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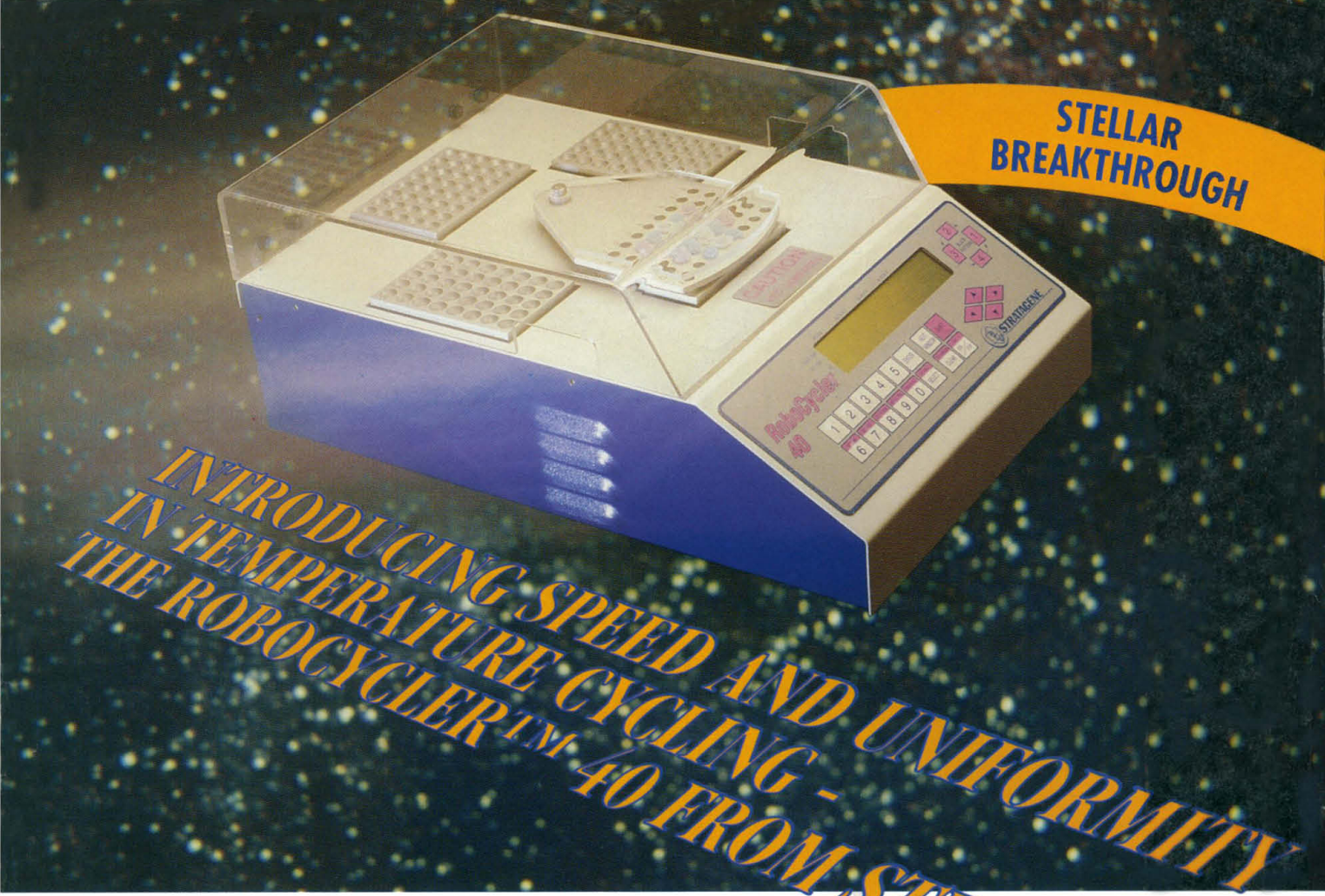
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**INSTRUMENTATION
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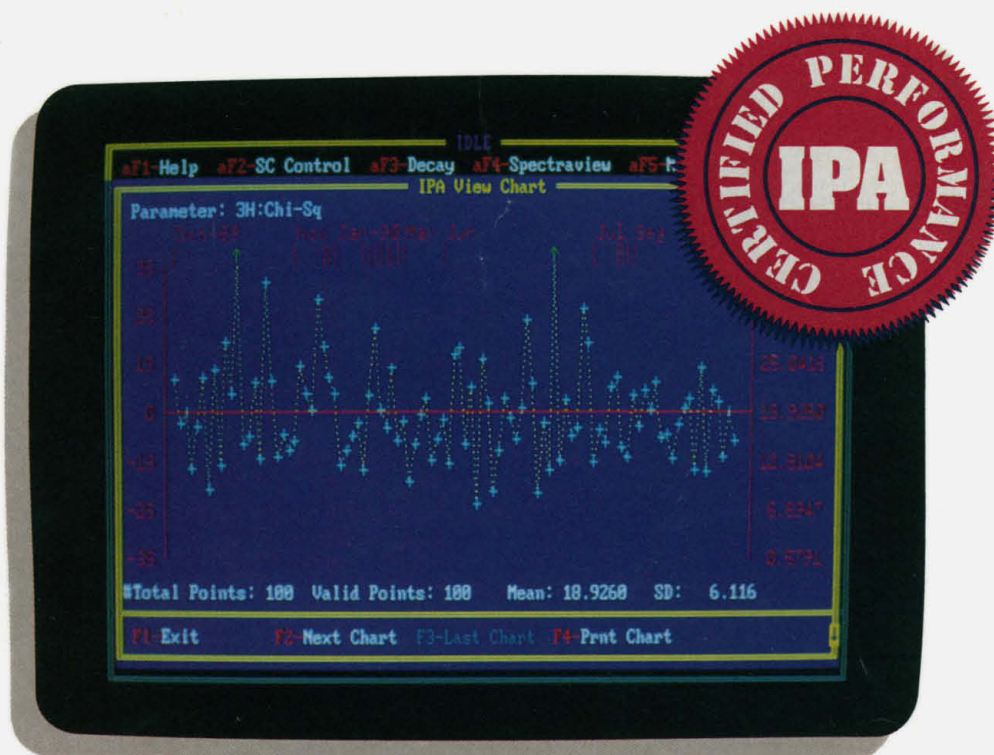
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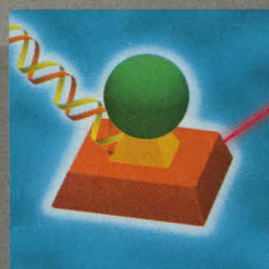
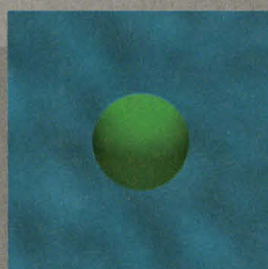
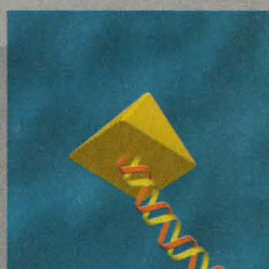
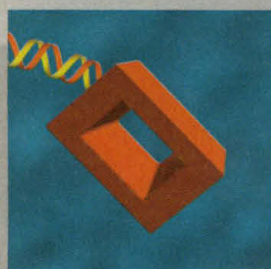
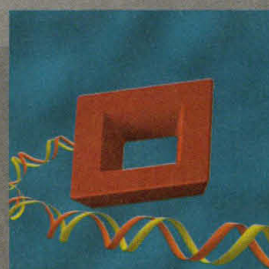
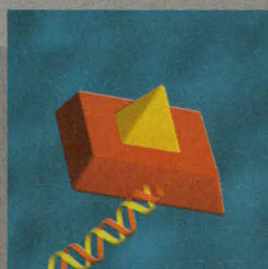
