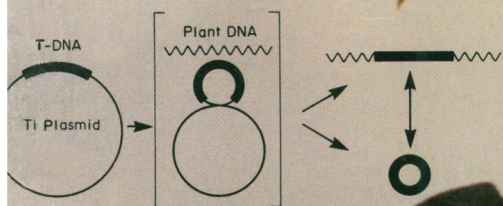


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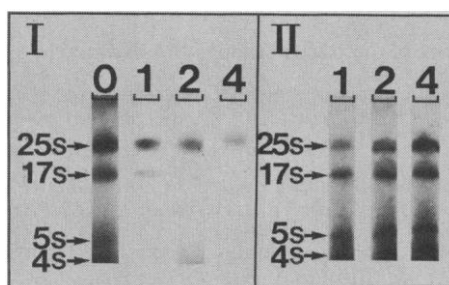
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- Stellwag, E. J. and Dahlberg, A. E., *Nucleic Acids Res.* 8: 299, 1980
- Towbin et al., *Proc. Nat. Acad. Sci. (US)* 76: 4350, 1979

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Recombinant DNA

Edited by John Abelson and Eleanore Butz

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Transfer of DNA from bacteria to plant cells and regeneration of a whole plant from tumor tissue. A shoot from a cloned teratoma tumor of Havana 425 tobacco induced by the soil bacterium *Agrobacterium tumefaciens* was grafted onto a Turkish variety host. The flowering shoot and teratoma which developed at the graft union both contained genetic information derived from *Agrobacterium*. Also shown is a diagram of possible models for the transfer of tumor-inducing (Ti) plasmid DNA from *Agrobacterium* to plant DNA. See page 1385. [Andrew Binns, Rockefeller University, New York City]

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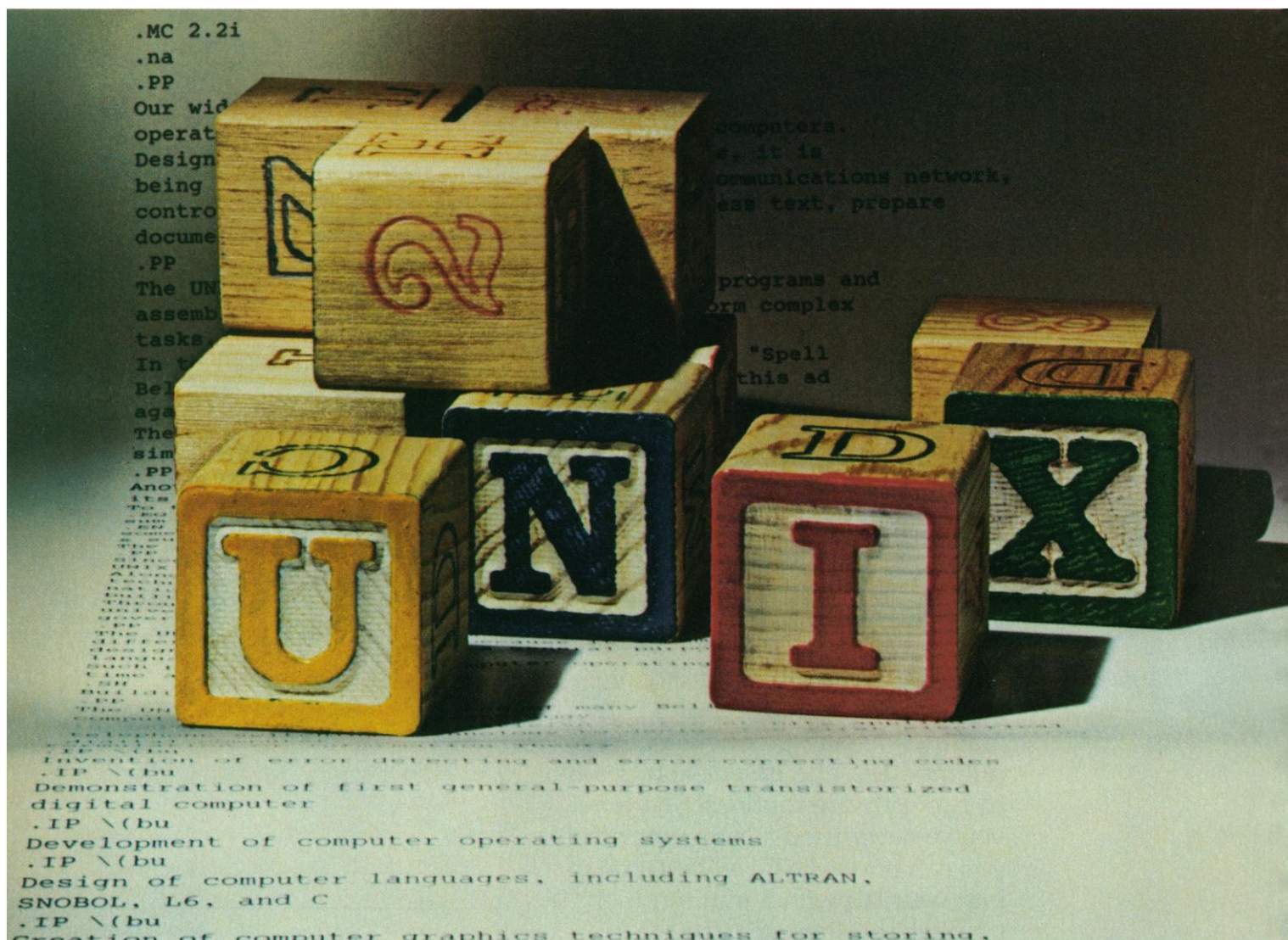
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The *UNIX* system allows users to take small programs and assemble them like building blocks to perform complex tasks. In text processing, for example, the command "Spell Bell Labs Ad" tells a computer to proofread this ad against a dictionary filed in its memory. The program that performs the task was created by simply combining several smaller *UNIX* programs.

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- Demonstration of first general-purpose transistorized digital computer
- Development of computer operating systems
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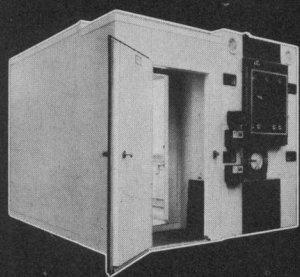
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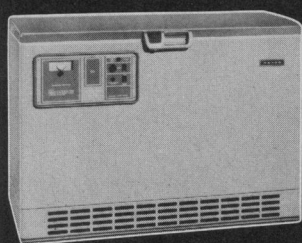


