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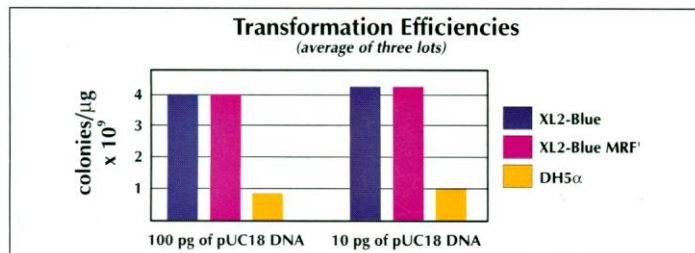
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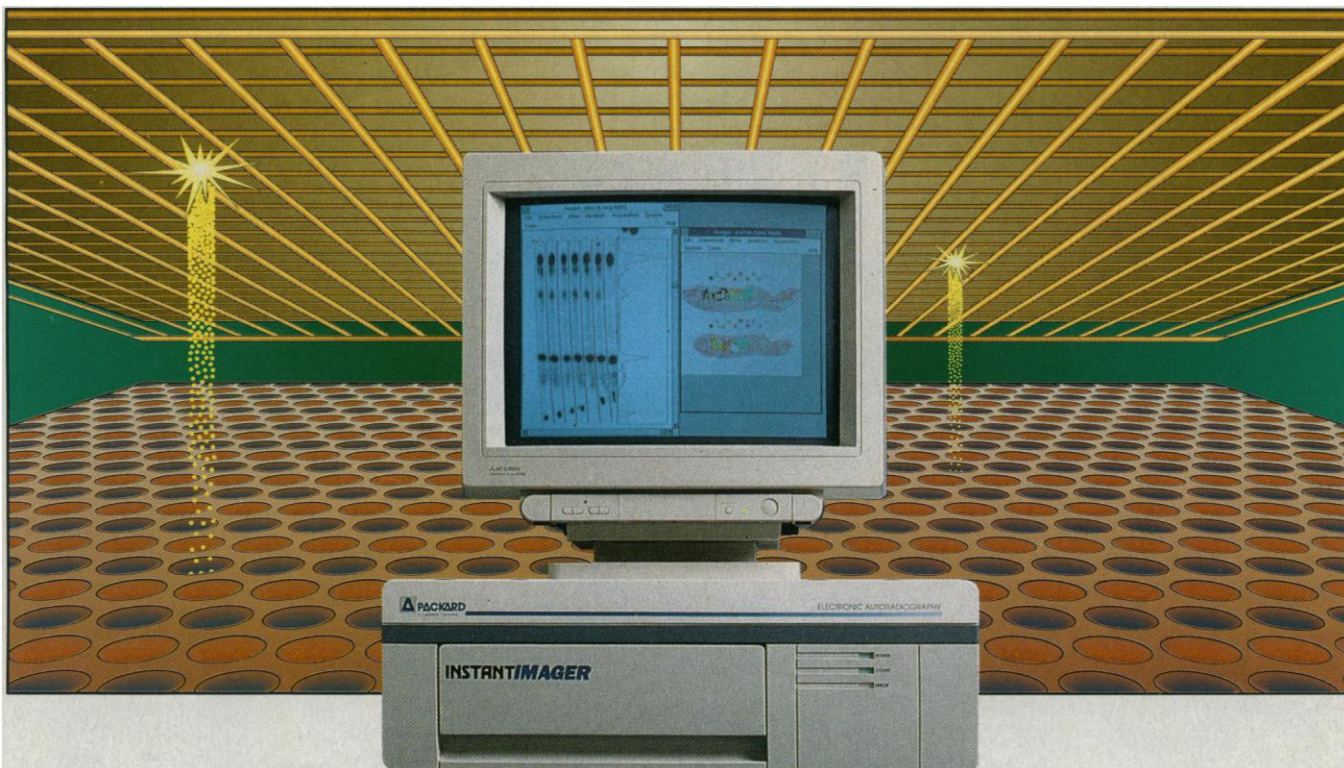


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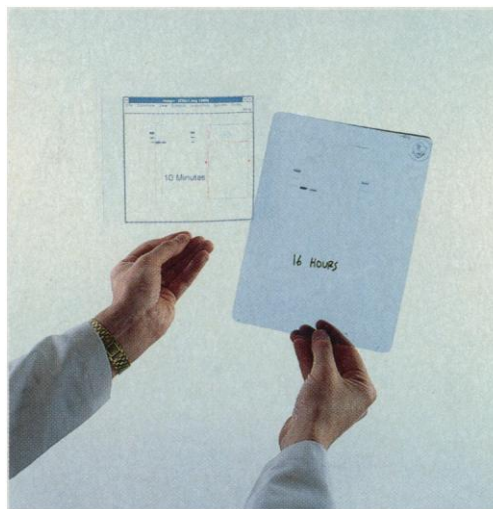
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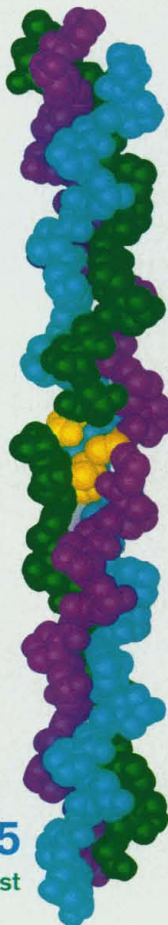
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## COVER

"Walking with the Ghosts of My Grandmothers" (1992), signature oil painting of artist Hollis Sigler's Breast Cancer Journal series. Through this series Sigler has tried to convey the emotional impact of a disease that affects one in nine women in the United States.

Two papers in this issue (see pages 66 and 120) report a major step forward in breast cancer research—the identification of the long-sought *BRCA1* gene, a critical determinant of hereditary breast cancer. [Photo: Michael Tropea]