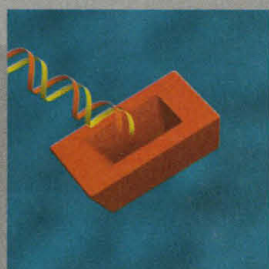
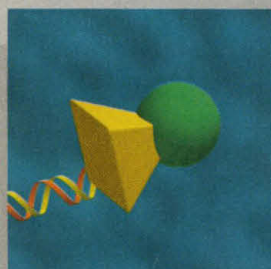
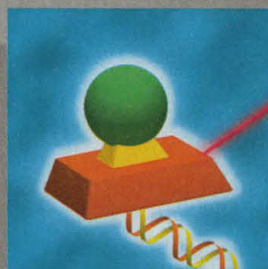
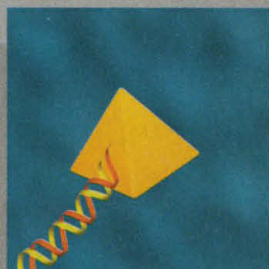
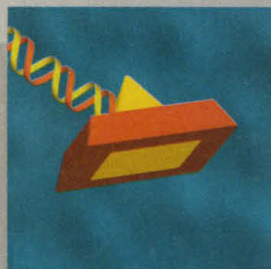
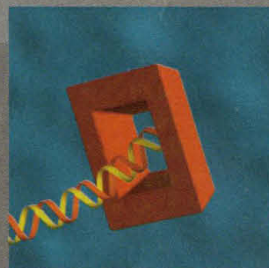
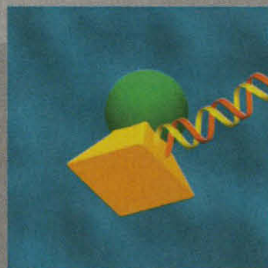
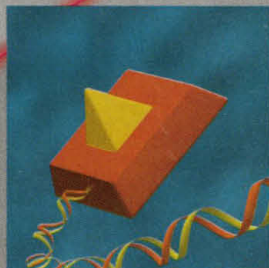
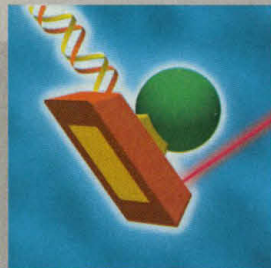
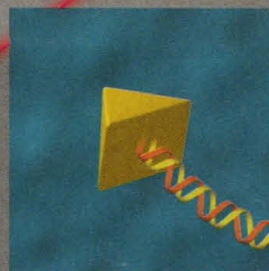
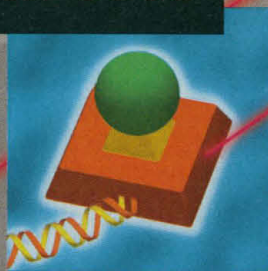
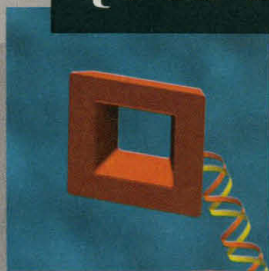
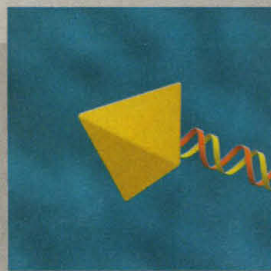


