulator at any elevation to the right or left of the stage plate.

With three adjustable injection pressures for holding, injecting and cleansing, the **Microinjector 5242** increases injection rate from the 100 cells a day typical of manual systems to 500 cells per hour. Other features: dosages in the picoliter range; an LED display of number of injections, pressure, mode and automatic or manual time; an acoustic signal when the injection sequence has been completed.



The **Heating Stage M** has built-in transistors (no electrical interference) and a temperature range of 3° C above ambient to approximately 50° C, with a stability of better than 0.2° C. The control unit monitors both programmed temperature and actual temperature for the heating stage and preheating plate.

The new Zeiss Micromanipulation/Microinjection Systems provide the researcher in physiology, cell biology, neurobiology with a complete workstation capable of transferring materials into the living cell with new levels of speed and accuracy.

EM 902: New Tool for Biomedical Research

The Zeiss EM 902 is an advanced analytical TEM that enables biomedical researchers to localize specific elements in the ultrastructure of tissues and cells. In employing a new technique, Electron Spectroscopic Imaging (ESI), the EM 902 operates on the principle that electrons in various elements – nitrogen, oxygen, phosphorus, calcium and sodium – exhibit different levels of energy loss. A fully integrated electron energy-loss spectrometer registers the electron energy-loss spectra (EELS) of a specimen, producing a high-resolution distribution map of the elemental components. The new TEM achieves an unprecedented point resolution as low as 0.5 nm.



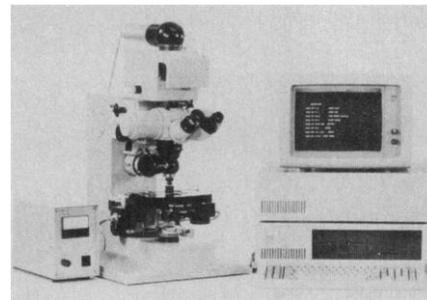
Extremely simple to operate, the EM 902 is suitable for research and routine applications. Besides the ESI technique, the EM 902 can be used for contrast enhancement on thin unstained sections, on thick sections up to 1 μm (the chromatic aberration equals that of a 1 million volt TEM), and for unlimited conventional electron microscopy.

New UMSP Microscope Photometer System

Flexible in design and easy to use, the new Zeiss UMSP System for high-resolution quantitative microscopy offers the biological researcher maximum problem solving capabilities.

The UMSP System teams the Zeiss UEM microscope with a modified IBM PC/XT, and user-friendly, state-of-the-art software developed for spatial and spectral analysis. Data acquisition is accomplished through either solid state camera or photomultiplier tube (PMT) depending on the specific application. The system can be configured with other Zeiss microscopes such as the Universal and Standard 16.

Powerful applications software such as the biologically-oriented Image Scan enable a researcher to measure the



grey level distribution and thereby generate a density map of a single cell. Simplicity in design of all hardware and software gives the user clear, logical and functional sequences for easy use and adaptable control of the system.

Video-Enhanced Microscopy for Submicron Observation

New techniques of video-enhanced microscopy from Zeiss allow the researcher to detect and record intra- and intercellular details at the submicron level. The recommended systems combine the famous Zeiss Axiomat™ microscope with a choice of compatible video units.

The unparalleled mechanical stability of the Axiomat microscope and its internally corrected planapochromatic lens produce the excellent image quality at high magnification required by techniques such as the patented Allen Video-Enhanced Contrast (AVEC) method.

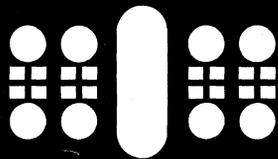
Features such as zoom capability can vary the image transfer as desired, optimizing the size of the specimen on the TV monitor with no loss of resolution. The image is further enhanced by electronic manipulation of the video signal. The instrument's single set of objectives covers the range of most commonly utilized optical techniques: brightfield, darkfield, phase contrast, POL and DIC.

In the inverted configuration for biological applications, the Axiomat microscope is connected to a video system by an optical interface developed by Zeiss.

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Preliminary announcement and call for papers

The Membrane Protein Symposium will bring together researchers concerned with the biochemistry of membrane proteins. The three-day program includes oral presentations, poster sessions, workshops, and discussion sessions. The following topics will be covered:

- Structure
- Ion channels
- Transport
- Receptors
- Signal transduction
- Methods

You are invited to submit an abstract describing original research in any of the above categories or in related areas. Abstract deadline: February 15, 1986. To receive an abstract form, contact

Shirley E. Schlessinger
Symposium Manager
Membrane Protein Symposium
400 E. Randolph Street
Chicago, IL 60601 USA
Telephone (312) 527-2011

Papers presented at the Symposium will undergo a normal review procedure. Accepted papers will be published in a collected Proceedings following the symposium. To expedite publication, completed manuscripts will be due at the time of the meeting.



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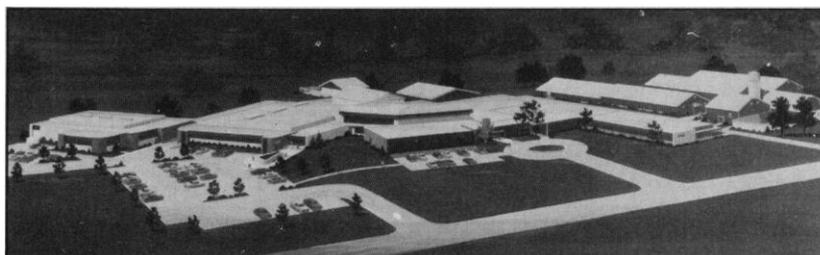
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DNA PROGRAM

Keynote Addresses

Interferon Genes and Their Expression: Charles Weissmann, University of Zurich, Zurich, Switzerland
Gene Expression in Mammalian Cells: Philip Sharp, Massachusetts Institute of Technology, Cambridge, MA

ONCOGENES

Session Chairman: Peter Gruss, University of Heidelberg, Heidelberg, West Germany
The Role of Papillomaviruses in Human Cancer: H. zur Hausen, University of Heidelberg, Heidelberg, West Germany
The new Gene Product: Gross Factor Receptor and Tumor Antigen: Robert Weinberg, Massachusetts Institute of Technology, Cambridge, MA
Modulation of the Malignant Phenotype by the Expression of MHC Class I Genes: Gilbert Jay, National Institute of Health, Bethesda, MD
Expression of AIDS Retrovirus: Paul Luciw, Chiron Corporation, Emeryville, CA

TRANSCRIPTION

Session Chairwoman: Pamela Mellon, Salk Institute, La Jolla, CA
Expression of Gonadotropin Genes: Pamela Mellon, Salk Institute, La Jolla, CA
Mechanisms of Transcriptional control in Animal Cells: Steven McKnight, Carnegie Institute, Washington, DC
Factors and Mechanisms Involved in the Regulation of Eukaryotic Transcription: Robert Raeder, Rockefeller Institute, New York, NY
Mechanisms of Human β Interferon Gene Regulation: Thomas Maniatis, Harvard University, Cambridge, MA

MEDICAL MOLECULAR BIOLOGY

Session Chairman: Walter L. Miller, University of California, San Francisco, CA
Molecular Biology of Steroid Hormone Synthesis: Walter L. Miller, University of California, San Francisco, CA
Molecular Biology of HTLV-III: Basis Studies and Applications for Prevention of AIDS: Flossie Wong-Stahl, National Institutes of Health, Bethesda, MD
Molecular Basis of Phenylketonuria and Potential Somatic Gene Therapy: Savio L.C. Woo, Baylor College of Medicine, Houston, TX
Models for Human Gene Therapy: Theodore Friedmann, University of California, San Diego, CA
Structure and Biology of Trions Causing Scrapie and Creutzfeldt-Jakob: Stanley Pruisner, University of California, San Francisco, CA

HORMONES

Session Chairman: John D. Baxter, University of California, San Francisco, CA
Hormonal Control of Growth Hormone Gene Expression: John D. Baxter, University of California, San Francisco, CA
Steroid Hormone Receptors as Trans-Acting Gene Regulators: Miguel Beato, Institute of Molecular Biology, Marburg, Germany
Structure and Expression of the Human Glucocorticoid Receptor: Ron Evans, Salk Institute, La Jolla, CA
Steroid Regulation of Transcription in Avian Species: Bert O'Malley, Baylor College of Medicine, Houston, TX

