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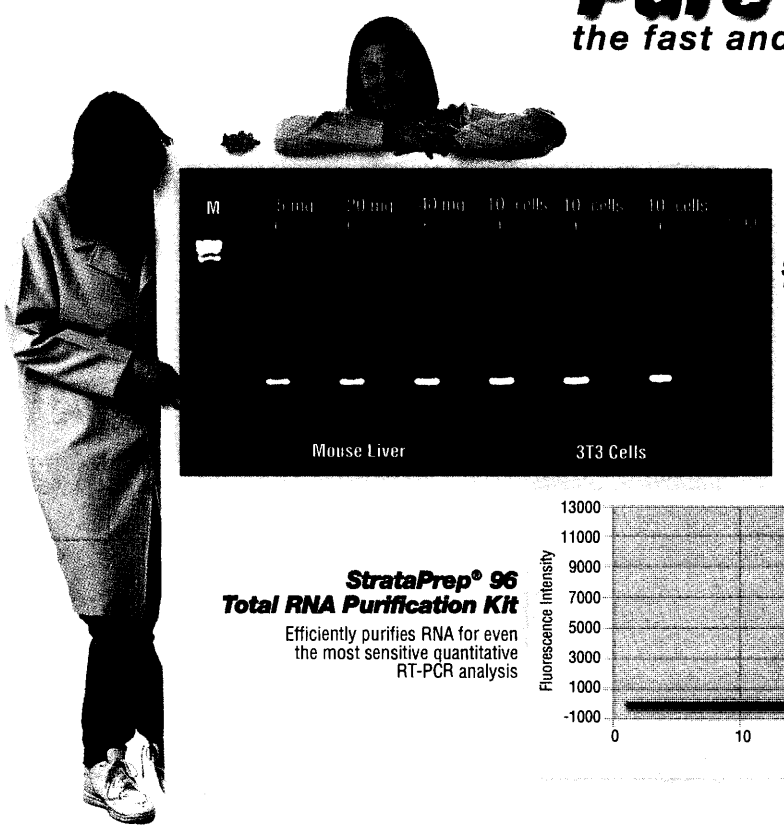

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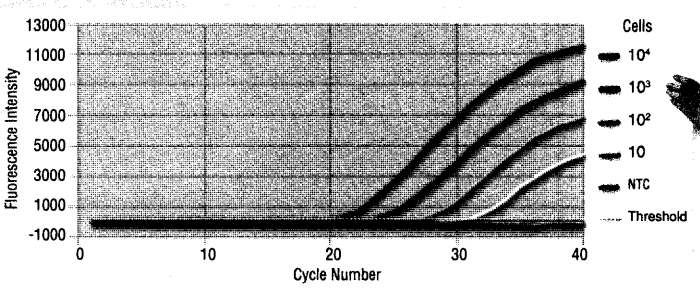

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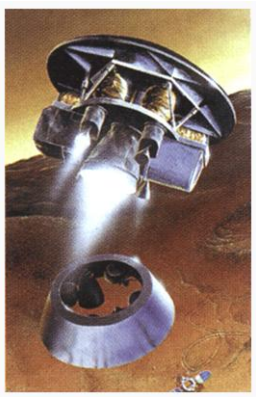
COVER The stalk structure (bottom) of the unicellular organism *Vorticella* (×120 magnification). This structure, shown in its contracted state, houses one of the most powerful biological mechanochemical springs known, extending and contracting the stalk up to 2 millimeters in milliseconds. A special section on the principles of movement, from molecular and cellular to organismal and robotic, begins on page 79. [Image: E. R. Degginger/Animals, Animals]



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NASA recovery mission

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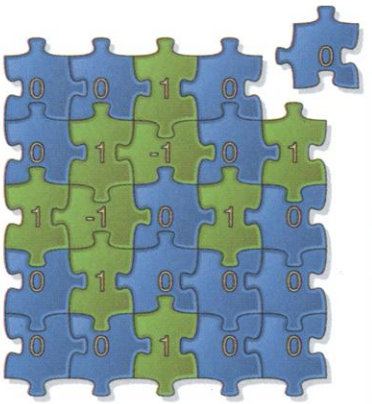

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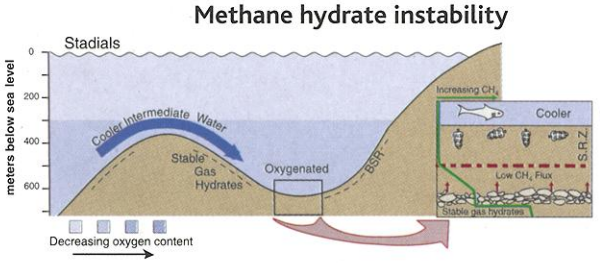

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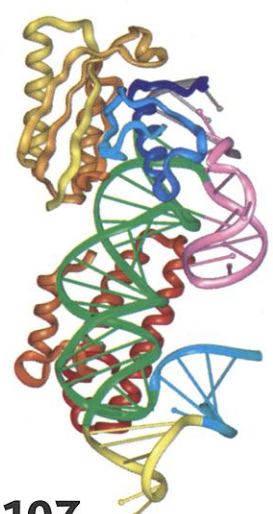

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The start of something big

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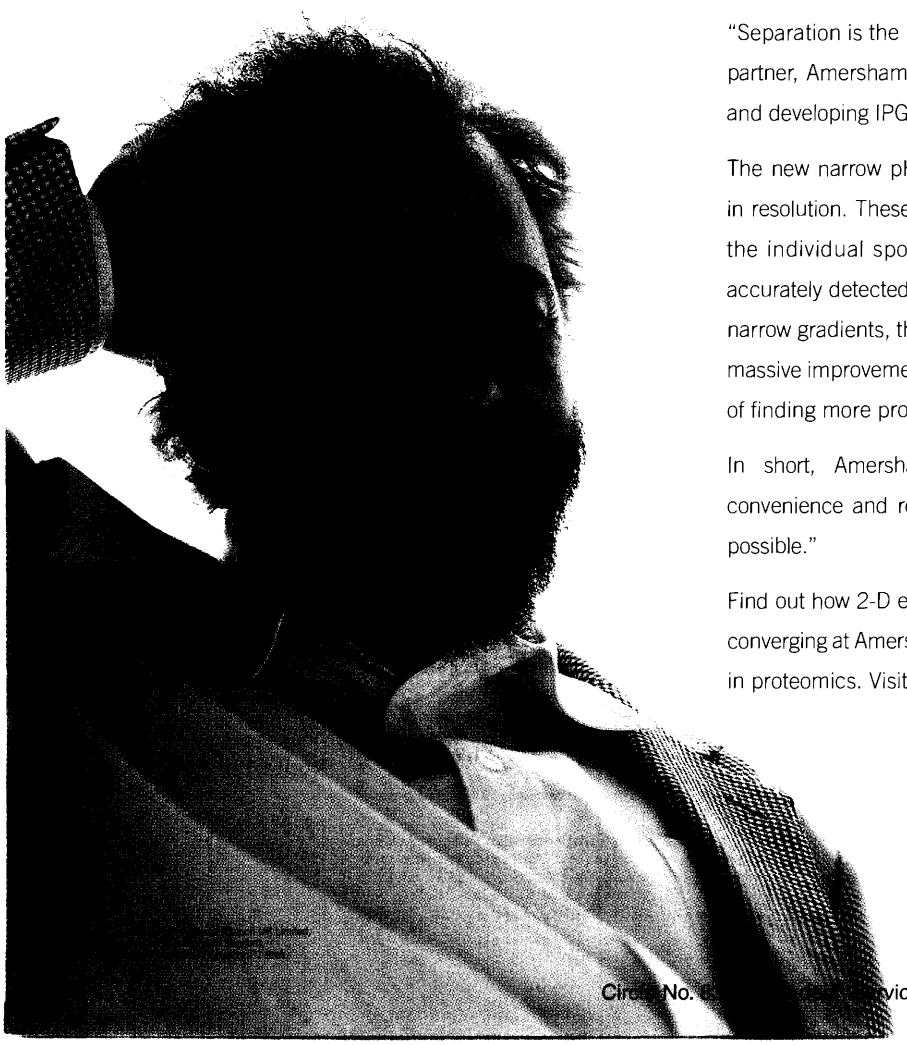

Dr. Hanno Langen, head of the proteomics group at Hoffmann-LaRoche genetics department.

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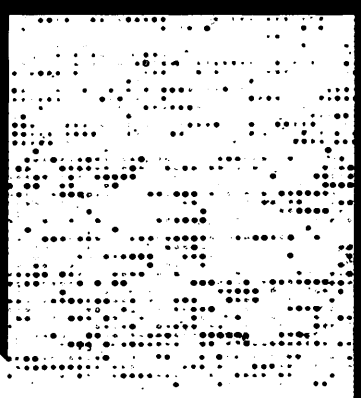

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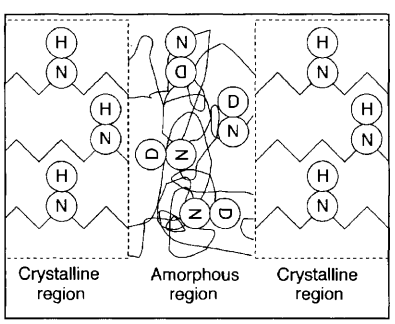
PLUMBING POLYMERS

Many microfabricated devices have been made from hard materials such as silicon, which can require multiple rounds of deposition and etching to create channels and openings. Unger *et al.* (p. 113) have assembled patterned layers of elastic polymers into microdevices. The cured polymer layers contain an excess of one of the two components from which they were formed—alternating the excess component allows the surfaces in contact to react to form a sealed structure. The authors fabricated micrometer-scale valves, which are actuated by air pressure, that show extremely small "dead volumes" and long cycle lifetimes. They then assembled a train of valves into a peristaltic pump.

MELTING IN THE STRETCH

Many polymers deform easily at relatively low temperatures, which makes processing them into particular shapes easier. What actually happens to polymer chains when the material is strained? Loo *et al.* (p. 116) used deuterium nuclear mag-



netic resonance to examine chain motions in nylon 6, which contains both crystalline and amorphous regions. Near the polymer's glass transition temperature, the chains in the amorphous regions showed enhanced liquid-like mobility as long as the polymer was being stretched; this mobility diminished once deformation ceased.

SHAPING CHROMOPHORES

An electro-optic (EO) modulator converts input electrical signals into the light pulses that run over fiber optic networks. Recent developments in both polymeric and inorganic EO materials have led to increases in their speed (modulation frequency) but require relatively high driving voltages (halfwave voltages of about 5 volts) that limit gain and increase noise. One difficulty in improving the polymeric materials is that their molecular chromophores tend to align at high loadings such that electrostatic interactions limit the EO effect. Shi *et al.* (p. 119) now show that chromophores designed with a particular shape avoid this difficulty and enable them to fabricate EO modulators that have halfwave voltages of less than 1 volt.

