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1. Lundberg, K.S., et al. (1991) *Gene* 108, 1-6

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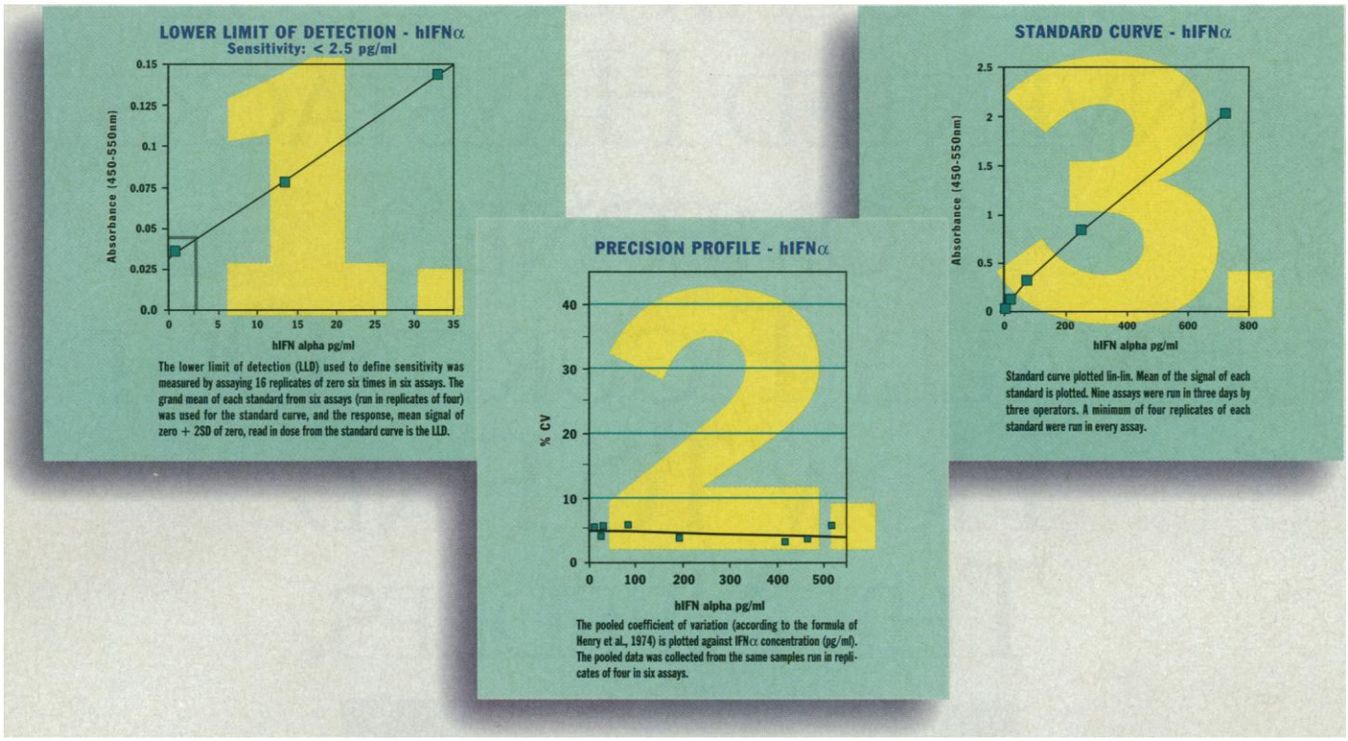

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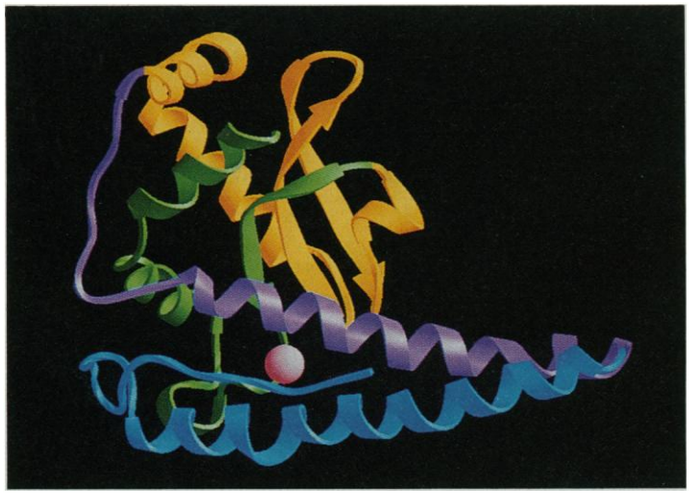
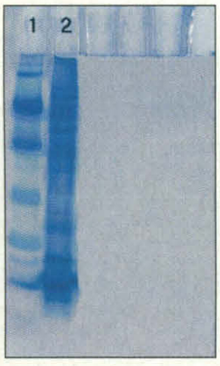
Twenty Years After Molecular Biologists Invented Haystacks, Someone's Finally Figured Out How To Find The Needles.