PLANTS

Session Chairman: Frederick Ausubel, Massachusetts General Hospital, Boston, MA
Molecular Genetics of Symbiotic Nitrogen Fixation: Frederick Ausubel, Massachusetts General Hospital, Boston, MA
Transposable Elements in Maize: Nina Sedoroff, Carnegie Institute, Washington, DC
Phytochrome Mediated and Organ-Specific Expression of Monocot and Dicot Genes in Transgenic Plants: Nam Hai Chua, Rockefeller Institute, New York, NY

DEVELOPMENTAL BIOLOGY

Session Chairwoman: Shirley Tilghman, Fox Chase Cancer Center, Philadelphia, PA
Developmental Regulation of Cloned α - Fetoprotein Genes in Cells and Mice: Shirley Tilghman, Fox Chase Cancer Center, Philadelphia, PA
Molecular Probes for the Development and Plasticity of the Neural Crest: Richard Axel, Columbia University, New York, NY
RNA Localization in Transcription during Frog Embryogenesis: Douglas Melton, Harvard University, Cambridge, MA
Genetic and Mutational Analysis of Embryogenesis in Drosophila: Eric Wieschaus, Princeton University, Princeton, NJ
Homeobox - Containing Mouse Genes and Their Expression During Mouse Developmental Processes: Peter Gruss, Univ. of Heidelberg, W. Germany

NEUROBIOLOGY

Session Chairman: James L. Roberts, Columbia University, New York, NY
The Identification of a New Brain Hormone: The Pro-GnRH Molecule and its Physiology: Peter Seeburg, Genentech, Inc., South San Francisco, CA
Gene Expression in Identified Aplysia Neurons: Richard Scheller, Stanford University, Palo Alto, CA
Expression of Opiate Peptide Genes in Heterologous Cell Systems: Edward Herbert, Oregon Health Sciences University, Portland, OR
Transcriptional Regulation of Gene Expression in Neuroendocrine Cells: James L. Roberts, Columbia University, New York, NY

YEAST

Session Chairman: Jack Szostak, Massachusetts General Hospital, Boston, MA
Behavior of Artificial Chromosomes in Yeast: Jack Szostak, Massachusetts General Hospital, Boston, MA
Positive Activation of the his 3 Promoter: Kevin Struhl, Harvard Medical School, Boston, MA
Genetic Recombination in Yeast: Rodney Rothstein, Columbia University, New York, NY
Ty Element Transposition: Jef Boeke, Massachusetts Institute of Technology, Cambridge, MA

POSTER SESSIONS AND EXHIBITS

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\$ 75 STUDENT REGISTRATION - Student status must be confirmed in writing by department chairman. Does not include journal subscription.
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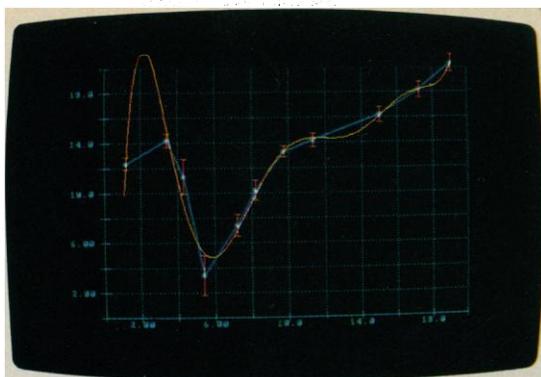
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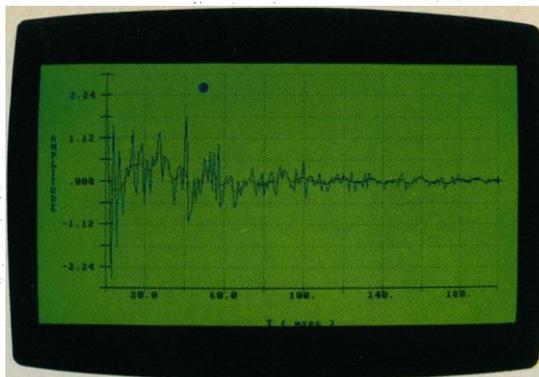
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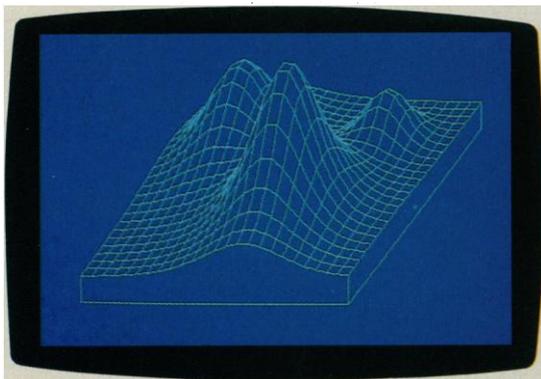


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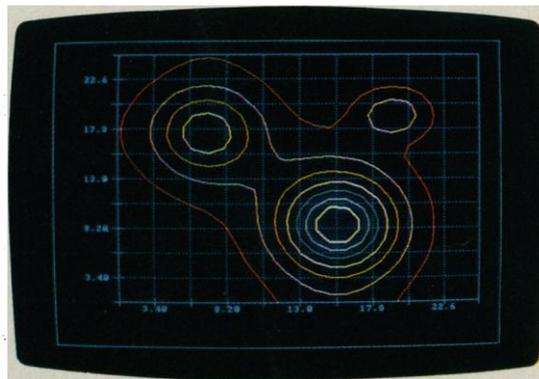