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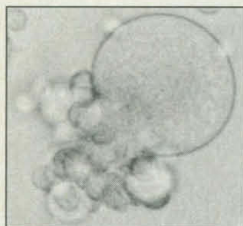
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COVER

Lipofectin-mediated delivery of oligonucleotides containing C-5 propyne to the nucleus of a human ovarian carcinoma cell, detected by fluorescence confocal microscopy. High concentrations (blue, red, and white) of oligonucleotides are mostly localized in the nucleus;

low concentrations (green, yellow, and orange) are found in the cytoplasm. Such nuclear localization of oligonucleotides appears to be critical for potent antisense gene inhibition. See page 1510. [Image: Richard W. Wagner]



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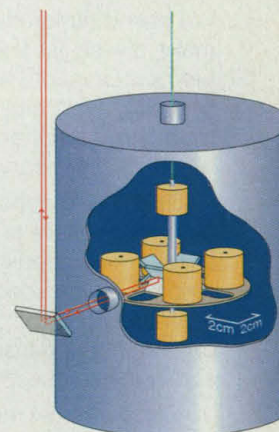


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Look and learn ... synaptic plasticity in the brain

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Dark gravitation



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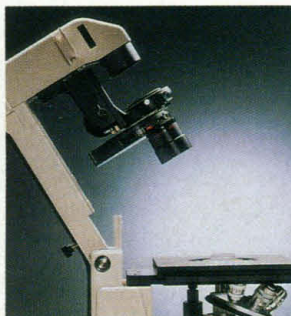
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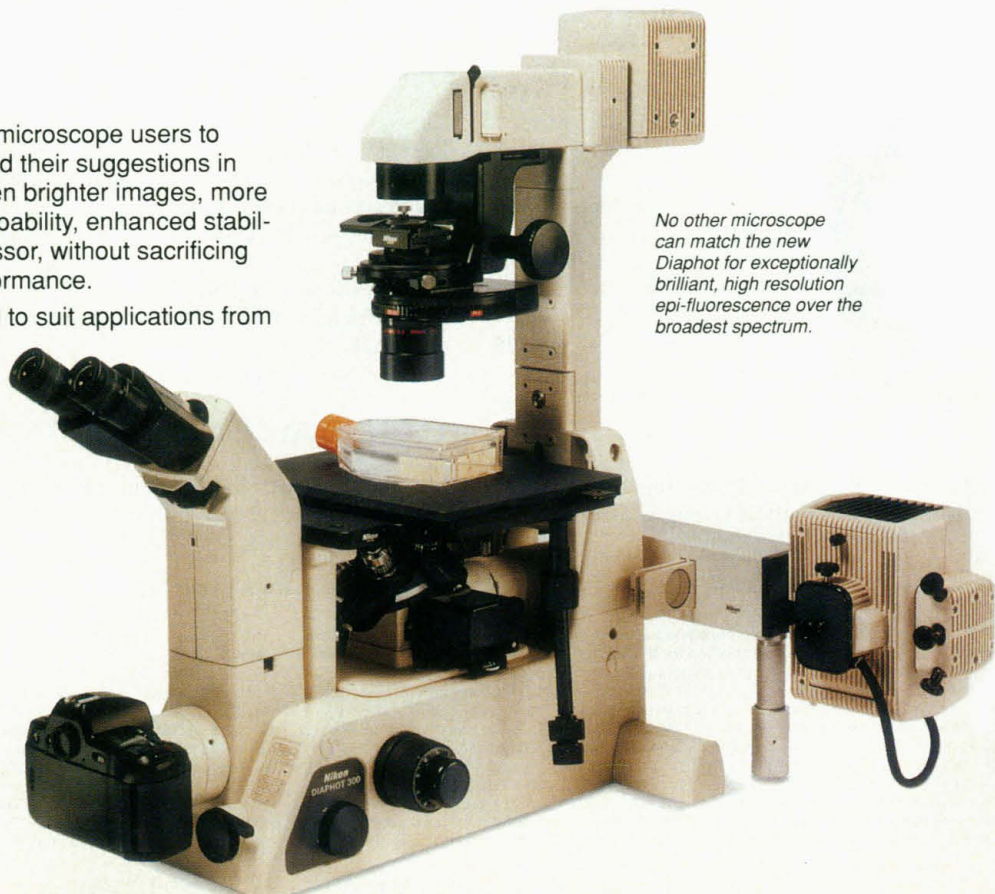
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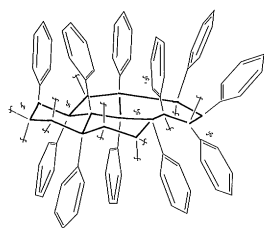
Hot sounds

Knowledge of the speed of sound through minerals under mantle pressures and temperatures is needed in order to use seismic velocities to characterize the composition and physical properties of the mantle. Zaug *et al.* (p. 1487) were able to measure the speed of sound in olivine, a major upper mantle mineral, in a diamond cell at pressures up to 12.5 gigapascals (equivalent to about 400 kilometers depth in the Earth). The results are inconsistent with previous extrapolations made from low-pressure data and suggest that the observed lateral variations in the upper mantle reflect changes in temperature rather than composition.

□

Diamond paint?

Diamond and diamond-like phases of carbon are attractive as coatings for surfaces that must survive harsh conditions of mechanical wear, but applying such a coating is not always straightforward. Visscher *et al.* (p. 1496; see news story by Amato, p. 1424) report a soluble, film-forming polymer material that decomposes upon heating to



form a diamond or diamond-like material at atmospheric pressure. The polymer precursor consists of poly(phenylcarbyne), which forms a random three-dimensional network of fused carbon rings. Uses may include hard carbon coatings and fabricating submicrometer structures by laser pyrolysis.

May help relieve inflammation and allergy

Many inflammatory responses in the body are triggered by the production of prostaglandins and leukotrienes from arachidonic acid. Drugs such as aspirin can help relieve inflammation by inhibiting the action of cyclooxygenase, the enzyme that initiates prostaglandin synthesis, but effective inhibitors of lipoxygenases, which initiate leukotriene synthesis, have been lacking. In a step toward the rational design of inhibitors, Boyington *et al.* (p. 1482) report the x-ray crystal structure of such an enzyme, soybean lipoxygenase-1, which is related to the mammalian enzymes. This enzyme has a two-domain structure in which the catalytic iron atom, which is not bound by a heme group, adopts a four-coordinate, distorted octahedral geometry. The two open coordination sites of the Fe^{2+} atom may then interact with the double bonds of arachidonic acid and molecular oxygen to ultimately catalyze the formation of the hydroperoxide product.

Chemical shifts in protein NMR

In the analysis of simple compounds by nuclear magnetic resonance, much information is gained from chemical shifts, which are the characteristic changes in resonance frequency caused by shielding effects. Protein structure determination by nuclear magnetic resonance usually relies on distance information gained from spin relaxation measurements because chemical shifts are difficult to calculate. De Dios *et al.* (p. 1491) have been able to make such computations tractable by using full ab initio methods only for the short-range shielding effects of nearby atoms. The calculated values correspond well with those determined experimentally for several proteins.

□

Regulating feedback

Patients with hyperphenylalaninemia have a deficiency in the phenylalanine hydroxylase pathway that converts phenylalanine (Phe) to tyrosine and yet have high plasma concentrations of tetrahydrobiopterin (BH_4), a cofactor for this enzyme. Harada *et al.* (p. 1507)

show that the enzyme that performs the initial step in converting guanosine triphosphate (GTP) to BH_4 , GTP cyclohydrolase I, is inhibited by BH_4 but only in association with another protein, p35. They also show that Phe can reverse the inhibitory effect of BH_4 and can reduce the cooperativity of GTP cyclohydrolase I so that GTP can be used as a substrate at lower concentrations. High BH_4 concentrations may also have to be considered in evaluating the neurological disorders in phenylketonuria (PKU), a disease in which Phe concentrations are high.

□

Antisense affinity

Although there are many approaches for modifying oligodeoxynucleotides (ODNs) for use as antisense agents, low binding affinities for the target site often lead to nonspecific gene inhibition. Wagner *et al.* (p. 1510) have synthesized phosphorothioate ODNs in which the U and C residues are modified at the 5' position with a propyne group. This modification so improves the affinity that inhibition of gene expression

could be seen at nanomolar concentrations when the ODNs were microinjected into cells.

□

Envelope proteins and HIV-1 replication

Progression from the asymptomatic stage of HIV-1 infection appears to be related to appearance of syncytium-inducing (SI) variants, which leads to loss of $\text{CD}4^+$ T cells. Groenink *et al.* (p. 1513) have characterized SI mutants and show that the V1 to V2 as well as the V3 region of gp120 are determinants of SI capacity. They also show that the propensity to undergo mutations that produce an SI phenotype is associated with the length and the number of potential N-linked glycosylation sites in the V2 hypervariable loop. Such information could be useful clinically because the V2 hypervariable loop can be analyzed 18 to 36 months before phenotypic changes occur.

□

In the pole position

The segregation and differentiation of the germ line in animals are key developmental events. In *Drosophila*, the germ line segregates early in embryogenesis and requires the presence of a specialized region (the pole plasm) postulated to contain the germ-line determinants. Kobayashi *et al.* (p. 1521) showed previously that mitochondrial large ribosomal RNA (mtlRNA) can induce germ cell formation in embryos whose pole plasm was destroyed by ultraviolet irradiation. They have now found that mtlRNA is localized to the pole plasm region of the embryo at the time of germ cell formation. Surprisingly, the mtlRNA is external to the mitochondria.

