

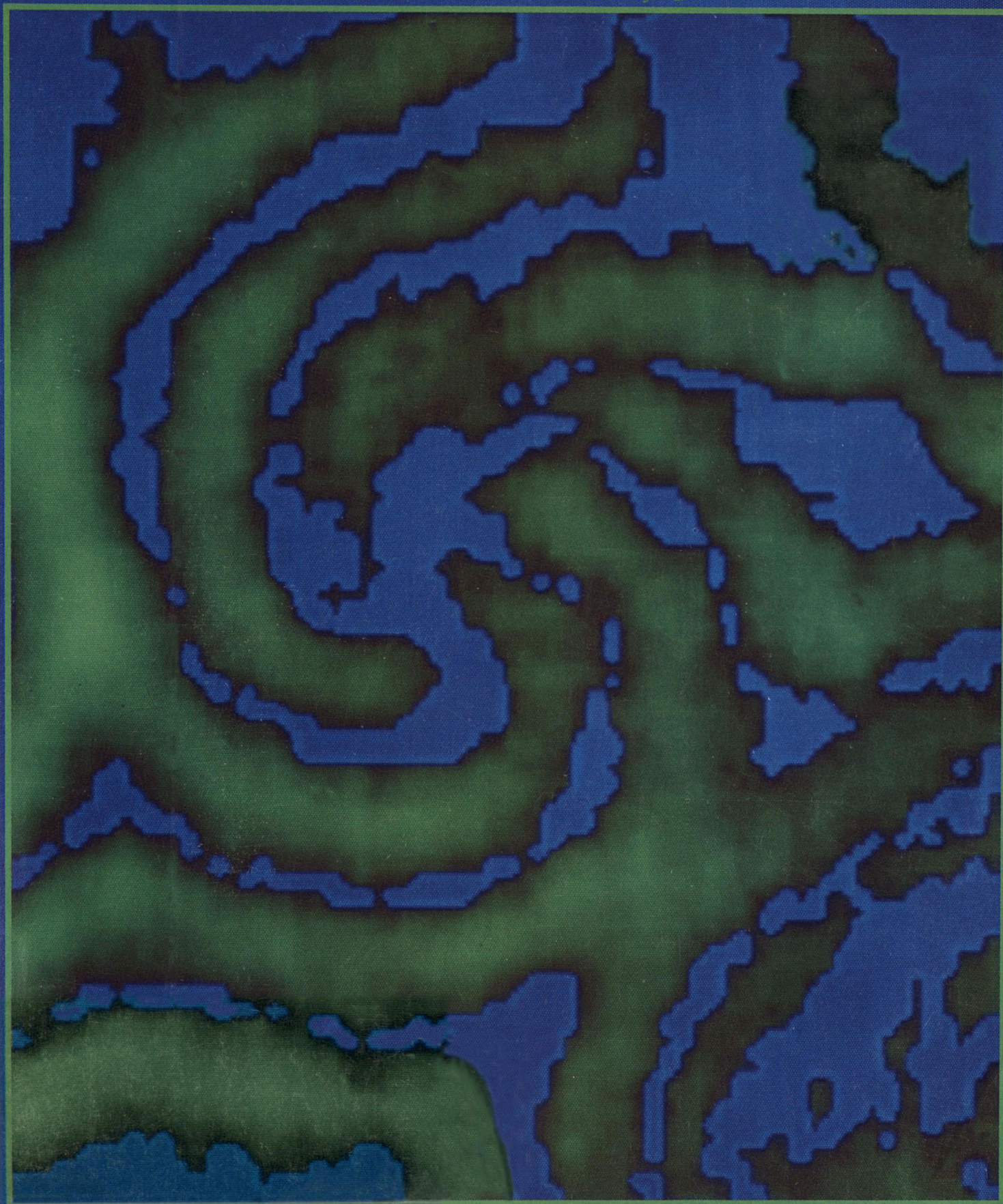
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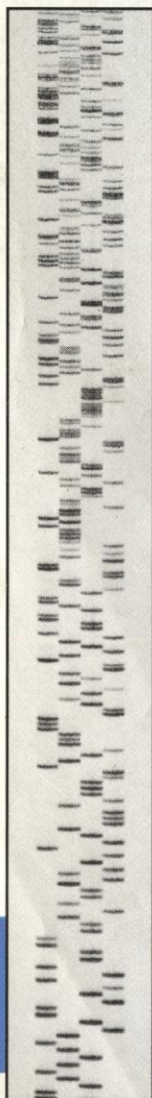


Figure Legend : Autoradiograph of sequencing gel using the BaseAce Sequencer and the FeatherVolt 2000 power supply. 1.0 µg M13 ssDNA was labeled with S-35 ATP and run for 3 hrs at 65 watts on a 6% acrylamide (7M Urea, 1X TBE) gel.



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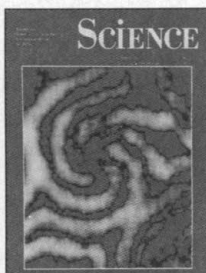
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COVER Spiral calcium wavefronts in a *Xenopus laevis* oocyte expressing muscarinic acetylcholine receptors observed by confocal microscopy. This spatiotemporal pattern of calcium activity (normal projection of five images collected over 10 seconds) is characteristic of a regenerative excitable medium and suggests that the calcium-mobilizing machinery behaves as such. See page 123. [Image by J. Leichter and co-workers]

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This Week in SCIENCE

HIV-1 domain structure

THE enzyme reverse transcriptase is essential for the proliferation of retroviruses. Reverse transcriptase is thus a target of antiviral therapies in diseases such as AIDS (which is caused by the retrovirus HIV-1), and many studies have focused on determining the structure of reverse transcriptase, how structure ties in to function, and what types of inhibitors might block various reverse transcriptase activities. Davies *et al.* have obtained high-resolution crystallographic data on the structure of a portion of the HIV-1 reverse transcriptase, the ribonuclease H domain, and describe its structure, folding, and binding to cations (page 88). Features of the HIV-1 domain are compared to and contrasted with those of a similar domain from *Escherichia coli* RNase. The H domain does not have enzyme activity when it is separated from the larger molecule but does resume activity—it degrades RNA in RNA-DNA duplexes—when recombined with the molecule's polymerase subunits. A model is proposed for how interactions of the H domain with other regions of the reverse transcriptase molecule account for its catalytic activities. The clinical potential of this research is discussed by Palca on page 31.

Making waves

IN the Pacific Northwest, off the coast of Washington, the Juan de Fuca plate is being subducted beneath the North American plate. Conflicting information obtained over the years has created uncertainty as to whether an earthquake could be produced at this plate interface or whether the subduction there is aseismic, characterized by two plates slipping steadily by one another. Using a network of eight stations set up in a region 30 by 20 kilometers, Savage and Lisowski have made precise measurements of the distances between various stations periodically during the past 9 years (page 101). The distances between stations ranged from 9 to 27 kilometers. Predictions based on the strain measurements

and on sea-level recordings (which serve as proxies for tectonic uplift) indicate that, although large segments of the plates are slipping smoothly by one another, strain is accumulating on the outboard 100 kilometers of the North American plate; when this locked segment ruptures, an earthquake will occur. Kerr comments on how these new data have sharpened seismologists' thinking about the earthquake to come in the Cascadia subduction zone (page 28).

Moving in waves

METABOLIC costs of movement along the ground are remarkably similar for diverse animals—from the smallest bugs to the largest beasts—with rigid skeletons. In these organisms, the muscles are attached directly to the skeleton, contractions cause the limbs to move, and it is actually possible to predict from knowledge of the body weight of the animal and its speed how much metabolic energy will be spent in movement. Gypsy moth caterpillars have a very different type of skeleton, a hydraulic skeleton, in which the muscles surround an incompressible fluid. Muscle contractions against this fluid cause the body to elongate. Measurements of oxygen consumption as caterpillars walked a motor-driven treadmill and video recordings of the body wave motions—which flow from the rear to the head—show that the hydraulic skeleton is much less efficient and versatile than a solid skeleton and that the relative cost of moving it is four to five times greater than the cost of moving a rigid skeleton (page 112). Casey explains how morphology, physiology, and biomechanics constrain speed and stride length and thereby control the caterpillar's locomotion.

Erythromycin derivative

THE pharmacologic efficacy of antibiotics can be changed if minor structural modifications are made in the parent molecule. Sometimes it is

possible to propose a desirable change and then to produce it synthetically or through bioengineering. One sought-after but elusive derivative of the antibiotic erythromycin is 6-deoxyerythromycin. This derivative is predicted to have enhanced stability in an acid medium, and thus it could have a longer active life in the stomach after it is ingested. (In underivatized erythromycin the hydroxyl group of the carbon 6 is a target for the decomposition pathway.) Weber *et al.* used a targeted gene integration procedure to disrupt a gene—*eryF*—in a region of the chromosome of *Saccharopolyspora erythraea* that is essential for the organisms' production of erythromycin (page 114). The 6-deoxy derivative of erythromycin was produced. It was stable in acid and, in animal experiments, proved to be as efficacious an antibiotic as was erythromycin against three pathogenic strains of bacteria.

Catching a wave

WHAT preserves the specificity of different cell stimulants such that each can deliver a distinctive signal to a cell while using a common intracellular "second messenger" system? One possibility is that the spatiotemporal pattern of release of the intracellular second messenger, which in many cases is free calcium ion, is informative and different for individual stimulants. A system for studying this phenomenon is described by Lechleiter *et al.* (page 123). Calcium release in an "optical slice" of a frog oocyte was followed with a confocal microscope. After the oocyte was stimulated with a neurotransmitter substance, spiral (cover), planar, and circular waves and colliding wavefronts were observed; their dynamic properties are like those seen in chemical systems for which models of "excitable media" have been developed. Epstein elaborates on the significance of the generation, propagation, and annihilation of calcium ion waves and the relation of these wave patterns to those of chemical and other biological systems (page 67).