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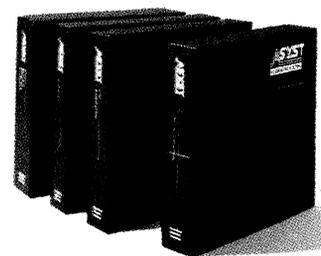
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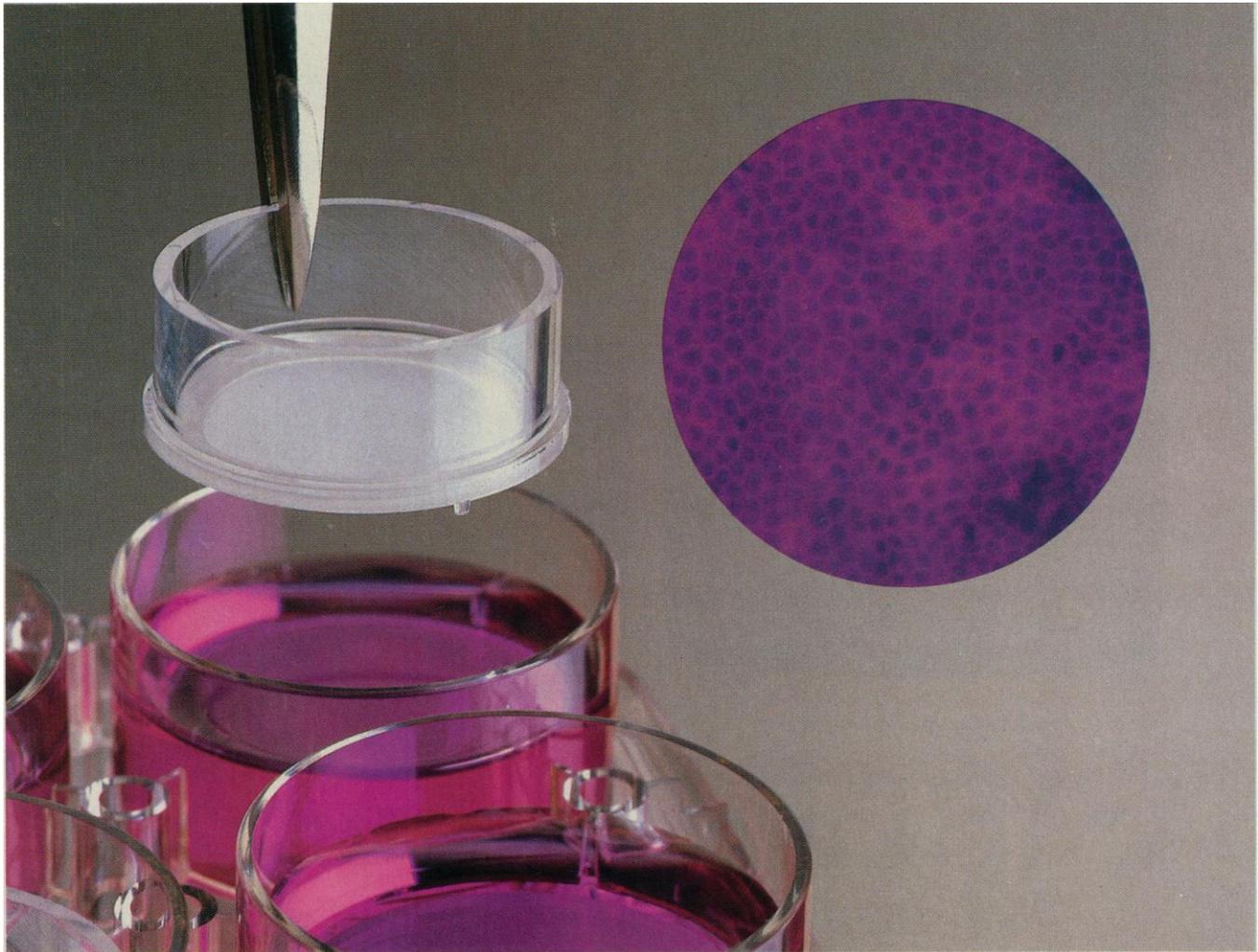
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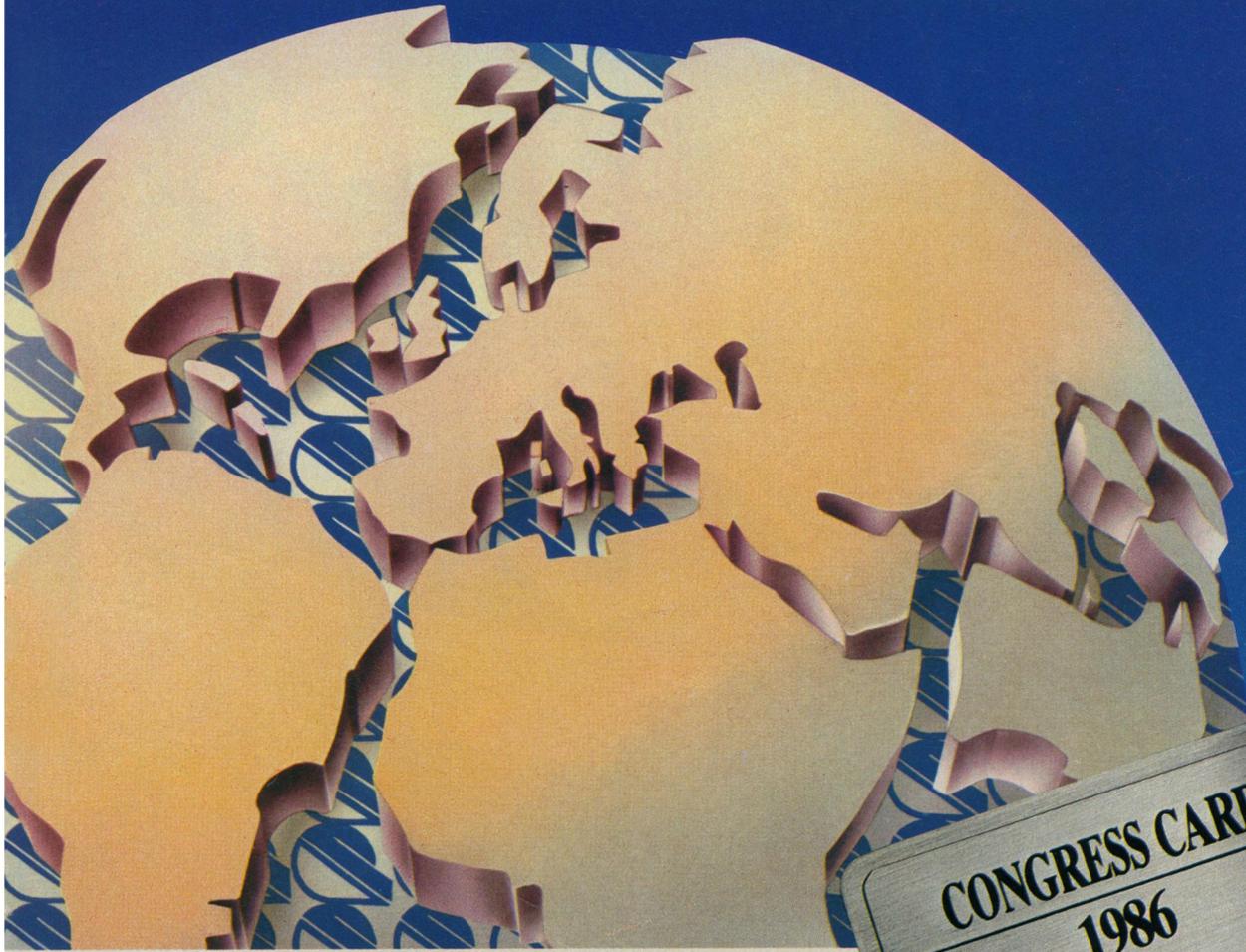
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Paris, April 7-9

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A.H. DeCherney (USA)

Dexamethasone-Suppressible Hyperaldosteronism

Rome, June 5-6

Scientific Organization: M.I. New (USA)

Corticosteroids and Peptide Hormones in Hypertension

Mannheim, Sept. 6-7

Scientific Organization: E.G. Biglieri (USA),
F. Mantero (I) and P. Vecsei (D)

Recent Advances in Adrenal Regulation and Function

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G. Chrousos (USA) and L. Loriaux (USA)