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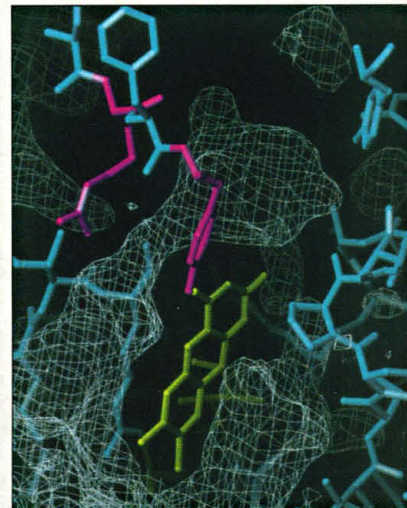
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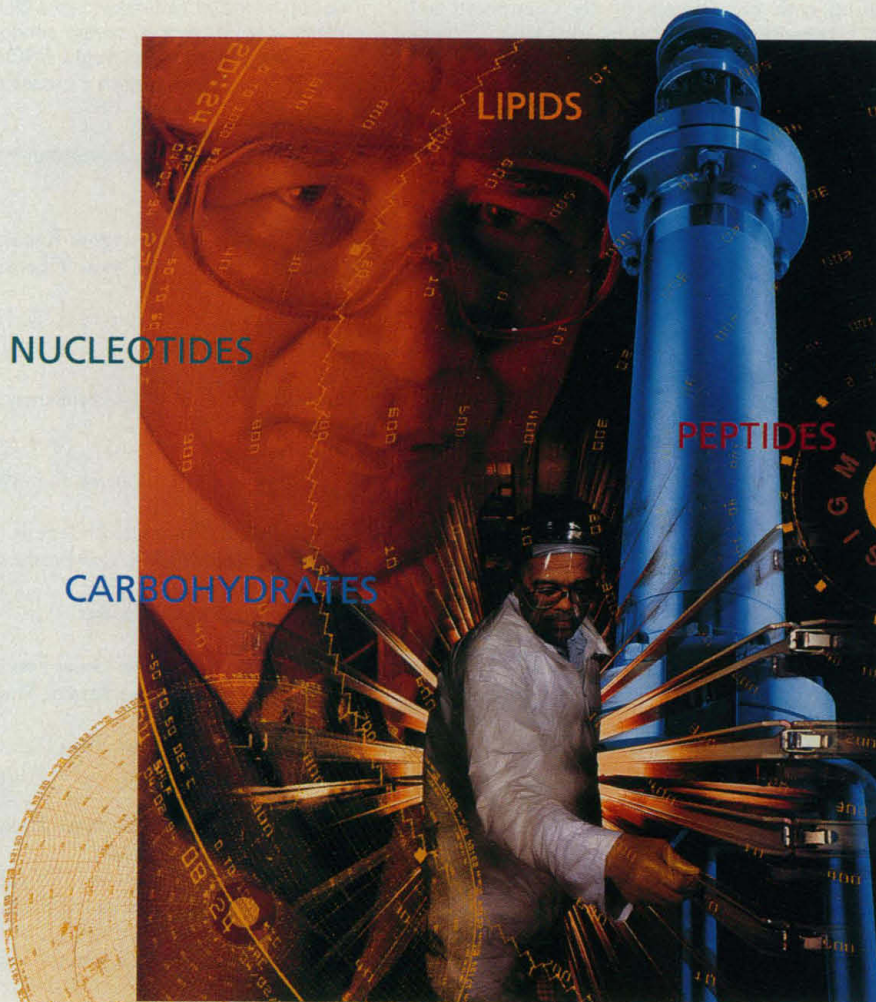
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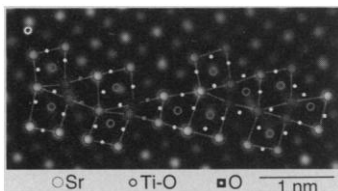
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## Going with the grain

Although grain boundaries in crystals play an important role in process such as diffusion and electrical conduction, their atomic structure is difficult to determine. McGibbon *et al.* (p.



102) present a structure of a grain boundary in a  $\text{SrTiO}_3$  bicrystal determined from a combination of high-resolution scanning transmission electron microscopy images, electron energy loss spectroscopy, and bond-valence sum calculations.

## High water mark

Dates of exposed ancient coral reefs provide a key record of sea level changes, particularly for the timing of interglacials when sea level was highest. A key question has been the timing of the last interglacial. Szabo *et al.* (p. 93) present 29 ages from 17 samples of reefs formed during the last interglacial on Oahu, Hawaii, which imply that sea level peaked 1 to 2 meters higher than today about 131,000 years ago. This date is somewhat earlier than that inferred from marine core records.

## Ocean oscillations

Understanding of the variability of temperature of the oceans at depths even a few meters below the surface has been poor. An early analysis of one station in the North Atlantic implied that temperature oscillated with a period of about 10 years and decreased overall during the past

## Biphasic catalysis without the water

Two-phase systems are often used in solution chemistry as a tool for maintaining product purity and recovering expensive catalysts. In phase transfer catalysis, a catalyst is dissolved in an aqueous phase and transported by a lipophilic cation into the organic phase. However, side reactions with water can occur, and many organic compounds dissolve poorly in water. Horváth and Rabái (p. 72; see the Perspective by Gladysz, p. 55) overcame these difficulties by replacing the aqueous phase with a fluorocarbon phase. Catalysts can be rendered soluble in the fluorous phase by attaching fluoro-carbon pendant groups. They present applications in olefin hydroformylation and rhodium catalyst recovery.

several decades. Levitus *et al.* (p. 96) have gleaned data from other stations in the Atlantic to extend this analysis. The data imply that temperature trends in the subtropical and subarctic gyres were opposite and that decadal-scale oscillations in temperature extend throughout the North Atlantic Ocean.

## Breast cancer gene

A strong candidate for *BRCA1*, a gene on chromosome 17q that confers susceptibility to early-onset breast and ovarian cancer, has been isolated by Miki *et al.* (p. 66). The gene specifies a protein containing a zinc finger. Germline mutations of the *BRCA1* candidate gene were found in members of 17q-linked families who are presumed to segregate *BRCA1* susceptibility alleles. A study of sporadic breast and ovarian tumors by Futreal *et al.* (p. 120) found no evidence of somatic mutations in the *BRCA1* candidate, suggesting that the gene may not play a critical role in these more common cancers.

## Triple helixes

Collagen and collagen proteins have a number of unusual sequence features, such as the oc-

currence of the small glycine residue at every third position, that cause them to adopt their characteristic triple-helix structure. Such a regular structure has made crystallographic studies difficult, in that these molecules often disorder in the solid state, so that only fiber diffraction data can be obtained. Bella *et al.* (p. 75) have obtained a high-resolution x-ray structure of a 30-residue collagen-like peptide in which one glycine has been modified to alanine. Their analysis reveals an extensive hydrogen-bonding network of the peptide with water molecules. Similar mutations occur in a number of human diseases; a local untwisting of the triple helix occurs in the vicinity of the substitution.

## Increased resistance

One in 20 Caucasians carry the mutation responsible for causing cystic fibrosis (CF). These carriers are healthy, whereas people who inherit two copies of the mutated gene are likely to die before reaching adulthood. Gabriel *et al.* (p. 107) used the CF mouse model to assess to what extent heterozygous mice possess an advantage that might explain the high incidence of the mutated gene in the human population. Mice carrying one

copy of the mutated gene were less sensitive to cholera toxin. Carriers of the gene might have a selective advantage of resistance to cholera or to other forms of secretory diarrhea.

## Editing guidelines

In the mitochondria of kinetoplastid protozoa, the sequence of a mature messenger RNA molecule is derived not only from the gene that encodes it, but also from a post-transcriptional editing process in which specific uridines are added or deleted. Seiwert and Stuart (p. 114) have developed an *in vitro* system for studying this editing process. Successful editing seems to depend upon adenosine triphosphate as well as upon base-pairing between the pre-mRNA and the guide RNA at the editing site.

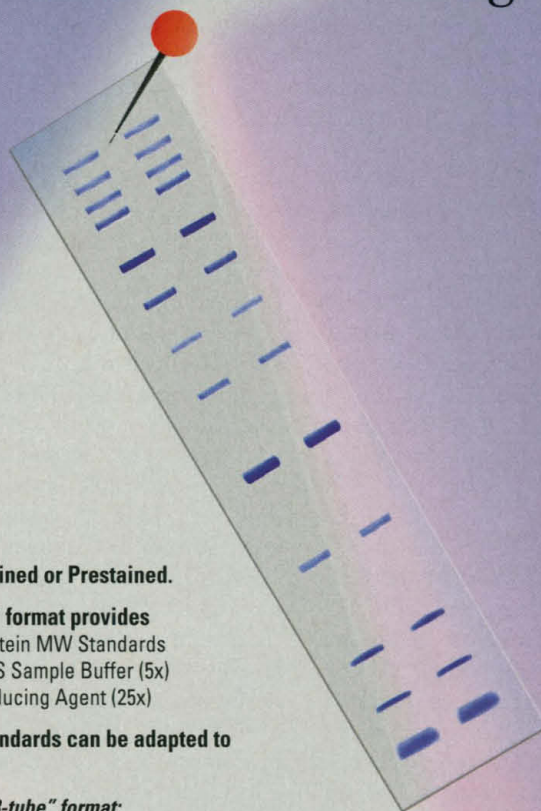
## More than cell cycle control

The function of cyclin-dependent kinases (CDKs) is not restricted to control of the cell cycle. The response of yeast to extracellular concentrations of phosphate is mediated by the CDK PHO85. In the presence of high concentrations of phosphate, an active complex of PHO85 and the cyclin PHO80 is formed, which leads to decreased expression of a secreted acid phosphatase. Schneider *et al.* (p. 122) show that in conditions where phosphate is limited, the PHO80-PHO85 complex is inhibited by PHO81, a protein with similarity to mammalian CDK inhibitors. Thus, similar mechanisms of regulation appear to modify the activities of CDKs that control either cell growth or responses to environmental stimuli.