FLUIDIZING FAULTS

Double-couple moment tensors provide a mathematical representation of shear motion on a fault and are used to study earthquake dynamics. About 75% of all earthquakes can be represented by a double-couple moment tensor (tension versus orthogonal compression). Dreger *et al.* (p. 122) derived seismic moment tensors and analyzed the broadband waveforms of earthquakes that occurred in a November 1997 swarm during inflation of the summit of the Long Valley Caldera, California. They found isotropic moment tensors (radial expansion away from a point source), which suggests that fluid was injected into a fault either by pressurization or by magmatic heating, causing coseismic volumetric expansion.

IRON ENRICHMENT

Iron has several stable isotopes. Although biological fractionation of iron isotopes occurs, for instance, in deposits and iron minerals that are associated with bacterial activity, it had been thought that nonbiological fractionation would be undetectable. Anbar *et al.* (p. 126) have conducted laboratory experiments showing, however, that purely chemical fractionation can be observed.

UNDERWATER DEGASSING

The atmospheric concentration of the greenhouse gas methane has varied dramatically over the past 400,000 years. Many of the increases are thought to be due to the expansion of wetlands, but the rapidity of others suggests a different cause—the dissociation of gas hydrates. Methane hydrates store tremendous quantities of carbon on continental margins and are destabilized by higher ocean temperatures. Kennett *et al.* (p. 128; see the Perspective by Blunier) tested whether such hydrates could have been an important source of methane during the past 60 thousand years by measuring the carbon isotopic composition of foraminifera from the Santa Barbara Channel. Their results show several episodes of massive methane release from the sea floor, consistent with catastrophic sediment failure during the brief warm periods called interstadials.

BUILDING PIECE BY PIECE

The advent of structural descriptions of the ribosome—a complex of three RNAs and 50-odd proteins—has resurrected the issues of assembly and function: Why are all of these distinct proteins needed and how do they assemble in an orderly and stoichiometric fashion? Agalarov *et al.* (p. 107) have determined the high-resolution structure of three of the small ribosomal subunit proteins in complex with a portion of the small ribosomal subunit RNA. They find that the first protein-RNA interaction stabilizes a reorganization of two three-helix junctions in the RNA; these, in turn, create the binding sites for two more of the small subunit proteins and provide the scaffold for subsequent steps of assembly.

GLIDING FARTHER UNDERWATER

How do marine mammals maintain long periods of aerobic exercise while diving on a single breath of air? By deploying submersible video cameras on free-ranging seals, dolphins, and a blue whale, Williams *et al.* (p. 133; see the news story by Pennisi) detected changes in locomotory behaviors. Lung compression and increased hydrostatic pressure at depth triggered the cessation of active stroking, which was replaced by prolonged gliding during deep dives. The energetic savings of gliding allow these mammals to lengthen the duration of submergence and to reach remarkable depths.

COORDINATE REGULATION

There are a variety of analytical methods for annotating coding regions in DNA sequences. However, it has been harder to identify regulatory elements in noncoding regions. Loots *et al.* (p. 136) noted that a set of genes are arrayed in the same order on human chromosome 5 and mouse chromosome 11, and identified conserved sequences that had the properties of long-range cis-acting elements. The largest candidate element was shown to regulate interleukin-4, -13, and -5 expression in transgenic mice.

CONTINUED ON PAGE 11

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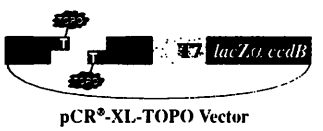

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THIS WEEK IN *SCIENCE*

CONTINUED FROM PAGE 9

ANCHORING THE CAMOUFLAGE

In order to evade immune surveillance the African trypanosome, the causative agent of sleeping sickness, coats itself with surface glycoproteins that can be shed rapidly due to their glycosyl phosphatidylinositol anchors. To synthesize these anchors, trypanosomes require a supply of myristate, the source of which has been a mystery. Morita *et al.* (p. 140) now show that the trypanosomes can synthesize myristate by themselves and that the myristate synthetic pathway is blocked and parasites are killed by the antibiotic thiolactomycin, providing hope for future therapy.

UNRAVELING PROTEINS BIT BY BIT

Protein folding remains a challenge for physical biochemists; in some cases, a plausible description of the folding pathway can be made, but the energies and kinetics of the intramolecular interactions are more difficult to measure. Unfolding of proteins has been experimentally more accessible, either with chemical denaturants or, more recently, by mechanical manipulation. Oesterhelt *et al.* (p. 143; see the Perspective by Forbes and Lorimer) offer atomic force microscopy studies of the light-activated proton pump bacteriorhodopsin as the latest application of single-molecule techniques and as a window into the complicated problem of how integral membrane proteins both fold and insert into lipid bilayers.

BLOOD CELL LINEAGES

Four transcription factors—GATA-1, GATA-2, GATA-3, and AML1—are known to be critical for mammalian blood cell development, but the relationships among them are not clear. Lebestky *et al.* (p. 146) have examined lineage control of blood cells in *Drosophila* and show that the *Drosophila* GATA homolog Serpent is required for the development of both classes of blood cells, plasmatocytes and crystal cells. The transcription factor Lozenge, which is similar to AML1 of mammals, is required only for crystal cell development, while Gcm is required for plasmatocyte development.

CHANGING DIRECTION

As axons travel from their birthplace to their ultimate point of connection, they follow guidance signals along the way. Kim and Wadsworth (p. 150) now show that the basement membrane can provide directional cues. Mutants of *Caenorhabditis elegans* lacking nidogen, a structural component of the basement membrane, show specific defects in the pathfinding of certain axons.

MERGER OF FAMILY FORTUNES

Somatostatin and dopamine are important neurotransmitters in the central nervous system. Their actions are mediated by members of a family of G protein–coupled receptors. For many receptors, homodimerization is an important aspect of functional regulation. Rocheville *et al.* (p. 154; see the Perspective by Milligan) show that this also can apply to two unrelated receptors like the ones for somatostatin and dopamine. The resulting heterodimers create a new type of receptor with increased physiological activity.

TECHNICAL COMMENT SUMMARIES

Serotonin and the Therapeutic Effects of Ritalin

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/288/5463/11a

Gainetdinov *et al.* (Reports, 15 January 1999, p. 397) found that locomotor activity in dopamine transporter knockout mice, whose behavior resembled that of children with attention-deficit hyperactivity disorder (ADHD), was decreased both by psychostimulants, including methylphenidate (Ritalin), and by serotonergic drugs. Gainetdinov *et al.* suggested that the "paradoxical calming effect" of psychostimulant drugs on many ADHD patients might stem from serotonergic effects. Volkow *et al.* find a "central problem" in this proposal, however: Unlike other psychostimulants such as cocaine and amphetamine, "methylphenidate does not increase the extracellular serotonin concentration in the brain." They also question whether the results of Gainetdinov *et al.* are directly relevant to ADHD treatments in light of several issues related to dosage and temporal response to medication. Gainetdinov *et al.* respond that "evidence from neurochemical, histochemical, electrophysiological, and behavioral studies" suggests that methylphenidate can affect the serotonergic system, and point out that "there is mounting evidence of potential clinical efficacy" in ADHD "for drugs with a predominantly serotonergic component of action."

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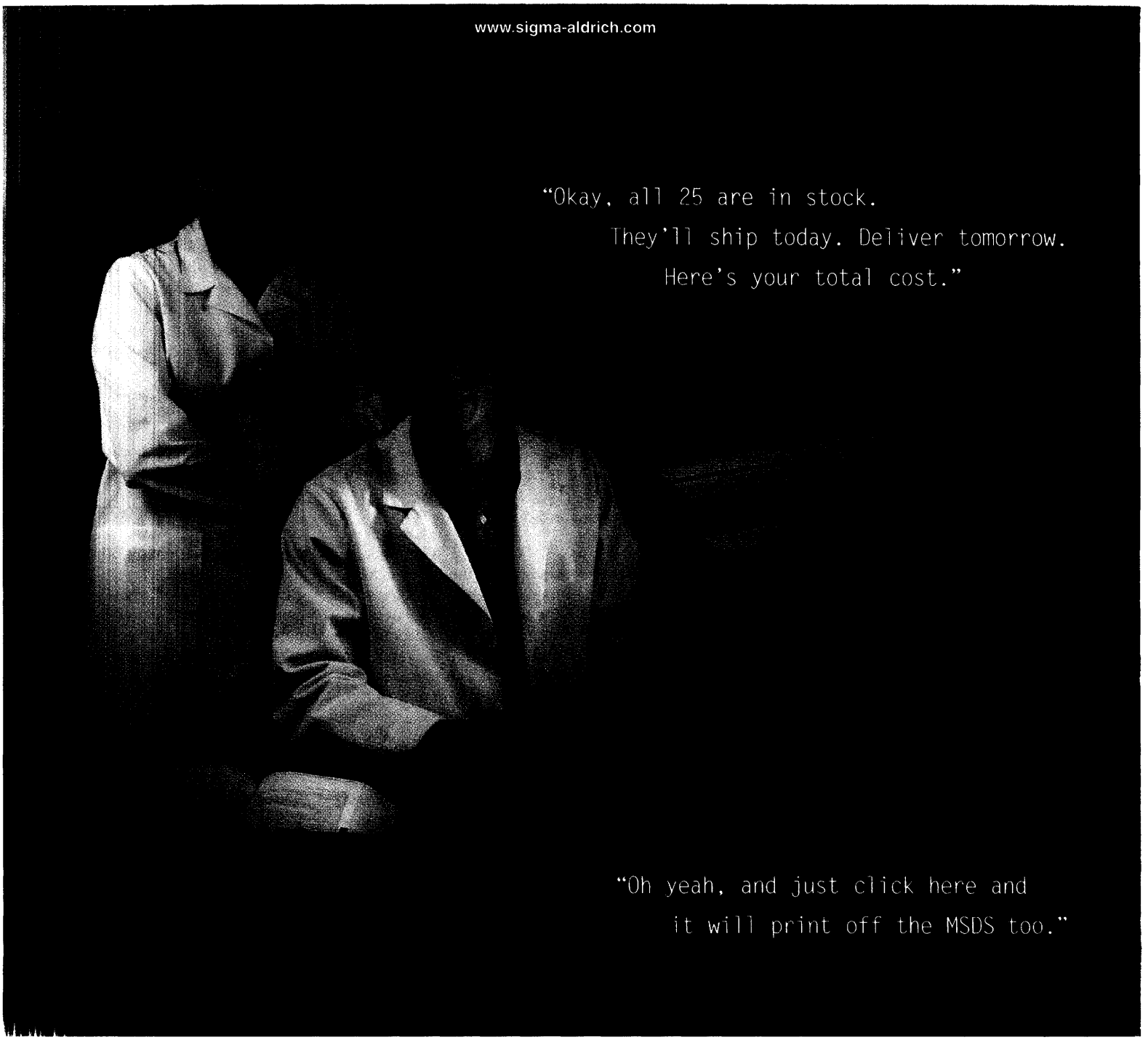