Fertility Regulation Today and Tomorrow

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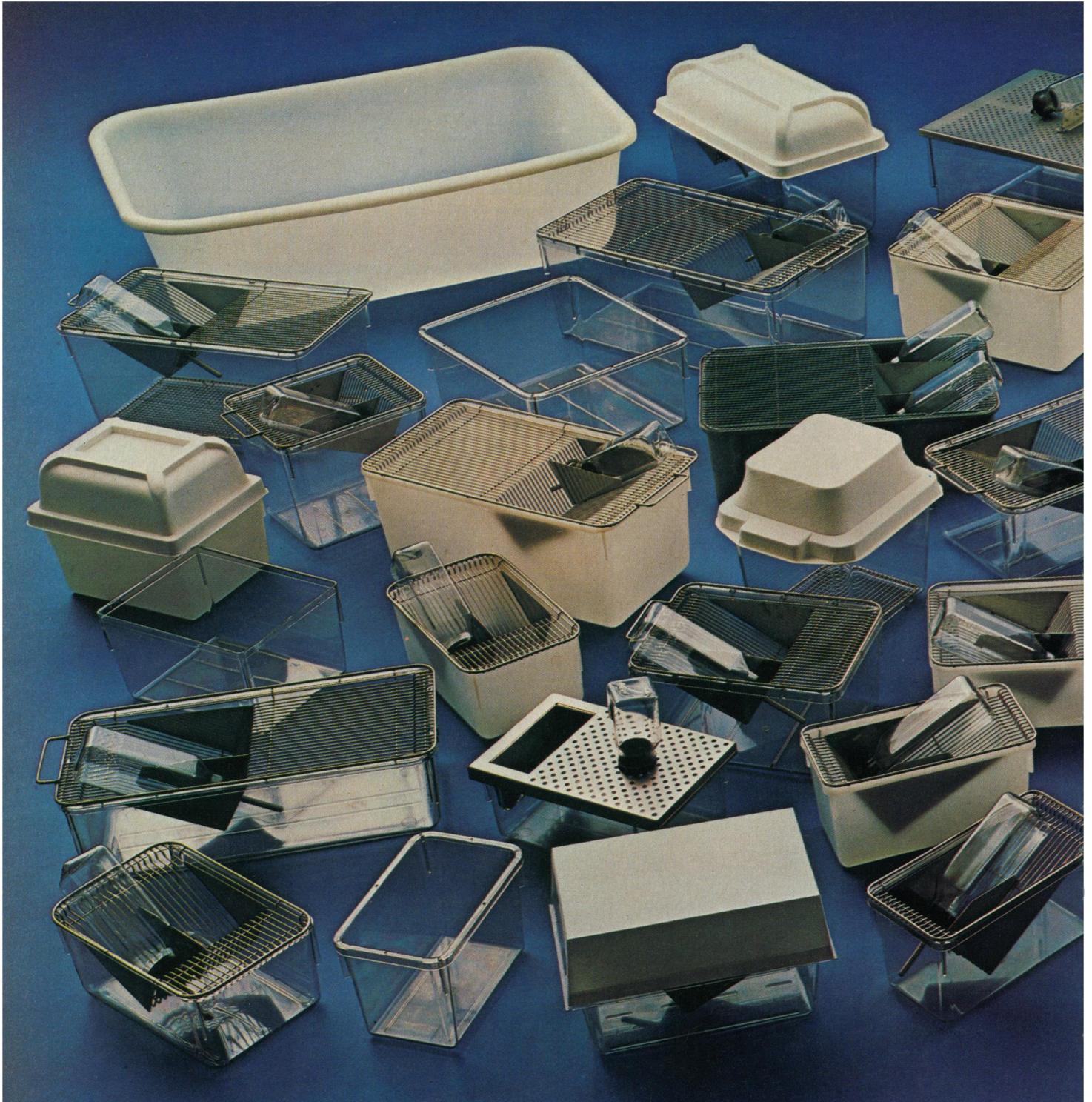
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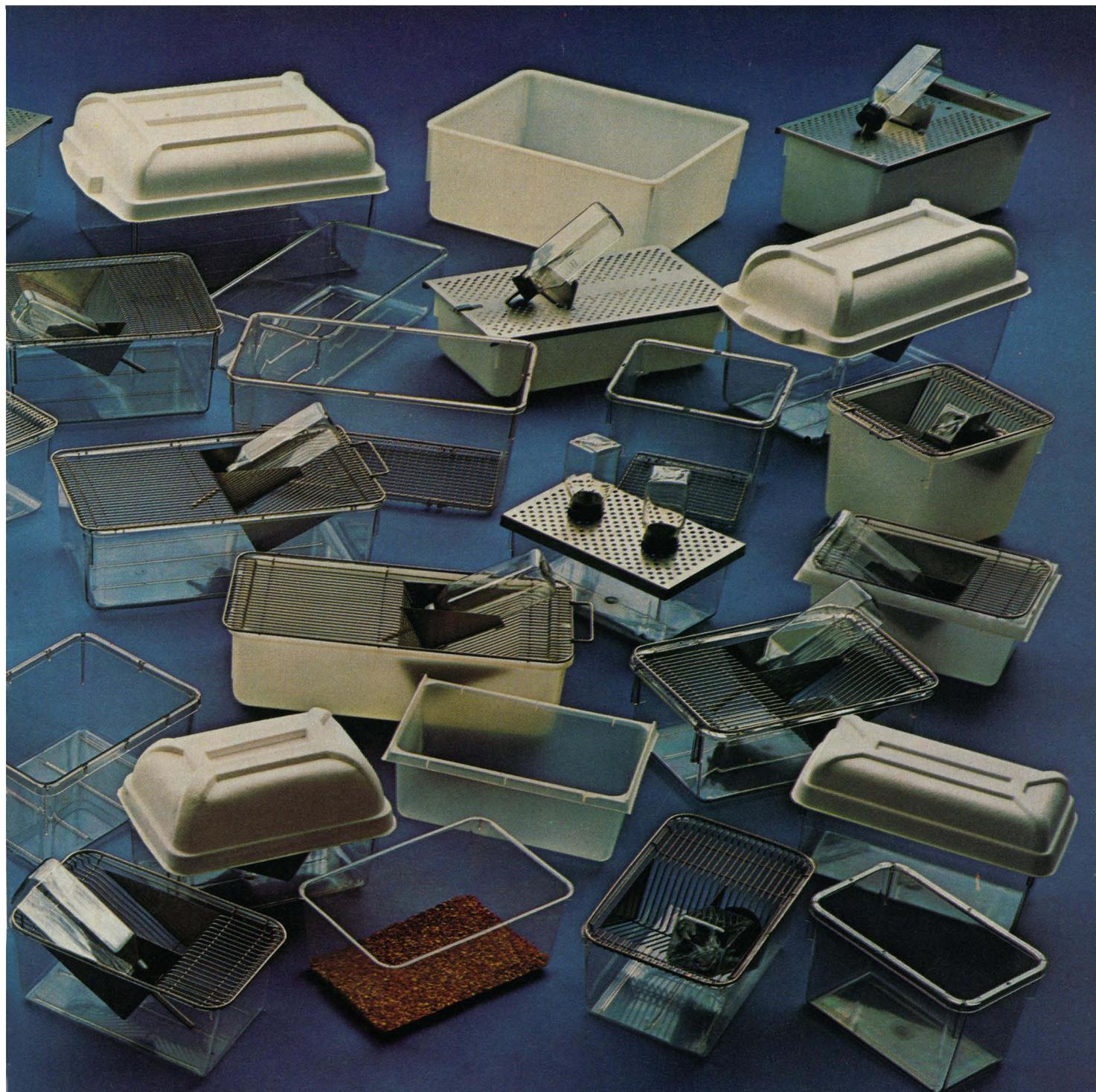
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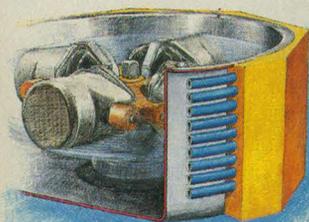
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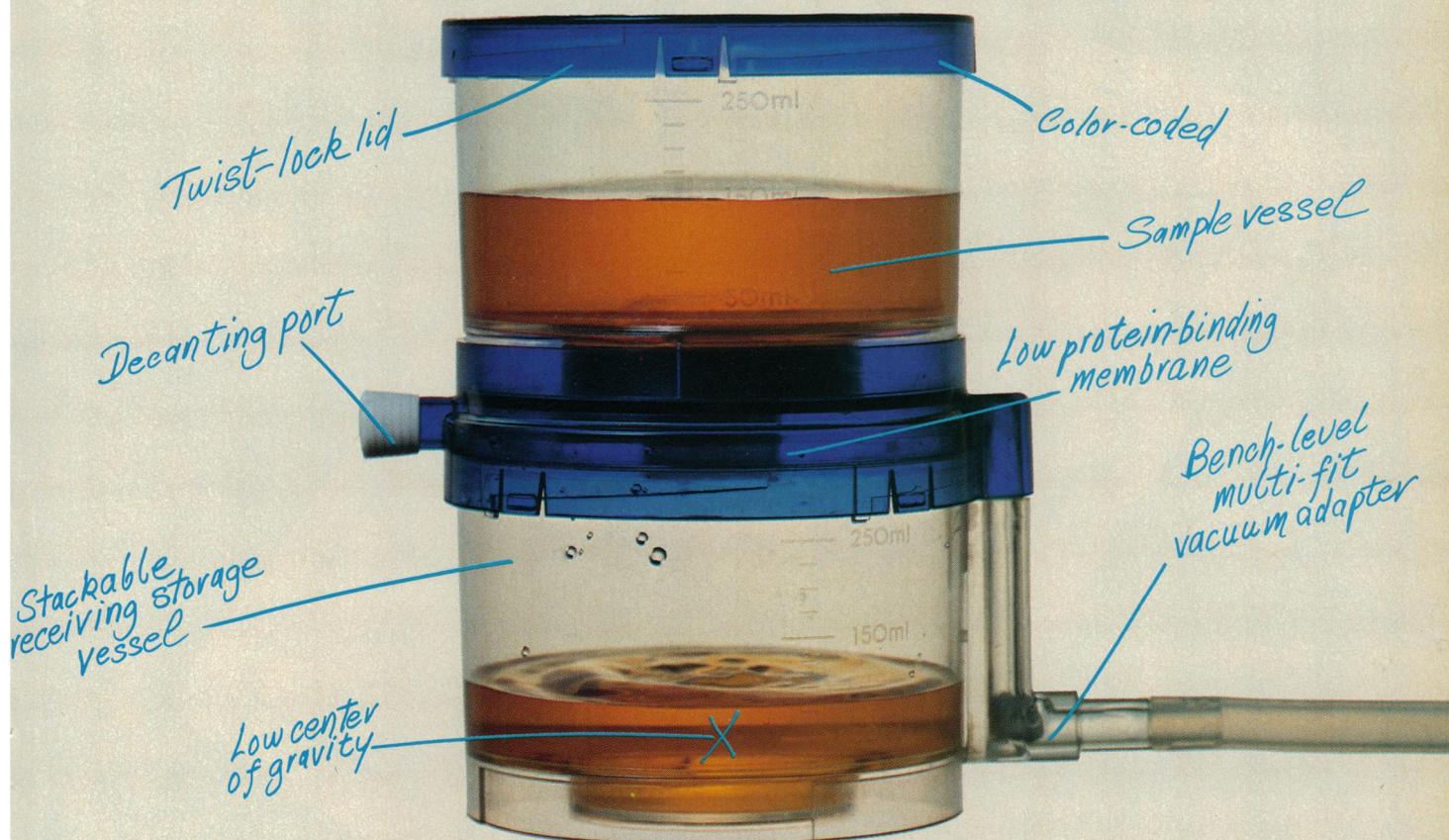