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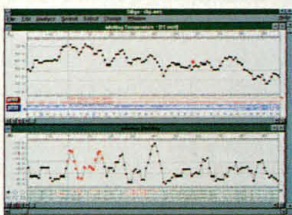


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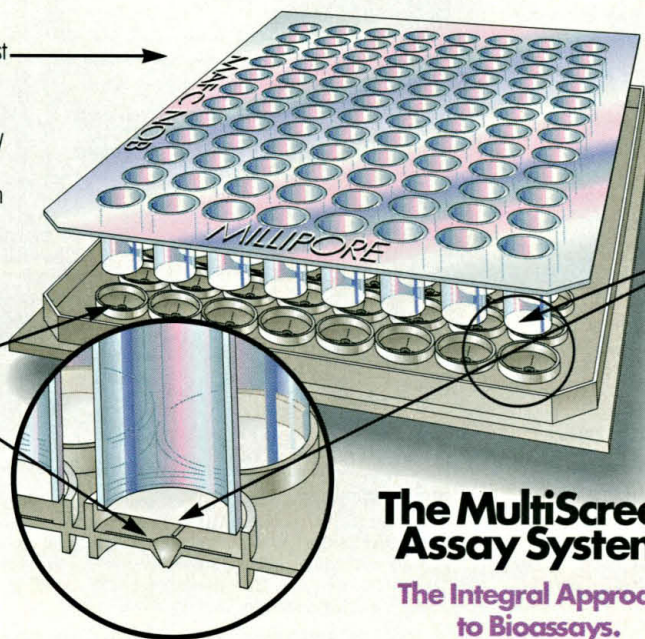
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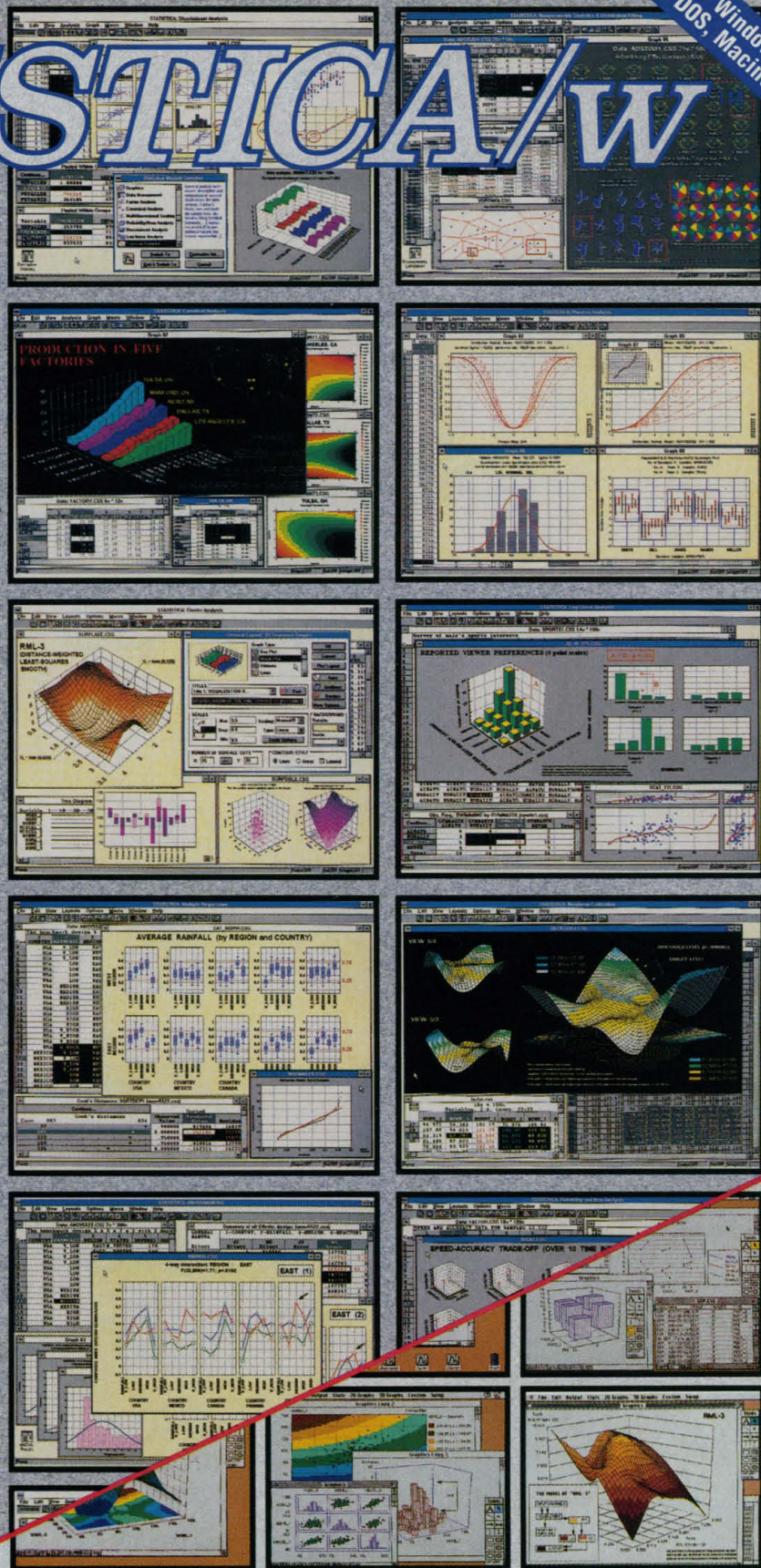


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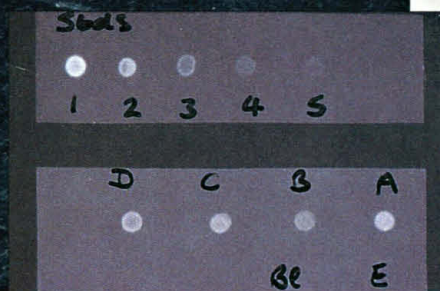
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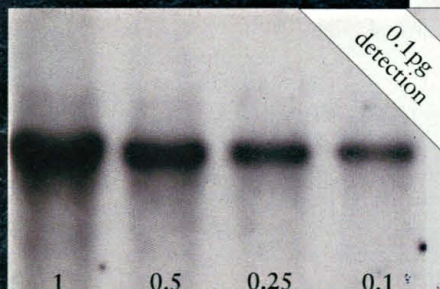