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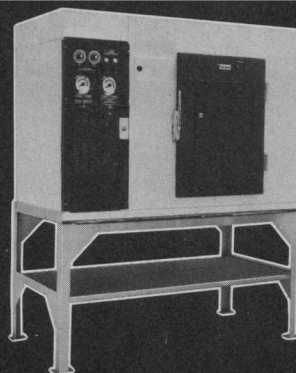
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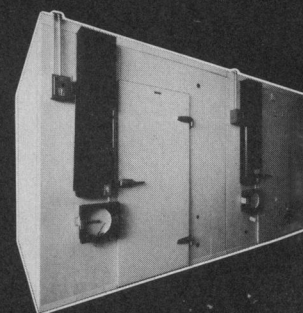
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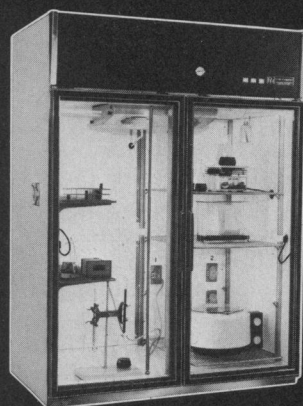
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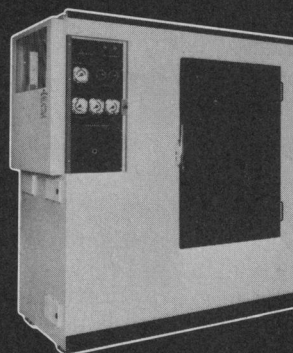
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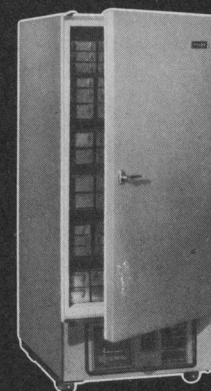
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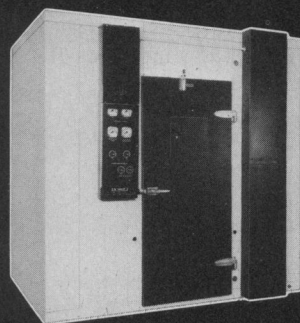
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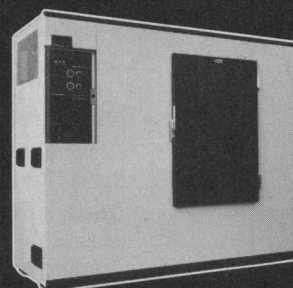
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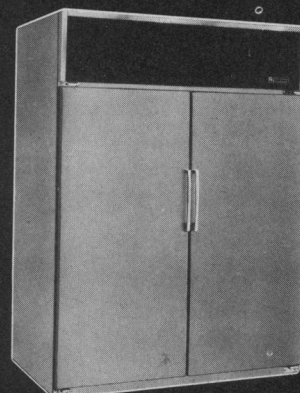
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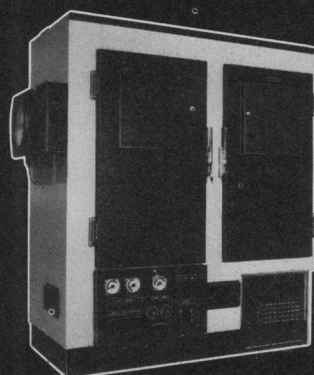
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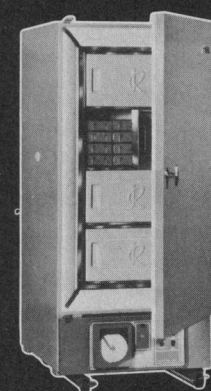
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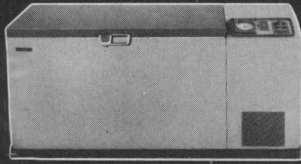
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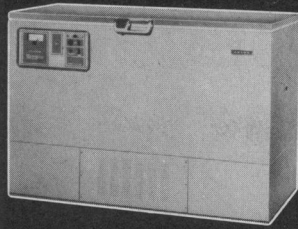
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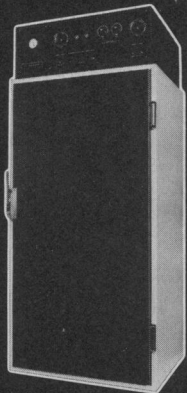
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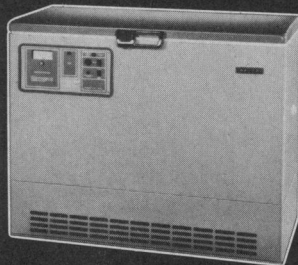
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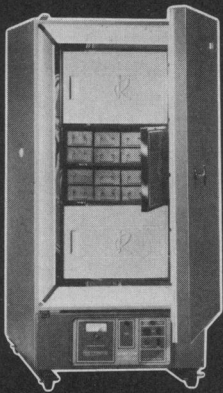
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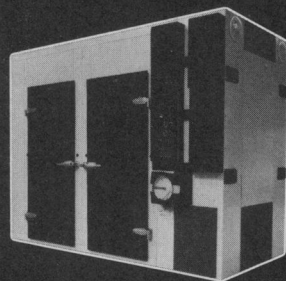
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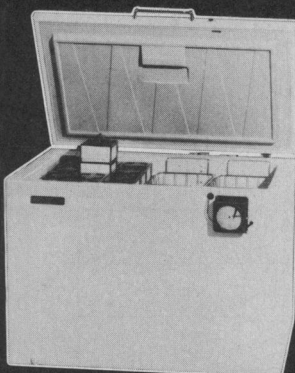
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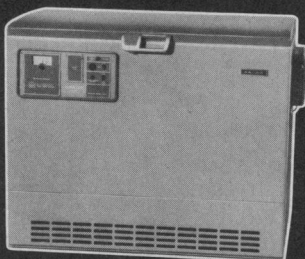
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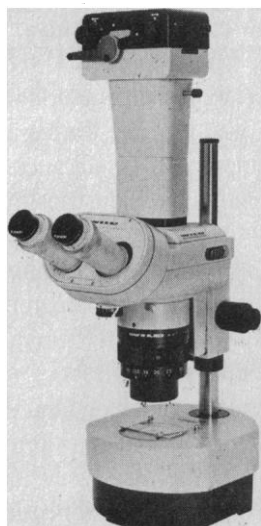


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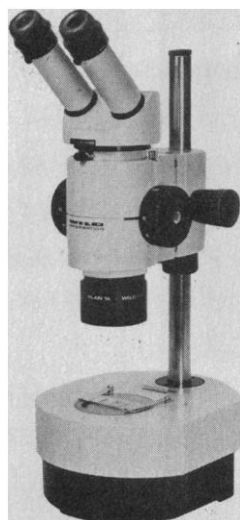
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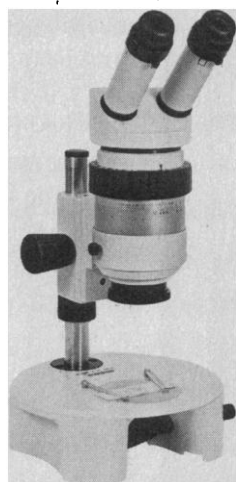
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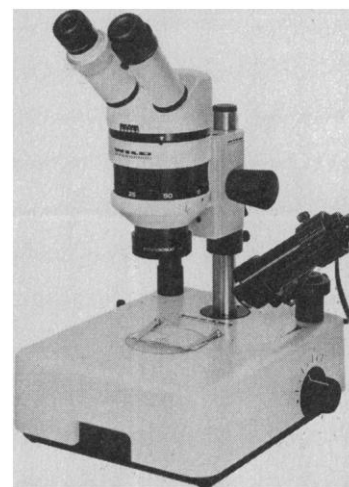
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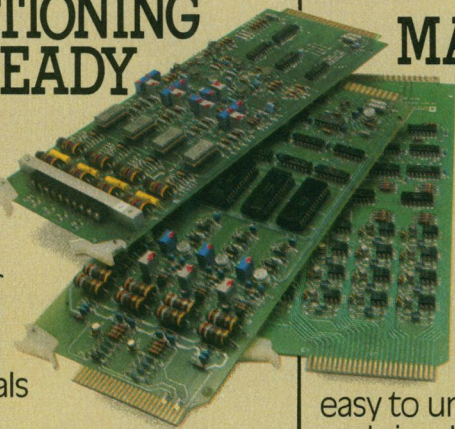
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A tall, stainless steel incubator system is shown against a textured, yellow and blue background. The top section has a control panel with multiple dials and digital displays. The main door is open, revealing several horizontal shelves inside. The bottom section is a solid, closed cabinet.

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Latin, "Omnis forma e DNA," — "All forms (of life) from DNA."