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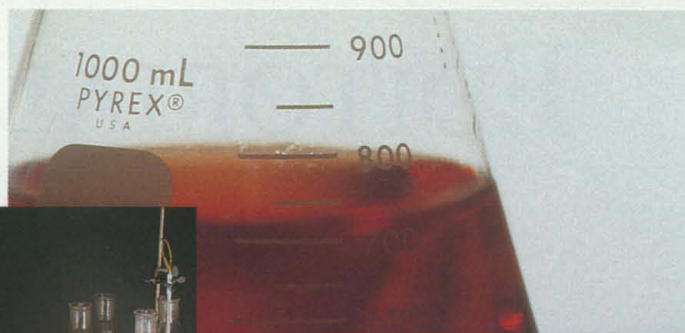
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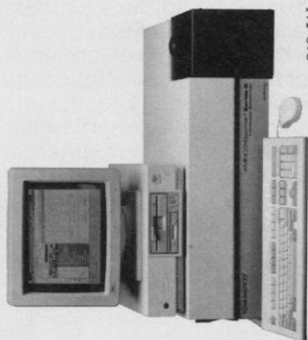
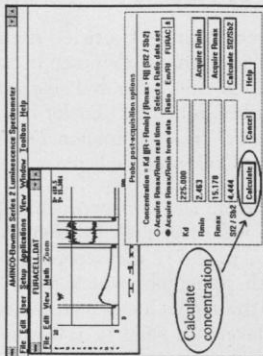
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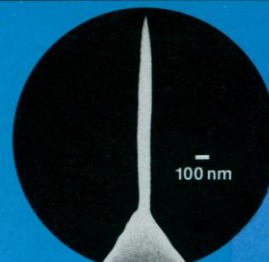
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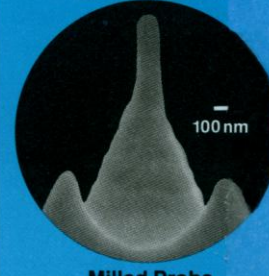
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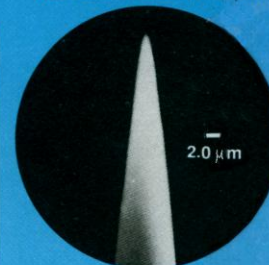


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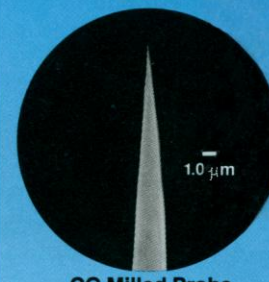


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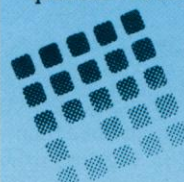


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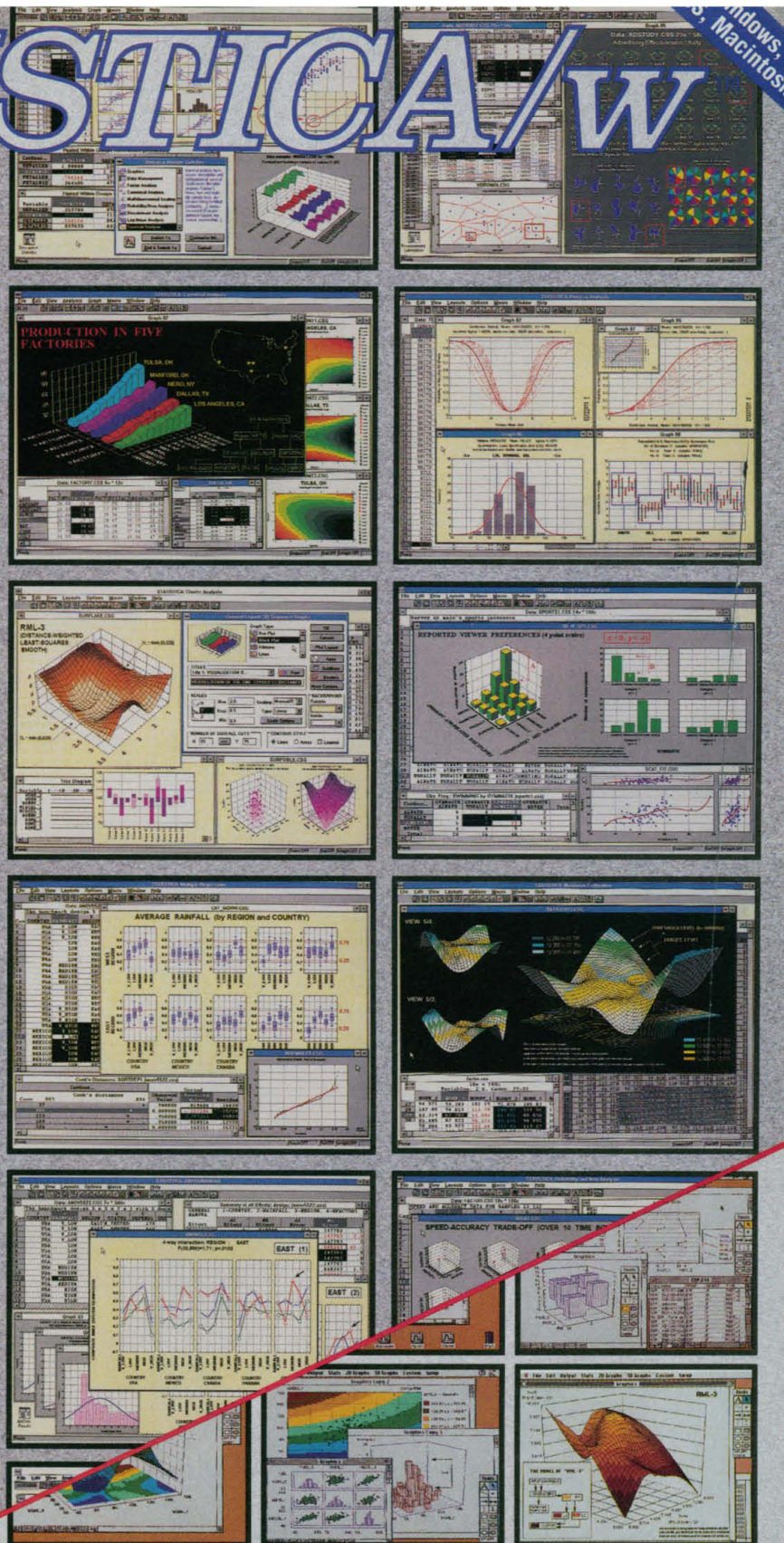