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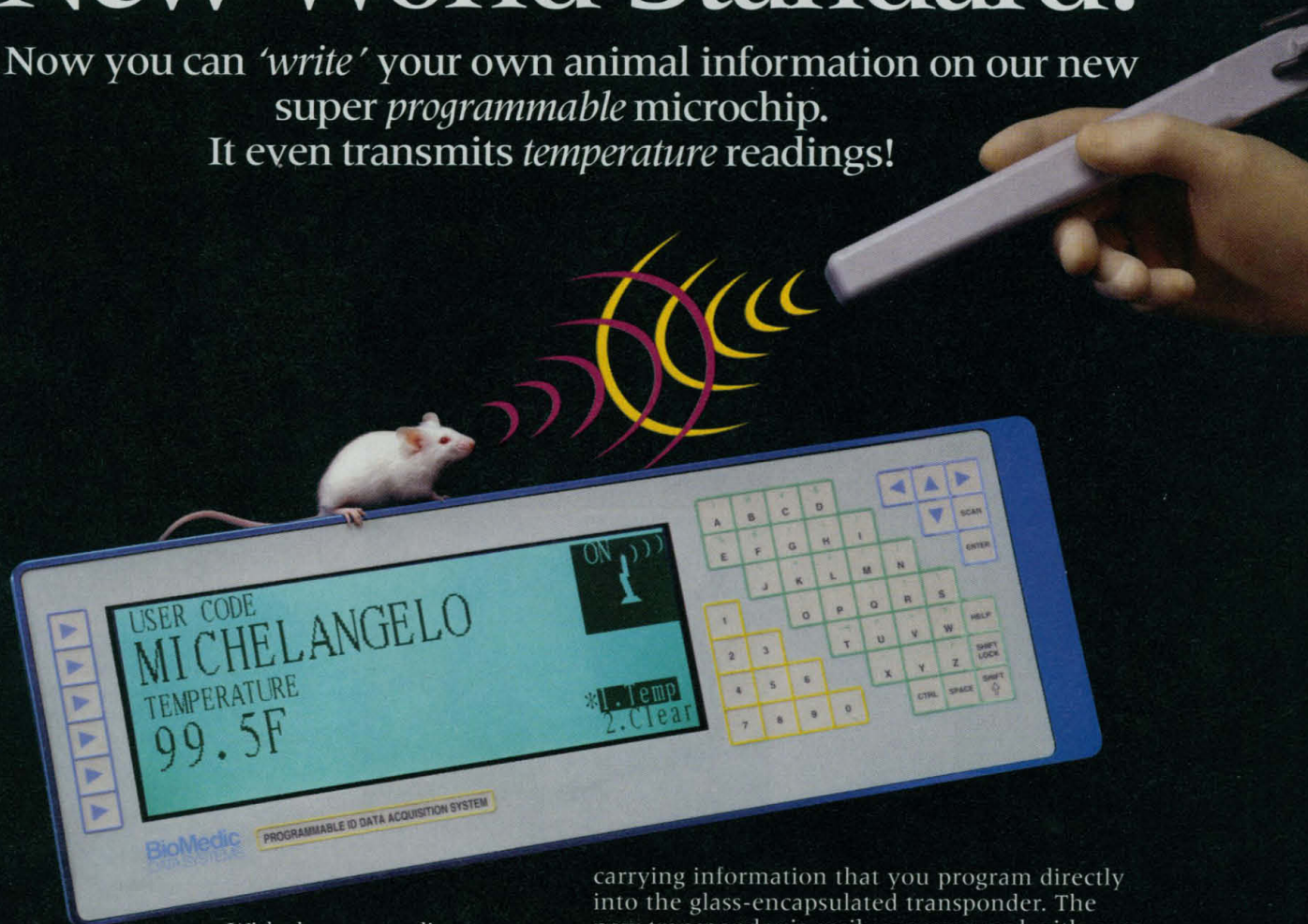
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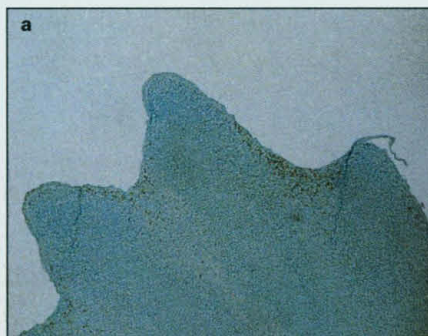
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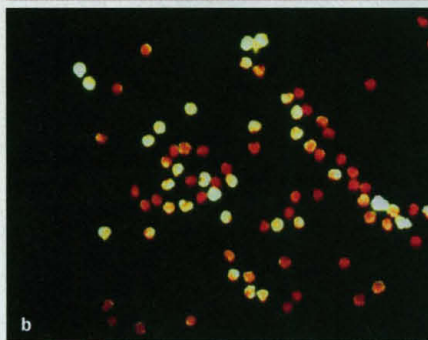
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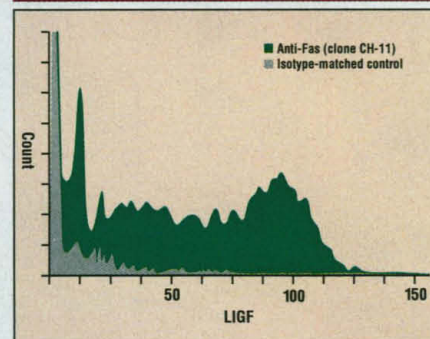
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<sup>1</sup> Yonehara, S., et al, (1989) *J. Exp. Med.* 169:1747-1756.

<sup>2</sup> JER Kerr, J Searle, BV Harmon & CJ Bishop, in: Potten, CS (ed) (1987) *Perspectives in mammalian cell death.* Oxford U. Press, pp. 93-128. Z Zakeri, D Quaglino, T Latham & R Lockshin, (1993) *EASEB Journal*; 7:470-478; and manuscripts submitted.

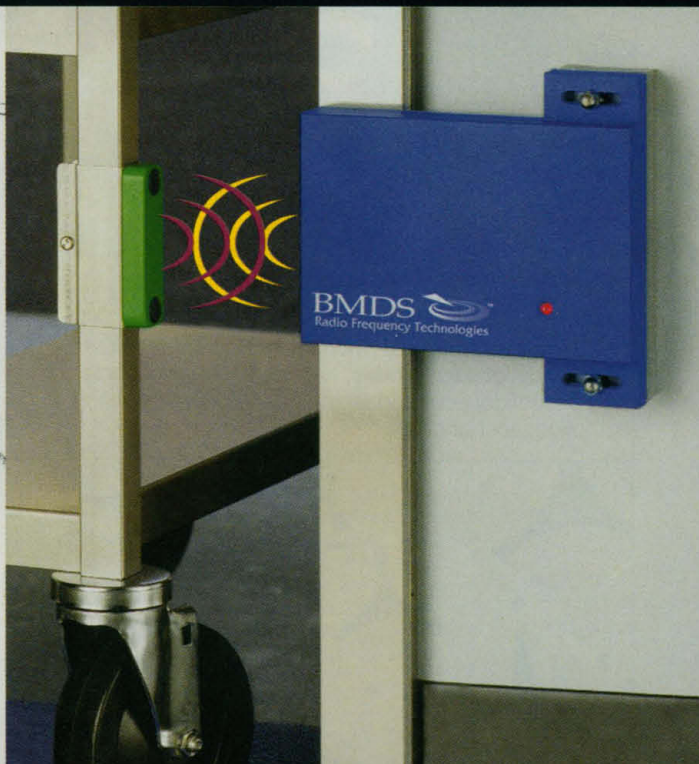
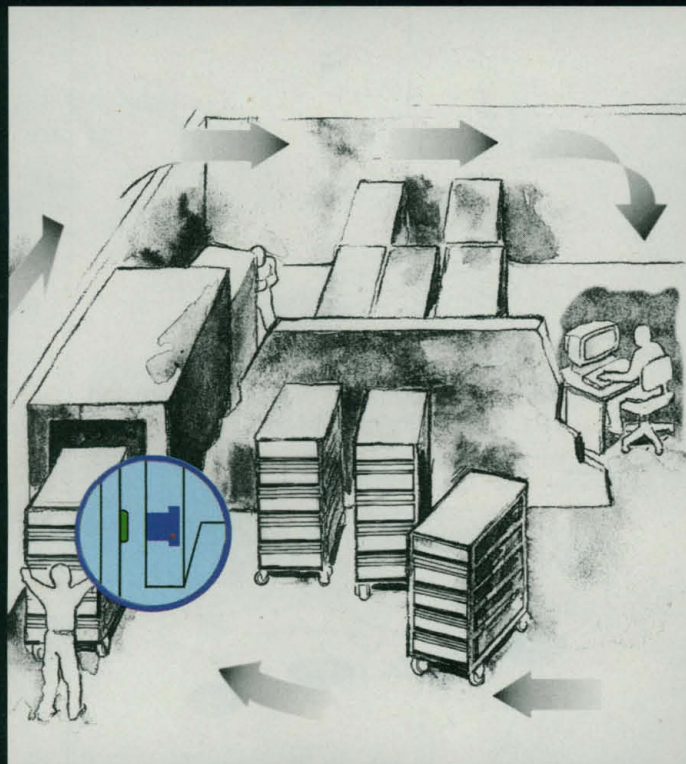
<sup>3</sup> X Li, W James, F Traganos & Z Darzynkiewicz, (1993) manuscript submitted.