Crude cytokine prep.
Lane 1: MW markers.
Lane 2: Crude.

You know it's in there.

Somewhere in that liter of crude extract, there's a few µg of your recombinant protein, if you're lucky.

It took you a year and a half to get this far. The important research won't happen until you purify the active protein. You've made several attempts with conventional chromatography columns and instruments and still don't have a clean molecule to work with.

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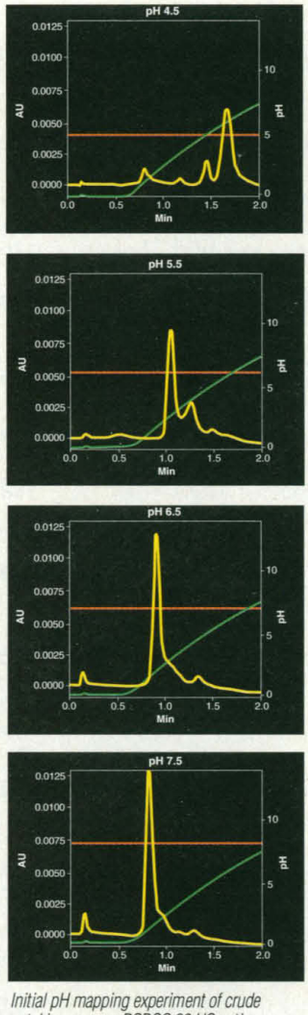

Initial pH mapping experiment of crude cytokine prep on POROS 20 HS cation exchange. Optimization of key separation variables including pH, gradient, loading, and flow rate can be completed in minutes.

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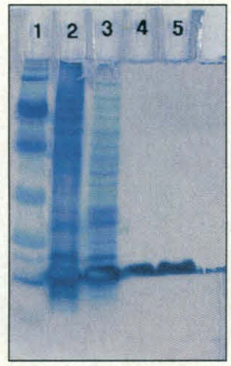

Lane 1: MW markers.
Lane 2: Crude.
Lane 3: Pooled fractions after initial cation exchange step.
Lane 4 & 5: Purified cytokine after second purification step with POROS 20 PH hydrophobic interaction column.

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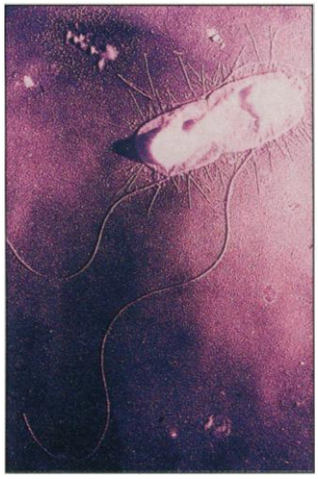