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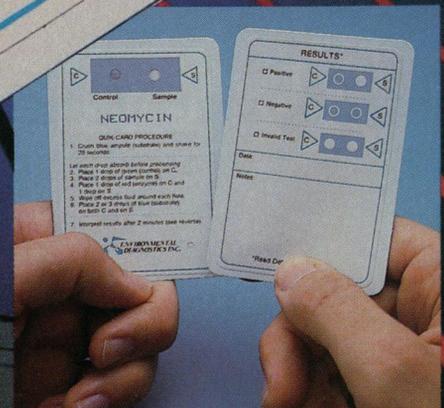
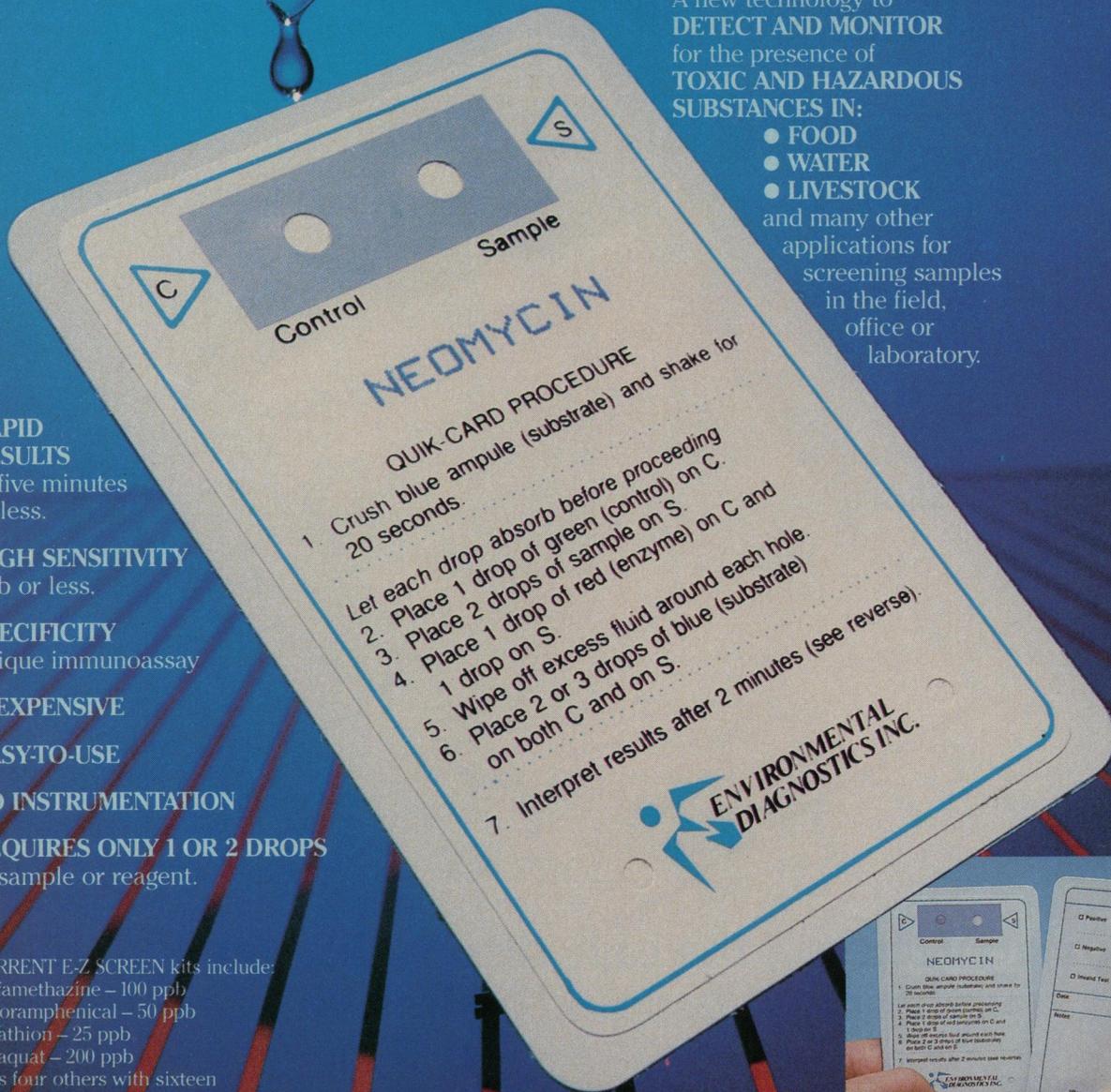
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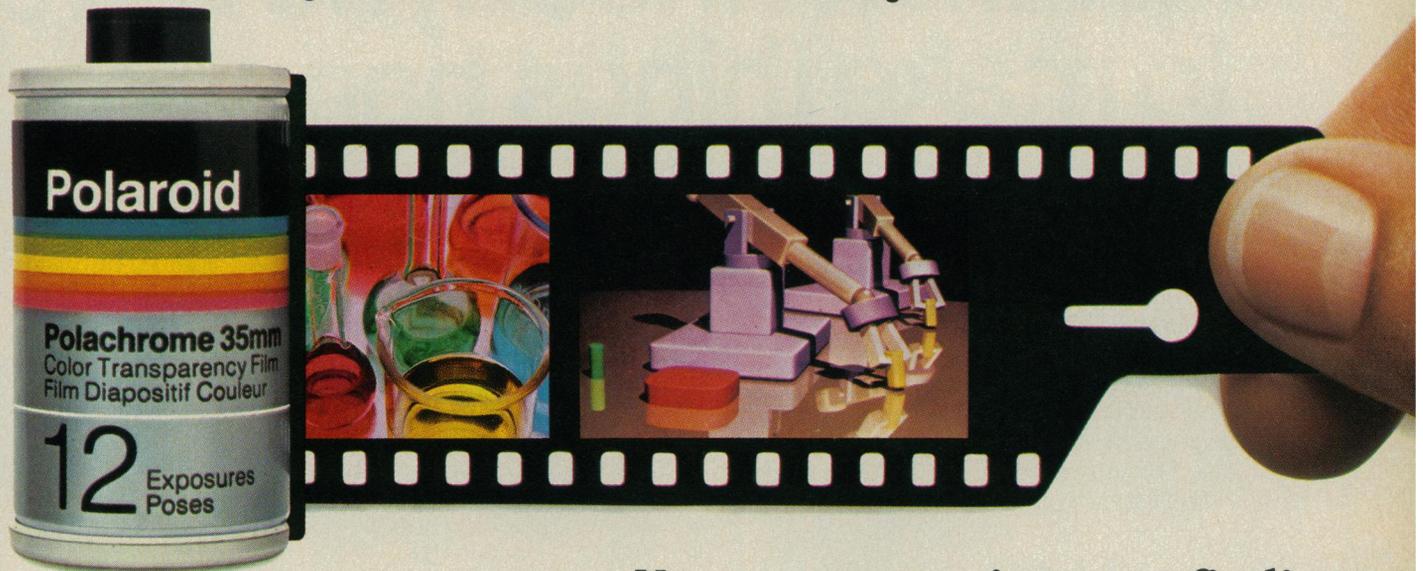
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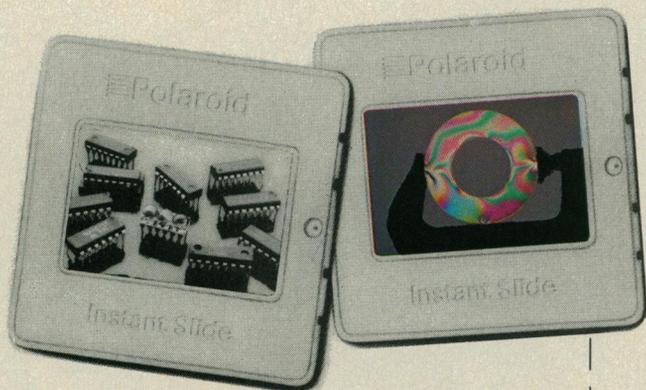
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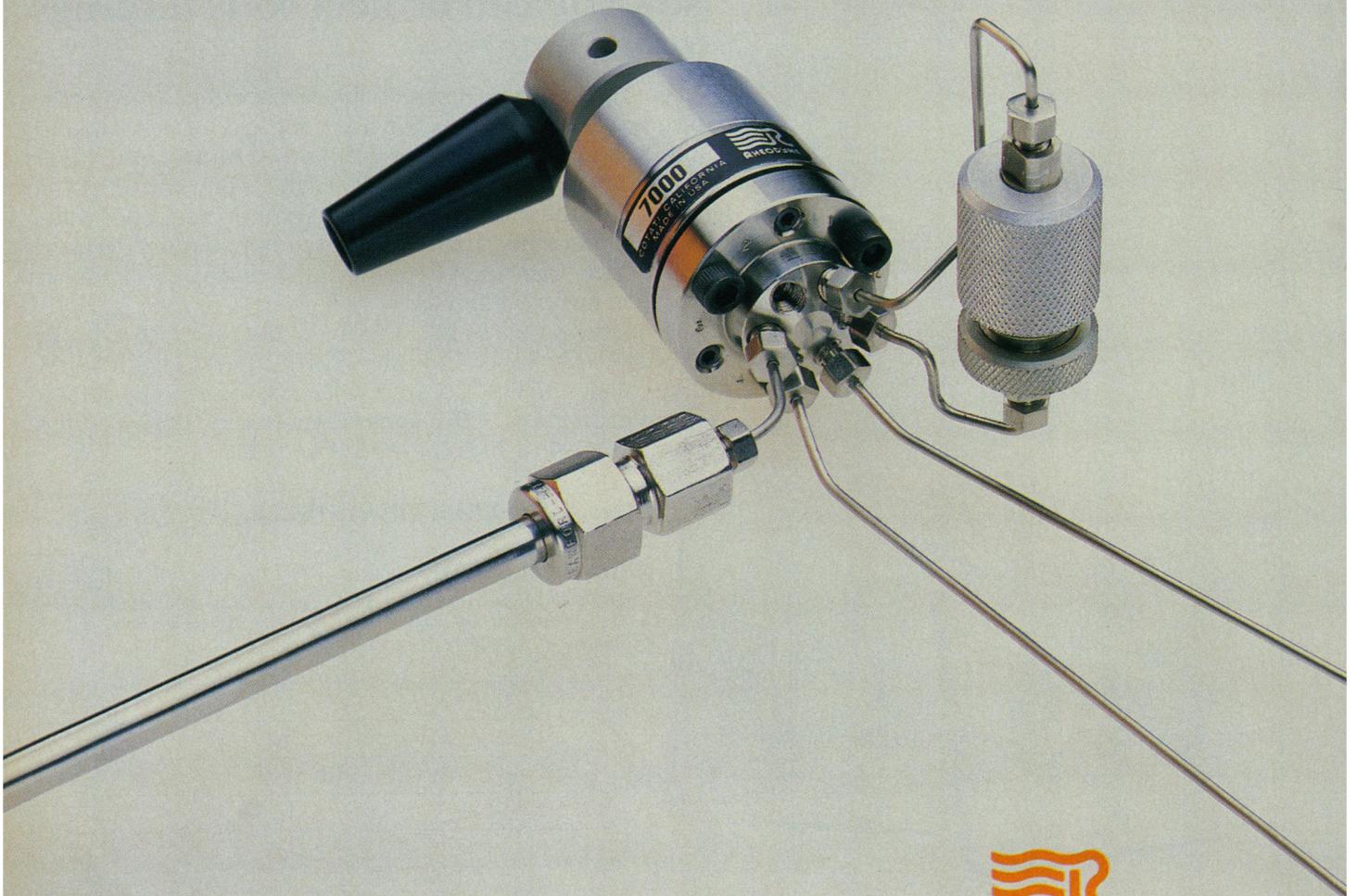
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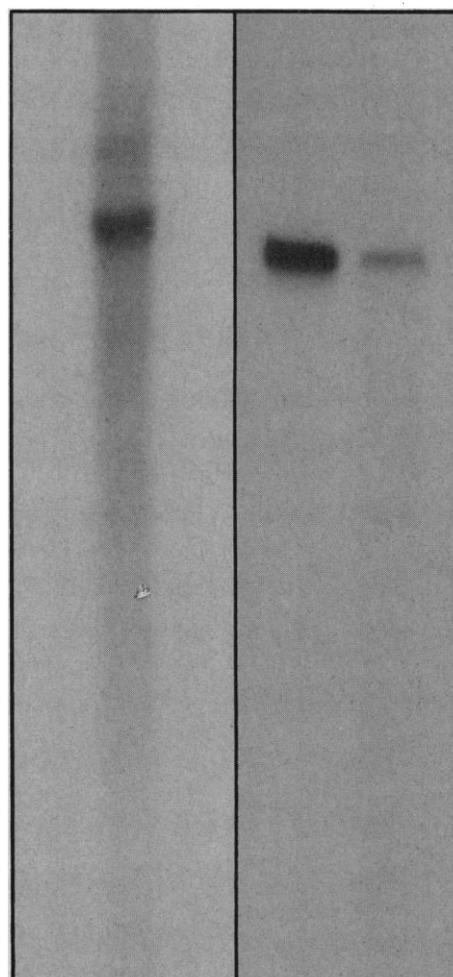
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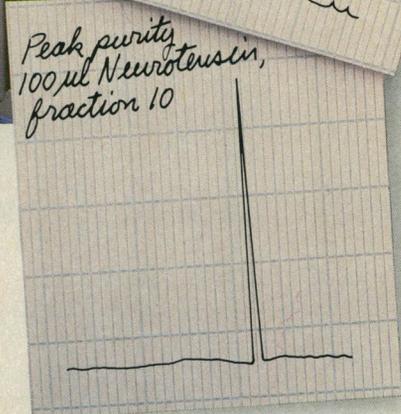