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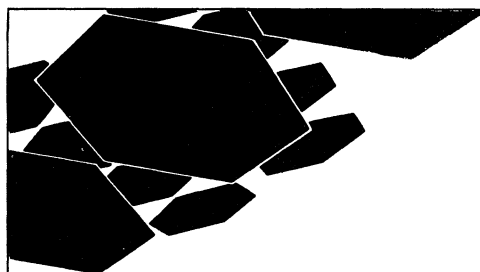
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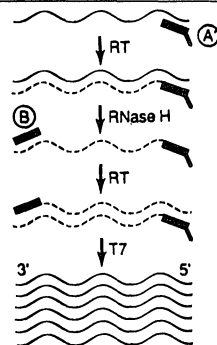
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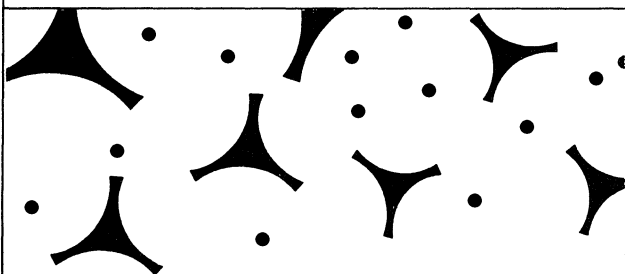
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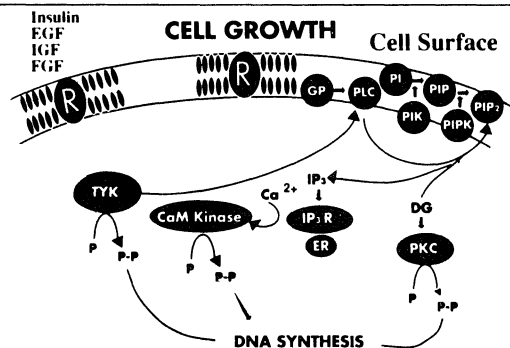
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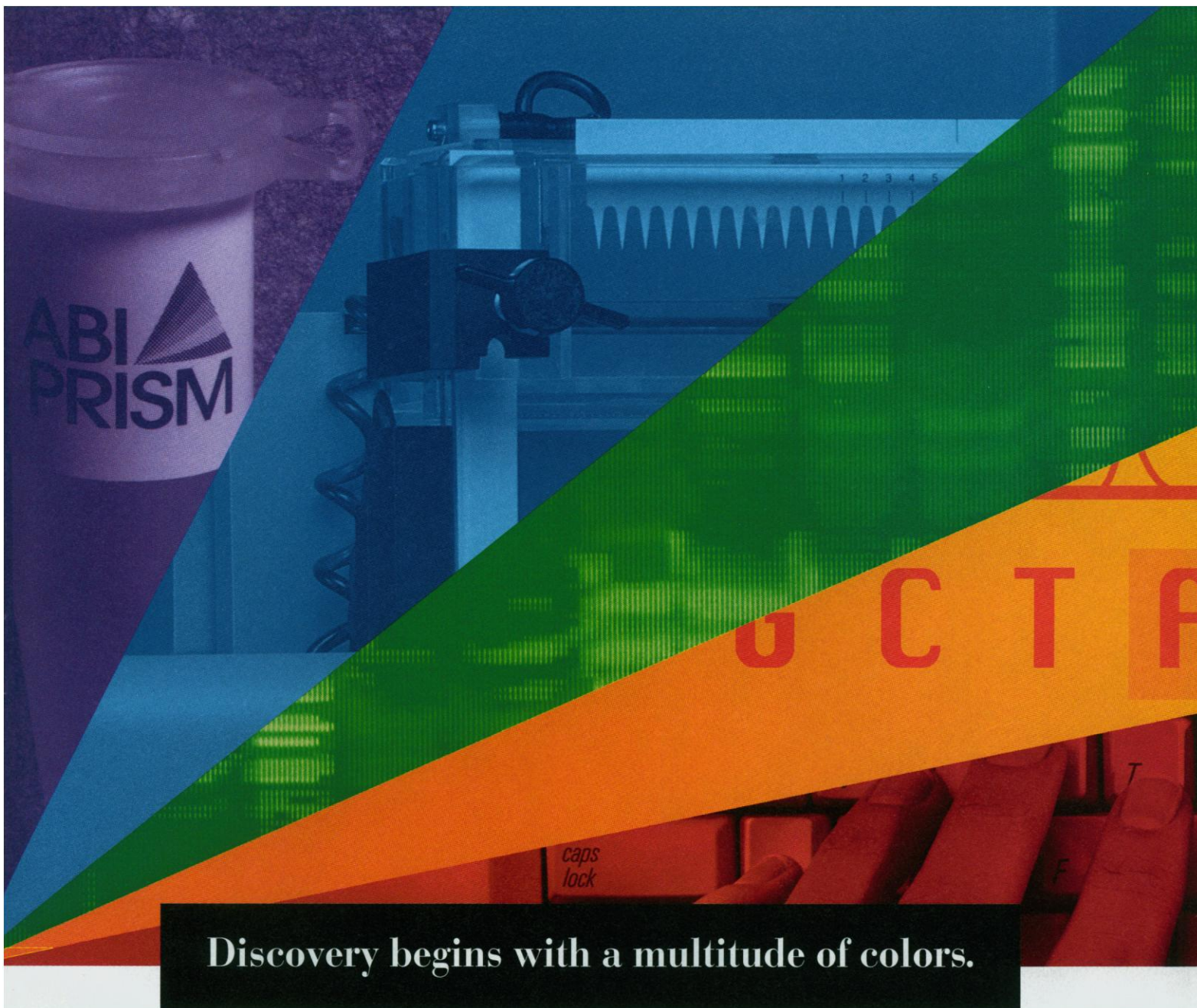
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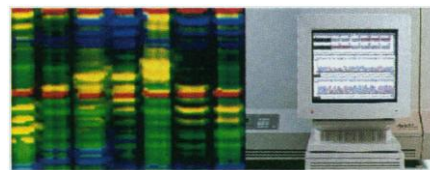
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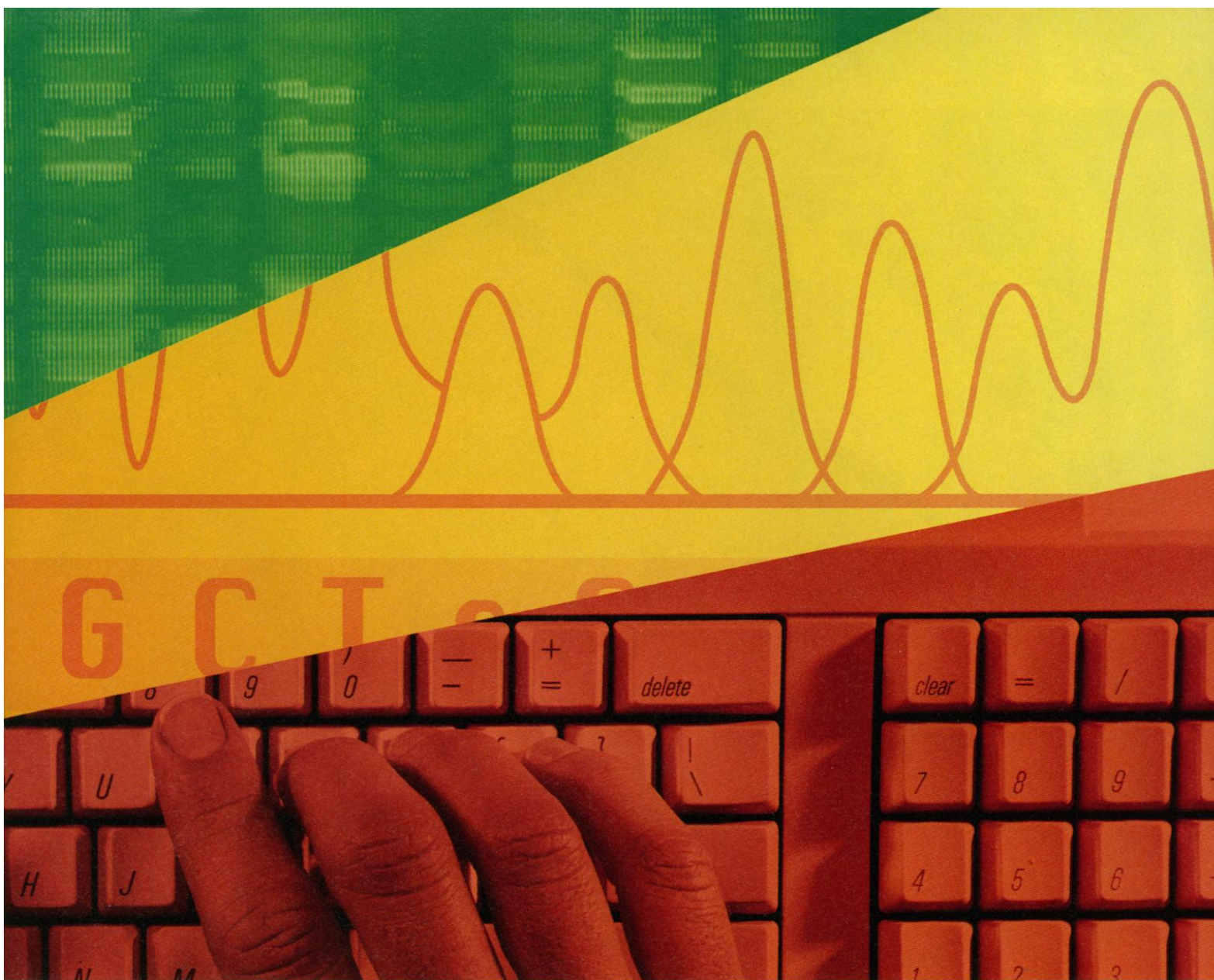