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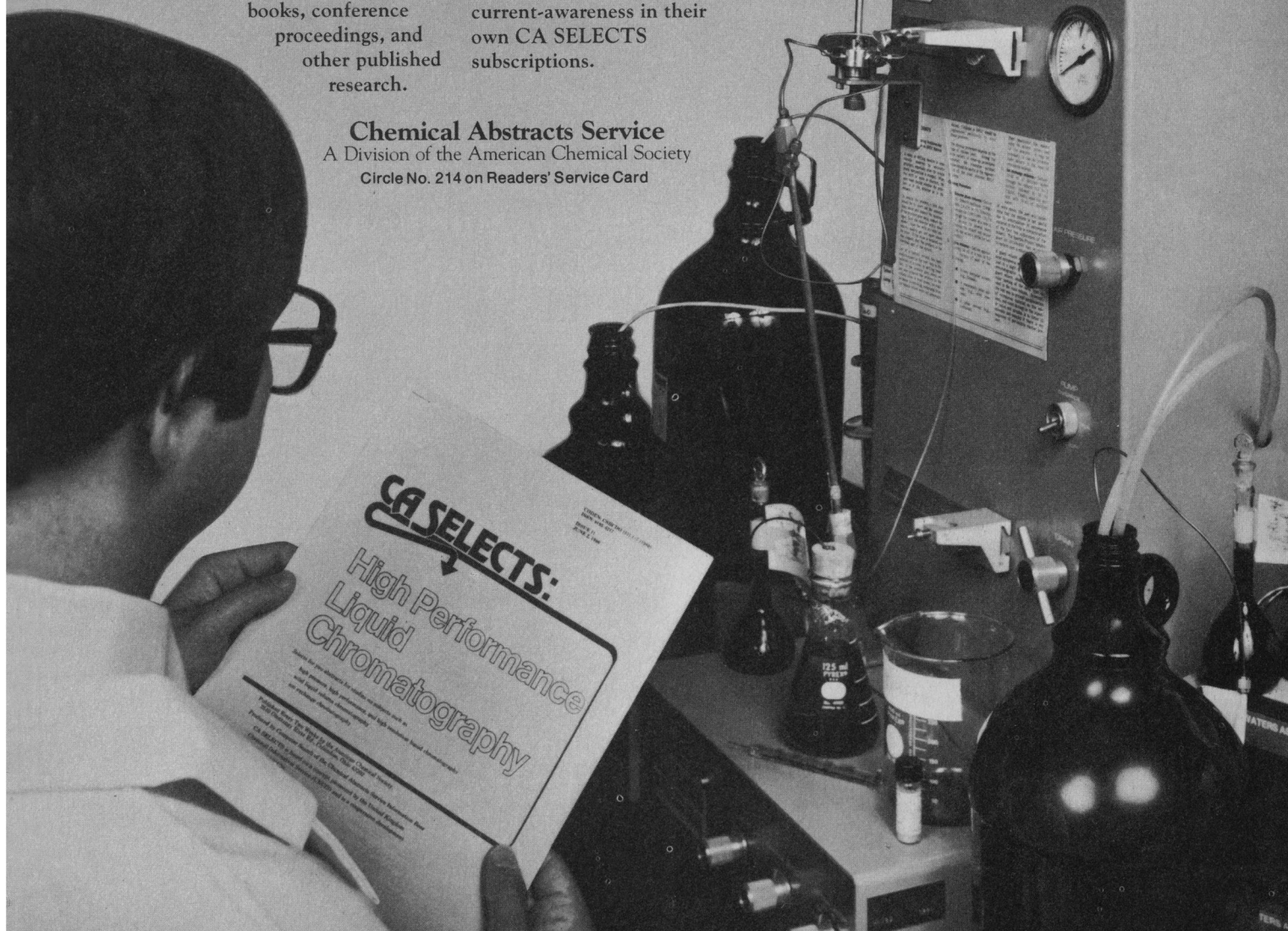
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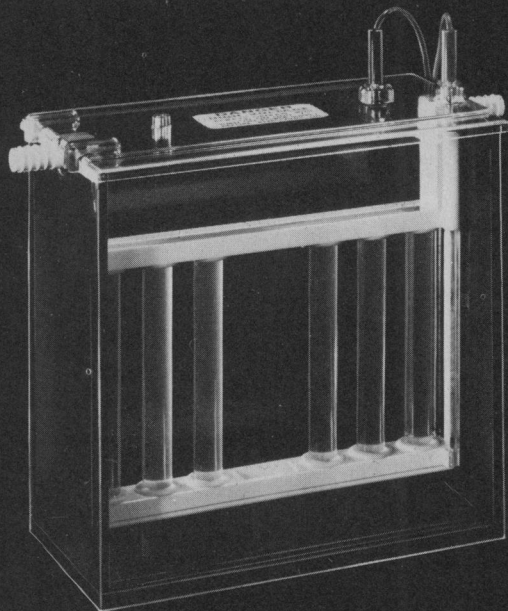
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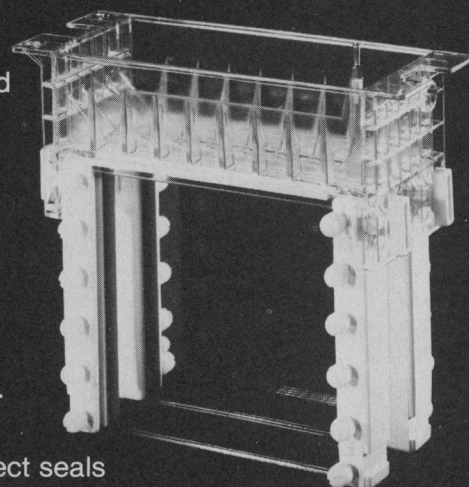


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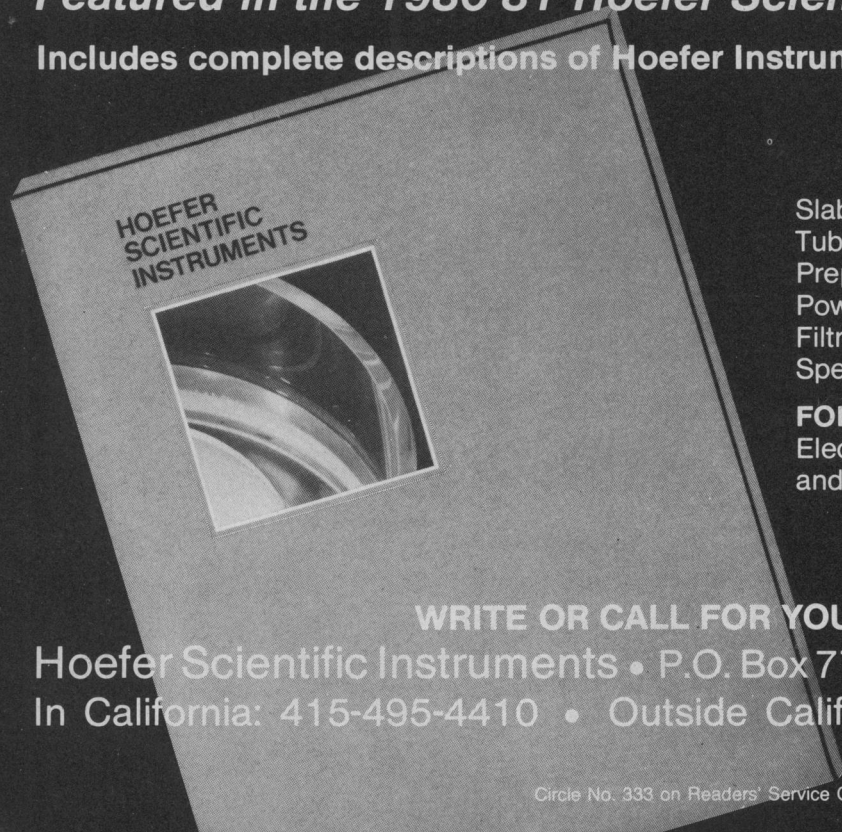