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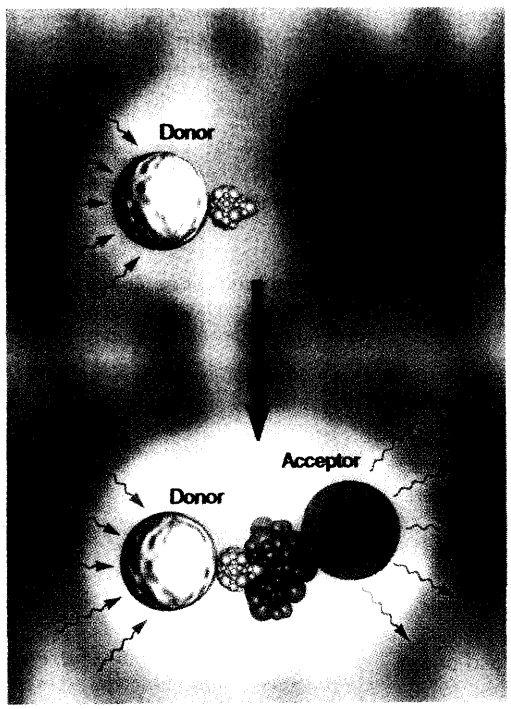

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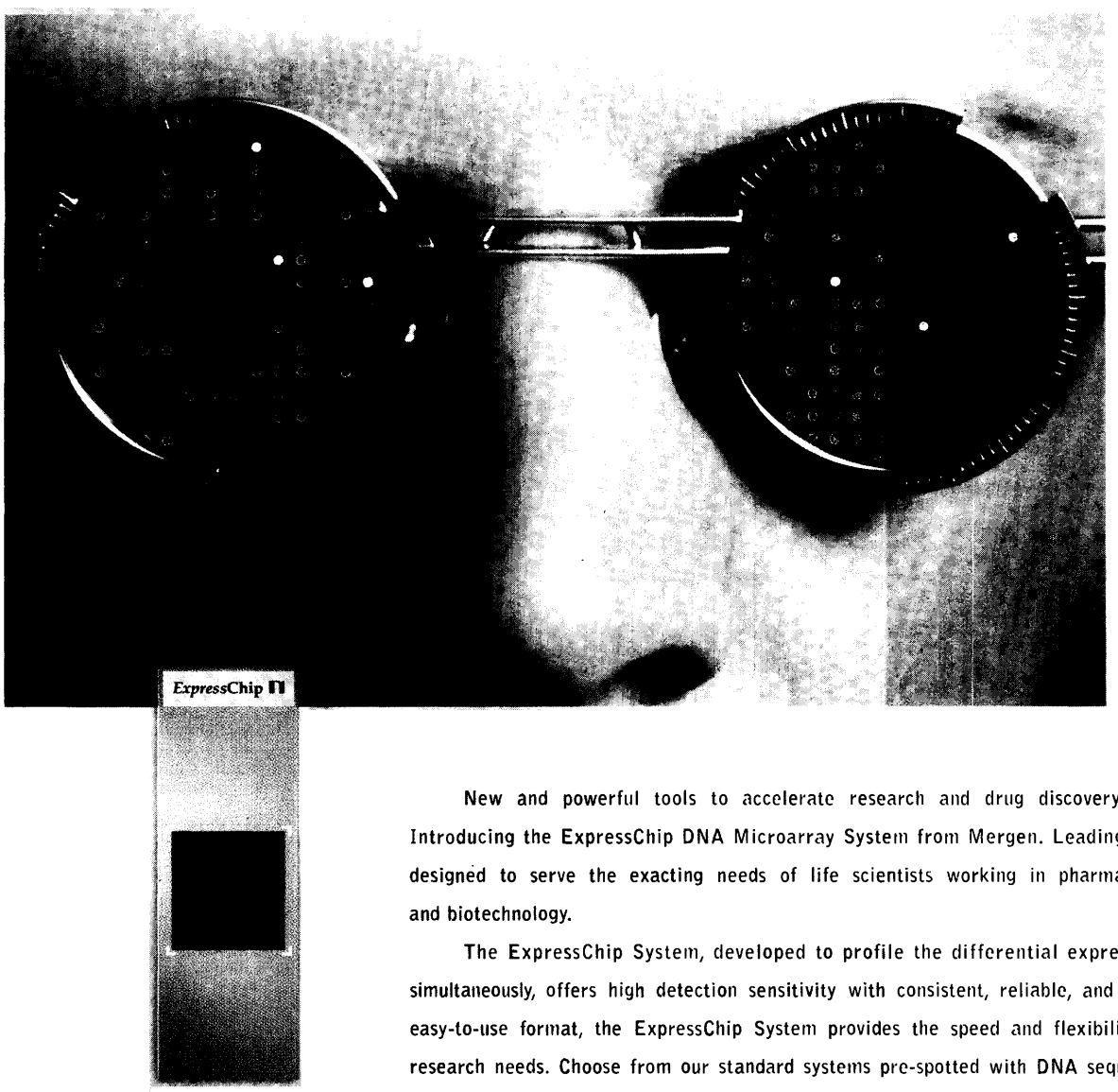

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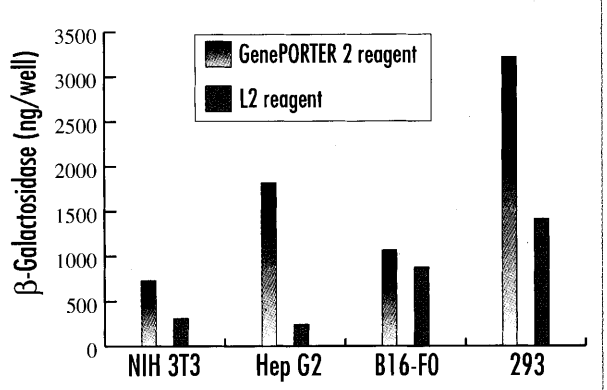

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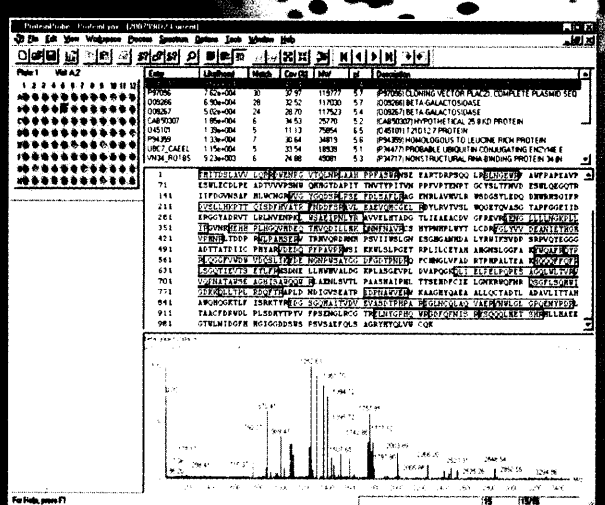

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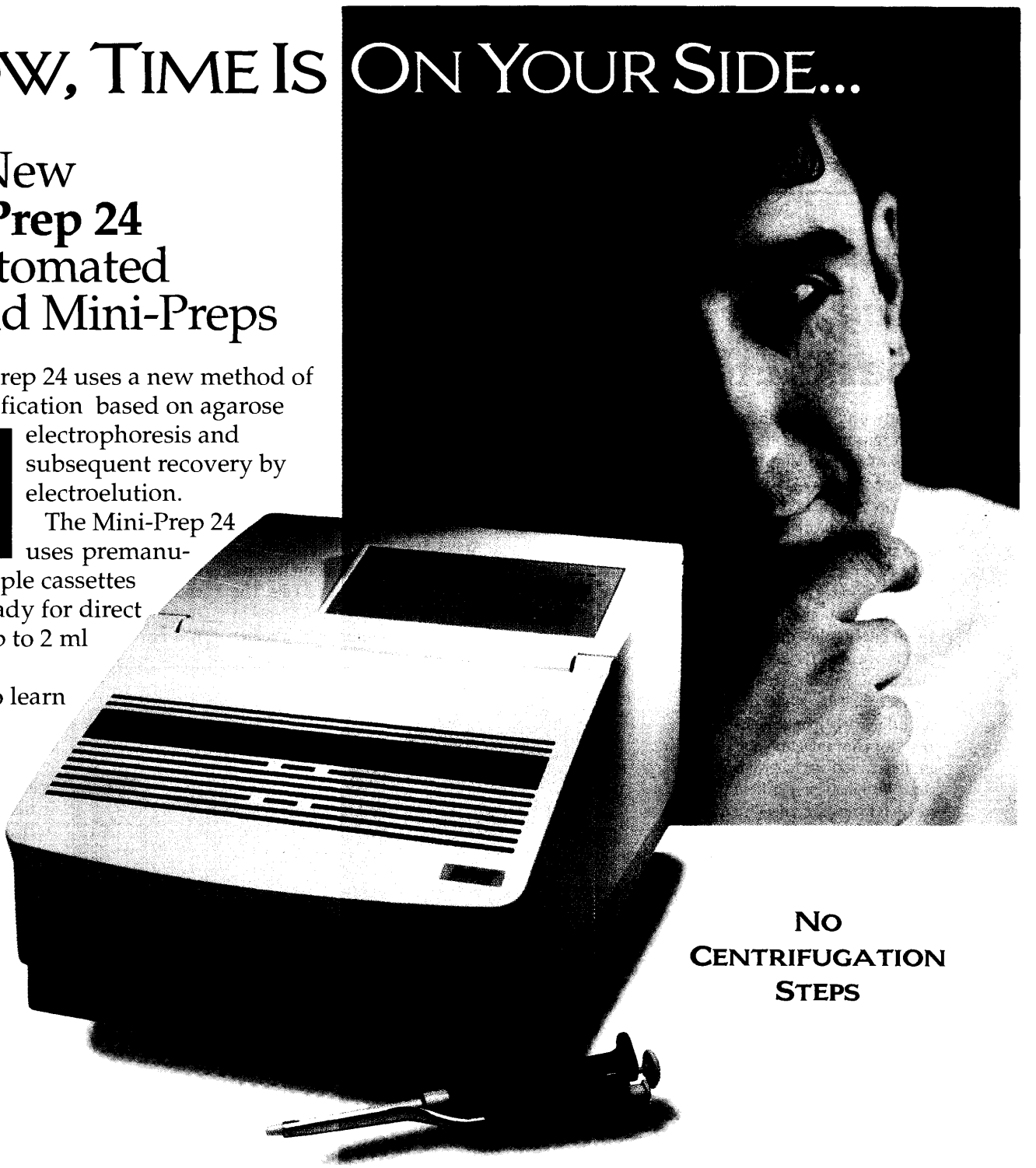