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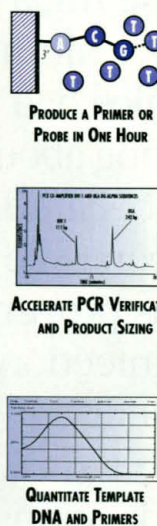
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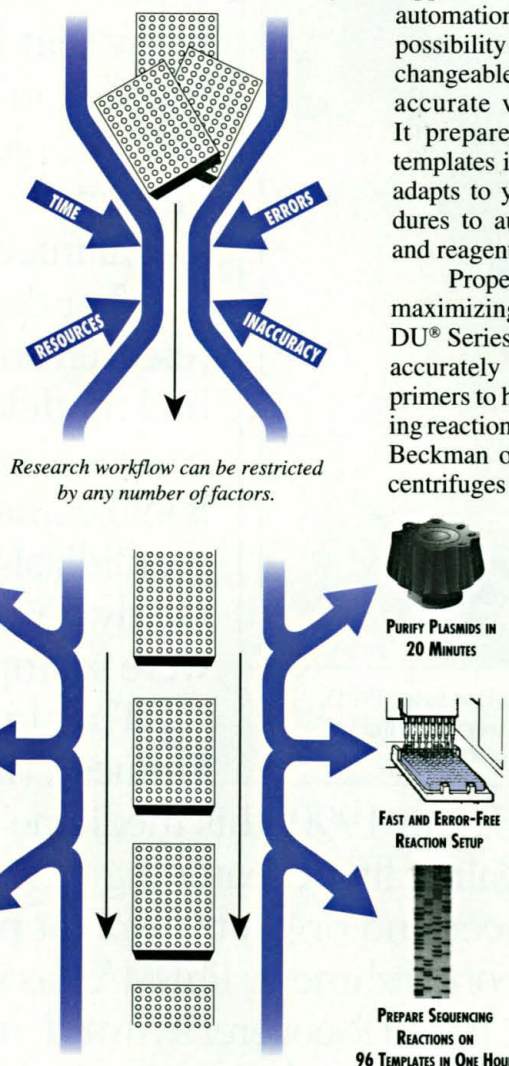
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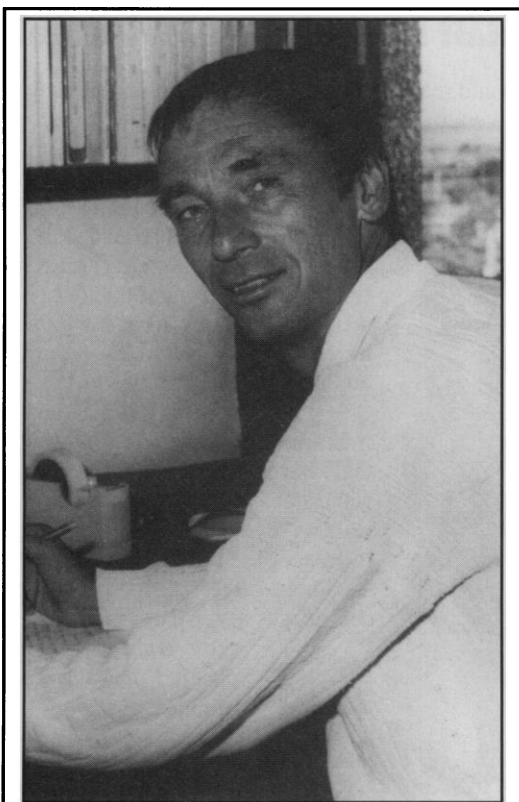
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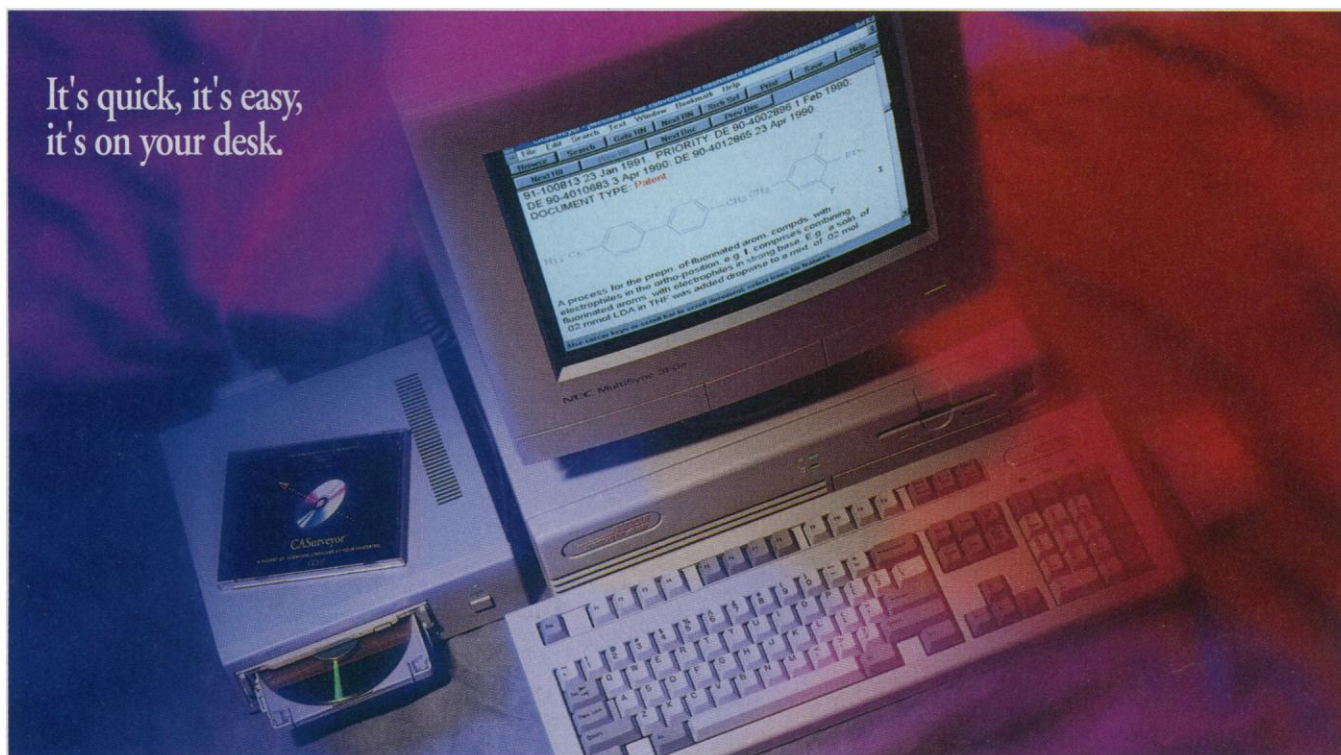
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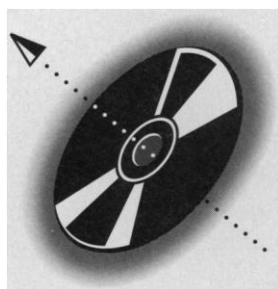
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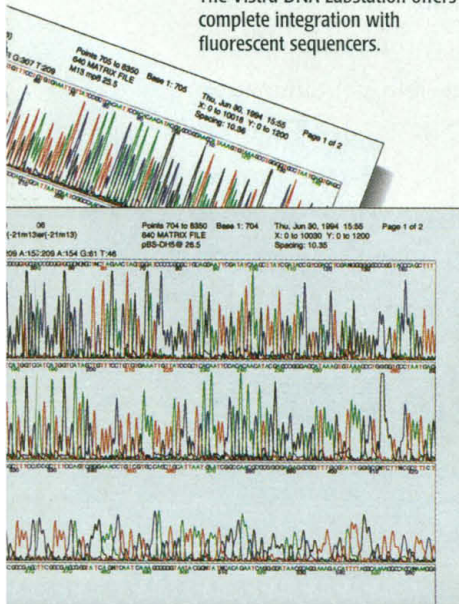