172
Escherichia coli
genome controversy

NEWS & COMMENT

RESEARCH NEWS

PERSPECTIVE

ARTICLES

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DEPARTMENTS

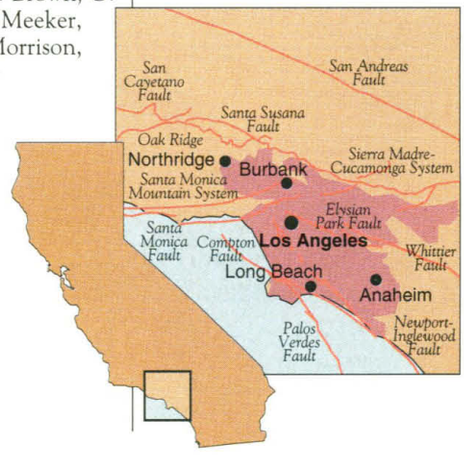
COVER

Fully open flowers of *Amsinckia vernicosa*, showing the reduced flower size typical of highly self-fertilizing species. Self-fertilization has evolved many times in plants. Extreme rates of self-fertilization provide an opportunity for estimating mutation rates to mildly deleterious alleles and the average dominance level of such mutations. These quantities and information on the reduced fitness of progeny from self-fertilization are important in genetic models of the evolution of sex, recombination, and self-fertilization rates. See page 226. [Photo: G. L'Heureux, McGill Biology Image Centre]

TECHNICAL COMMENTS

176, 199, 206 & 211

Bad breaks for Southern California



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NOMINATIONS FOR THE 1996 LOUIS JEANTET PRIZE FOR MEDICINE

Nominations are being sought for the 1996 Louis Jeantet Prize for Medicine. One to three prizes will be awarded. They will amount to a maximum of 2 million Swiss Francs (approximately 1.4 million US Dollars) in 1996. These prizes will provide substantial funds for the support of biomedical research projects (fundamental or clinical) of the highest quality. Candidacies in clinical research are strongly encouraged.

Candidates (either individuals or research groups) must be nominated by scientists, physicians or institutions having detailed knowledge of the candidates' research. The Louis Jeantet Prize for Medicine is not intended to honour past accomplishments but to help and encourage the winners' continued research activity. Candidates shortlisted for the final selection will therefore be asked to provide a research project to which the financial support of the Prize could give decisive impetus.

The previous winners of the Louis Jeantet Prize for Medicine have been **Luc Montagnier, Michael Berridge** and **Désiré Collen** in 1986, **Sidney Brenner, Walter Gehring** and **Dominique Stehelin** in 1987, **Bert Sakmann, John Skehel** and **Rolf Zinkernagel** in 1988, **Roberto Poljak, Walter Schaffner** and **Greg Winter** in 1989, **Nicole Le Douarin, Harald Von Boehmer** and **Gottfried Schatz** in 1990, **Pierre Chambon, Frank Grosveld** and **Hugh Pelham** in 1991, **Paul Nurse, Christiane Nüsslein-Volhard** and **Alain Townsend** in 1992, **Jean-Pierre Changeux, Richard Henderson** and **Kurt Wüthrich** in 1993, **Thierry Boon, Jan Holmgren** and **Philippe Sansonetti** in 1994, **Dirk Bootsma** and **Jan Hoeijmakers, Peter Goodfellow** and **Robin Lovell-Badge,** and **Peter Gruss** in 1995.

The following general points should be noted:

1. The Prize is intended for researchers working in European countries, members of the Council of Europe. The candidates need not, however, be themselves nationals of any of these countries.
2. Applications must be submitted, confidentially, on the official forms only. These are obtainable from:

   The Secretary of the Science Committee
   The Louis Jeantet Foundation for Medicine
   P.O. Box 277
   CH—1211 GENEVA 17
   Switzerland

   Further information will be sent with the nomination form.
3. The deadline for applications is February 15, 1995.

   The name(s) of the winner(s) of the 1996 Louis Jeantet Prize for Medicine will be announced in January 1996. The Prize Ceremony will take place in Geneva (Switzerland) in April 1996.

edited by DAVID LINDLEY

Dissecting the dark

Measurement of the present cosmic abundances of deuterium, helium, and lithium constitutes an increasingly refined probe of nucleosynthesis during the first few minutes of cosmic history. To make models and measurements agree, Copi *et al.* (p. 192) argue that at least some of the notorious cosmological dark matter must be baryonic. If the total density of the universe is at or close to the critical value, however, as many observations indicate, most of the dark matter must be non-baryonic.

■

Polymers to order

Polymer properties such as elasticity can depend on the way in which the monomer building blocks are joined. For example, isotactic polypropylene, in which all the pendant methyl groups are arranged in the same way, is a crystalline thermoplastic, whereas atactic polypropylene, in which the methyl groups are arranged at random, is an amorphous gum. Coates and Waymouth (p. 217; see the Perspective by Wagener, p. 191) have developed a transition metal catalyst for the polymerization of propylene that allows the degree of stereoregularity (the mix of atactic and isotactic content) and hence the physical properties of the polymer to be varied simply by changing the propylene pressure and the reaction temperature.