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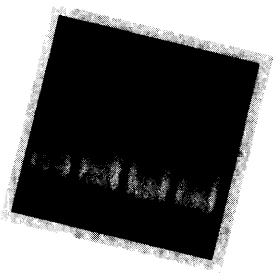

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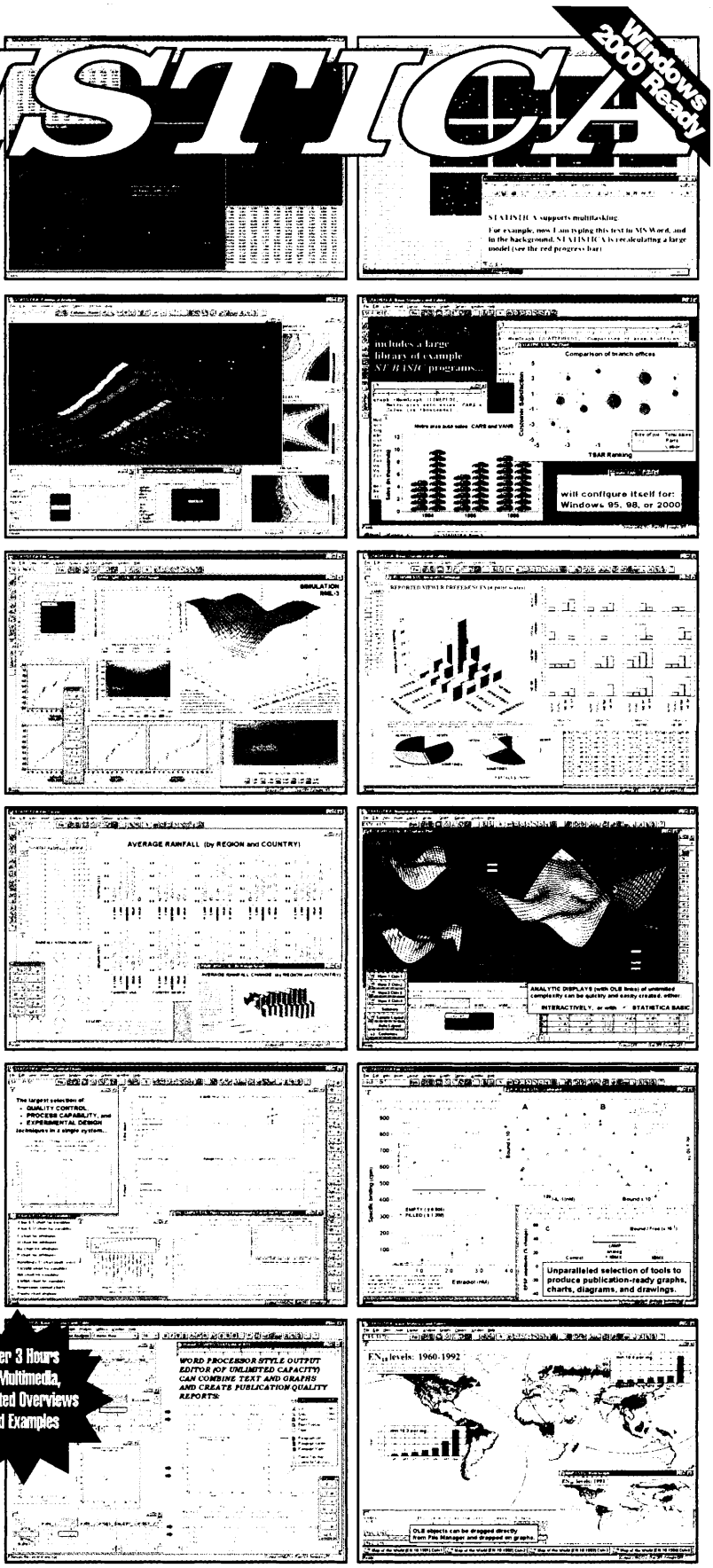

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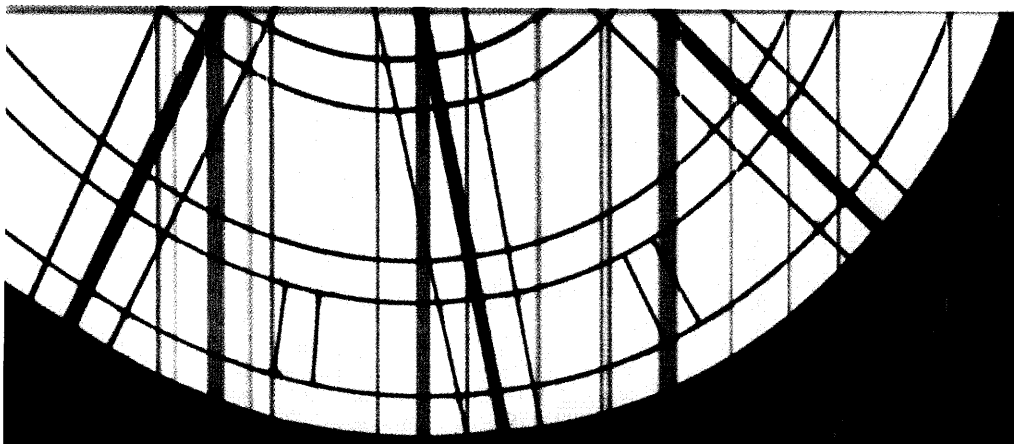

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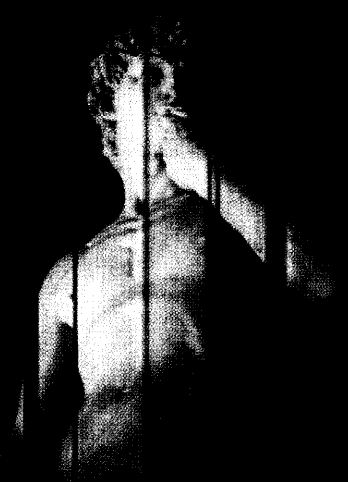

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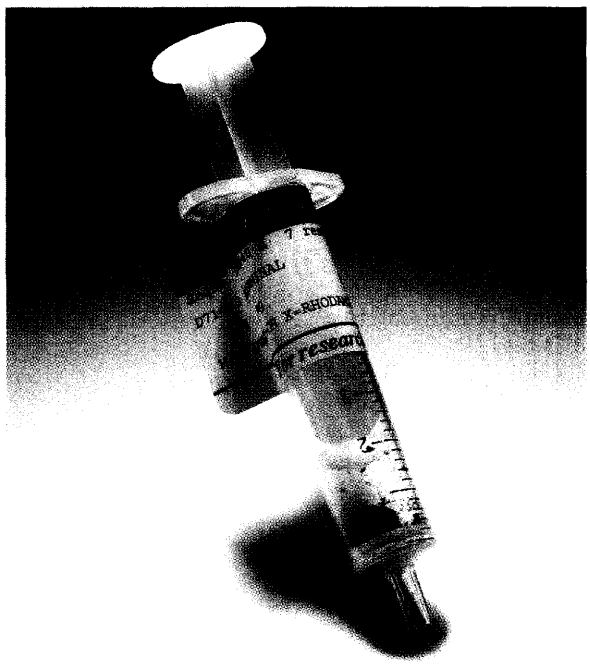

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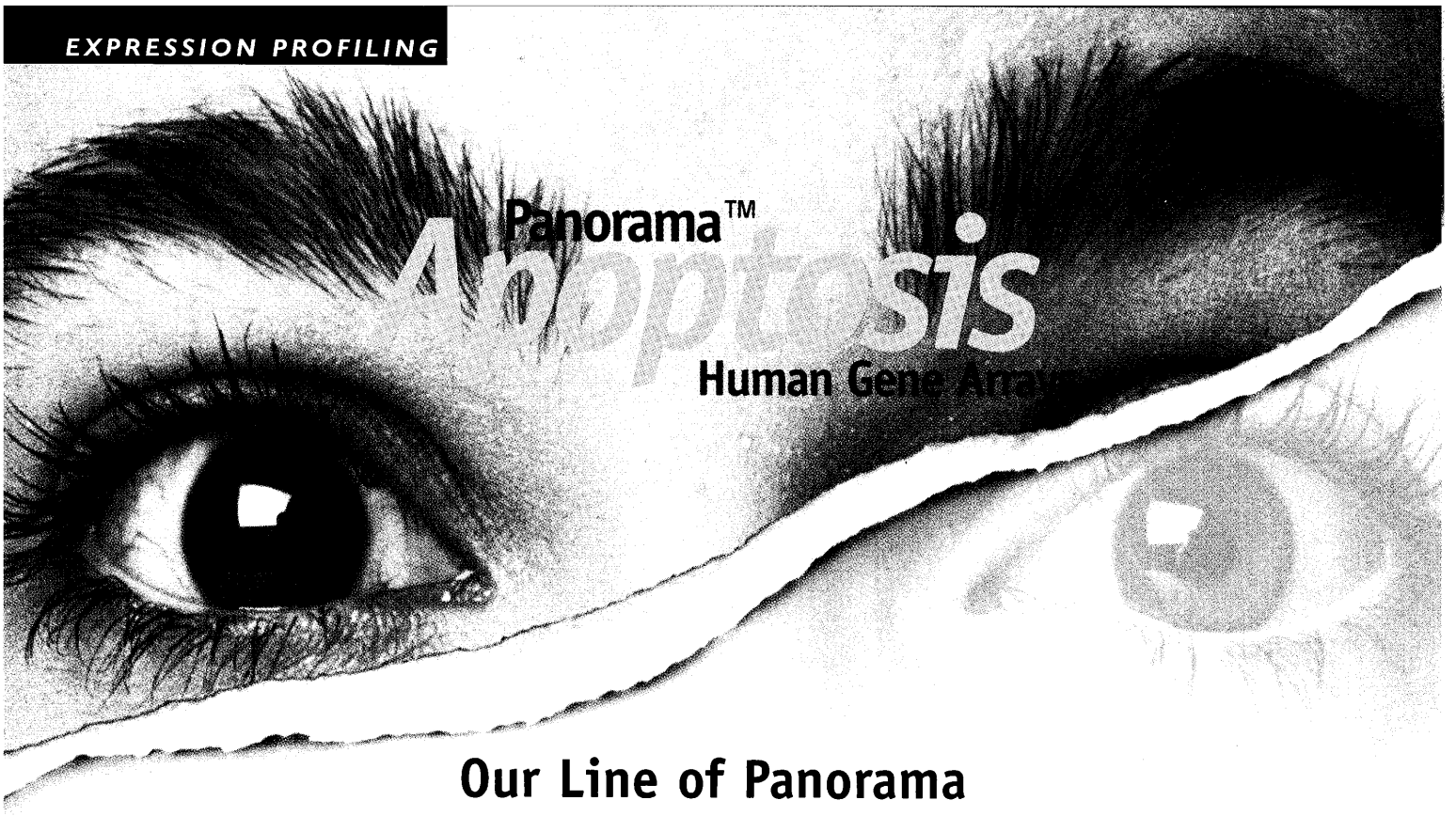