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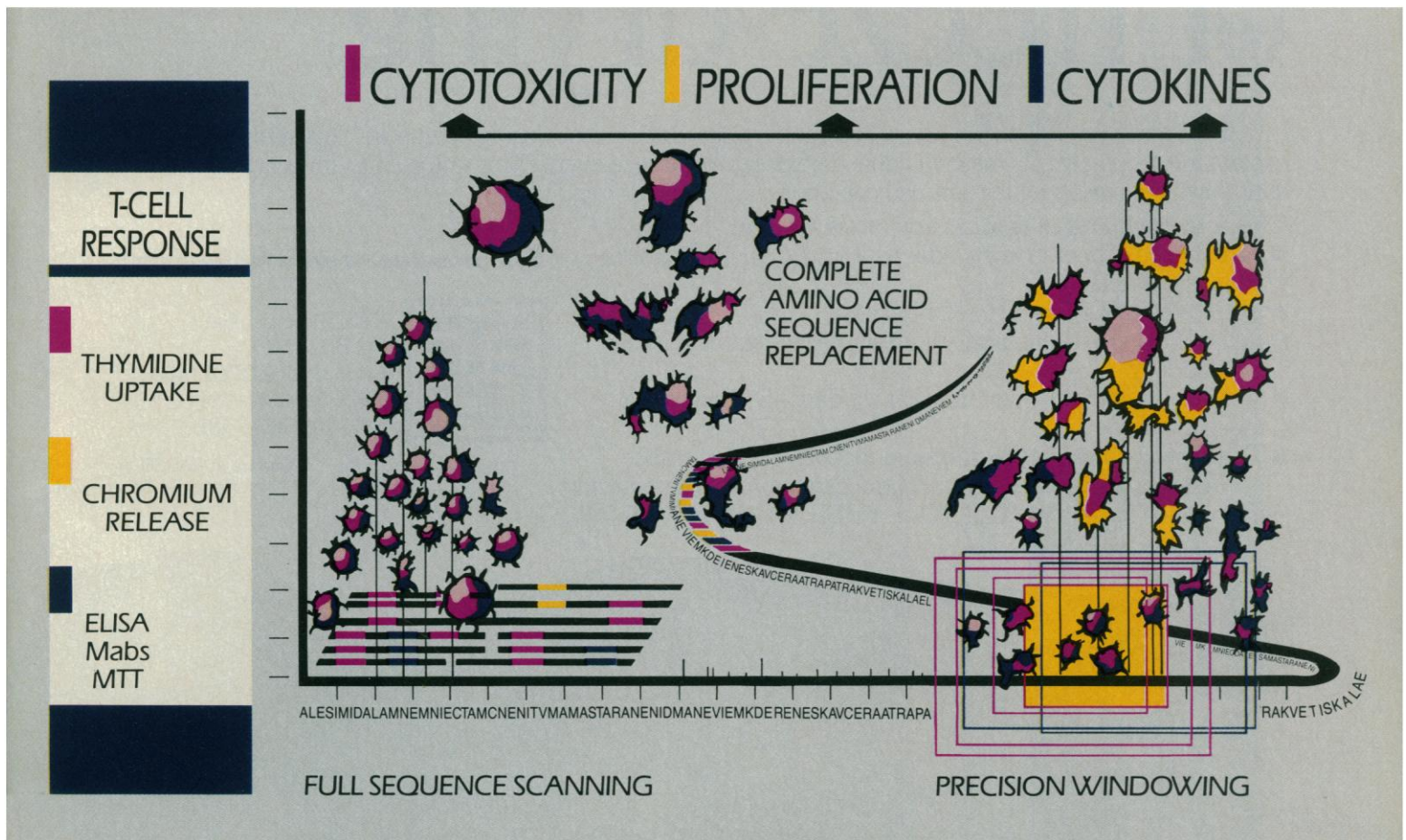
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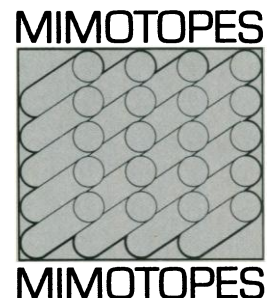
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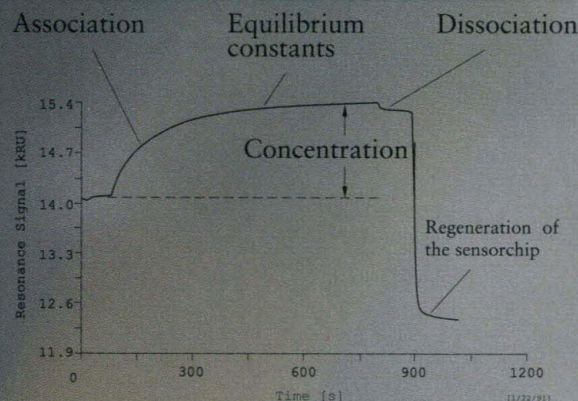
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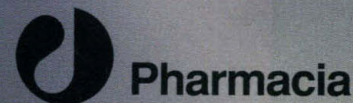
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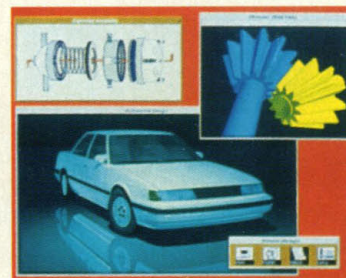
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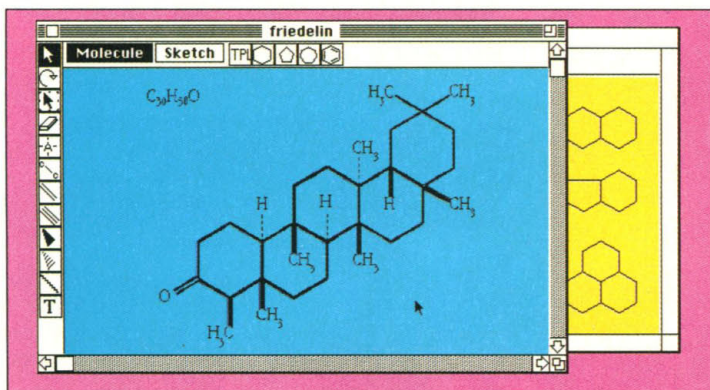
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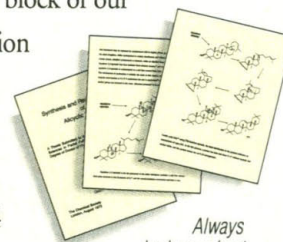
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Latest LSC technology cuts sample and cocktail costs; increases throughput

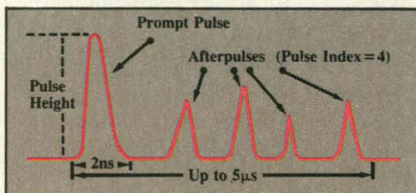
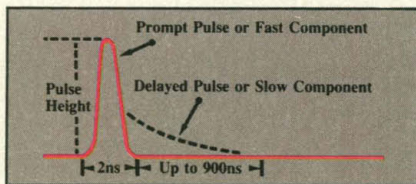
In the past, liquid scintillation counting used traditional technology to overcome background noise. Now, there's a new, more sensitive technology – TR-LSC or Time-Resolved Liquid Scintillation Counting – that reduces background noise by an additional 30%-40%, and more. This new patented technology is available only in Packard's Tri-Carb® liquid scintillation analyzers.

Originally developed for extremely low level counting, TR-LSC technology has now been applied to a broad range of applications. While these don't always require high sensitivity, additional benefits have been realized. By increasing sensitivity, TR-LSC reduces sample and cocktail consumption while shortening the time required for accurate counts. The benefits? Lower cocktail costs, lower disposal costs, and increased throughput.

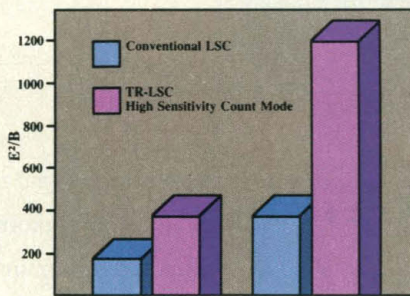
How TR-LSC is superior to older technology

Traditional counters are based on two-dimensional pulse analysis: pulse height and pulse counts. They provide a level of sensitivity that's merely adequate for most applications.

Patented TR-LSC adds a third dimension to pulse analysis: a pulse index that measures over time the afterpulses associated with background. In doing so, TR-LSC clearly distinguishes between beta pulses and background pulses. By identifying, and reducing, background noise, TR-LSC provides a great level of sensitivity (see chart comparing E^2/B values) and more accurate counts.



The typical beta scintillation pulse (top) is very fast and may be followed by a delayed component. The typical background pulse is followed by a series of afterpulses. Patented TR-LSC distinguishes between the two.



Typical E^2/B values for ^3H and ^{14}C using traditional and TR-LSC counting.

Achieve accurate counts on samples as small as 25 µL

Traditional technology limits sensitivity. The improved sensitivity of TR-LSC, however, allows you to achieve accurate DPM results for single and dual label samples in volumes as small as 25 µL. That can add up to substantial savings in sample and cocktail costs.