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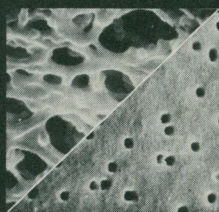
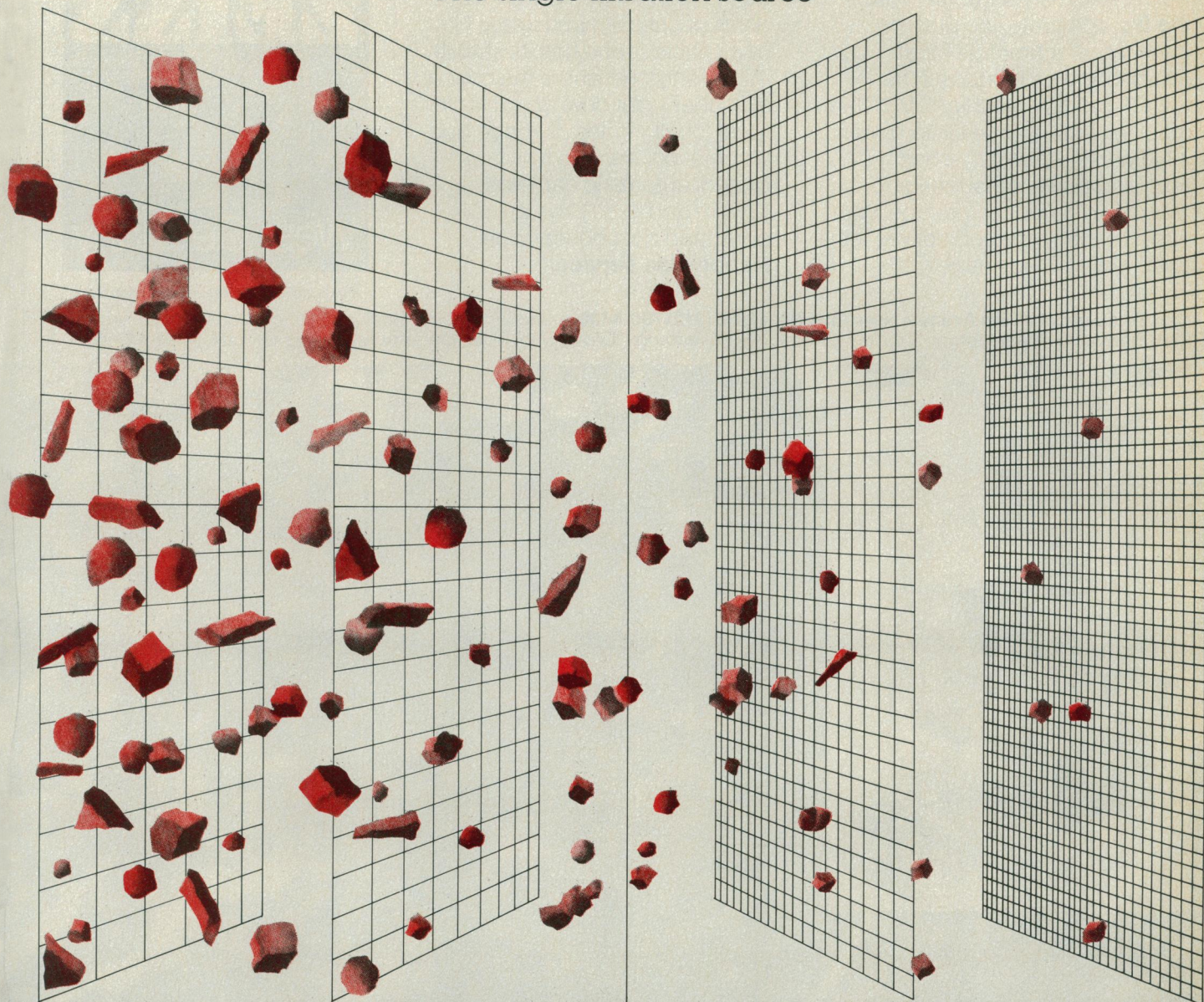
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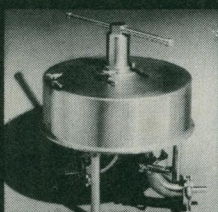


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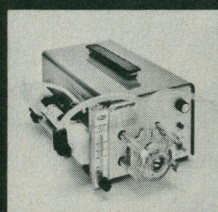


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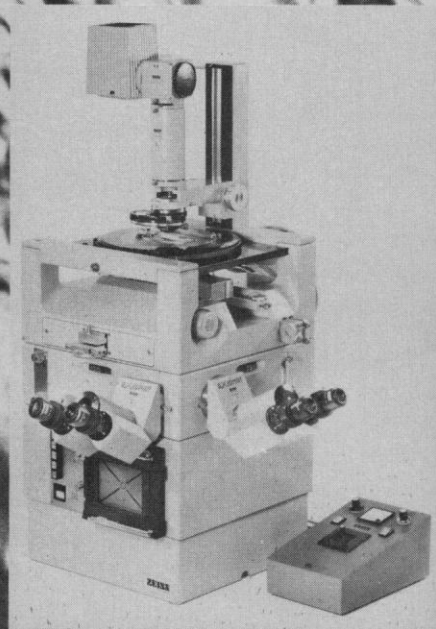
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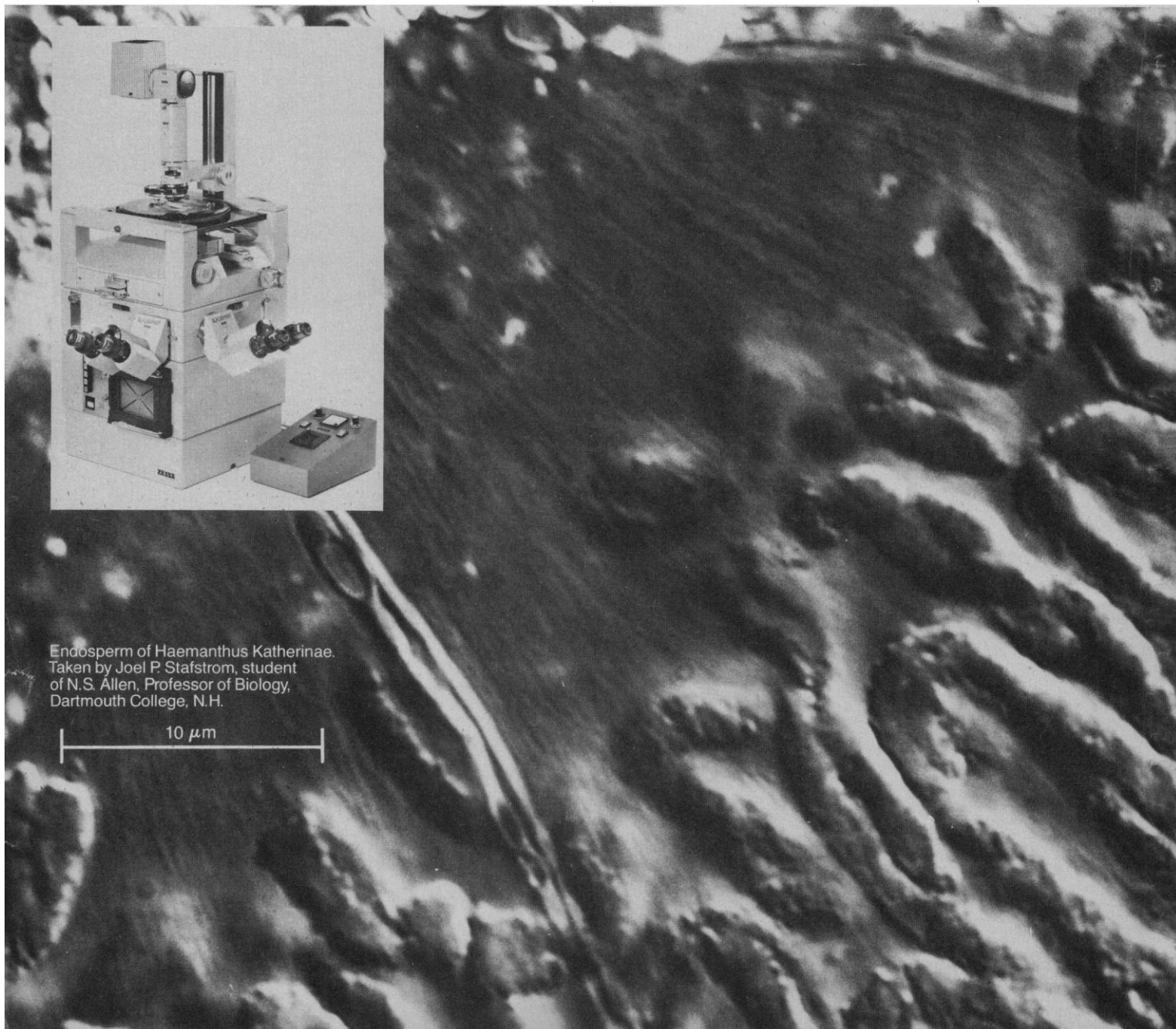
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Endosperm of *Haemanthus Katherinae*.
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10 μm