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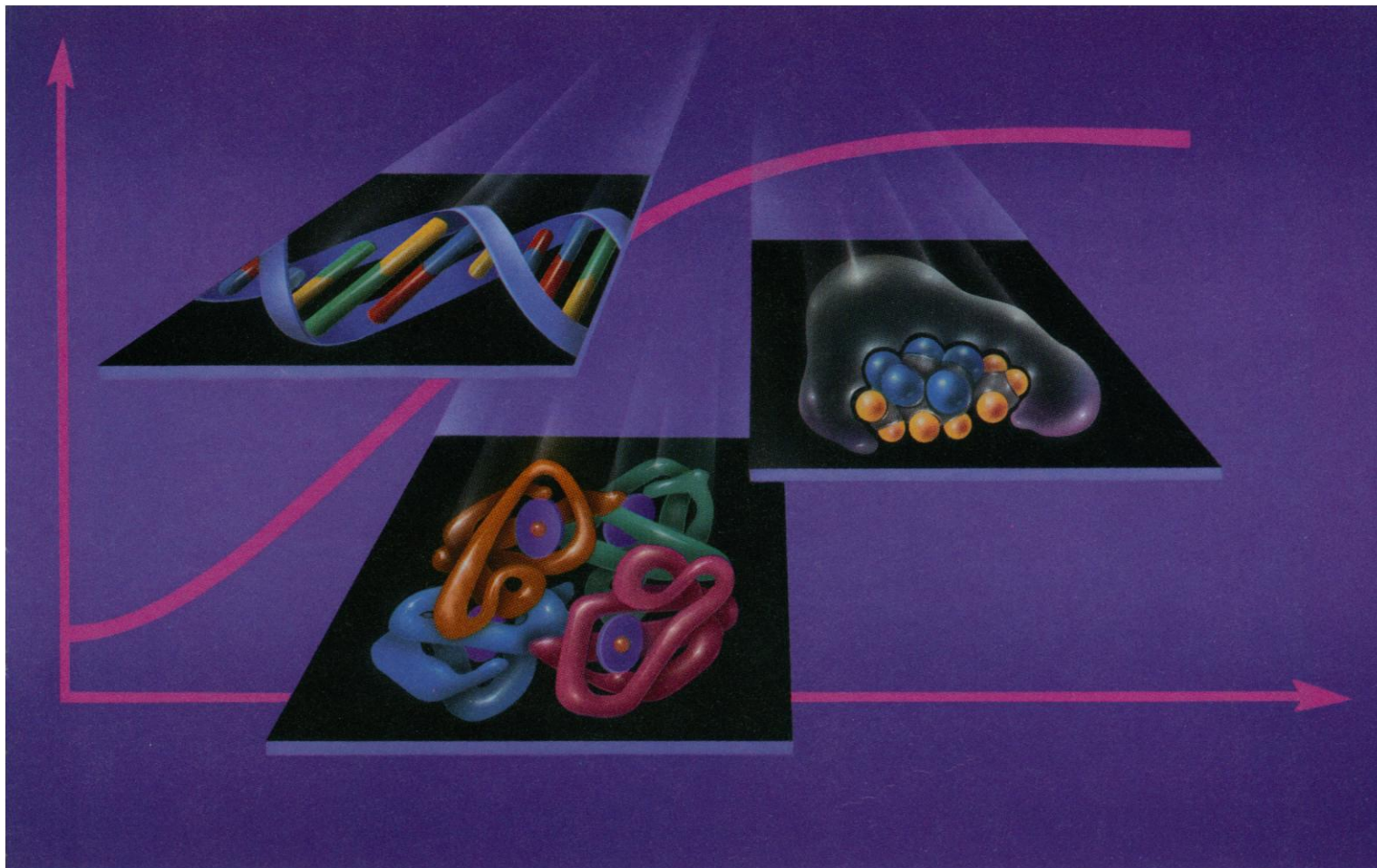


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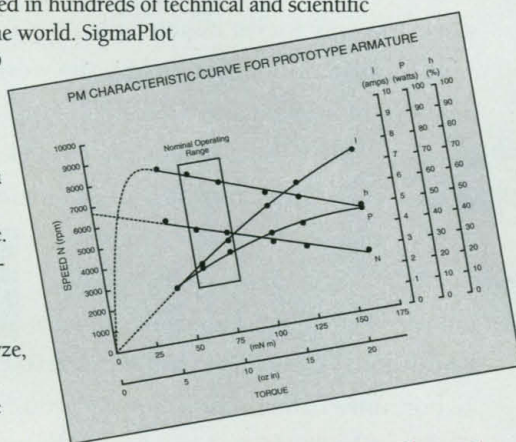
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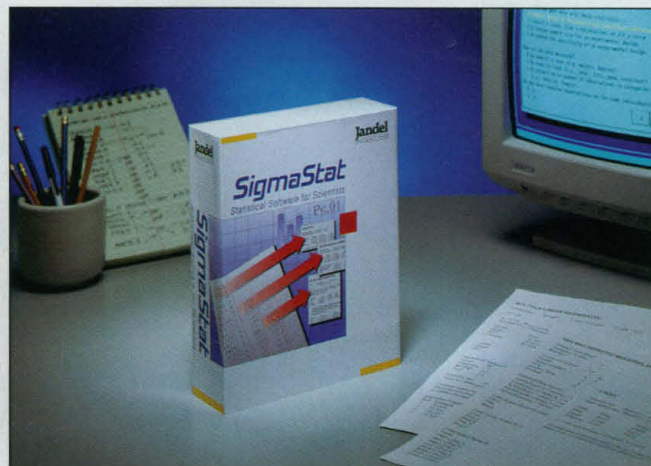
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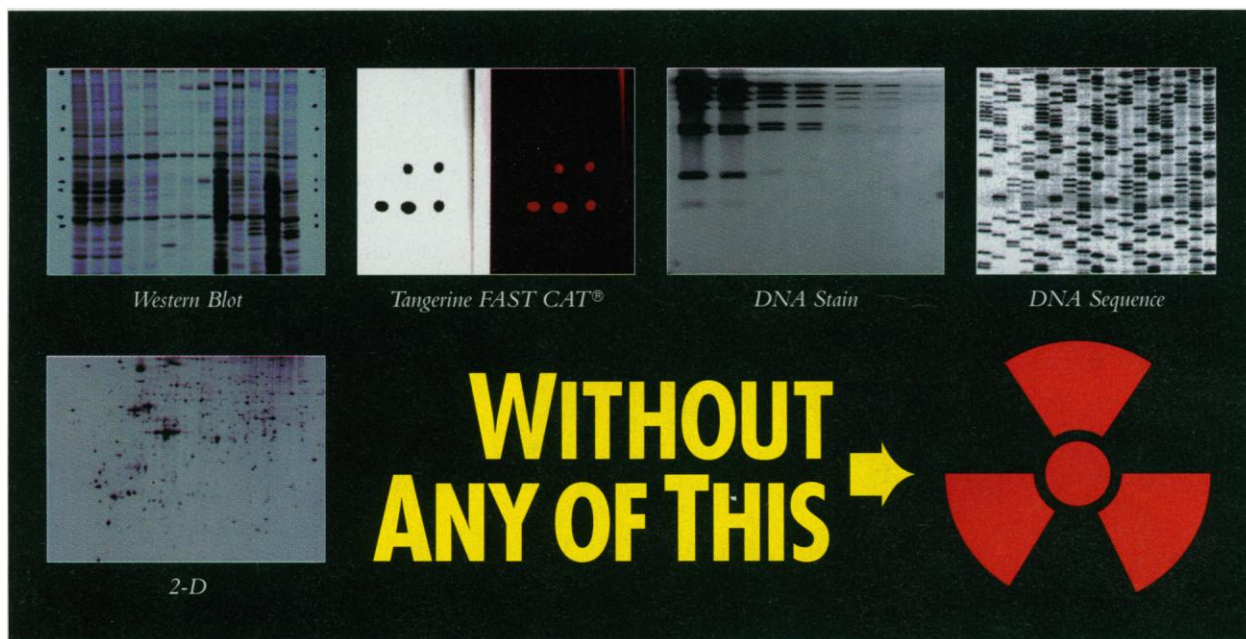