Slash radioactive waste disposal costs

Counting smaller samples will also reduce radioactive liquid disposal costs, which can be \$500 per drum, or higher. While you may not pay this cost directly, your operating budget could be affected. With TR-LSC you can cut operating costs while reducing environmental hazards.

Increase sample throughput by over 80%

Just as TR-LSC reduces the volume of sample and cocktail required for accurate counting, it also reduces the time required for an accurate count. By cutting background in half, high sensitivity TR-LSC lets you count nearly twice the number of vials of a 250-DPM sample, in the time it would

take to count a single vial using conventional technology. For lower activity samples, the increase in throughput with TR-LSC is even greater.

Automatic data interpretation, too

Another advanced feature available only with Tri-Carb analyzers is automatic tandem processing. This unique capability processes your counting data automatically using one software program after another – RIA packages, spreadsheets, word processing, or custom-written programs – until the results are printed in whatever format you have specified. All this is done automatically, without operator intervention, for up to 30 users.

Free Investigator's Guide provides a complete explanation of the benefits of TR-LSC

More information on TR-LSC, and other exclusive Packard features, is available in a new publication, the Investigator's Guide to TR-LSC Technology and Tri-Carb Liquid Scintillation Analyzers. For your free copy, mark the reader service number below or call us today.



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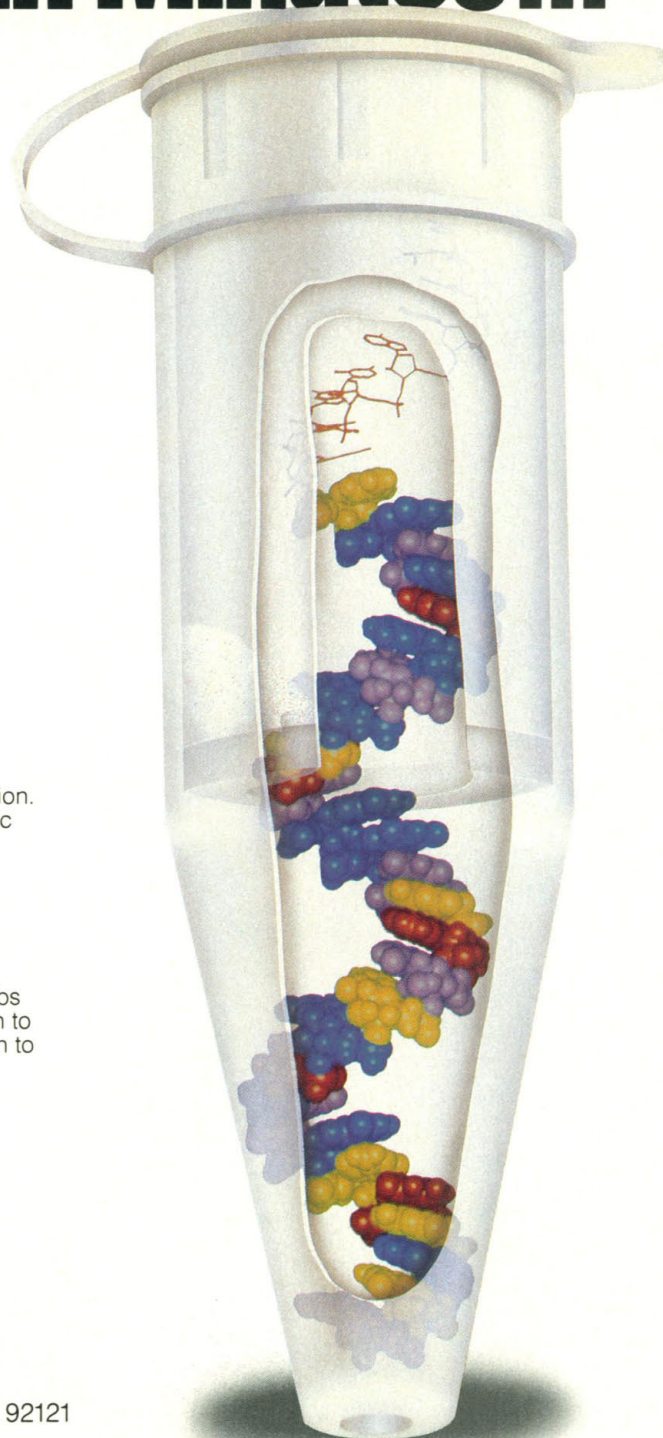


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*patent pending. mRNA model courtesy of BIOSYM

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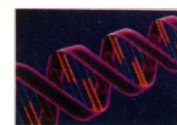
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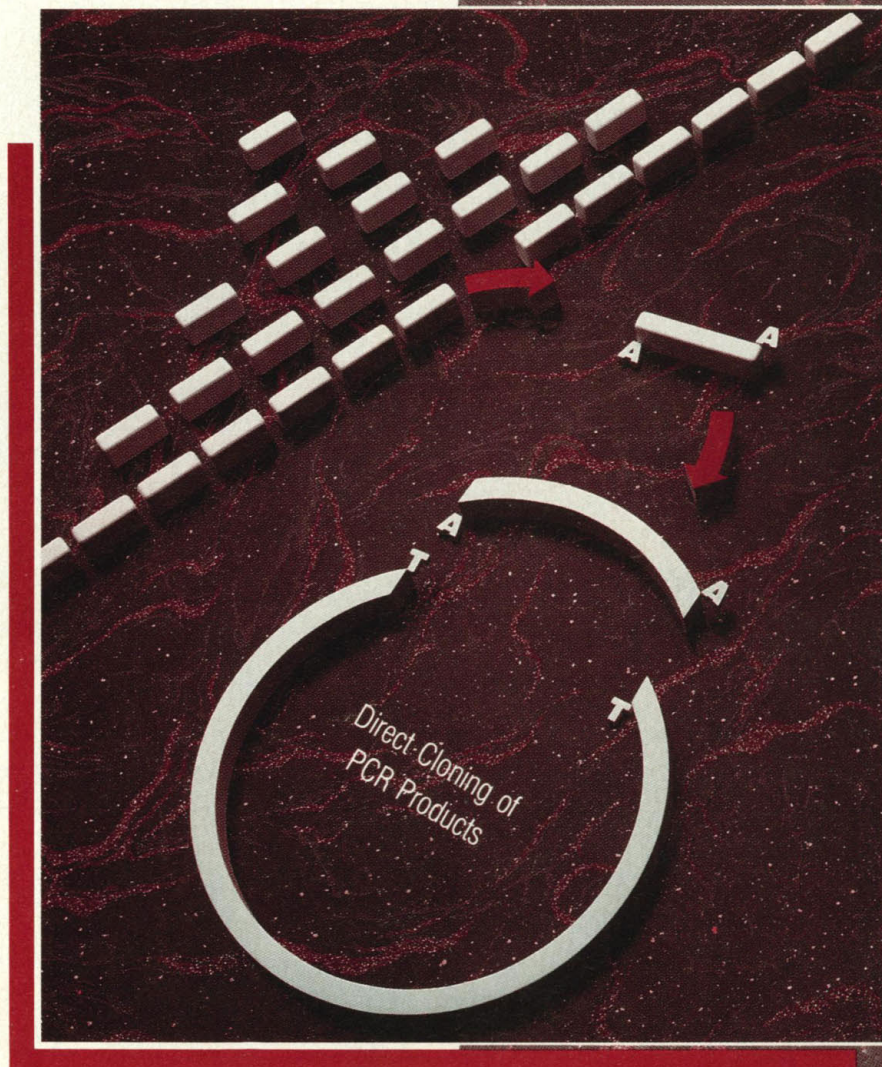
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*PCR is covered by U.S. Pat. #'s 4,683,202 and 4,683,195 issued to Cetus Corporation.

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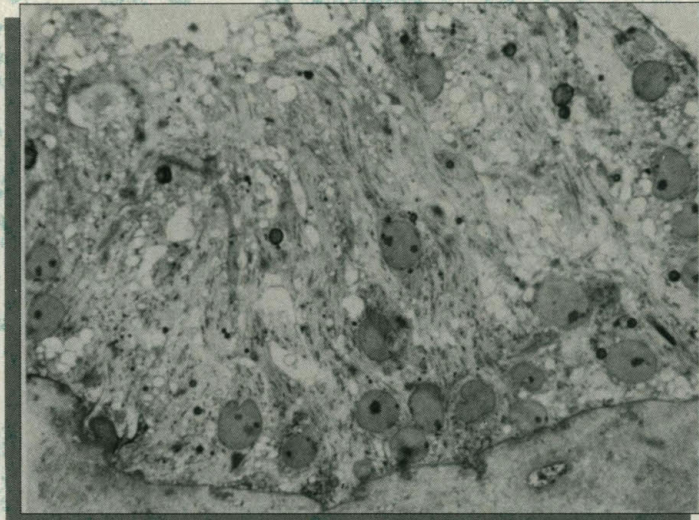
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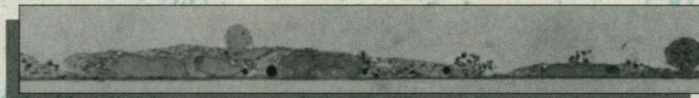
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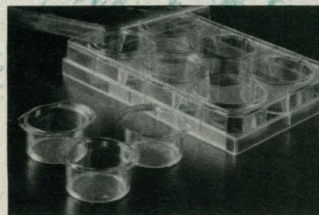