■

Inorganic fullerenes

Arc discharges and plasma conditions are generally needed for synthesizing carbon fullerenes and nanotubes. Feldman *et al.* (p. 246) have synthesized MoS_2 in the form of nested fullerenes or as nanotubes through the gas-phase reaction of MoO_{3-x} and H_2S at elevated temperatures (800° to 950°C). Turbulent flow conditions in the reactor produced the highest yields, and an inorganic fullerene phase with a narrow size distribution could be obtained.

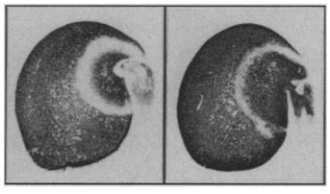
The stress of waiting

The measured accumulation of strain across the Los Angeles region is more than can be accounted for by recorded seismic activity in the past two centuries, suggesting that there is a potential for moderate to large earthquakes, with magnitudes larger than the recent Northridge quake (M_w 6.7), to occur in the future. Dolan *et al.* (p. 199) and Hough *et al.* (p. 211) present two separate analyses of this problem, both concluding that the typical interval between larger quakes, up to M_w 7.6, is a few hundred years or more. In a related study Heaton *et al.* (p. 206) predict through a modeling study that the effect of ground motion associated with such quakes may cause collapse even of newly designed buildings close to the epicenter. Additional lessons learned from the Northridge quake, which occurred 1 year ago, are discussed in a news story by Kerr (p. 176).

■

Viral disturbance

Pea seed–borne mosaic virus infects the plant embryo early in development and, as the infection proceeds, spreads into the cotyledons. Wang and Maule (p. 229) have studied the



effect of the invading virus on the metabolism of the host cells. Viral replication occurs early in infection, and thus in pea cotyledons is localized to the infection front; in the same region, the virus suppresses the expression of host genes and disturbs host protein translation. These changes plausibly underlie the appearance of viral symptoms in the plants.

Coping with salt

A little bit of salt may be tasty, but too much is hard on the metabolism of many types of cells. Murguía *et al.* (p. 232) have found that, in yeast cells, the salt tolerance gene *HAL2* encodes a nucleotidase that participates in the general sulfur metabolism of the cell and is inhibited by sodium and lithium. When *HAL2* is overexpressed, the cells can tolerate higher than normal amounts of extracellular salt. Understanding the mechanisms of salt tolerance may aid the development of crop plants with greater salt tolerance, an important agricultural goal as heavy irrigation tends to make soil increasingly salty.

■

Wood alcohol

Efforts to produce ethanol from lignocellulosic biomass, such as agricultural and forestry residues, have been hindered by the lack of microorganisms that can efficiently ferment pentose sugars, which commonly occur in hemicellulose. Zhang *et al.* (p. 240; see Random Samples, p. 171) have engineered the bacterium *Zymomonas mobilis*, which already has some advantages over yeast in the fermentation of glucose to ethanol, so that it can digest xylose. The genes for the enzymes required for xylose assimilation and the pentose phosphate pathway were transformed into *Z. mobilis*, which was able to ferment both xylose and glucose to ethanol.