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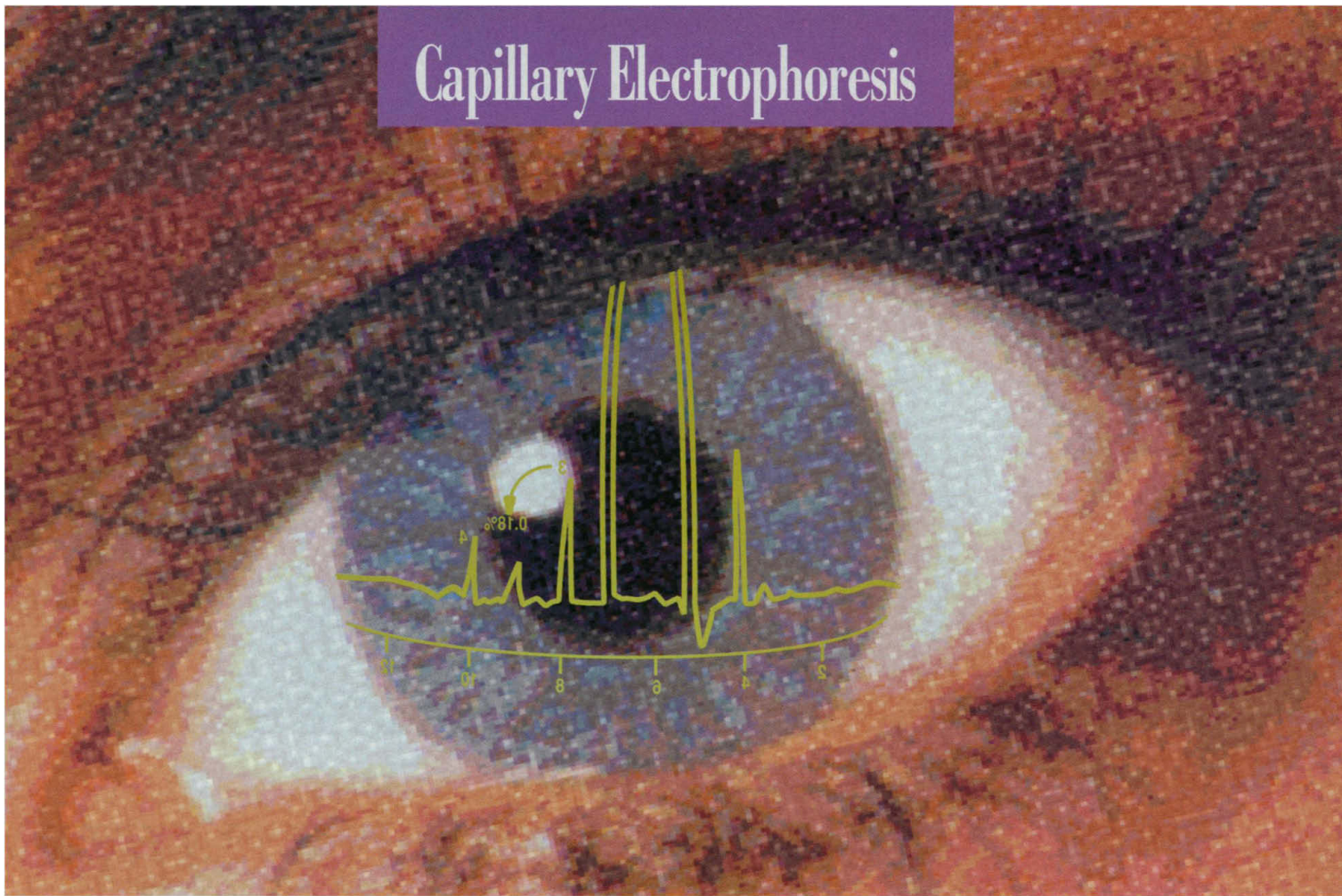
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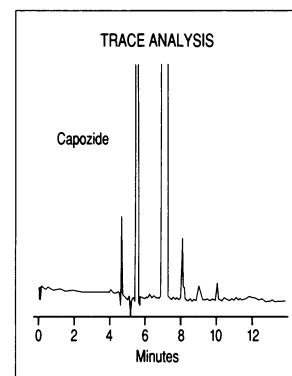
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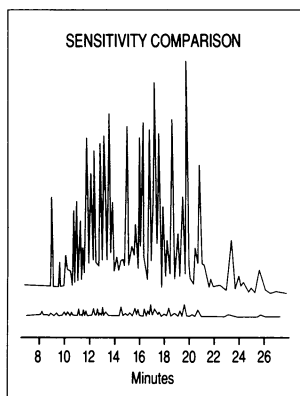
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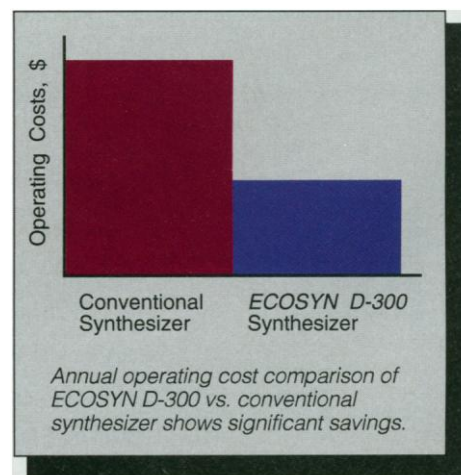