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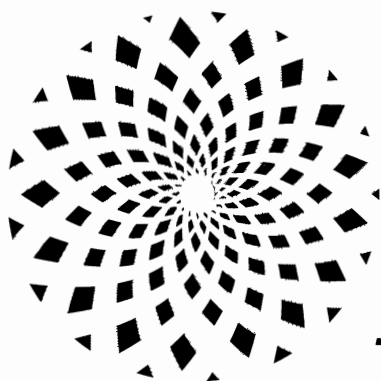
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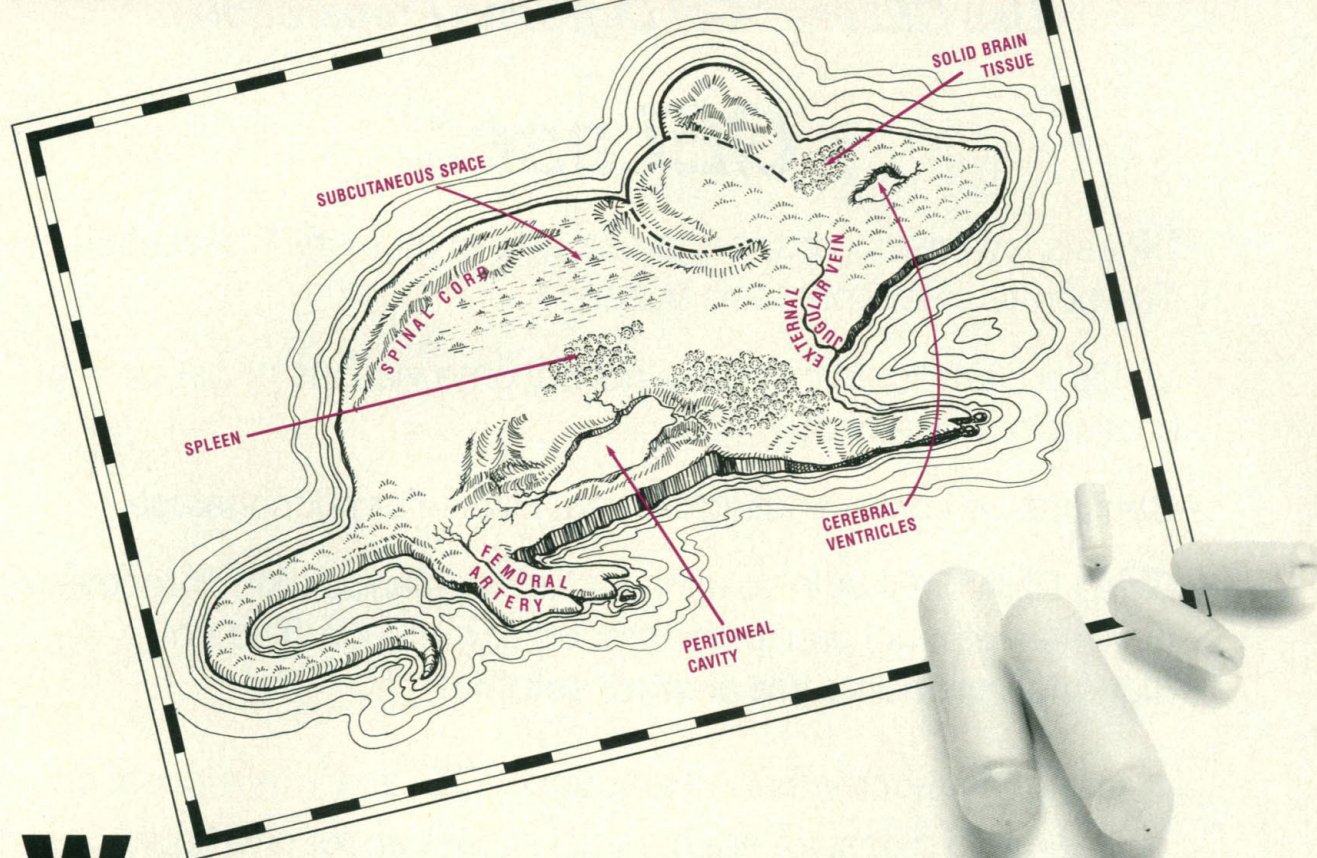
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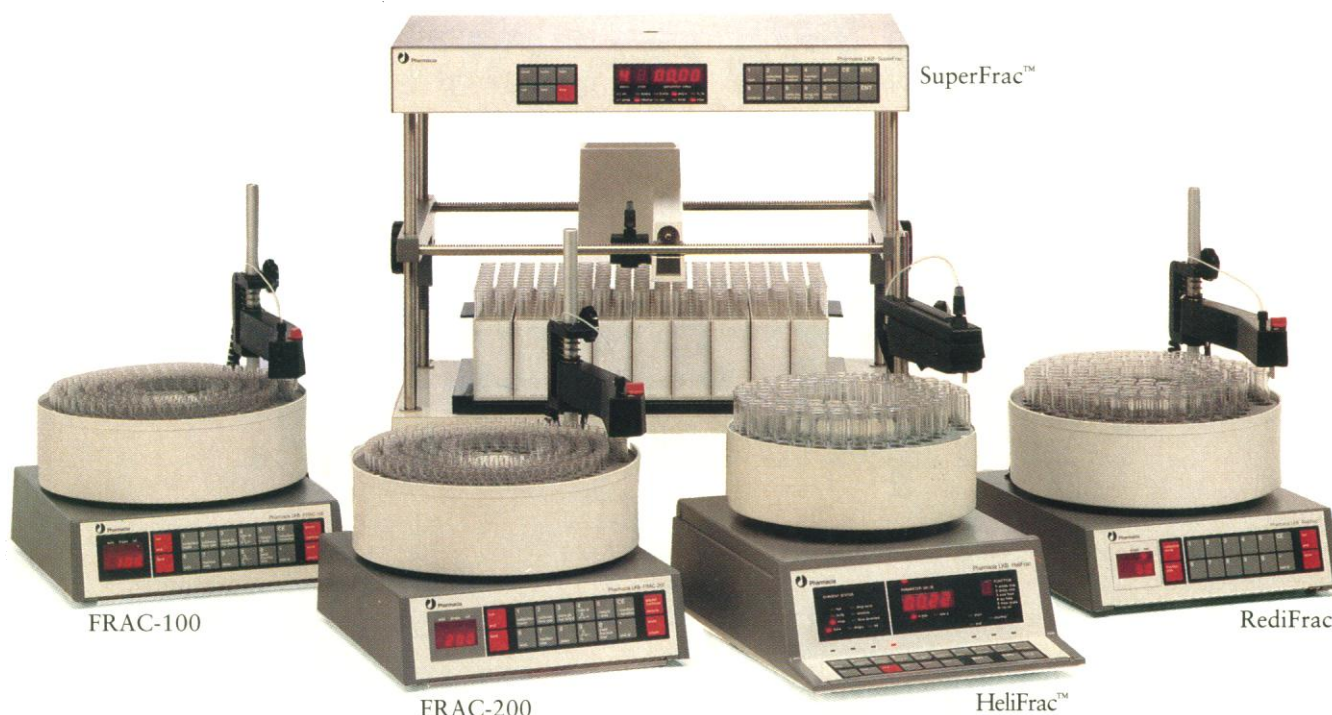
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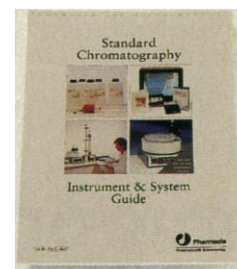
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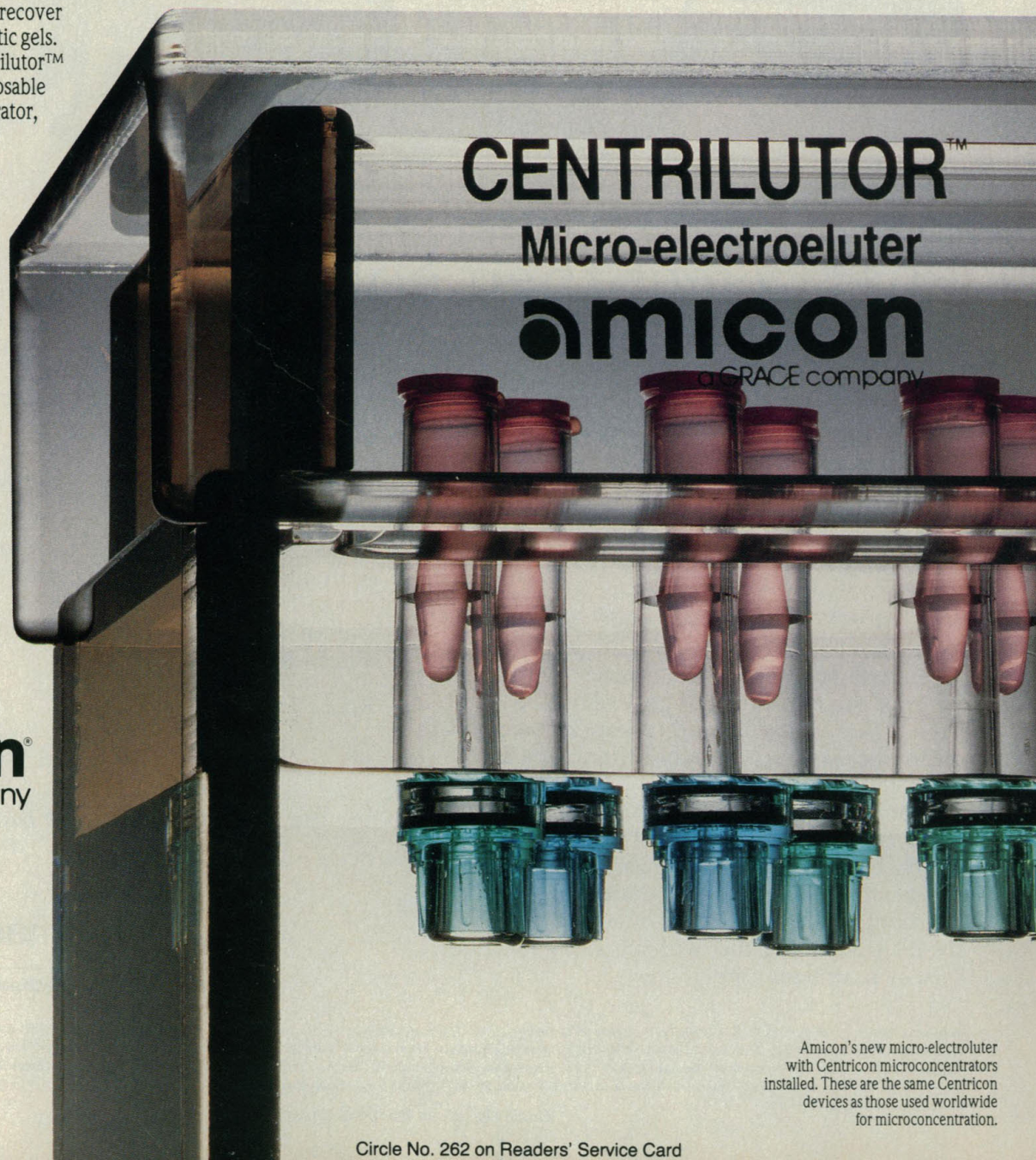
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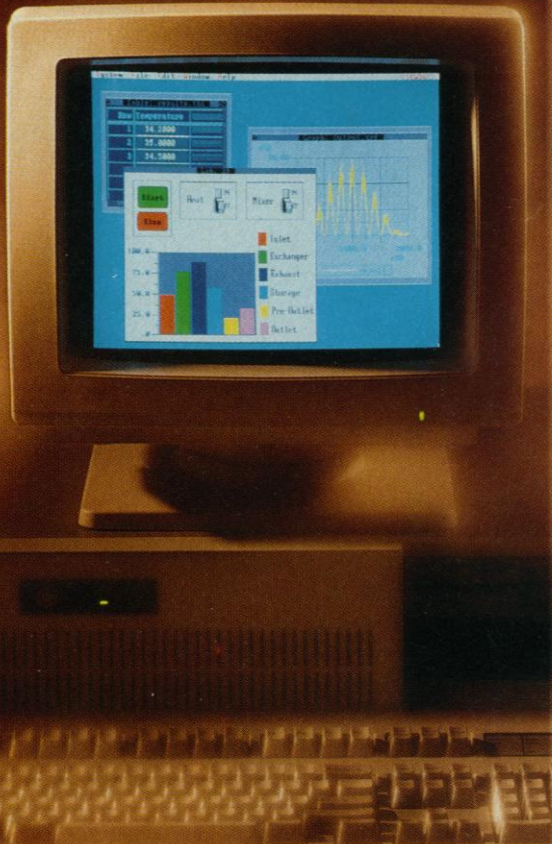