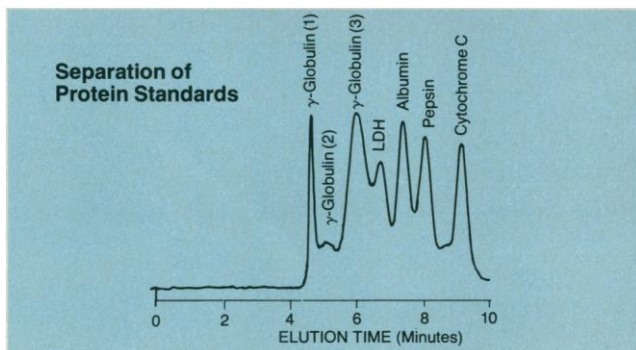
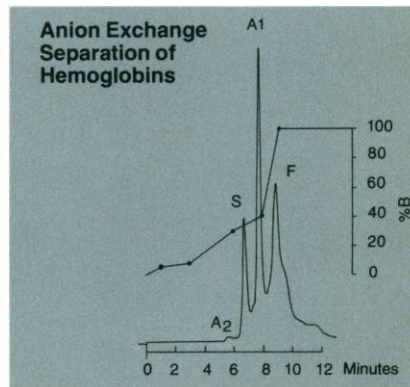
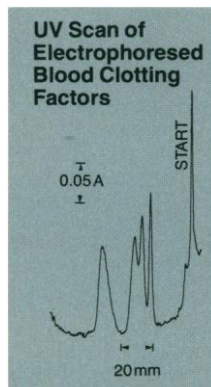
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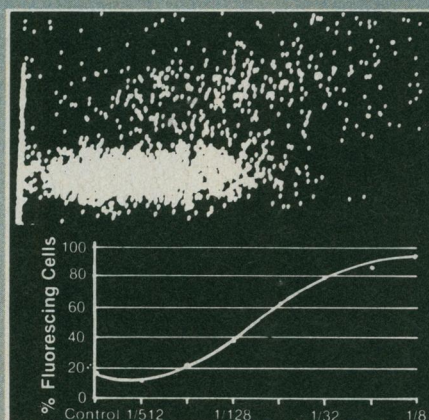
No other commercially available cell sorter and analyzer approaches the power, precision and versatility of the Ortho Systems 30/50. The instrument is offered in two basic configurations: System 30—a high resolution, 21 parameter analytical flow cytometer, and System 50—which adds cell sorting capabilities to the System 30 flow cytometer. Both feature dual lasers as standard equipment for increased analytical power.

System Components

To appreciate the far reaching capabilities of these Ortho instruments, consider that the System 50 combines: two lasers—a .8 milliwatt helium-neon for ultra high precision scatter measurements and a 5 watt argon type for fluorescence measurements (optional argon-ion, and krypton-ion lasers with U.V. capability are available); four detectors—two of the photomultiplier type for right angle scatter, and fluorescent emission detection (S-20 response, 185 nm–850 nm), and two solid state sensors for axial light loss and narrow angle forward scatter; a sophisticated optical system incorporating fiber optics; a multiplexed multichannel analyzer, with C.R.T. display; the signal processor unit; and an advanced cell sorter module (System 50). Additionally, the Model 2150 com-

puterized 8 parameter data handler/sorter controller is available as an option*. The 2150 System features simultaneous data acquisition, and realtime processing while sorting is in progress.

*Complete Model 2150 specifications available on request.



1. Upper: Direct immunofluorescence test (cytogram). Lymphocytes from CLL patient incubated with FITC labelled anti-human IgG. Lower: Titration of V-25 Leukemia cells from C-57 black mice different dilutions of FITC conjugated rat radiation leukemia virus antibody.

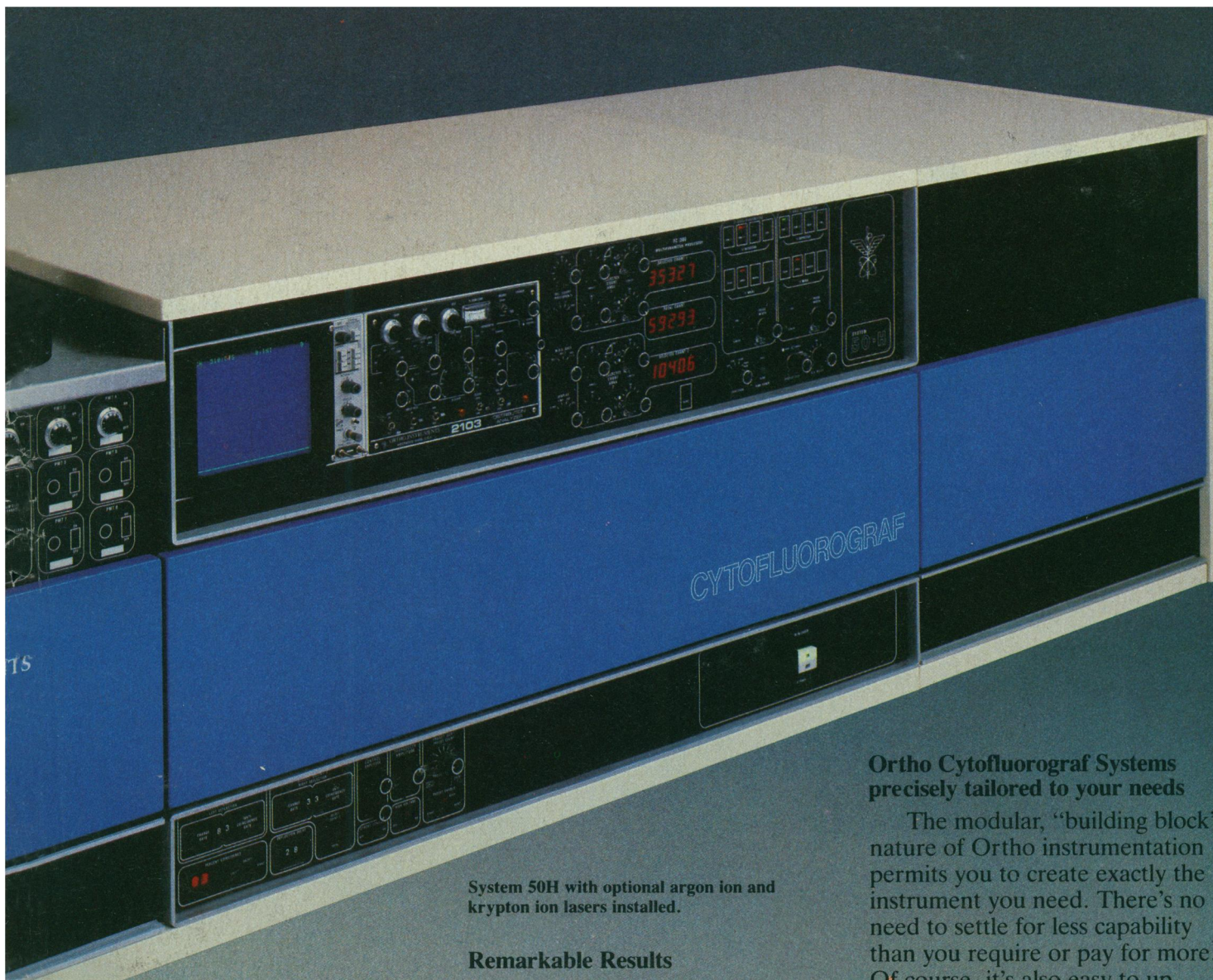
System Capabilities

These modules allow the System 50 to provide and analyze morphological information and sort on this basis, a significant first for a flow cytometric instrument. With four detectors and the ability



2. Cytogram of somewhat clumped Erlich ascites tumor cells, stained for DNA with ethidium bromide. Correlation of pulse area measurement (X) with pulse height (Y) permits distinguishing G2 cells from 2 x G1 aggregates.

to display pulse height, pulse area or pulse width analysis for each—

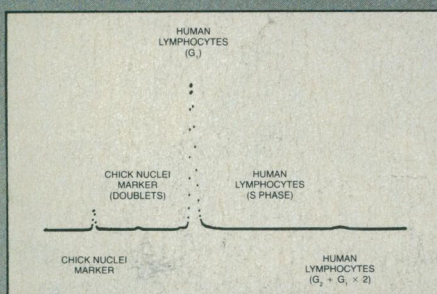


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The histograms and cytograms displayed were produced by the System 50. Evaluate them. And consider the difficulty of deriving this data by any other means. The capabilities of this unique Ortho instrument will speak for themselves.