■

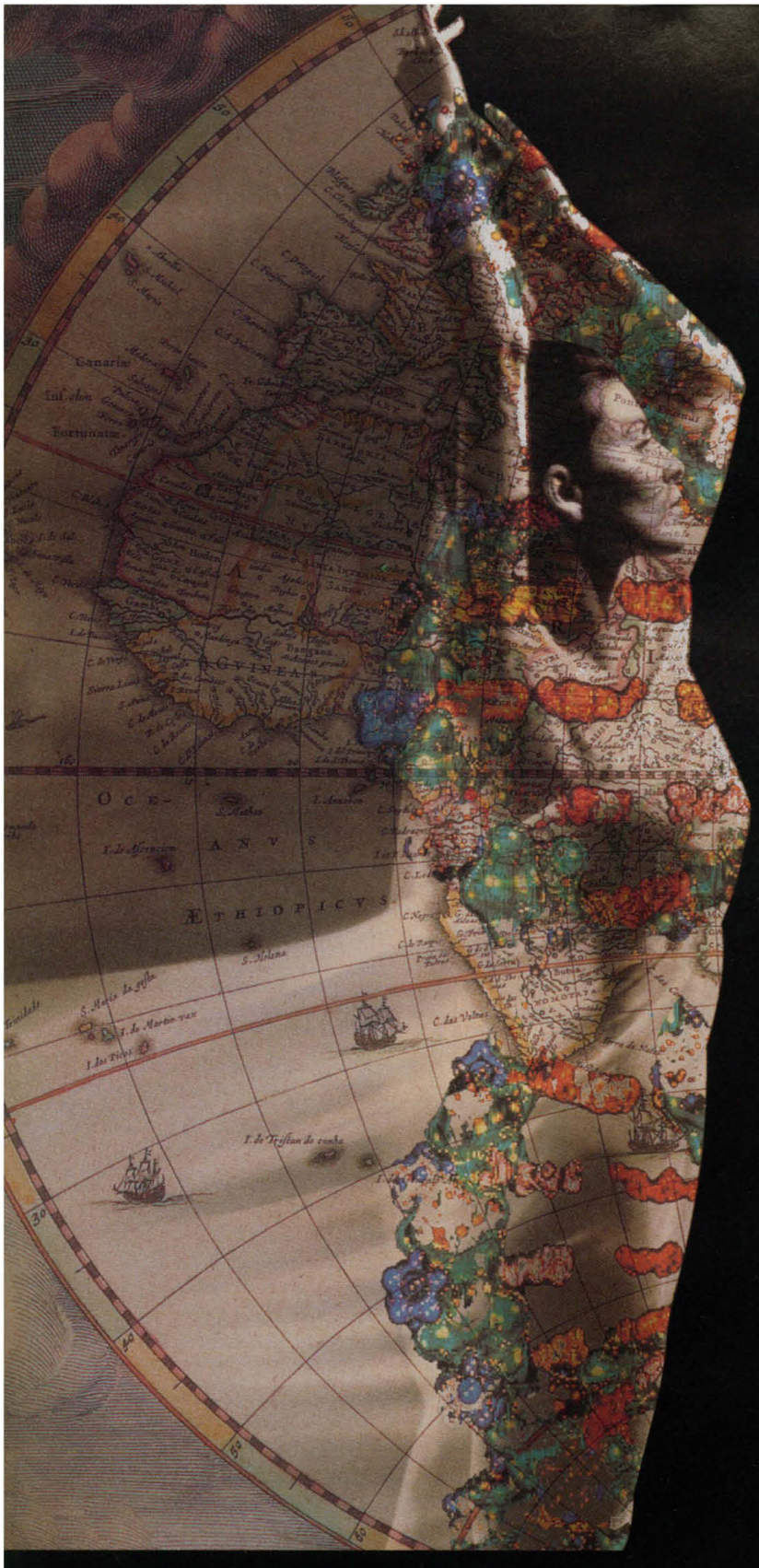
Primitive biochemistry

In the primordial world, an ancestral RNA enzyme (ribozyme) may have catalyzed both RNA polymerization and peptide bond formation. Dai *et al.* (p. 237) present data that may support this scenario. They show that a variant form of a group I ribozyme, optimized by in vitro evolution for its ability to cleave phosphodiester bonds, can also cleave an unactivated amide bond. These results have implications for both the evolution of catalytic function and the origin of protein synthesis.

■

From the outside in

Generation of a cytotoxic T lymphocyte (CTL) response is normally initiated by an antigen-presenting cell bearing major histocompatibility complex (MHC) class I molecules bound to a peptide synthesized by the cell, but in a few cases pathogens or particulate antigens also generate a CTL response. Kovacsovics-Bankowski and Rock (p. 243) show that macrophages can transport these extracellular antigens into the cytosol, from which point they are dealt with by the normal MHC class I pathway. These results suggest that it may be possible to induce a CTL response by means of inert particulate proteins without the use of a live vaccine to introduce the antigen into cells.