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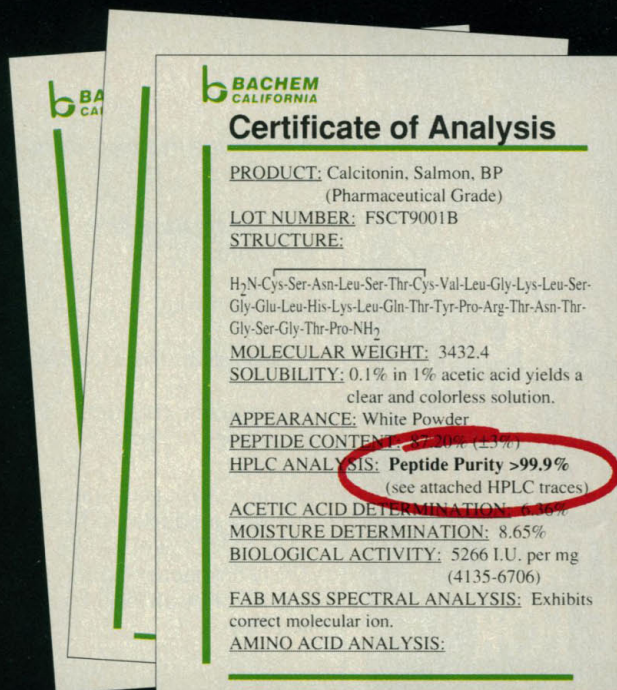
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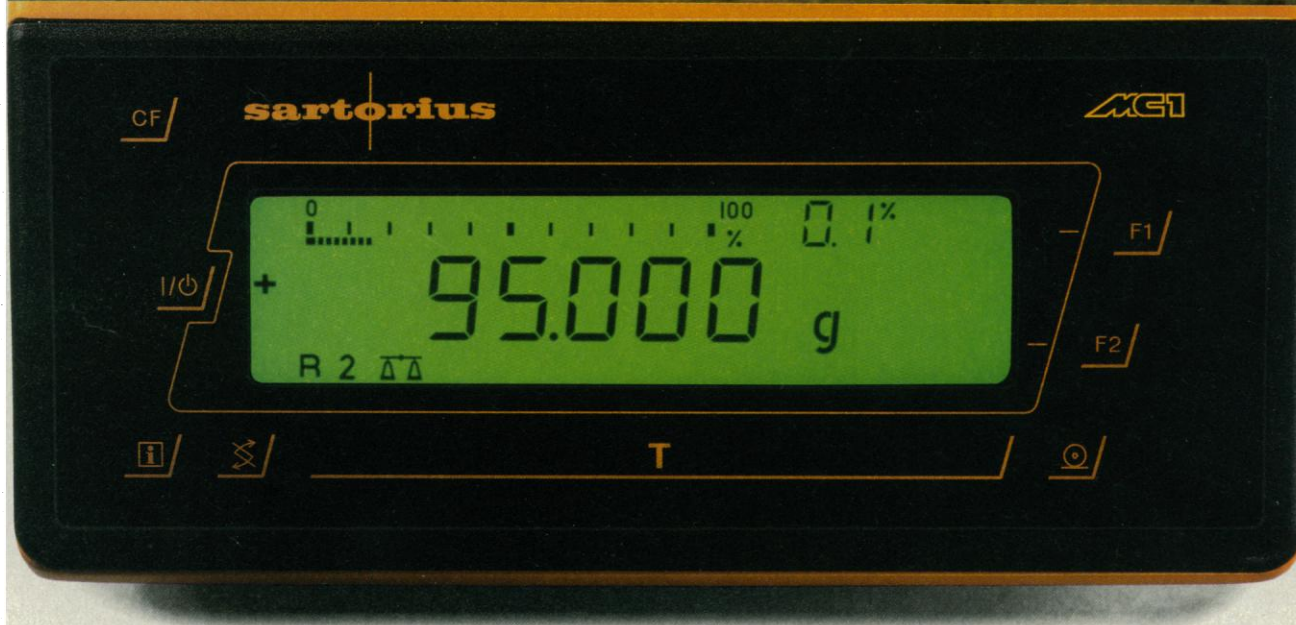
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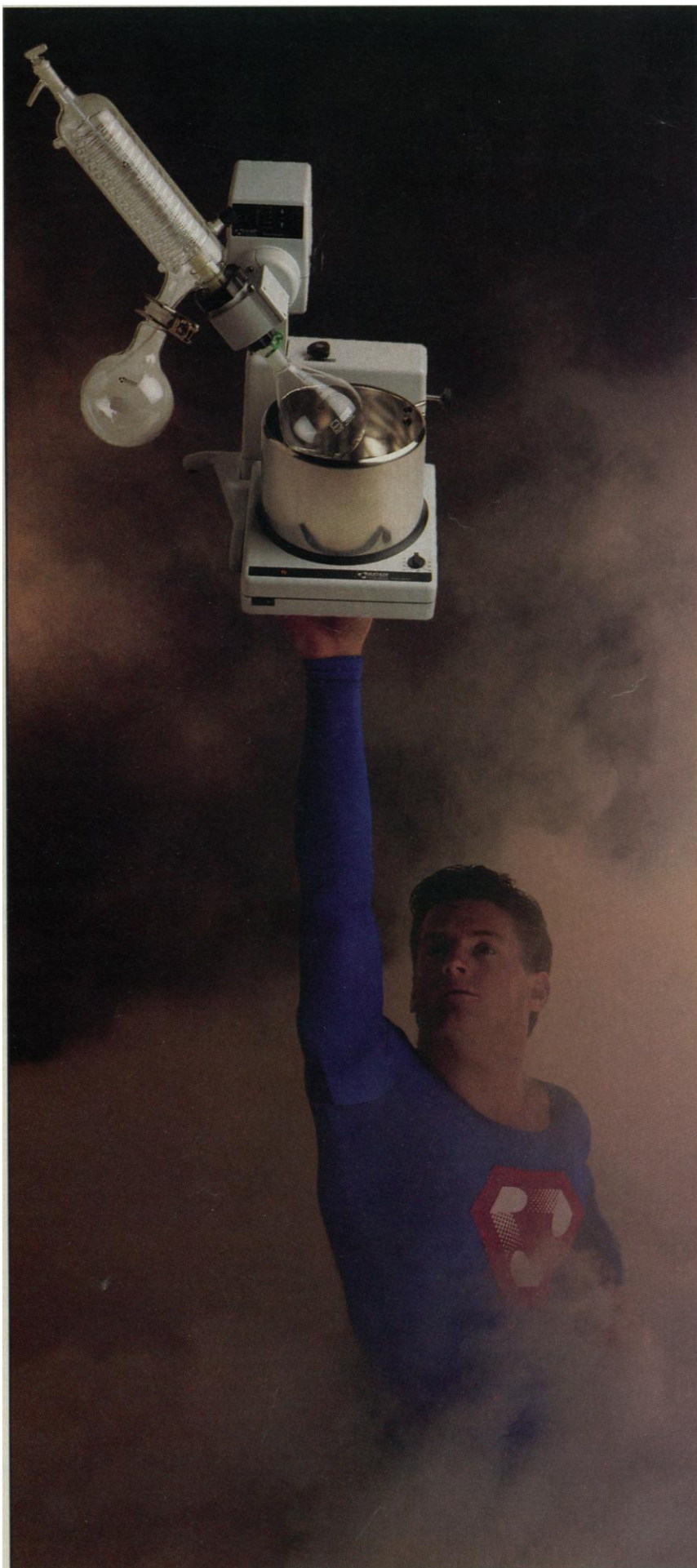
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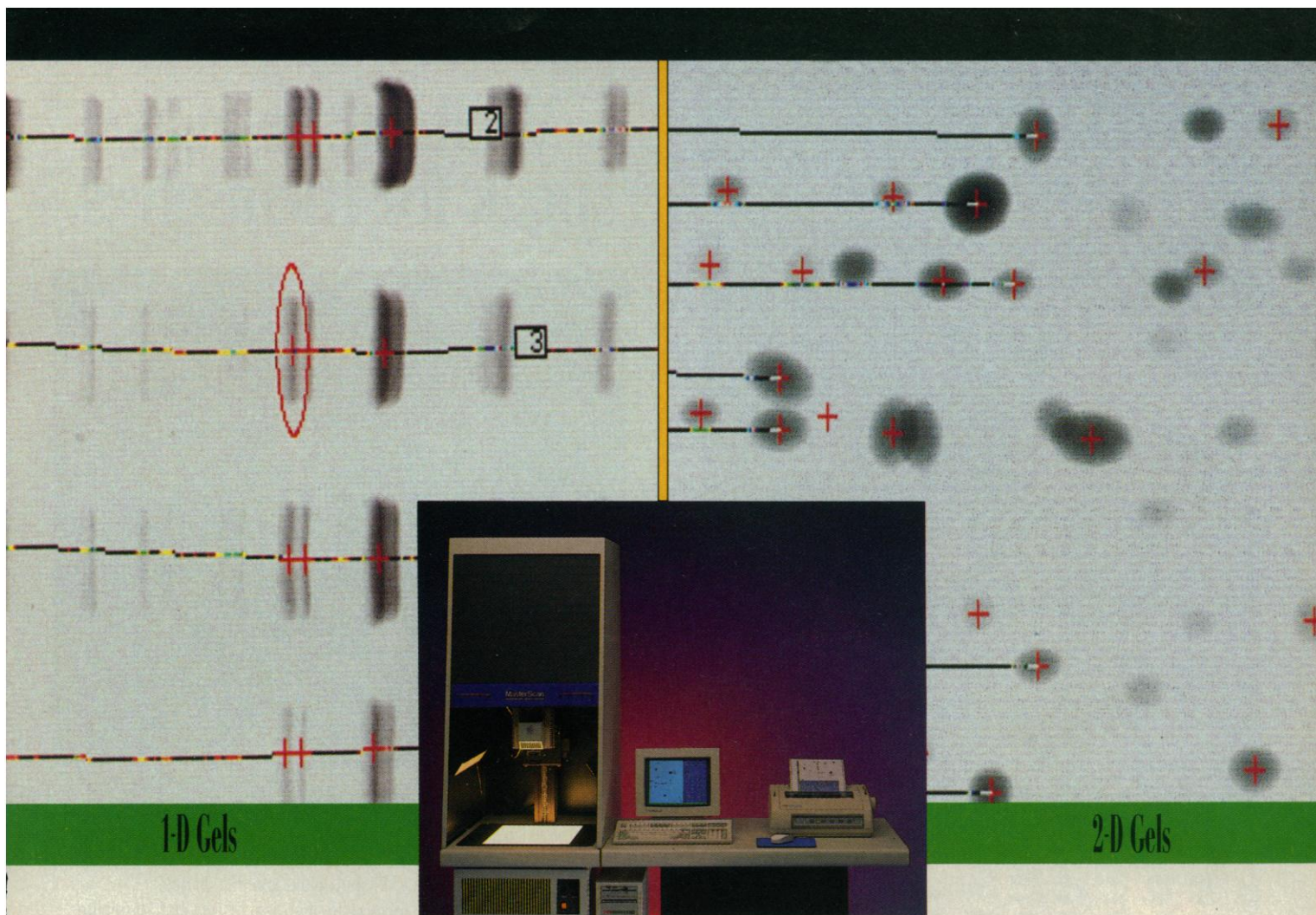
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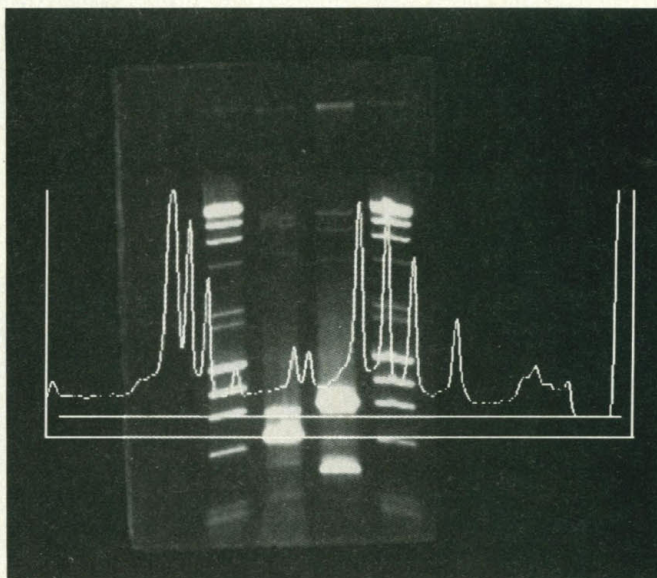