Our Line of Panorama Gene Arrays Has Expanded *(again!)*

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- Caspase and Caspase Substrates
- Cell Cycle Regulators
- Cytokines, Growth Factors, & Receptors
- Neuronal Factors
- Signal Transduction Proteins
- TNF Superfamily

The genes are spotted in duplicate on nylon membranes and analyzed using standard molecular biology techniques.

Product Numbers:	*PRAP0002*	*2 Panorama Human Apoptosis Gene Arrays*
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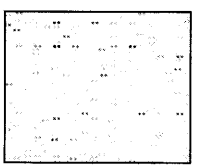
- Mouse Cytokine (coming soon)
- Mouse Apoptosis (coming soon)



Panorama Microbial Gene Arrays

PCR-amplified open reading frames representing all protein coding sequences, arrayed in duplicate on nylon hybridization membranes.

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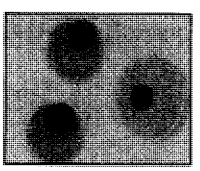
- *B. subtilis*
- *H. pylori* (coming soon)
- *C. jejuni* (coming soon)



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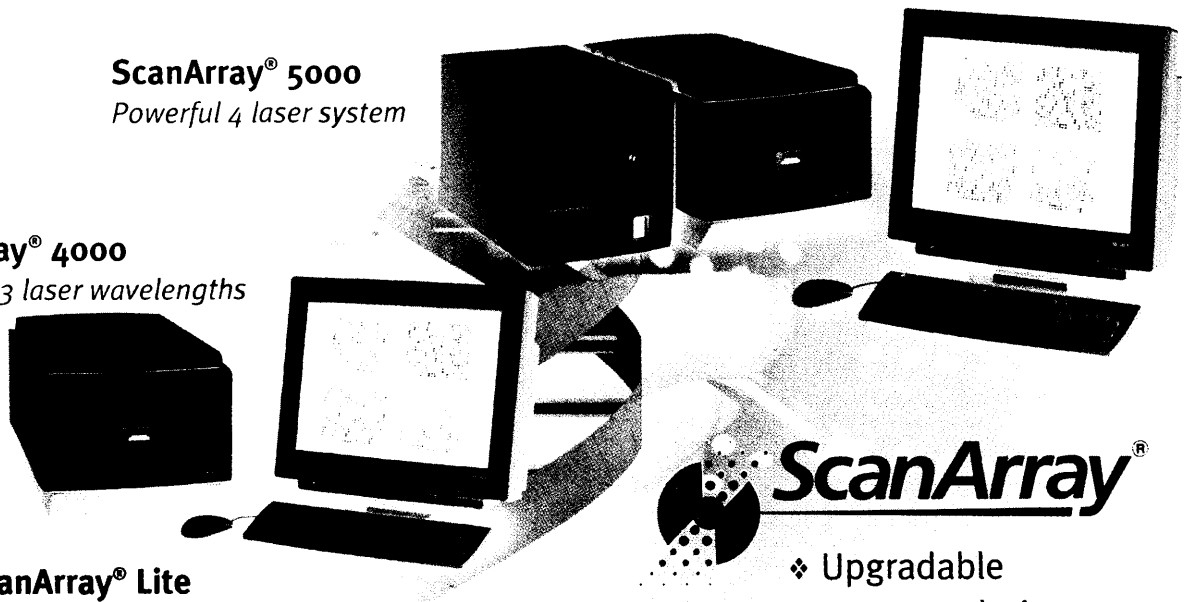

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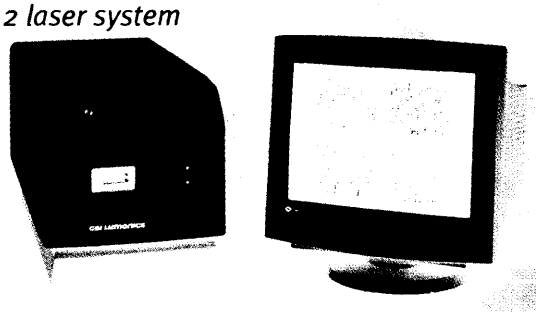

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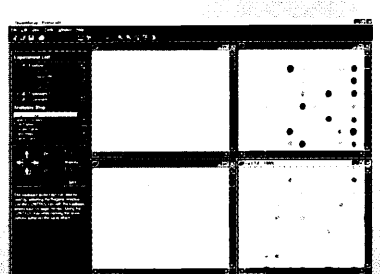

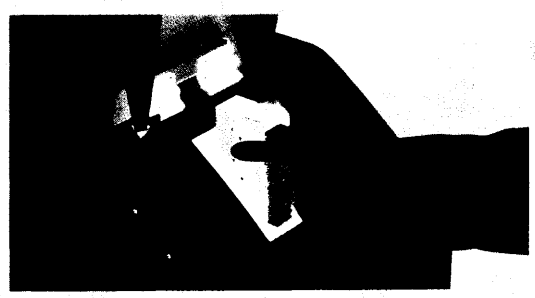

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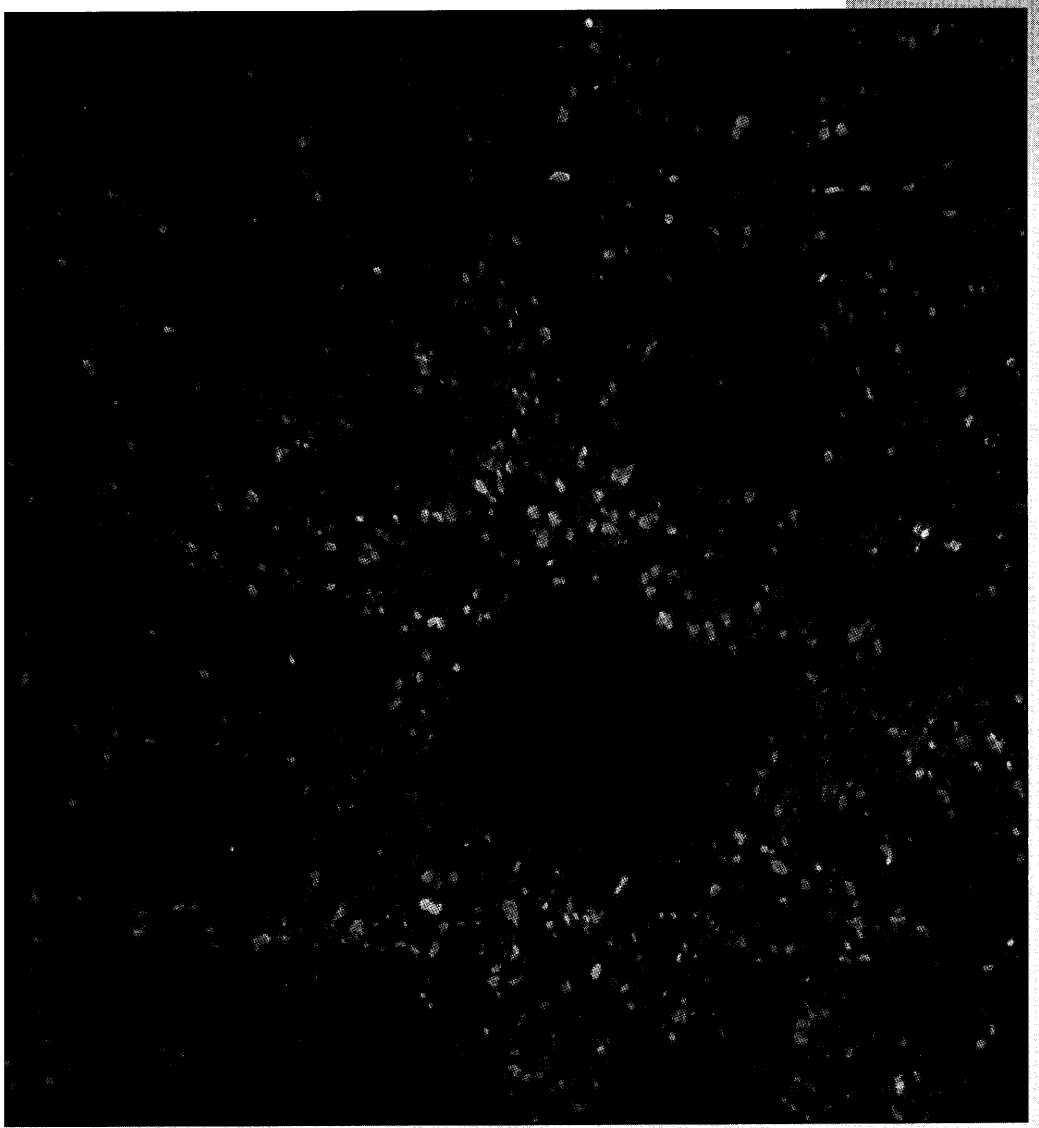

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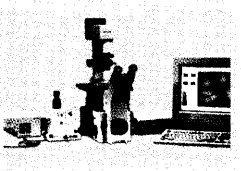