In order to provide customers with complete support, Ortho maintains an Applications Laboratory that is available for confirmation and consultation services. Additionally, an international network of service technicians is ready to aid customers should calibration or repairs ever be required.



3. Histogram of human lymphocytes utilizing a chick nuclei marker for standardization and stained for D.N.A. with Propidium Iodide. C.V. = 1.65% (Human Lymphocytes)

a total of 21 distinct measurement parameters can be studied.

The System 50 also features: two bi-dimensional regions of interest, dual histogram multi-channel analyzer with cytogram mode, super-sil quartz optics with which the cells are analyzed and easy sample entry.

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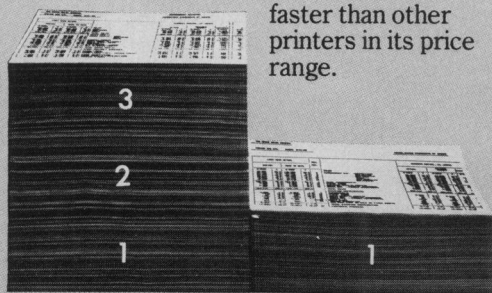
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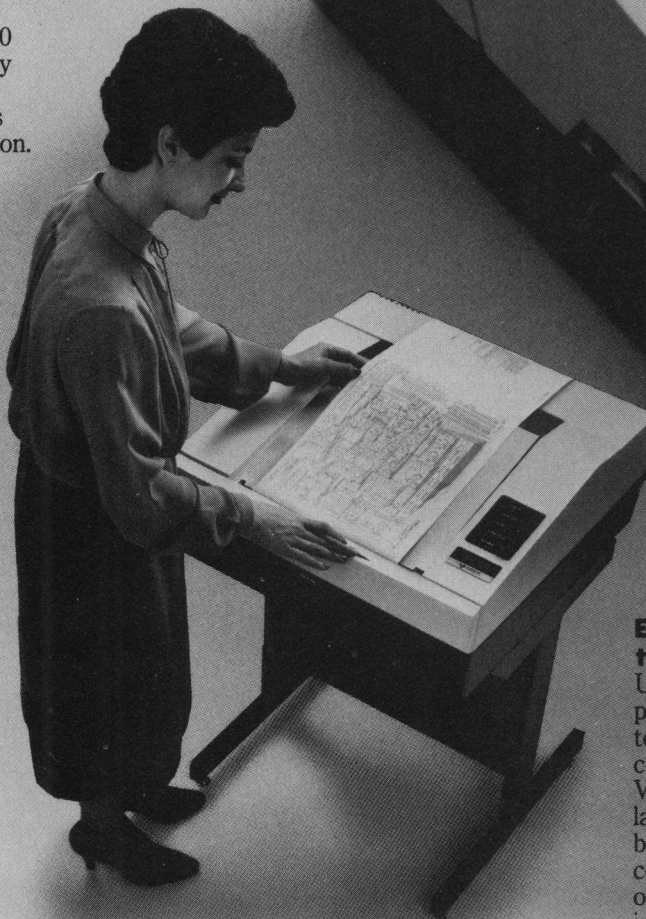
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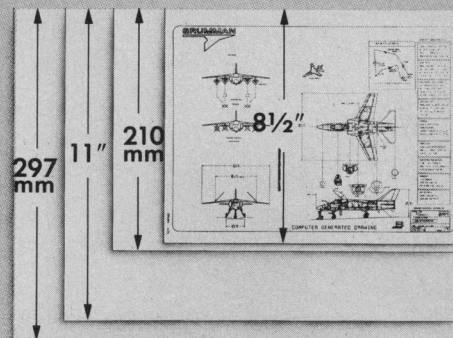
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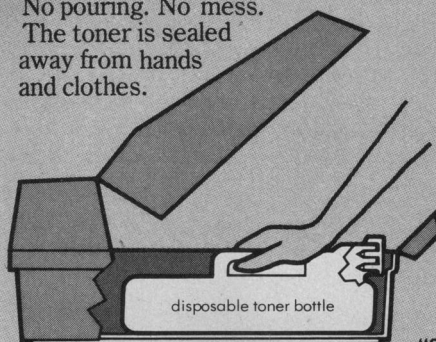
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¹Maxam, A.M. and Gilbert, W., *Methods Enzymol.*, 65, 1980

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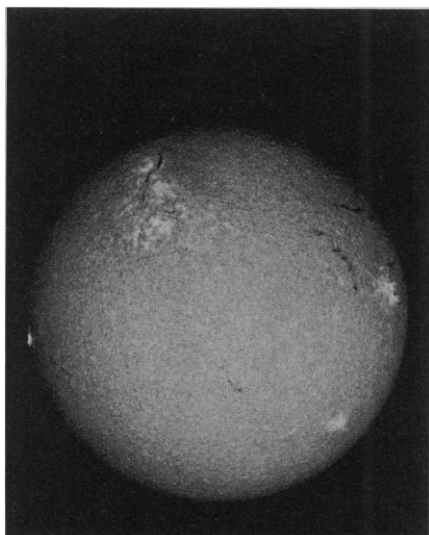
Its unusual combination of performance characteristics allows Technical Pan Film to fill a void in the matrix of black-and-white photorecording films. These characteristics have made 2415 a worthy successor to KODAK Solar Flare Patrol Film (ESTAR-AH Base) SO-392 and KODAK Photomicrography Monochrome Film SO-410—and a valuable alter-

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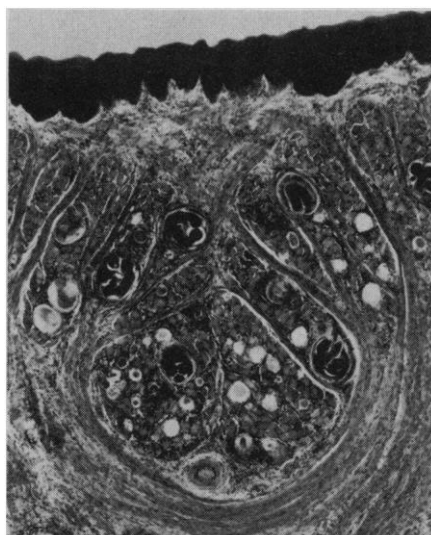
You won't find a Kodak film with a broader range of scientific and technical applications. At the same time, you may wish to load a roll into your 35 mm camera to record some stunning pictorial photography.

For additional information on Technical Pan Film, write to Eastman Kodak Company, Department 412L-153, Rochester, NY 14650. (A brief indication of your application may help us respond more effectively.)

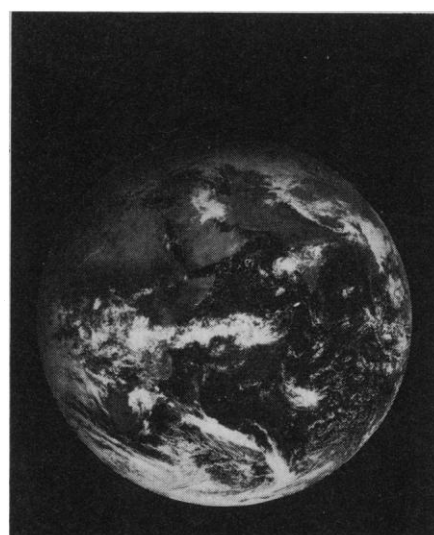
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Hydrogen-alpha photograph of solar flares. Sacramento Peak Observatory, Sunspot, N.M.



Photomicrograph of *trichinella spiralis* in muscle, 175 $\times$. Tungsten-halogen source (3200 K) with KODAK WRATTEN Filter No. 58.



Meteorological imagery from geostationary satellite. VIZIR laser-beam recording by Société Européenne de Propulsion (France).