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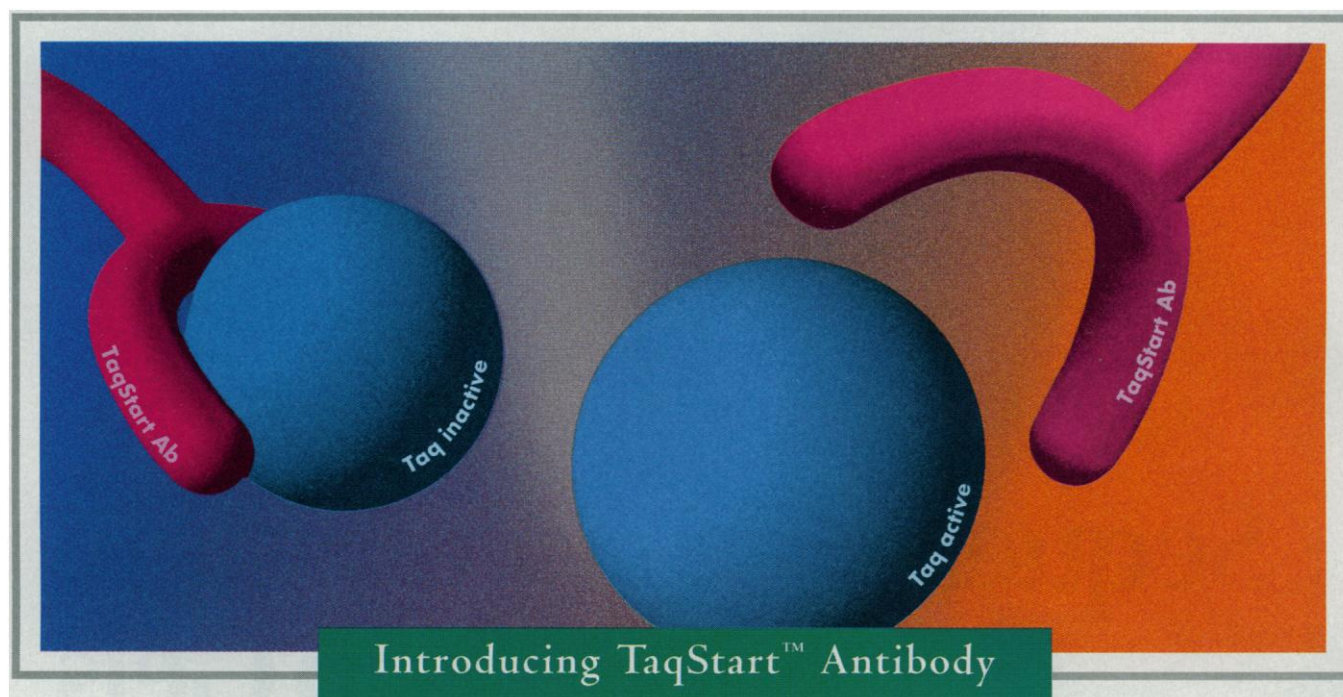
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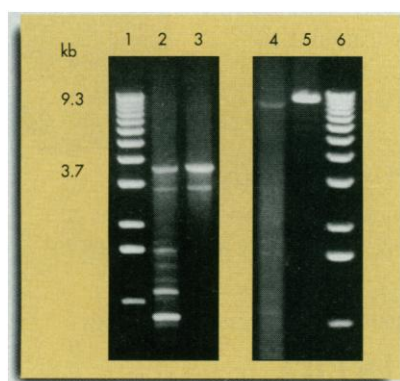