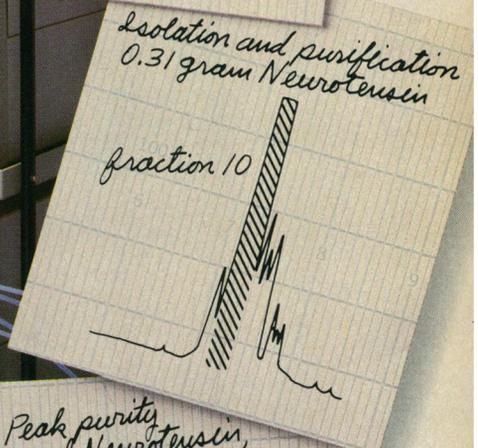
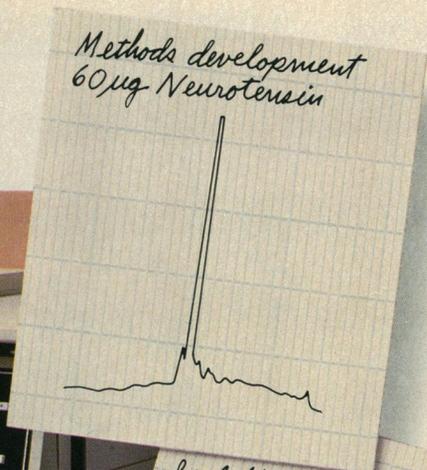
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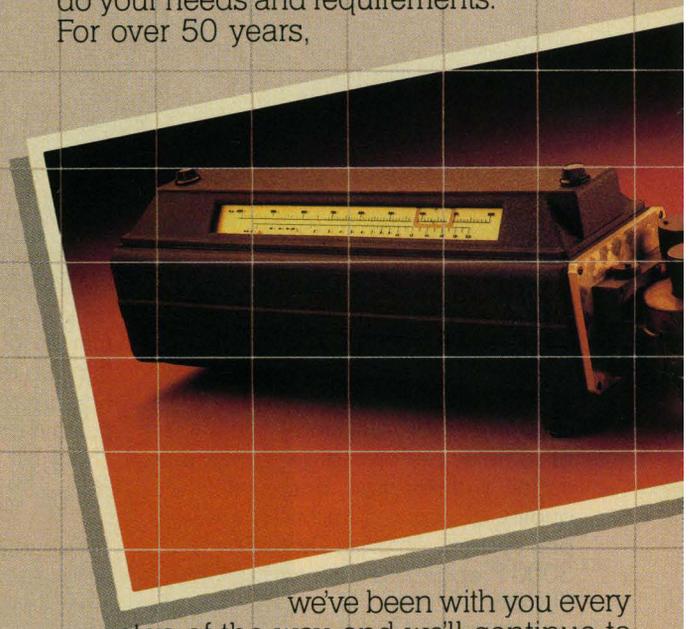
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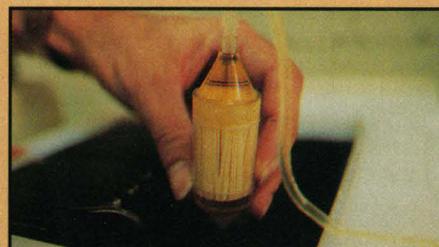
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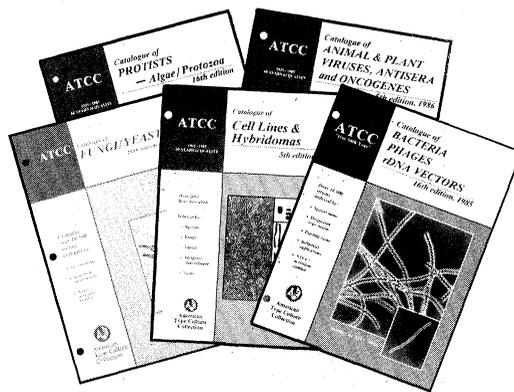
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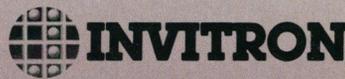
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In Pursuit of the Renewable Frontier