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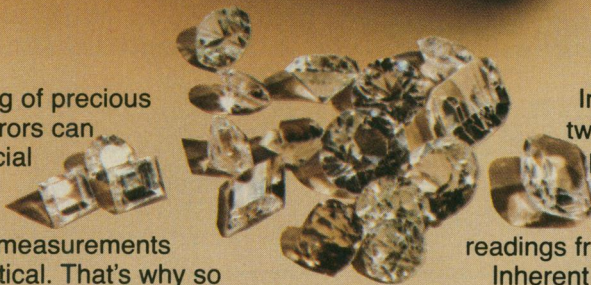
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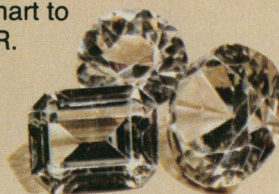
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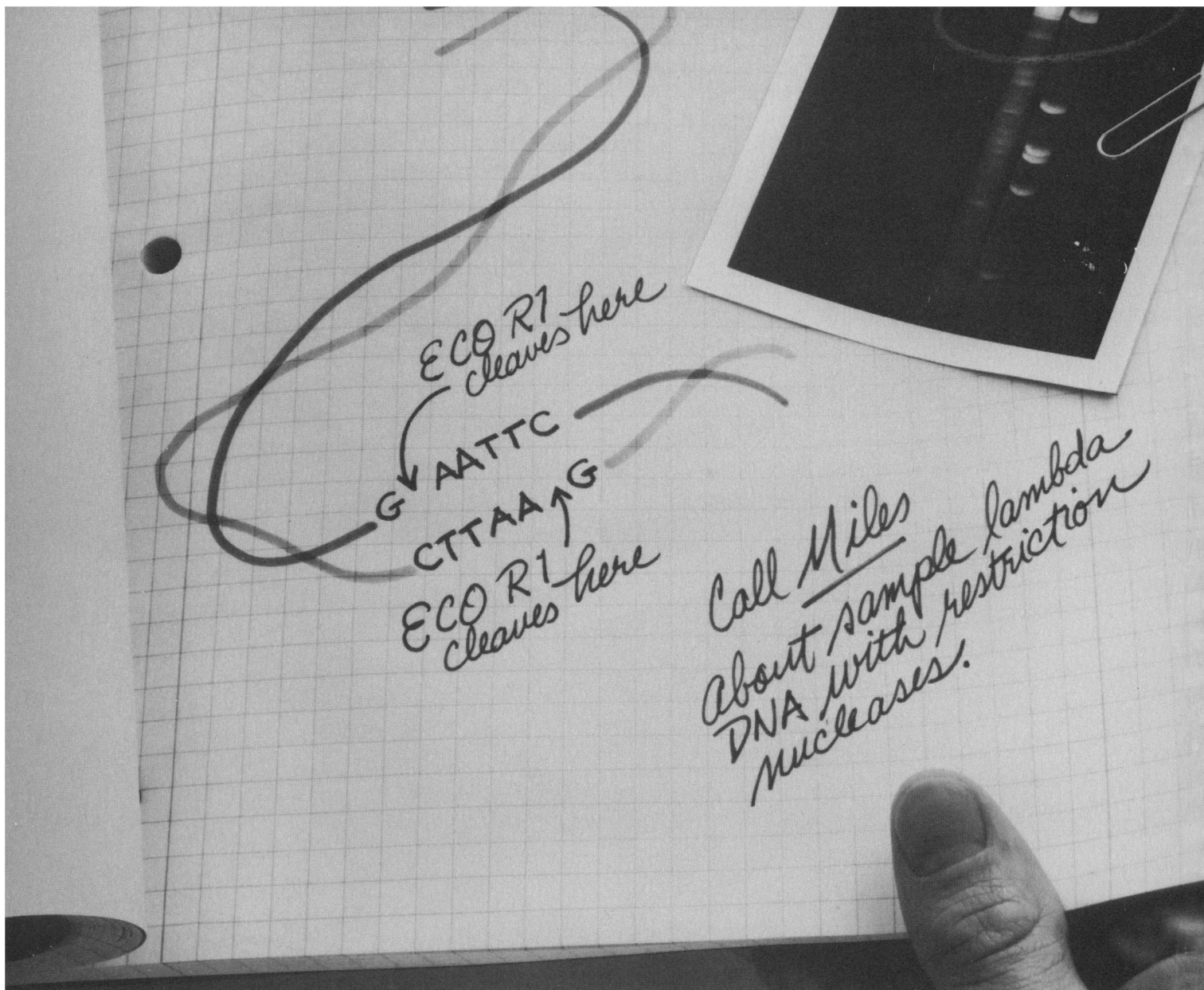


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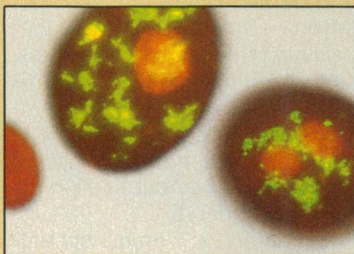
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Platelet Subpopulations in Immune Disorders

Platelet immune destruction has been studied using FACS for quantitation of IgG and C3 on individual platelets. Analysis of samples with counts as low as 1000/mm³, using as little as 1 ml of blood, are possible. Many subjects with evidence of immune platelet destruction show one subset of platelets reacting with both anti-IgG and C3, while a second subset is unreactive.

FACS Analysis of Leukemic Cells

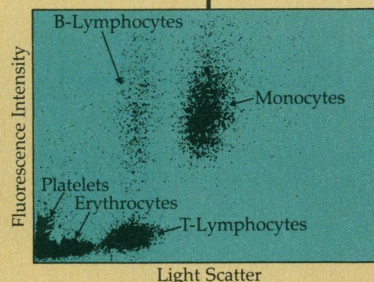
Cell-surface-binding fluorescent ligands have been used by researchers to distinguish between leukemic cell types and between leukemic cells and their presumed normal counterparts. Binding sites for cholera toxin have been found to be normally expressed in chronic leukemias but greatly diminished or absent in acute leukemias irrespective of their morphological type. Antibodies specific

for the common form of acute lymphoblastic leukemia (ALL) have been produced in rabbits and shown to define a cell surface antigen of non-T, non-B type ALL.

Stem Cell Analysis and Sorting Using Light Scatter

Morphological discrimination of the hematopoietic stem cell—the colony forming unit of spleen (CFU-s)—has been made using light scattering measurements, without fluorescence staining, in FACS. Light scatter is measured simultaneously from different directions. Correlated analyses of mouse bone marrow cells have then been used for sorting and microscopic identification. CFU-s are found among those cells classified by light scatter as large lymphocytes, or blast cells.