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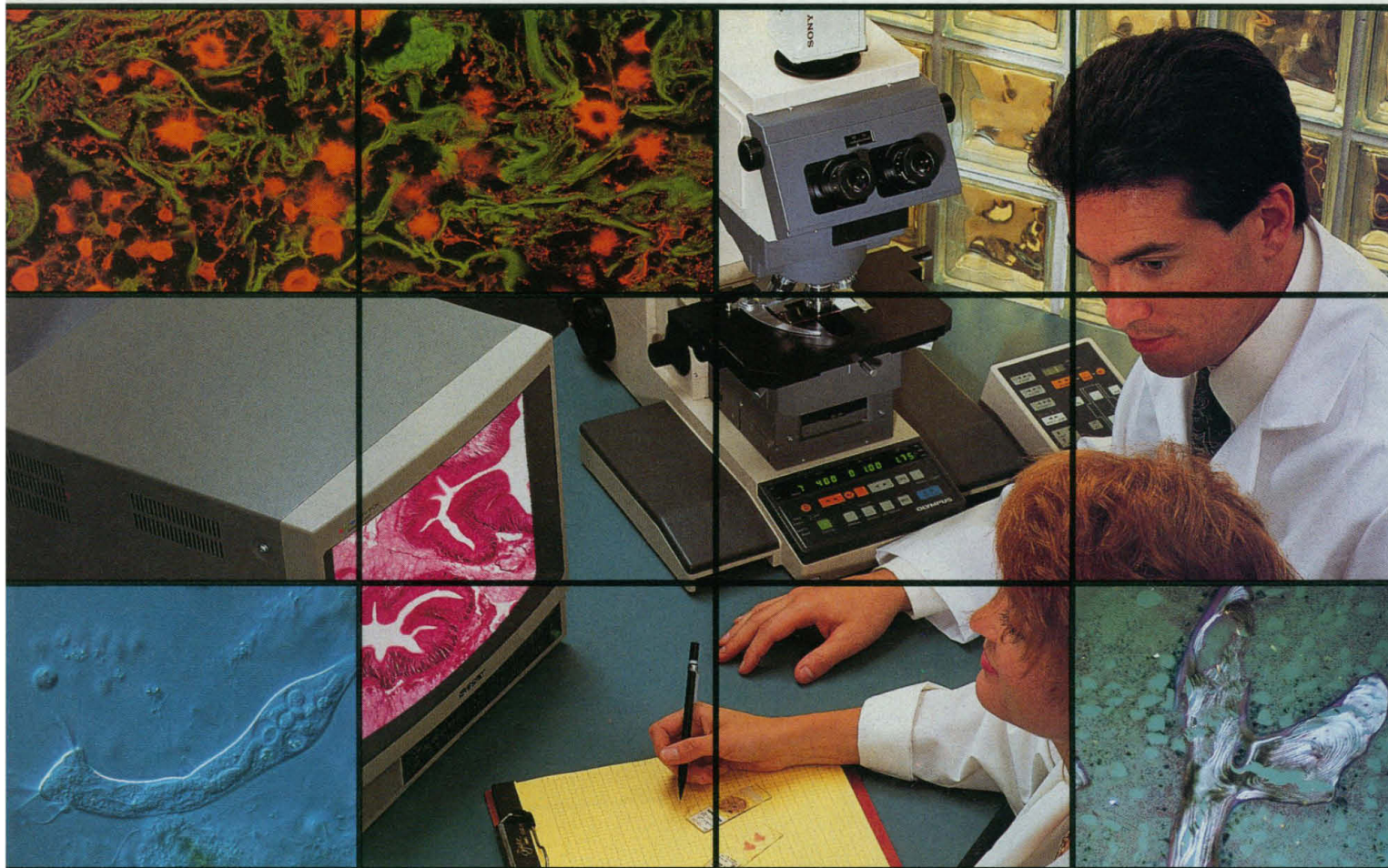
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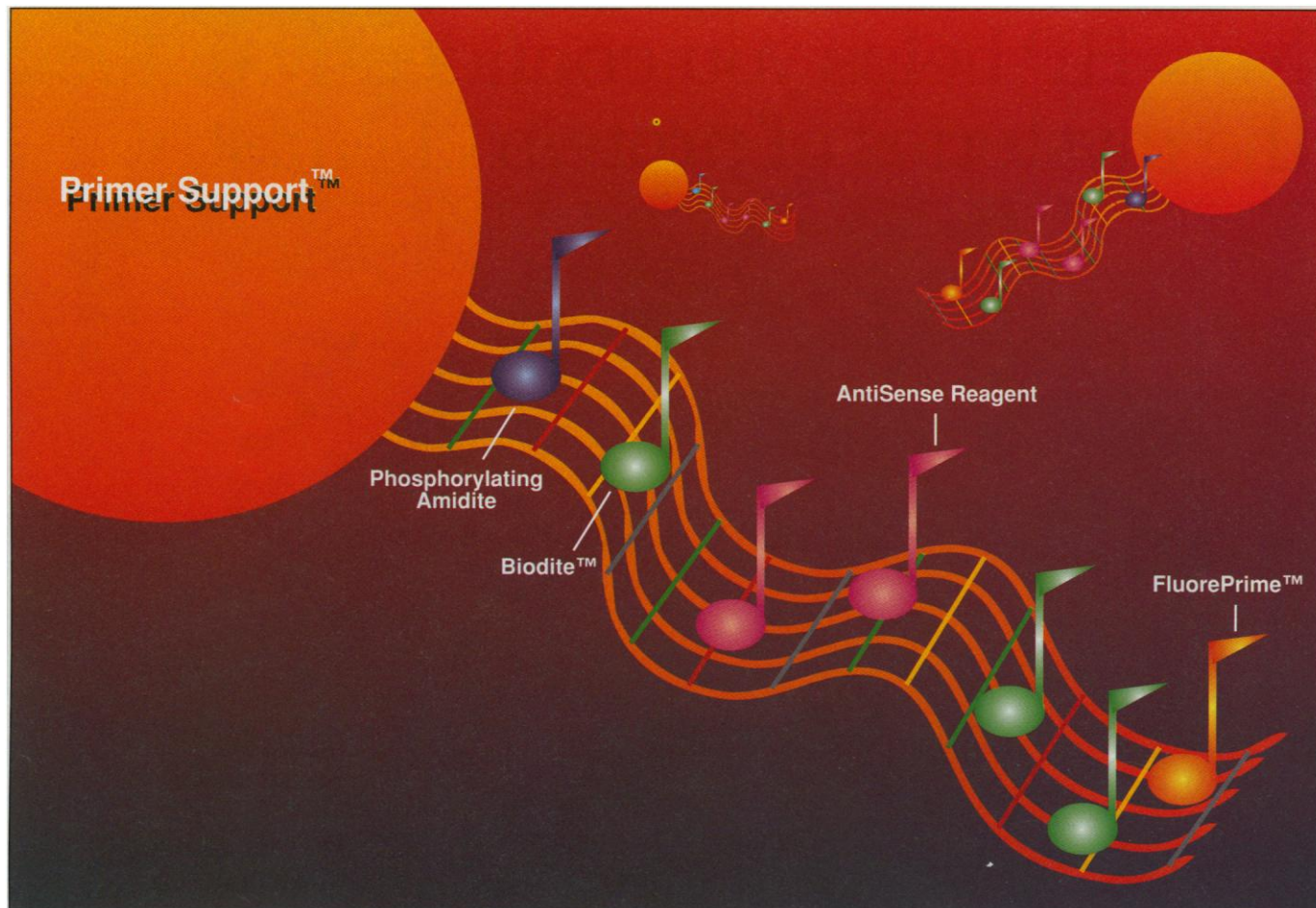
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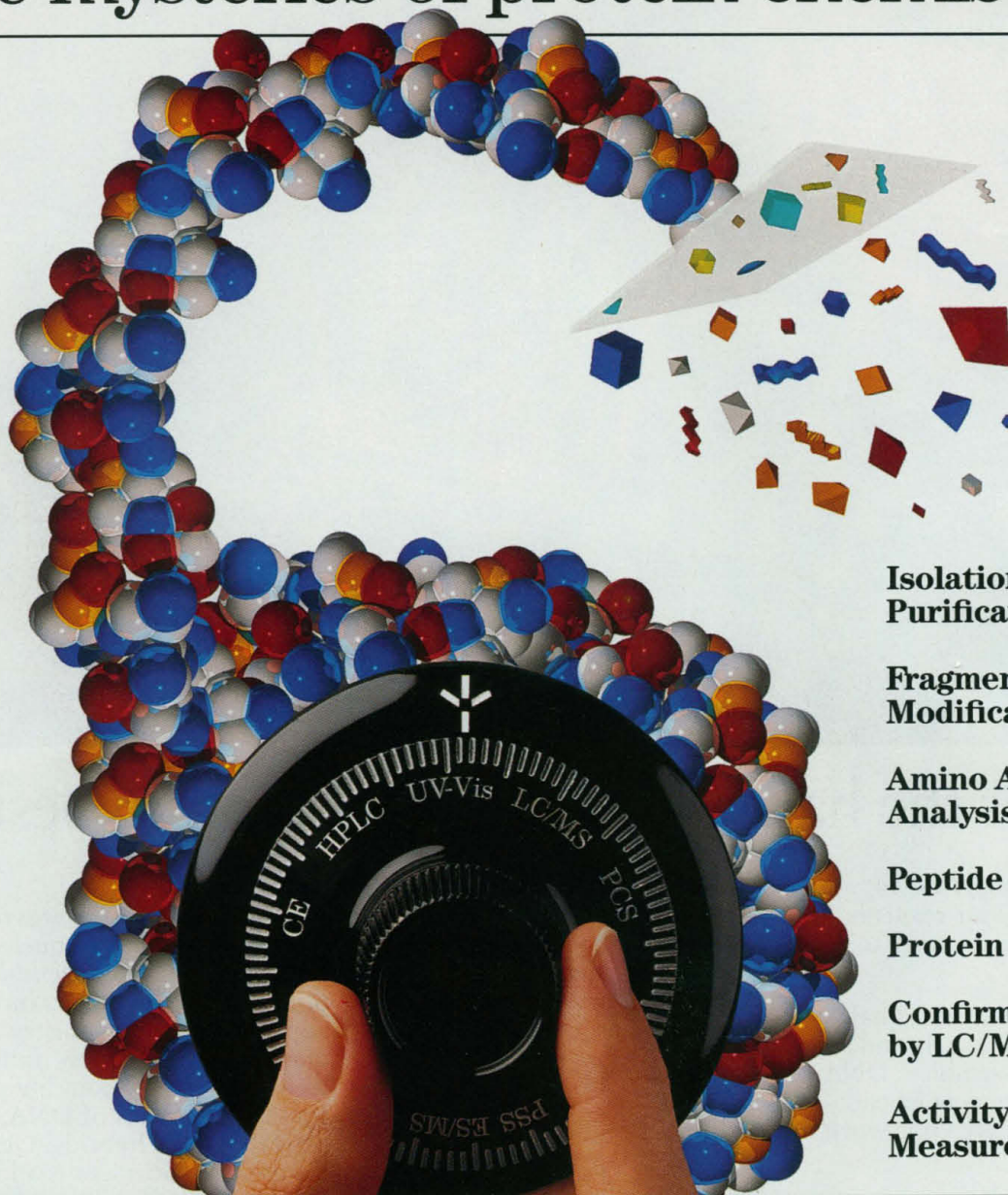