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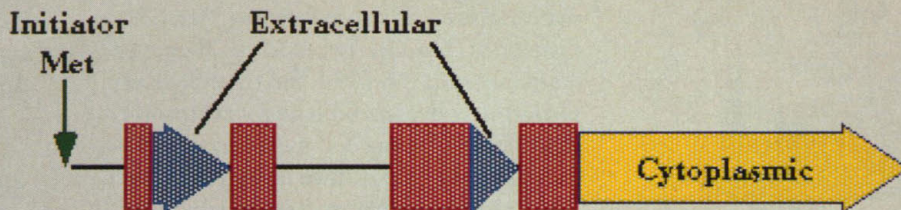
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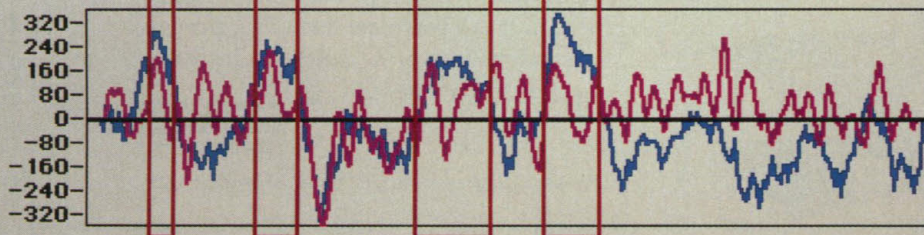
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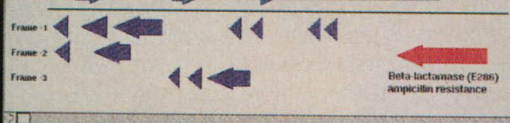
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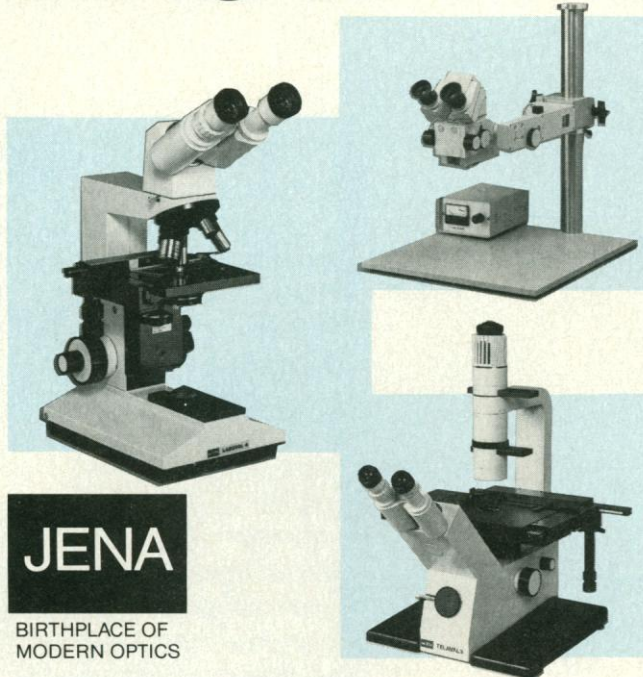
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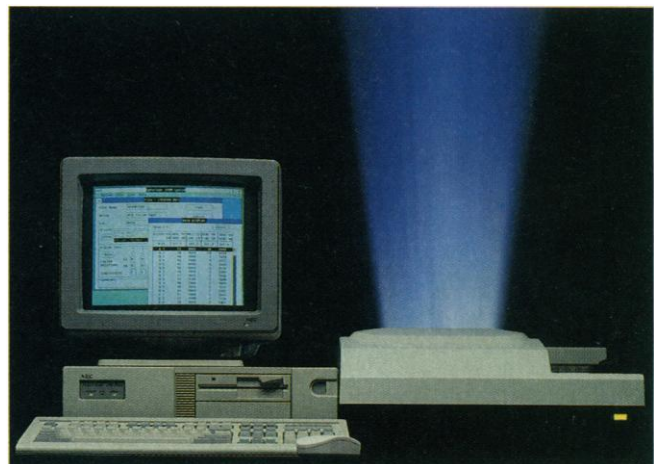
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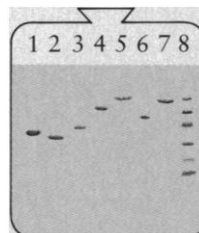