The endearing feature of intellectual frontiers is that they are in endless supply. Explorers of continents fight their way through wildernesses until they arrive at the water's edge, and then sigh that there are no new mountains to conquer. Researchers, on the other hand, are part of an ever-expanding universe, inevitably creating new territories to explore as they complete the maps begun by the discoveries of the past.

No area of research illustrates this phenomenon more clearly than modern biology, which many believe is in its Golden Age. This issue of *Science* presents a *Frontiers in Biology* collection that contains an illustrative—but certainly not exhaustive—list of areas that have great potential for the future.

In the first article, Jim Hudspeth deals with an area of fantastic scientific challenge: the mechanisms of hearing. The cochlea is the most complex mechanical apparatus in the human body, with a million moving parts designed to convert sound waves into electrical signals. It relays to the brain a complex mixture of sounds, some of which are only slightly higher in energy than background noise.

Dennis Drayna and Ray White analyze an ancient problem, the inheritance of disease, using an unusual opportunistic combination of religion and recombinant DNA. Because Mormon families have large numbers of children, a tradition of record-keeping through many generations, and a generosity in terms of a helpful interest in community causes, an abundance of information about their hereditary lineage is available. The use of restriction enzymes, the delicate surgeons of DNA structure, adds a new tool to population genetics. The combination provides an ability to follow genetic diseases through generations. It has led to the mapping of the X chromosome and to a vast potential for increasing our understanding of genetic disease and for providing clinical help for individuals.

Differentiation is a puzzle constantly searching for new techniques, and Helen Blau and her co-authors discuss one of these that shows particular promise. By fusing two cells from different species, a hybrid cell is created that contains the nuclei of both cells. The resulting hybrid cell is stable and can be studied over long periods of time, making it appropriate for the study of muscle development and the timing of signals for gene expression during differentiation.

An example of "the medium is the message" is a new hormone, the atrial natriuretic factor, which plays a key role in water control, electrolyte balance, and blood pressure. It is described by Adolfo de Bold and offers hope for new therapeutic interventions in hypertension and heart failure.

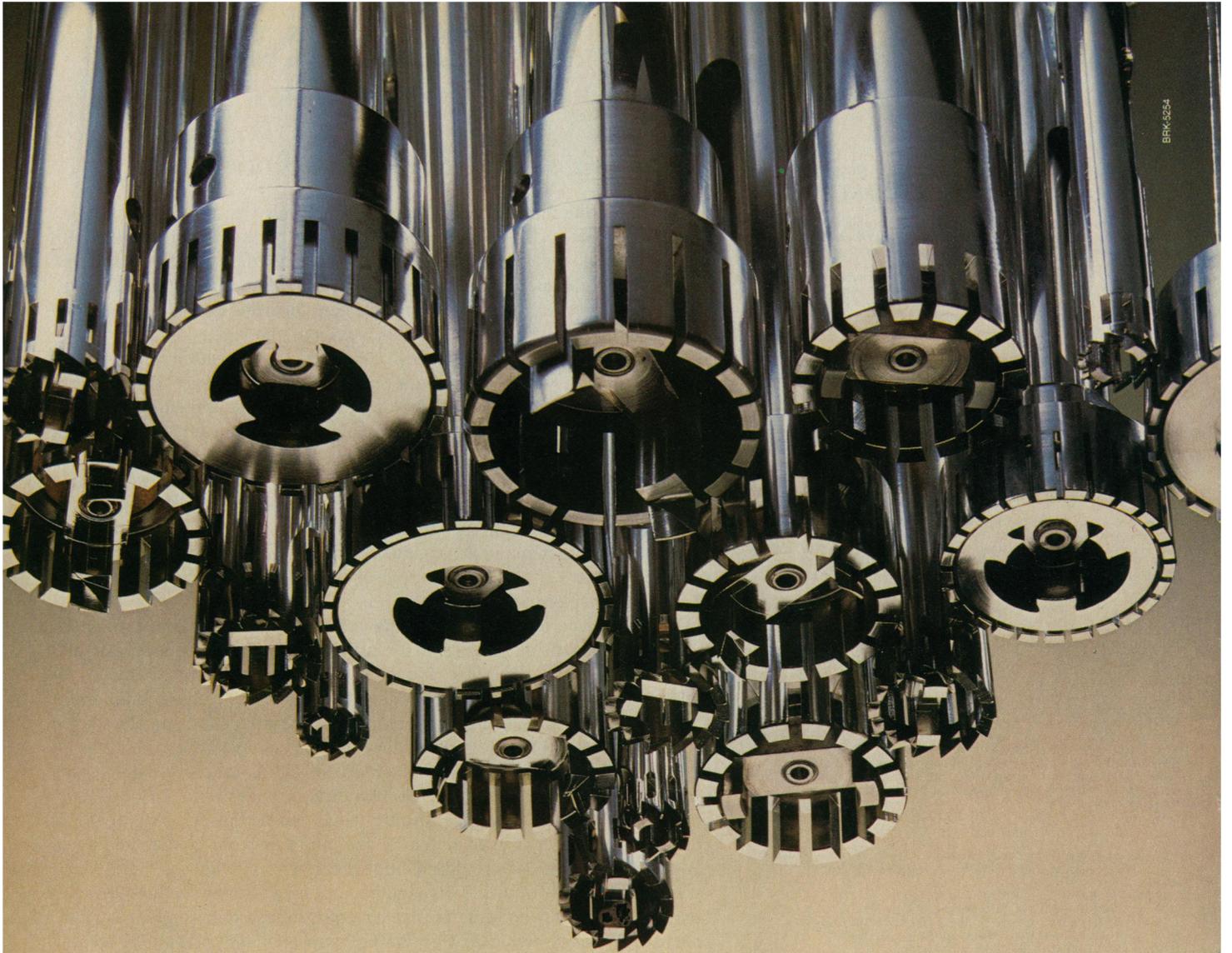
The melodramatic world of the oncogene, those genes that have been frequently identified as being "at the scene of the crime" of cancer but have so far not been convicted of a clear-cut offense, is discussed by Robert Weinberg in a "whodunnit" that considers the current evidence but enticingly leaves the final chapter to be written in the future.