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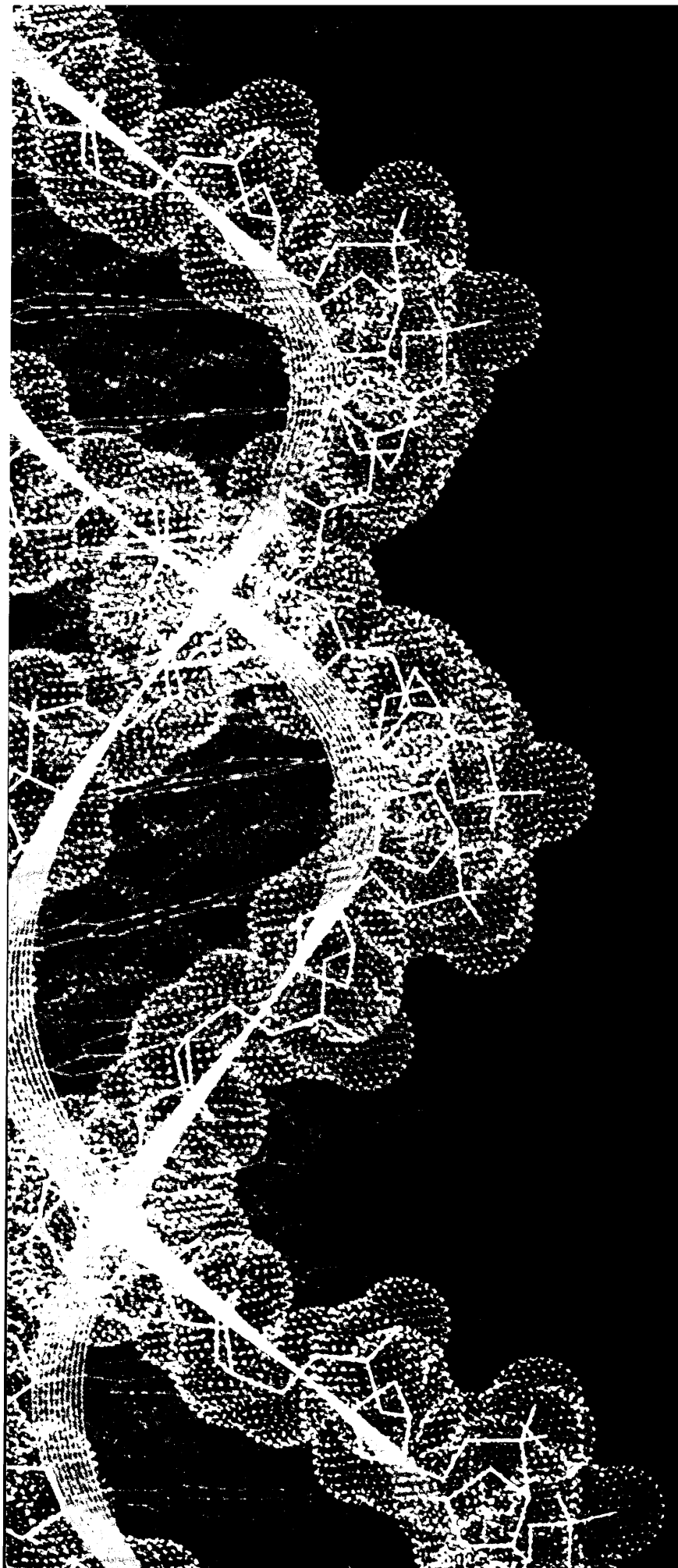

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Image: A false color scanning tunnel micrograph of a double-stranded DNA molecule taken at the Lawrence Livermore Laboratory.

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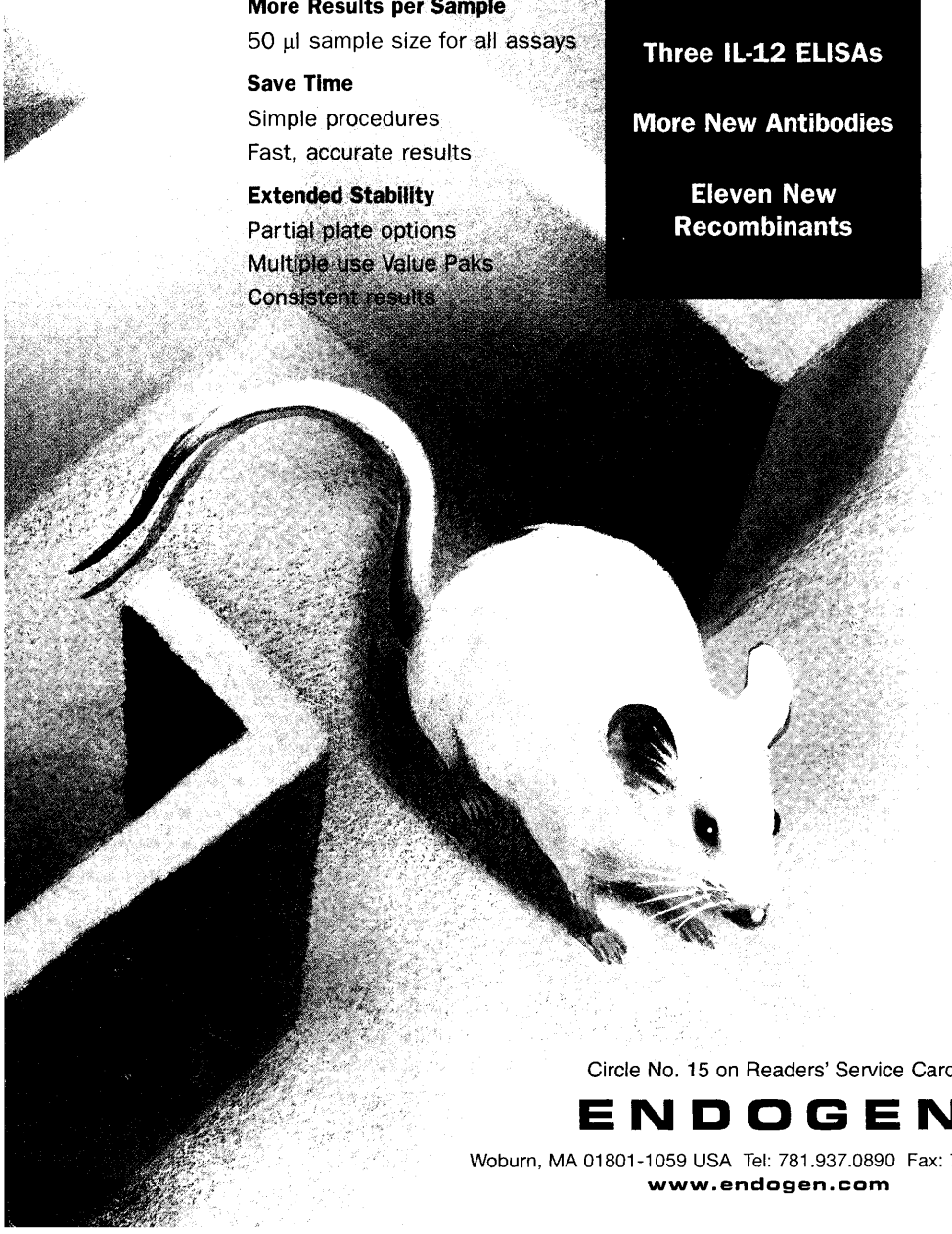

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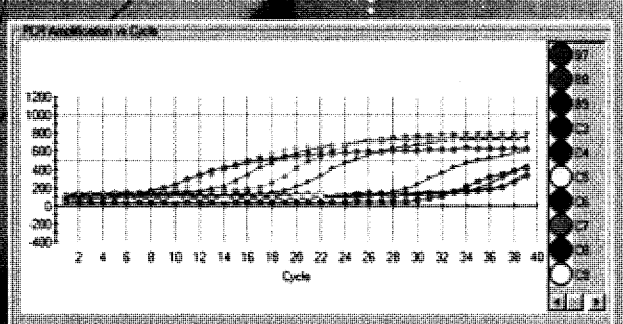

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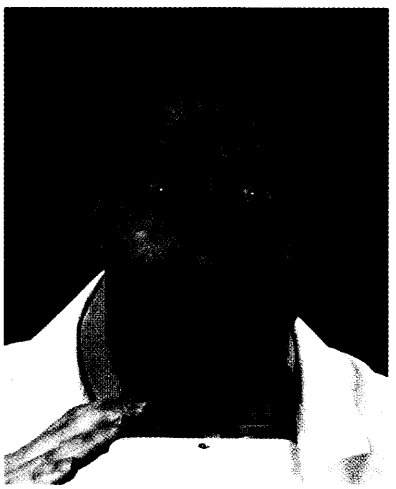

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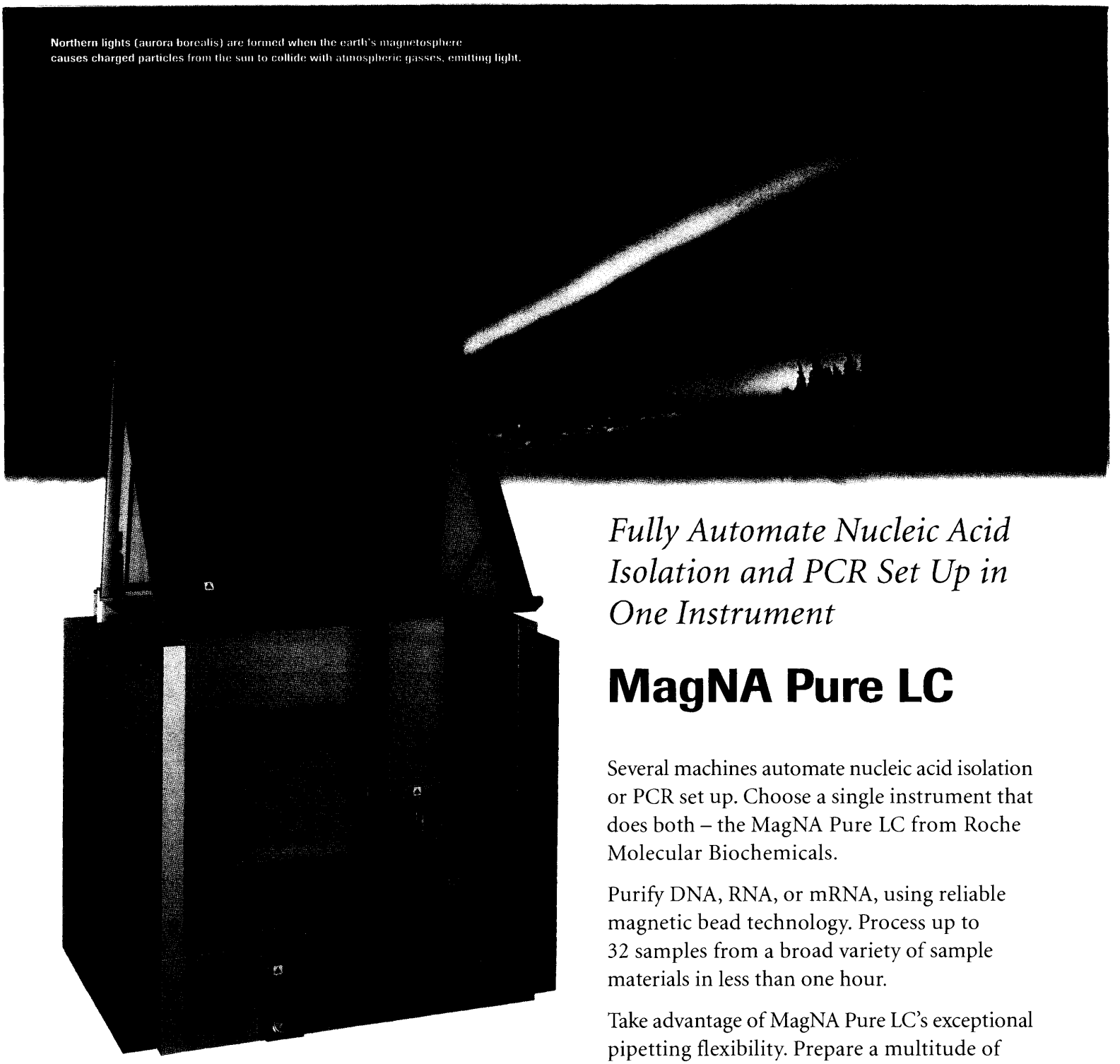