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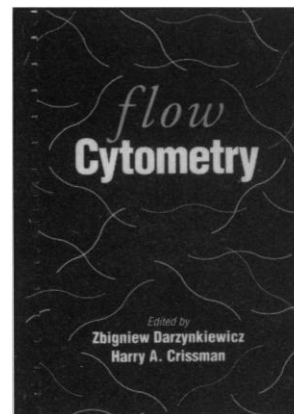
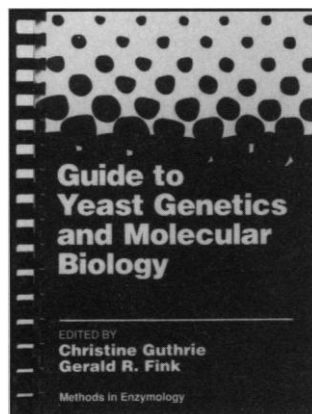
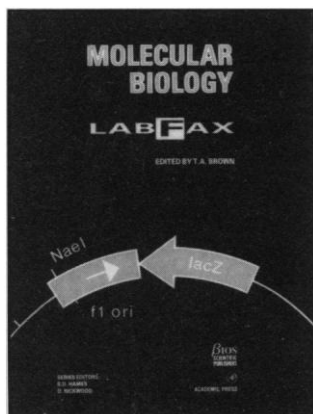
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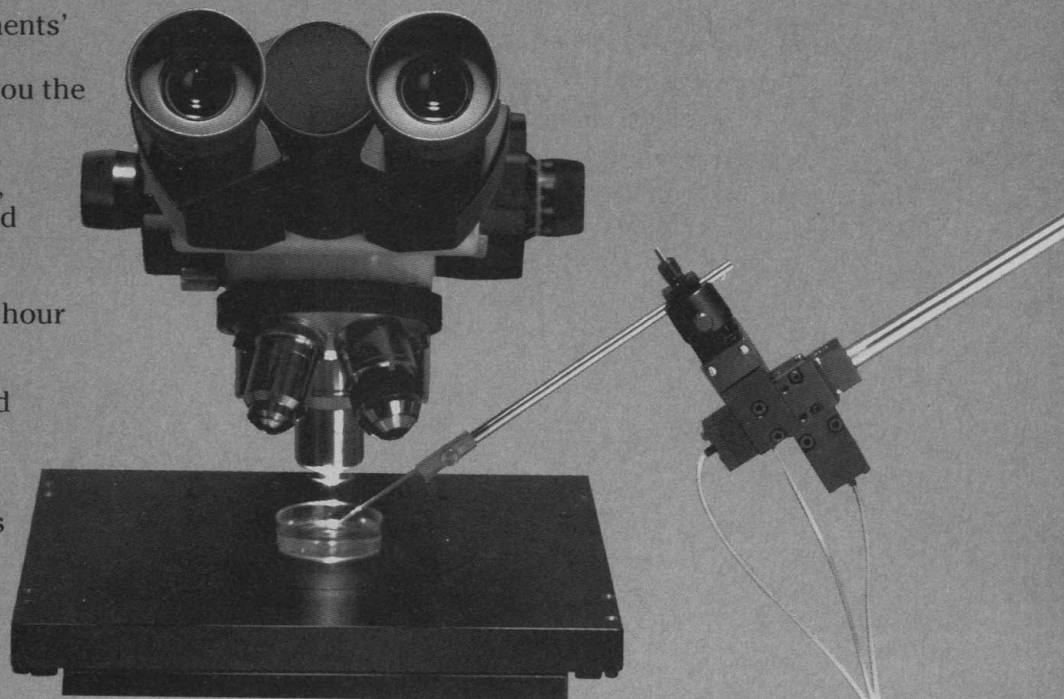
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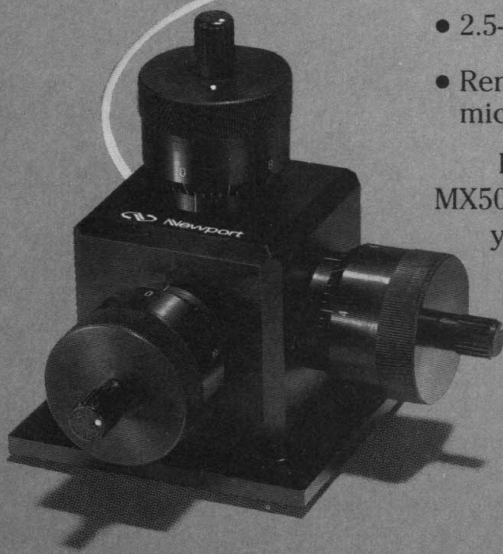
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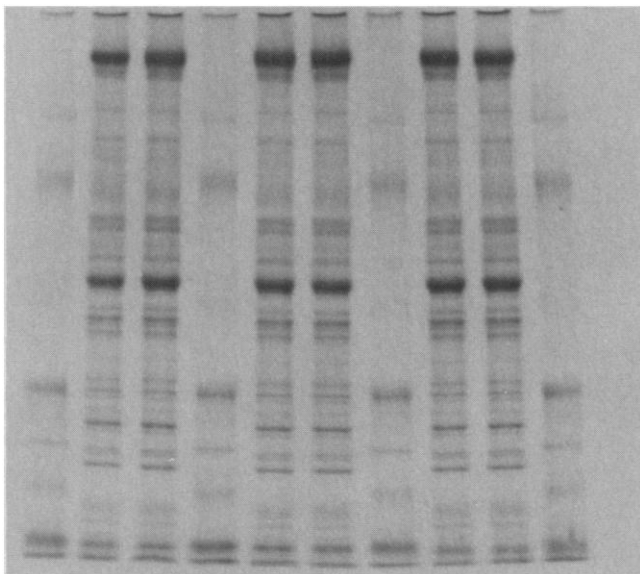
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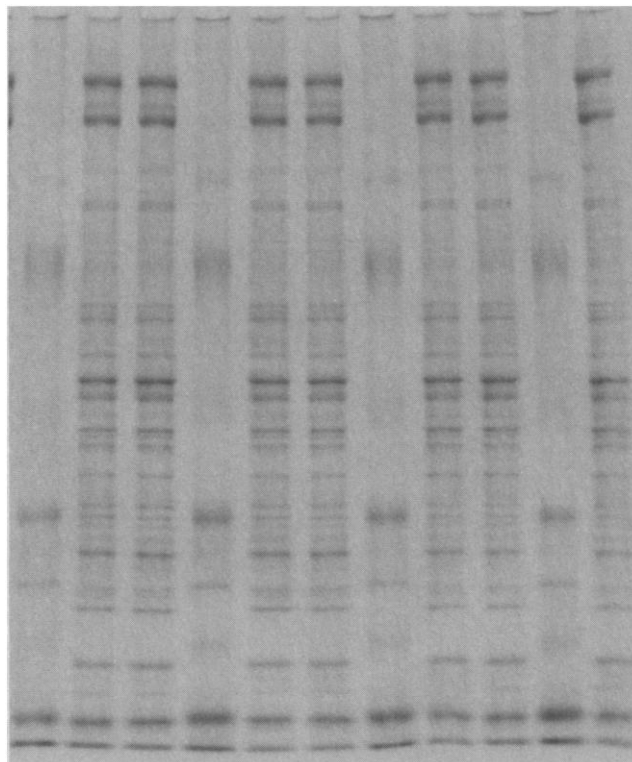
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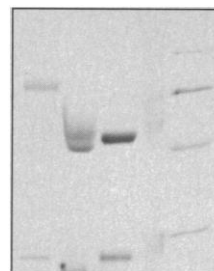
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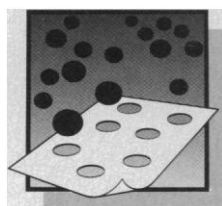