The finding that susceptibility to disease may be inherited in ways quite different from the inborn errors of metabolism has led to correlation of the immune apparatus with the tendency to contract certain diseases. Robert Goodenow and co-workers focus on one aspect of this problem that is of great interest in modern science: the role of the major histocompatibility complex in the immune surveillance of cancer cells.

As this issue goes to press and we plan new issues of frontiers in physics, chemistry, astronomy, and other areas, an editor cannot help but reflect on the personality of individuals who are satisfied by such an unceasing quest. Are we scientists just curious children who have never grown up? Are we the most idealistic of people, bravely confronting the ultimate challenges for the good of mankind? Or are we the most selfish of its citizens, who have discovered the ideal way of life: solving nature's crossword puzzles while being subsidized in our happiness? Whatever the answer, we are all, in the words of the poet, "emperors of the endless dark, even in seeking."

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Deadline 17 January 1986

The next Annual Meeting of the AAAS will be in Philadelphia, PA, 25-30 May 1986, at the Franklin Plaza, Bellevue Stratford, and Hershey Philadelphia hotels; plan to attend. Information about program activities, as well as housing and registration forms, will appear biweekly in *Science*, beginning with the 31 January 1986 issue.

Although it is too late to submit suggestions for symposia for the 1986 Annual Meeting, contributed papers can be sent in up to 17 January 1986. The contributed paper sessions will be either of the POSTER or SLIDE type; see below for instructions and abstract sample.

POSTER SESSION: Each contributor will have a bulletin board on which to place text and graphics (oversized for easy reading)

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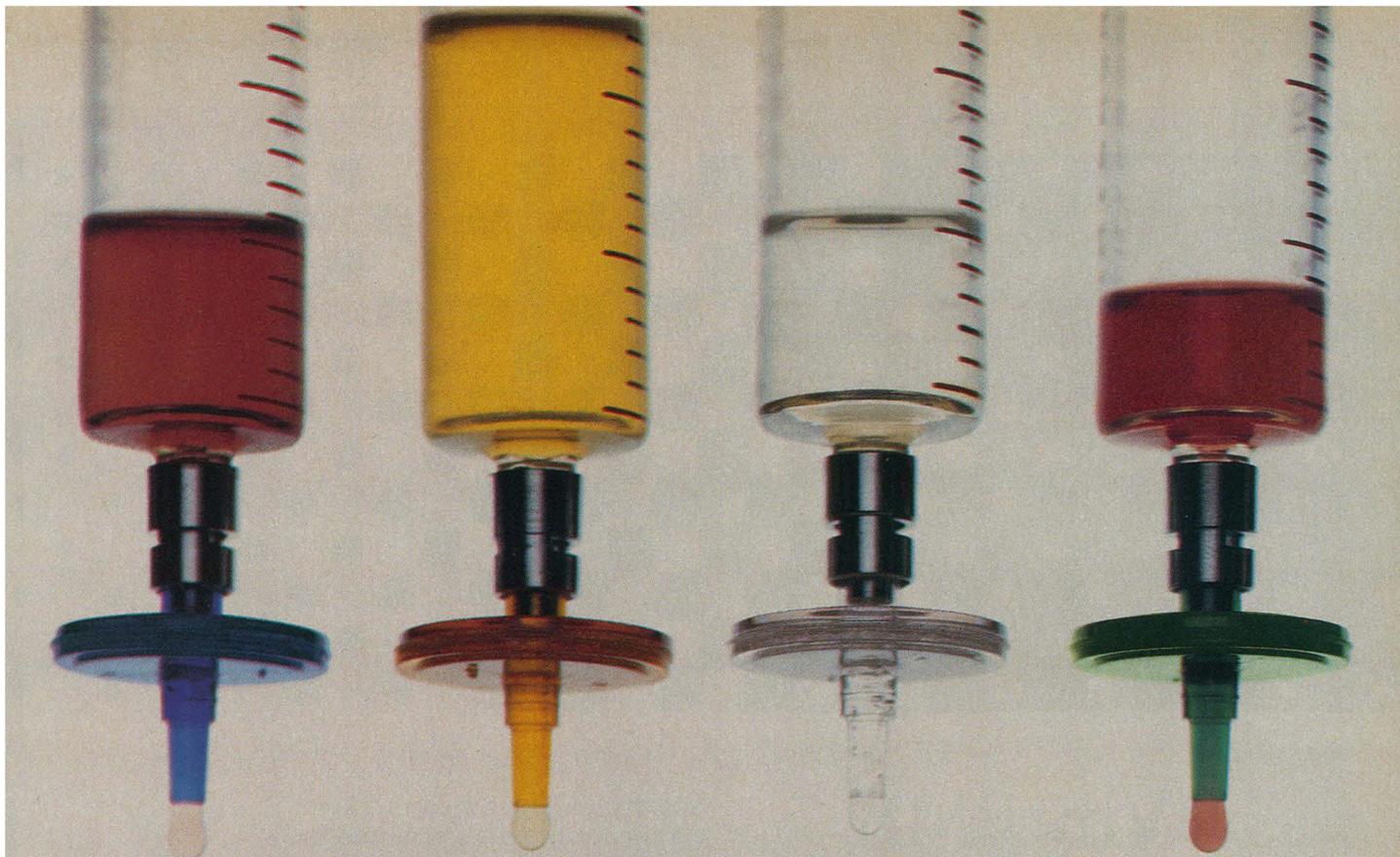
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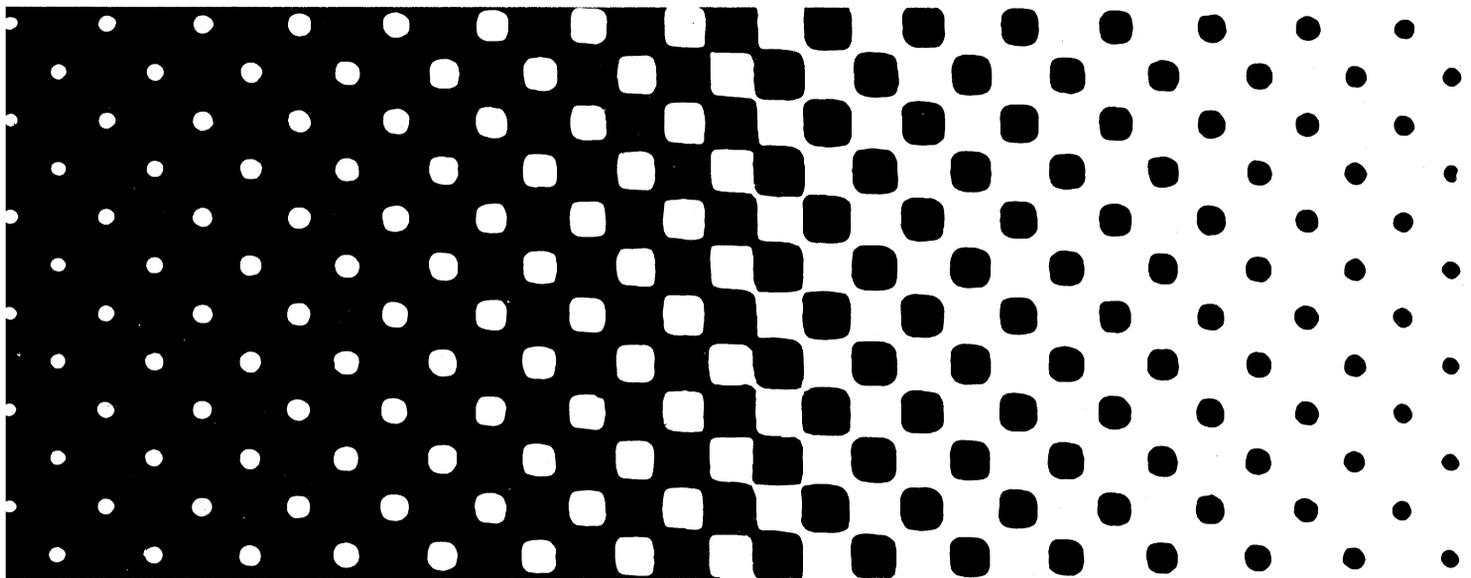
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