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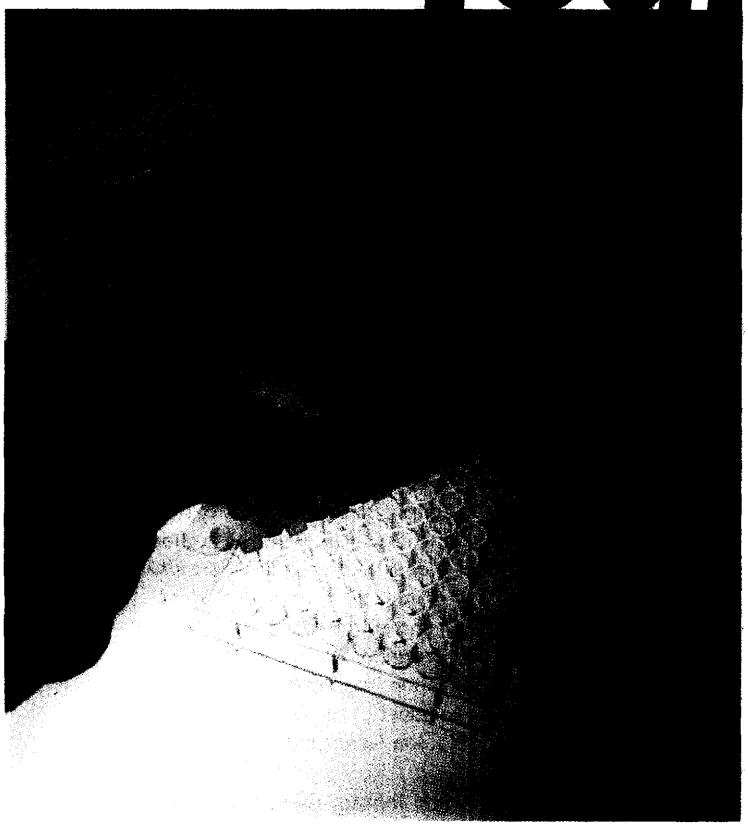

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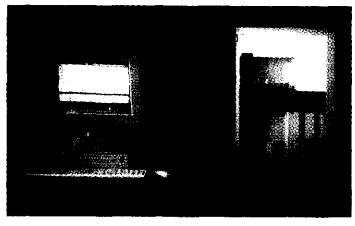

A New Opening. One entry point to the proteomics area is to search for binding partners for the new gene products. Both for understanding what the molecules do and as a help in developing new drugs. But identification gives just basic structural information. The dynamics of molecules are as important. You want to know: How specific is the interaction? How fast? How strong? How much of the compound is there?

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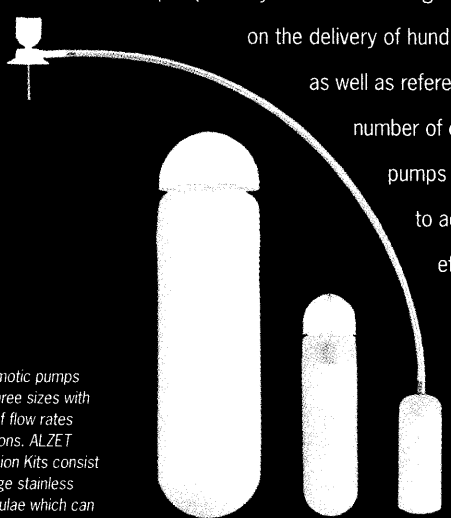

Fig. 2

ALZET osmotic pumps come in three sizes with a variety of flow rates and durations. ALZET Brain Infusion Kits consist of 28 gauge stainless steel cannulae which can penetrate 3-5 mm below the skull surface.

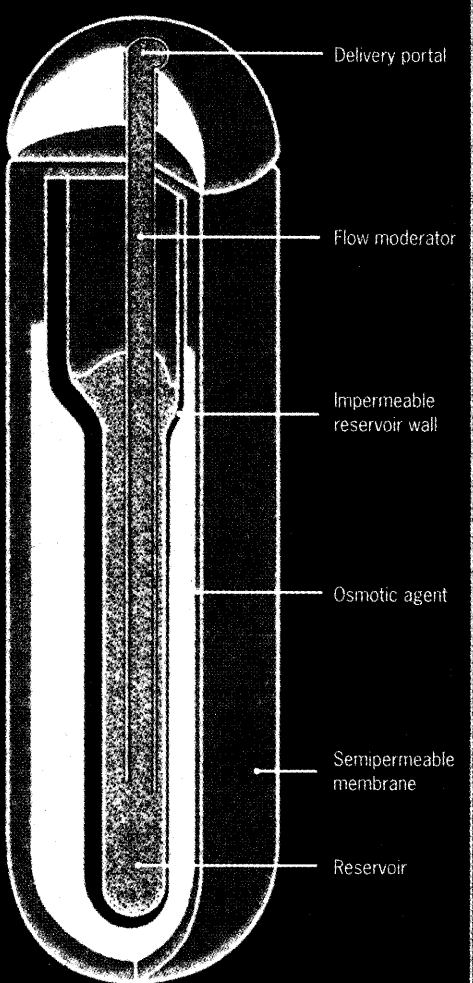

Fig. 1

The ALZET pump operates as interstitial fluid is attracted into the pump by the osmotic layer at a rate limited by the outer, semi-permeable membrane. As the osmotic layer hydrates, it compresses the flexible reservoir, which expels drug from the delivery portal of the pump.

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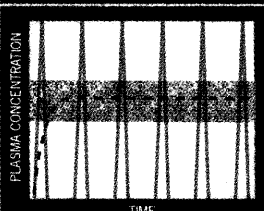

Eliminate Fluctuations in Plasma Drug Concentration

Fig. 3

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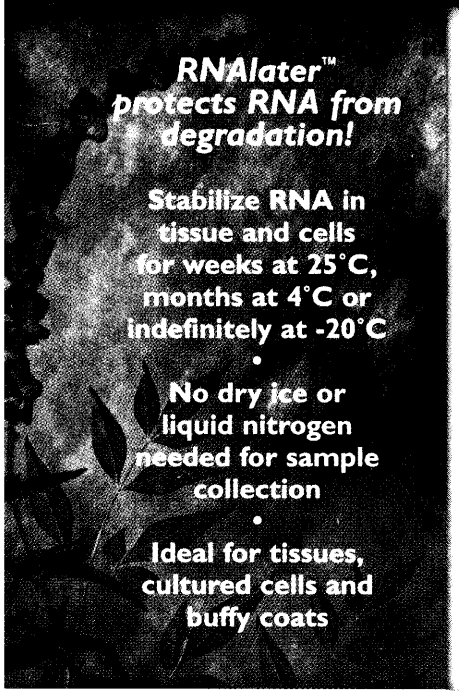

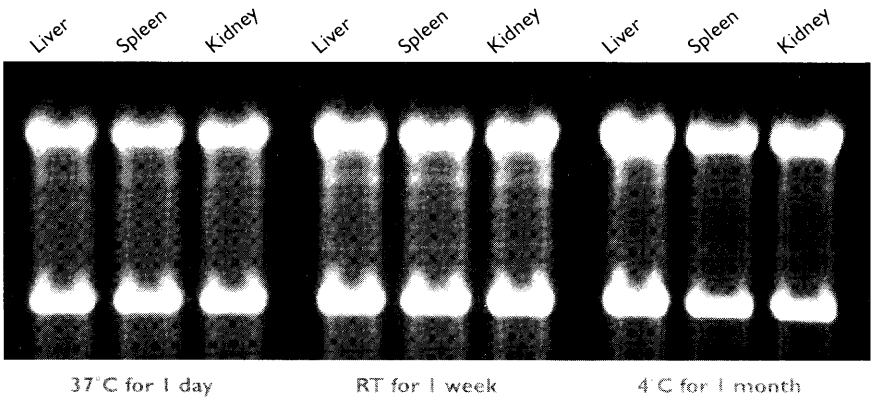

Figure 1a. Quality of RNA isolated from Tissue Stored in RNA*later*™ Solution. Fresh mouse tissues were dissected and stored in RNA*later*™ at 37°C for 1 day, room temperature for 1 week, or 4°C for 1 month. RNA was isolated using TRI Reagent® (MRC) and analyzed using denaturing agarose gel electrophoresis.