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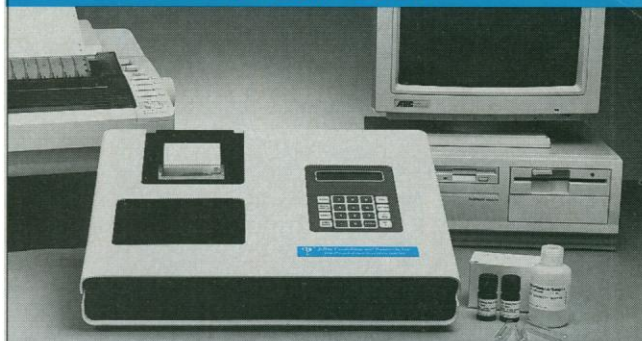
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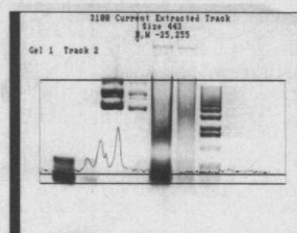
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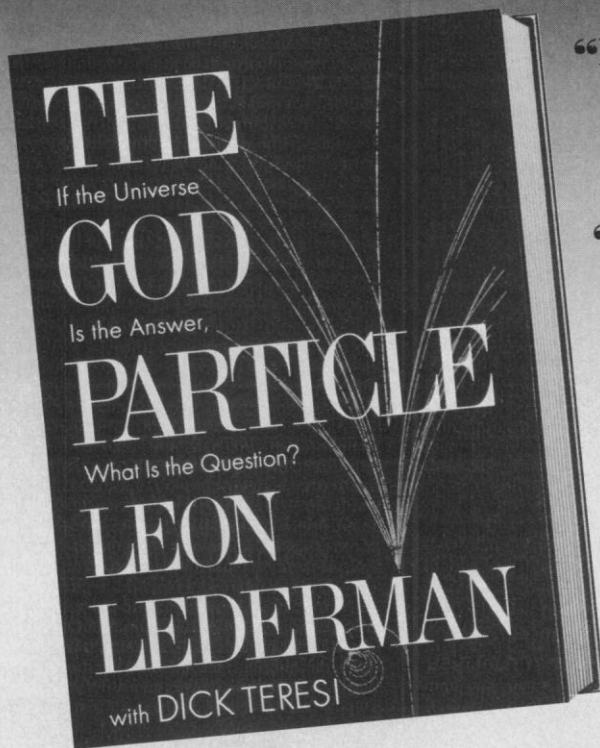
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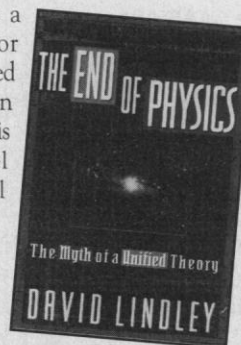
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