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Lane 2: 2.0 kb  
Lane 3: 4.0 kb  
Lane 4: 6.0 kb  
Lane 5: 8.0 kb  
Lane 6: 10.0 kb  
Lane 7: 12.0 kb  
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Lane 11: 34.8 kb

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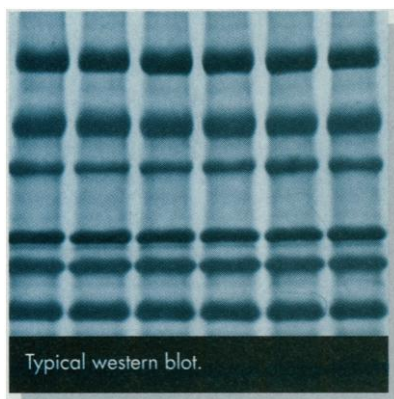
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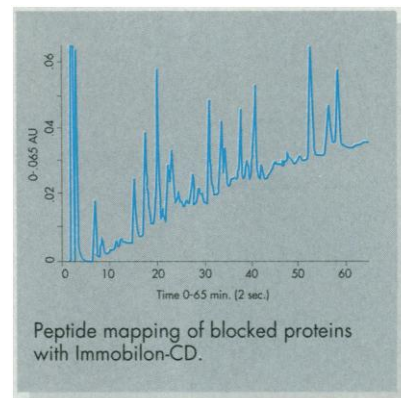
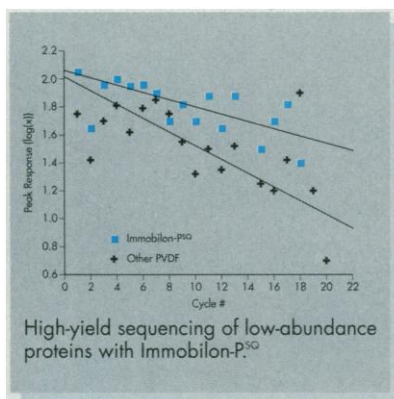
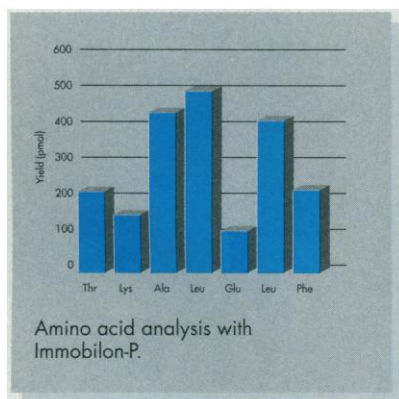
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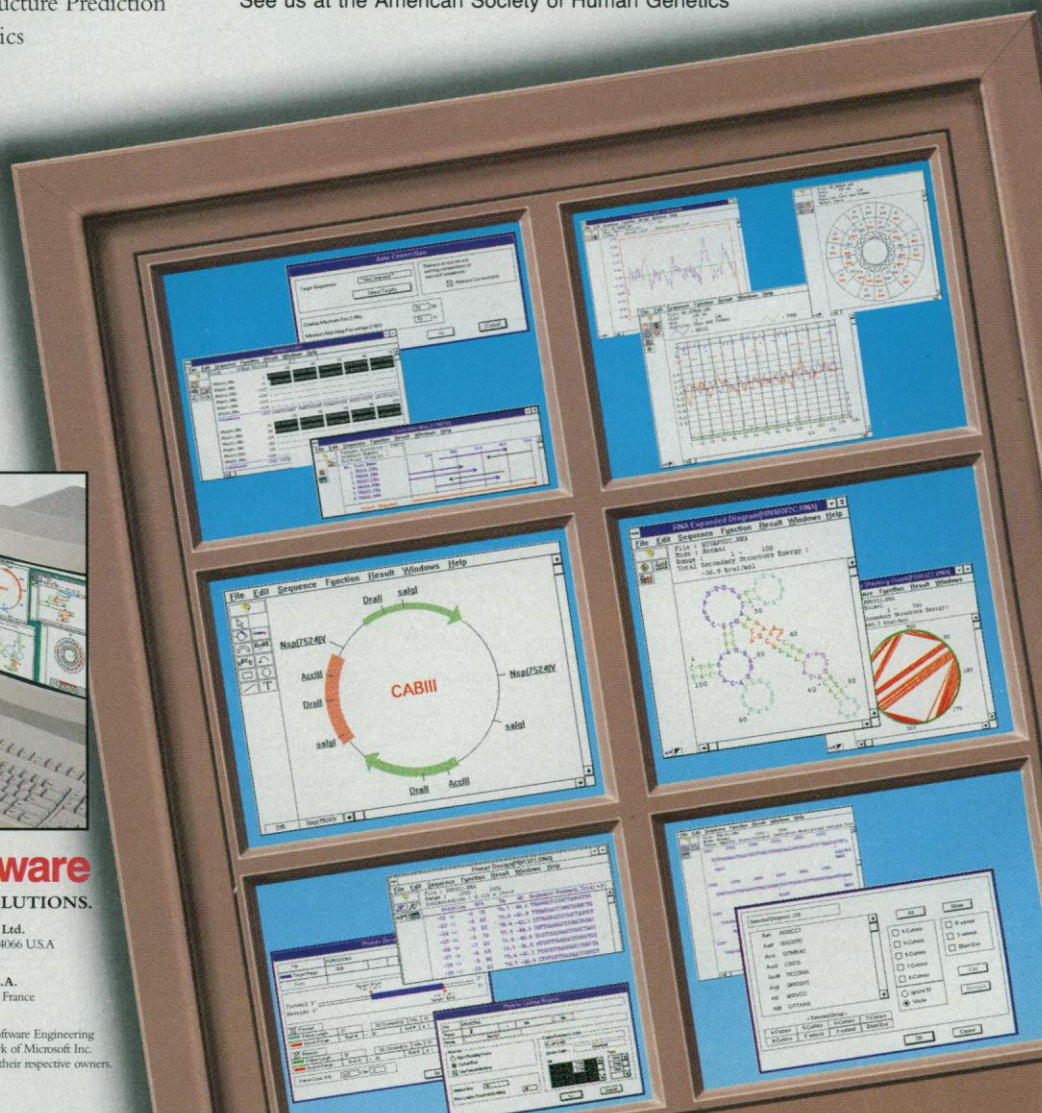
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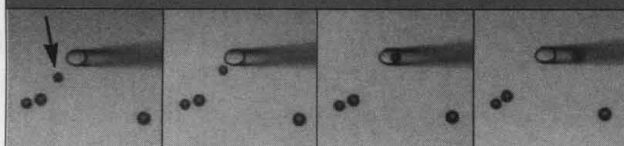
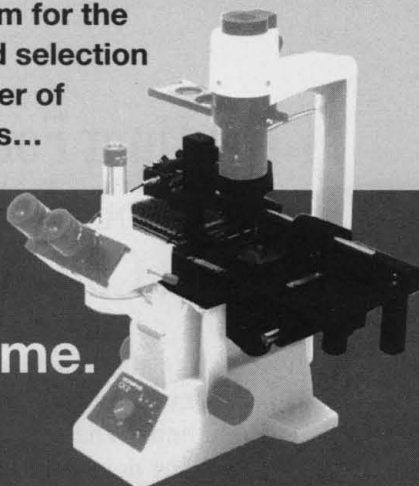
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