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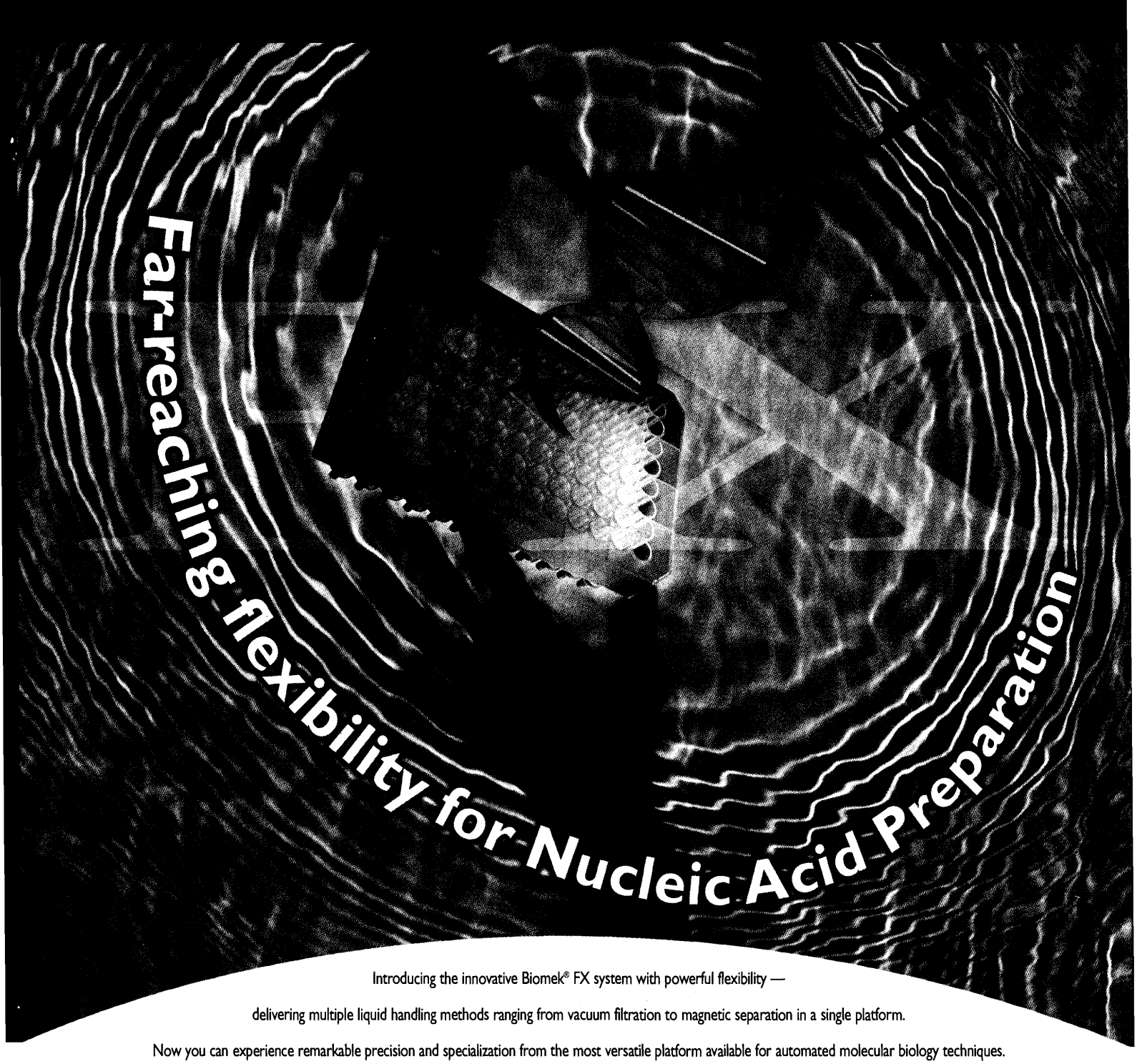

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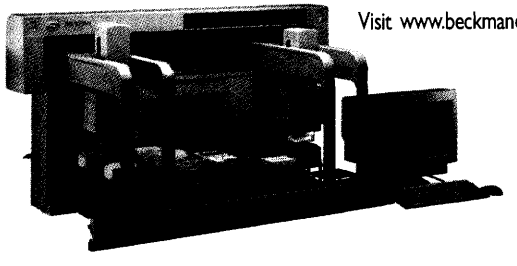

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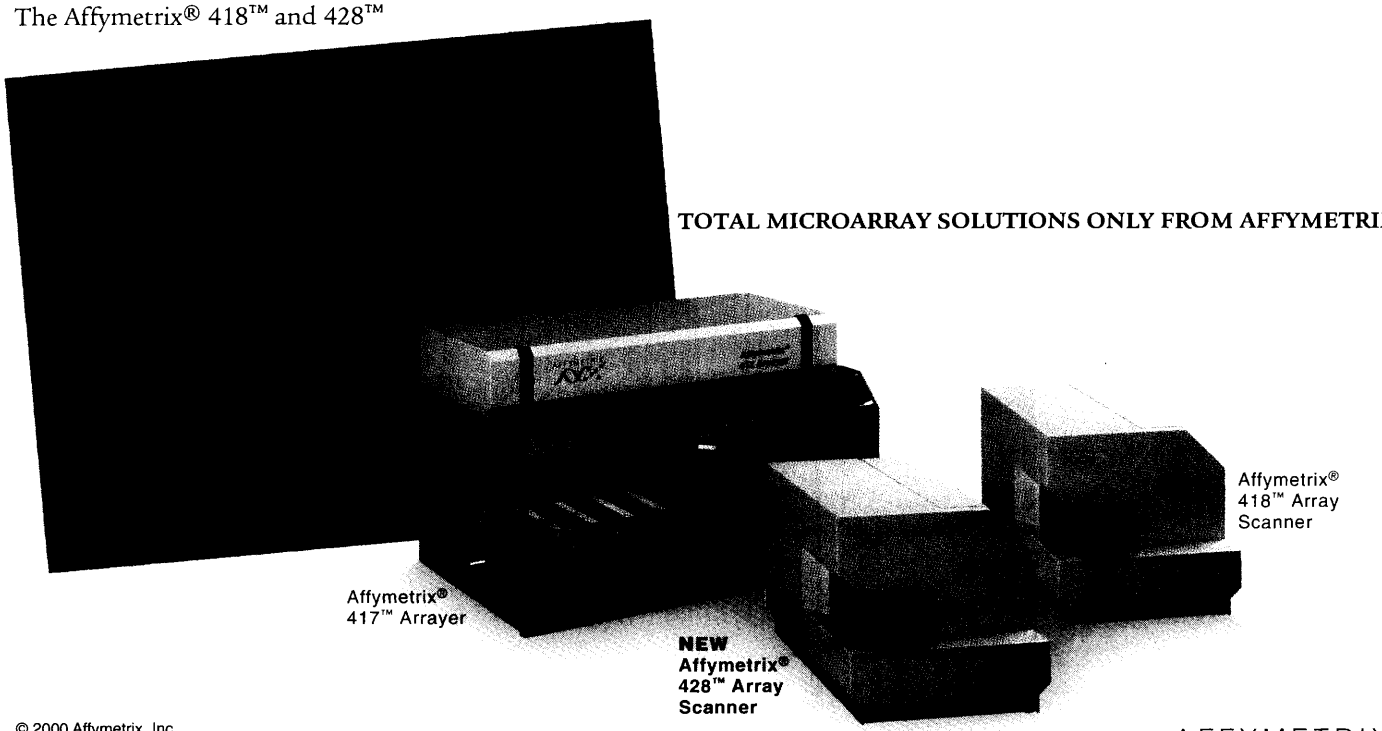

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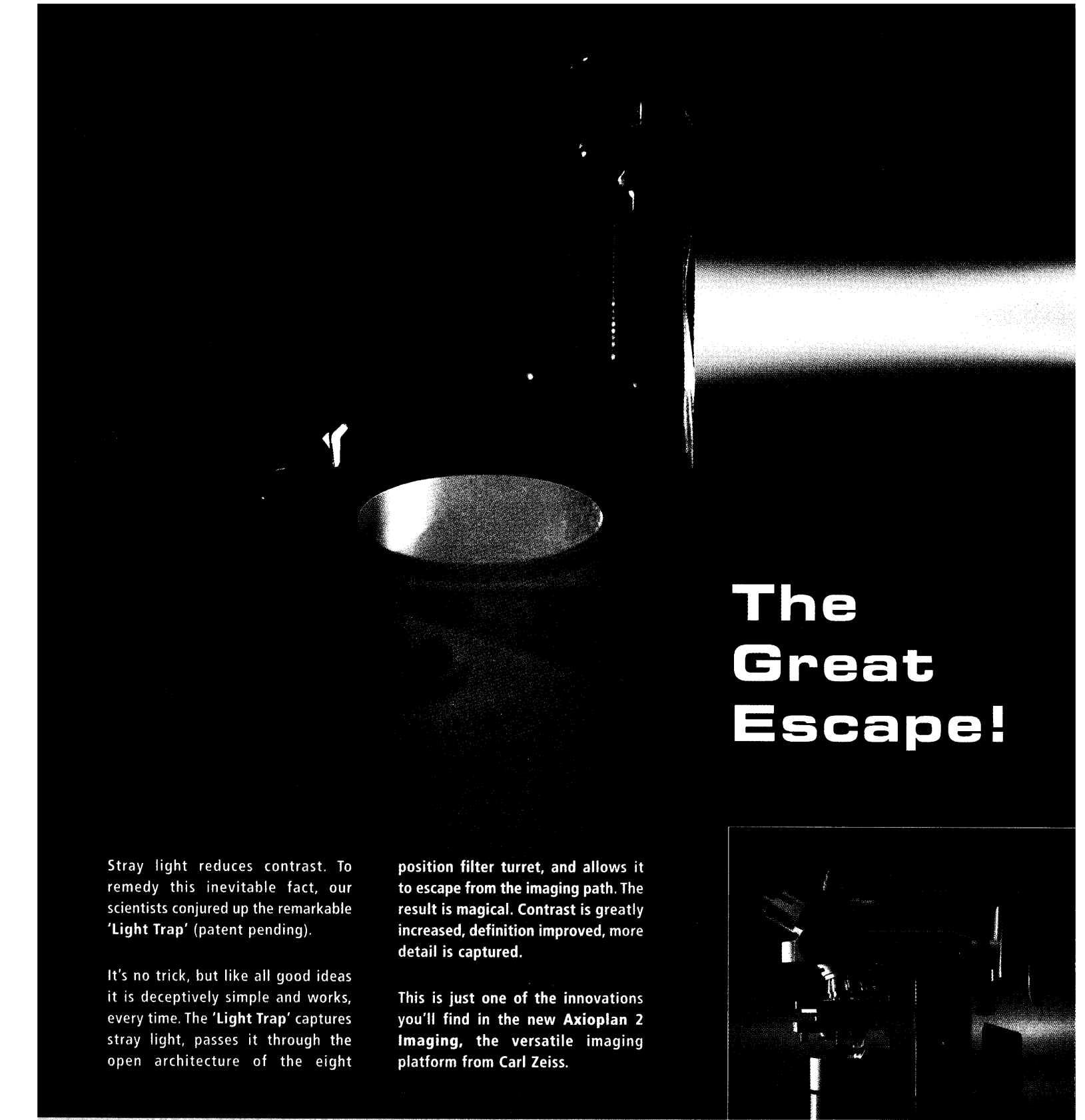

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