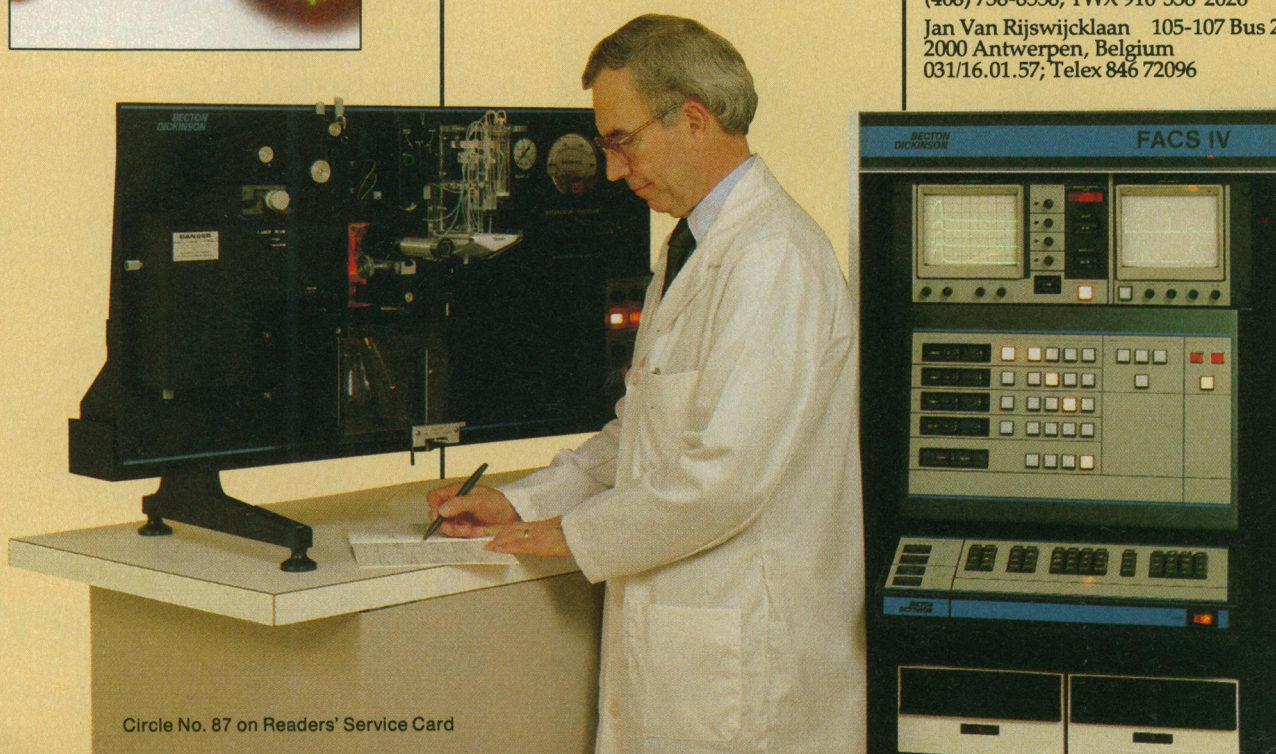
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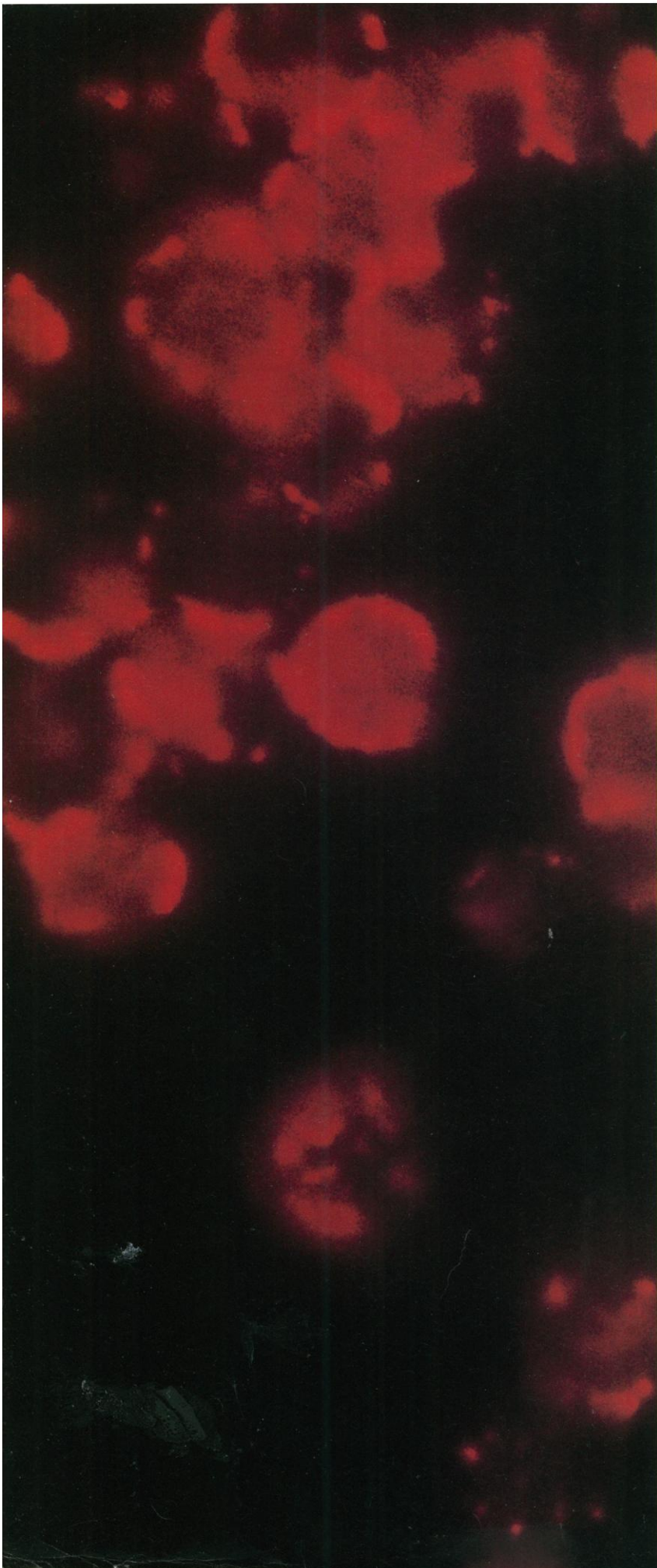
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Monoclonal antibody to human T cells creates new research opportunities.

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Recombinant DNA Revisited

Thoughtful people might well begin to wonder at yet another celebration marking a new generation of major discoveries in molecular genetics. But it is true that since 1953, when the Watson-Crick model for DNA structure was proposed, there has been a dizzying succession of advances, each deepening our understanding of biology at the molecular level. It has been a 30-year high for those who participated, although for the most part we did poorly in imparting to others the reasons for our excitement.

In this regard, the recombinant DNA debate had a happy effect. The daily papers and television now report frequently on the activities of biologists. Lately, these reports have been upbeat, as the production of rare and medically significant materials nears reality. This is a marked change from the hair-raising headlines of a few years ago. Most people now understand that the extreme views heard at the height of the debate were groundless. No novel hazards have emerged from the research, and the cautious approach instituted at Asilomar in 1975, and continued by national guidelines in many countries, has not seriously hampered the progress of research.

Dramatic differences exist between the reports appearing in the mass media and those in this issue of *Science*. The manufacture of important biological agents like insulin and interferon by recombinant DNA procedures is the fruit of the basic research of the past. Here are reported the foundations for the future. It would be foolhardy to try to predict specific outcomes. We can be certain only that they will be unexpected and astonishing. And we ought not fear these unknowns. Rather we should work to ensure that the singular intellectual bounties of our era are exploited for the good of all.

The present articles, regardless of any future impact, stand on their own for their originality and remarkable insights into how the genes of all organisms, including man, are arranged, expressed, and regulated. Once we thought the DNA of complex organisms was inscrutable. Now we cope with it readily. We thought of DNA as immovable, a fixed component of cells. Now we know that some modules of DNA are peripatetic; their function depends on their ability to move about in a genome. There are already sufficient examples of peripatetic DNA for us to be certain that it is a universal element in differentiation and development. We thought genes were continuous stretches of DNA. Now we know coding regions may be interrupted dozens of times, and spliced together in the form of messenger RNA when needed. We have learned that genes are fungible; animal genes function perfectly well within bacteria and bacterial genes within animal cells, confirming the unity of nature. We need no longer depend on chance events to generate the mutations essential for unraveling intricate genetic phenomena. Specific mutations can be constructed at will, and millions of mutant genomes readily produced for study. We already see that some standard questions about evolution must be rephrased to account for new information.

Recombinant DNA techniques alone did not accomplish all this. Coincident improvements in methods for the chemical and enzymatic manipulation of DNA were equally important. First, the discovery and exploitation of restriction endonucleases allow us to cut up large genomes into reproducible small segments. The segments are ready-made for insertion into a recombinant DNA vector because of the special termini generated by the endonuclease cleavage. Next, it is feasible and indeed common to determine with precision the sequence of thousands of base pairs on a DNA segment. Finally, there is the matter of scale; nanogram, even picogram amounts of DNA can be characterized with precision because of the availability of highly radioactive phosphorus-32 and simple electrophoretic techniques carried out on semisolid gel supports. Together, these methods have opened opportunities unimaginable even 5 years ago. And molecular biologists alone did not accomplish all this. They had unprecedented support from enlightened societies and governments. It has been a joint venture, and we should celebrate together.—MAXINE SINGER, *Chief, Laboratory of Biochemistry, National Cancer Institute, Bethesda, Maryland 20205*

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