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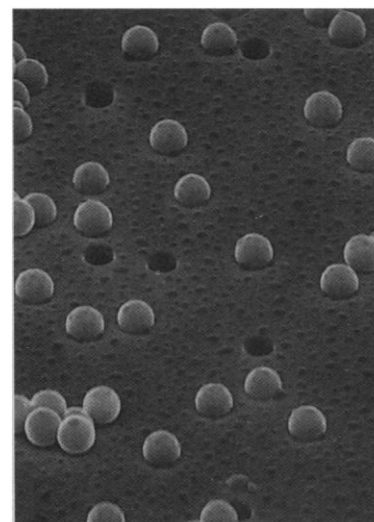
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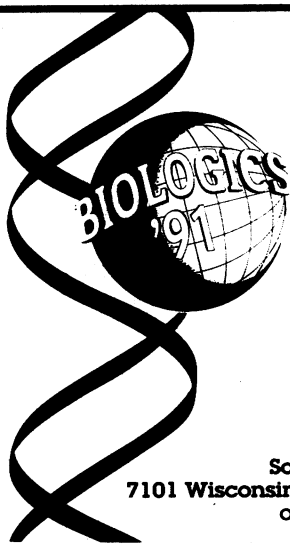
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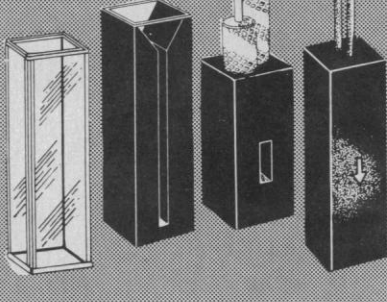
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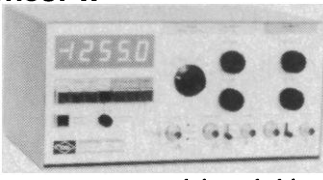
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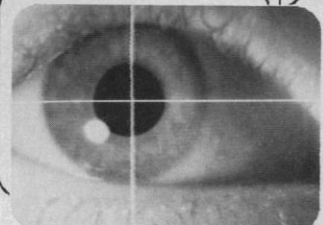
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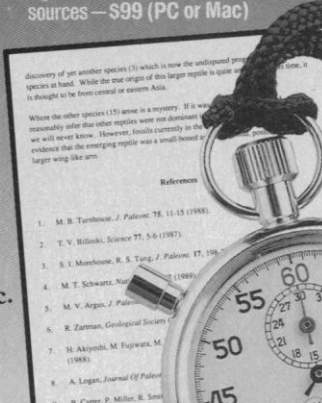
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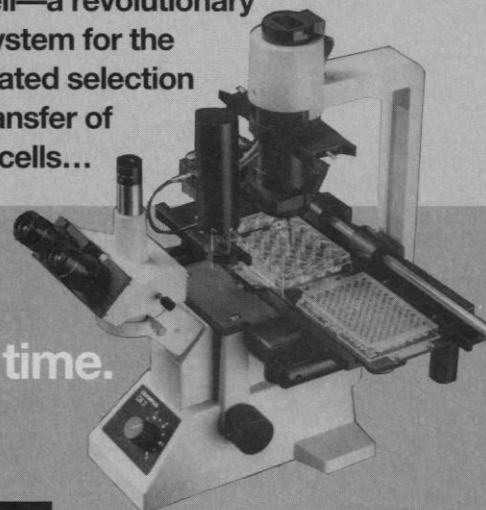
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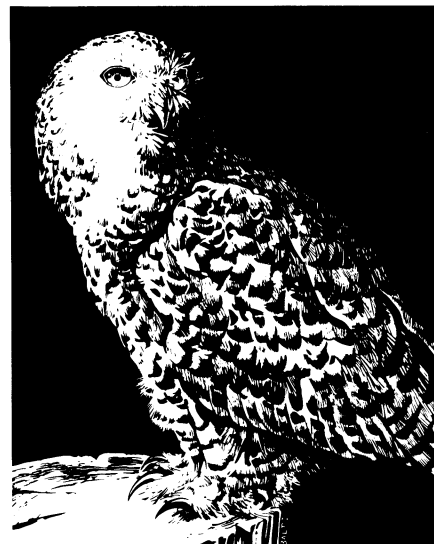
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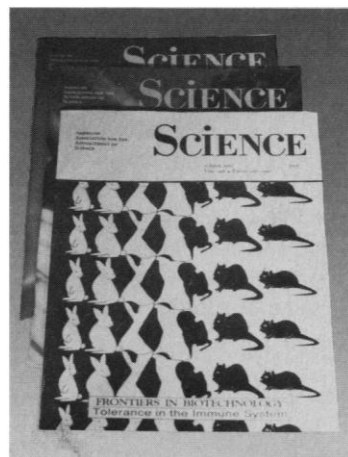
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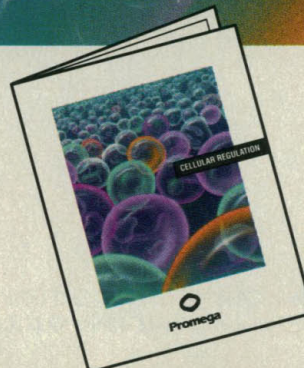
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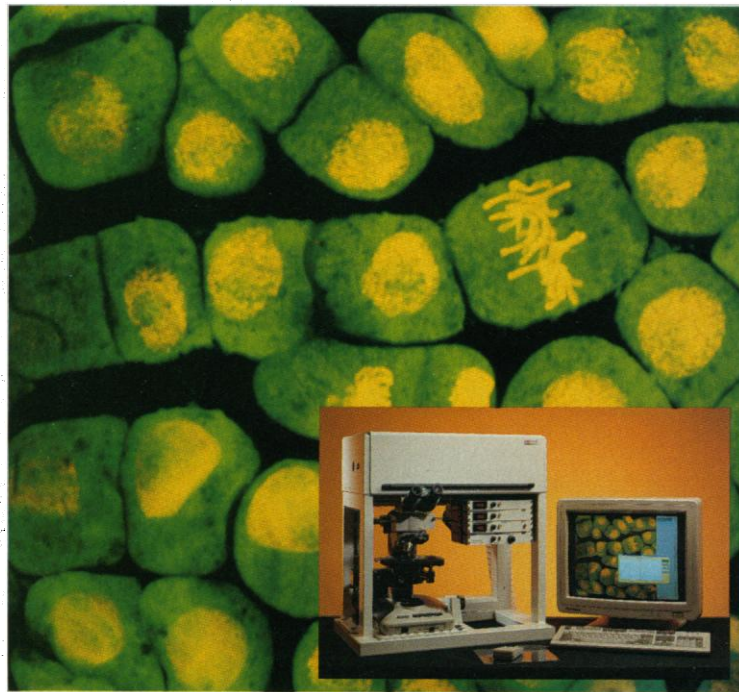
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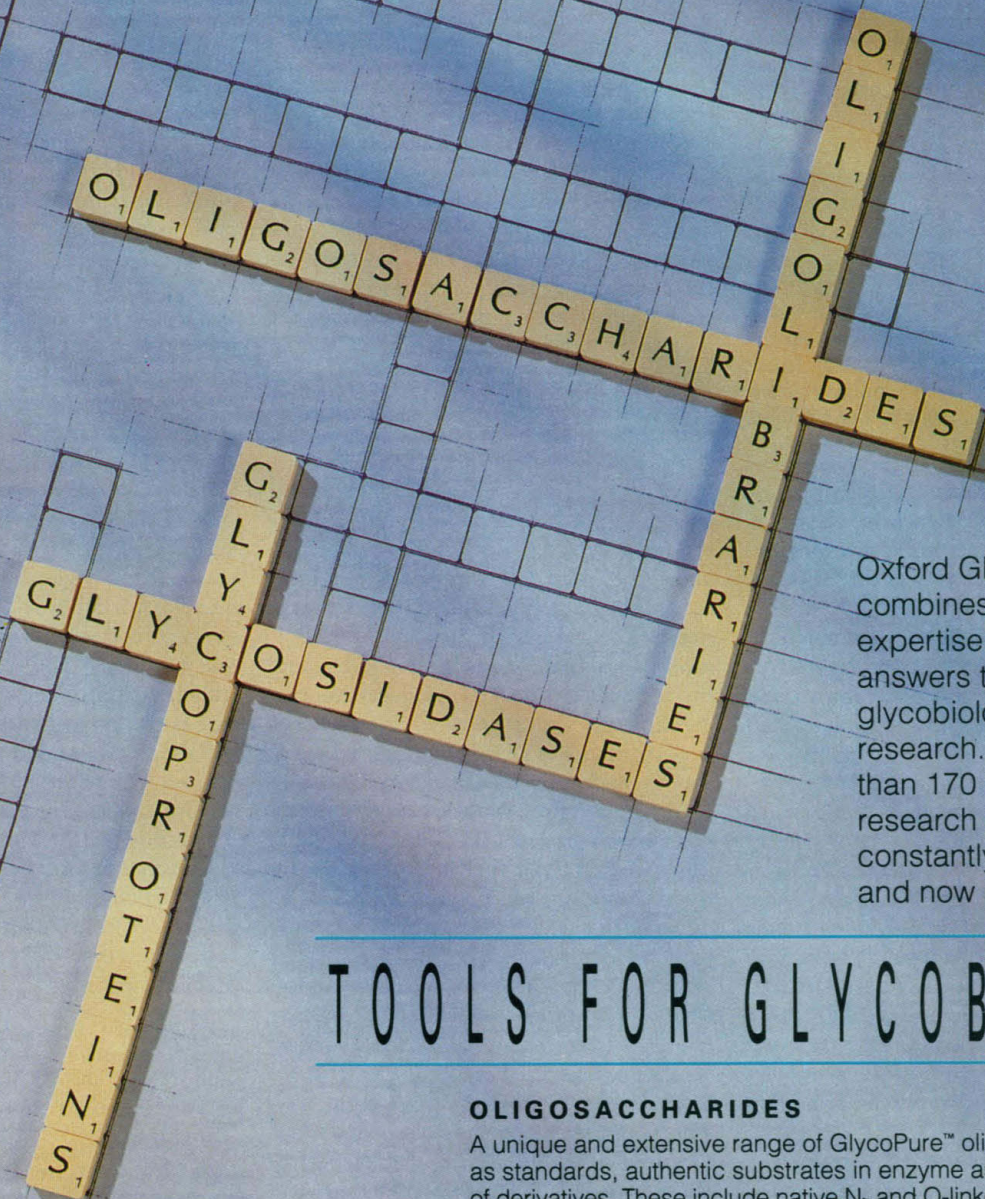
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