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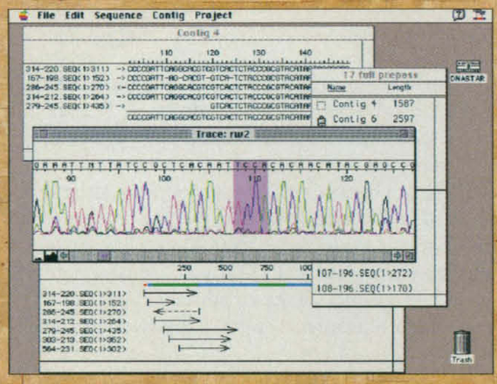

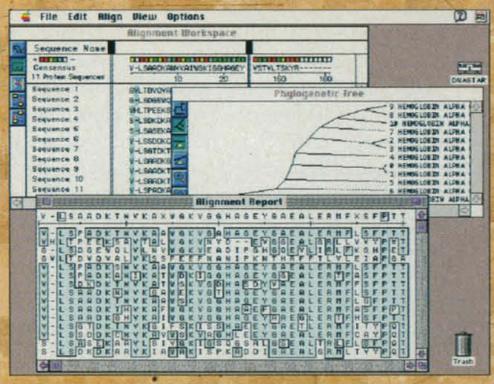

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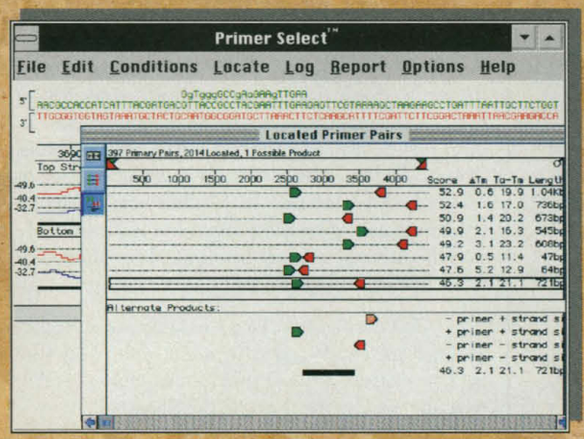

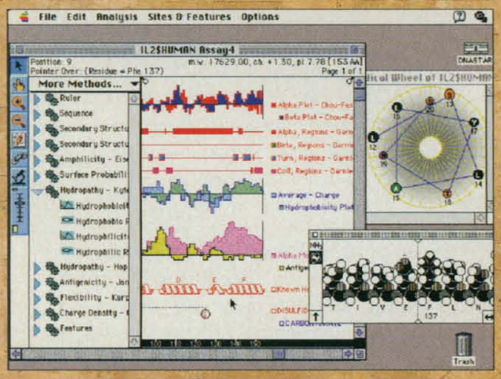

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New Technique Revolutionizes Microscopic Study of Living Cells

Some of the most significant biological research being done today involves the study of cellular dynamics inside living tissue. Using the Nikon RCM-8000 realtime confocal microscope and a special water immersion objective developed by Nikon, scientists are observing phenomena never before seen by the human eye. These include changes in calcium concentration during cell contractions, protein sub-unit transport mechanisms in living cells, neuronal cell-to-cell interactions and communications, and early developmental structures in living embryos.

Scientists have found that many of the optical microscopy techniques currently available are not well suited for the study of cellular dynamics inside living tissue.

Working with thinly cut sections of fixed tissue placed up against the cover glass, researchers are able to produce superb images using techniques such as confocal microscopy, DIC and epi-fluorescence. The problem arises when they try to study living cells *in vivo* or *in vitro* surrounded by physiological solution.

In the past, researchers have tried to achieve higher resolution by using plan apochromat or fluor high numerical aperture (NA) oil immersion objectives. This technique works well when the details or events being studied are no more than 15μm below the cover glass, but cannot be used when the area of interest is 100μm to 200μm deep.

Spherical aberration is a problem

The problem is the different indexes of refraction of the oil and glass (1.515) and the aqueous physiological solution (1.33). The light rays are bent toward the higher refractive index at the glass interface, causing severe spherical aberration. This is seen as a loss of intensity and contrast, inability to collect and resolve small spatial frequencies and reduced accuracy of reproduction — all in direct proportion to how deep beneath the cover glass the area of interest lies.

Spherical aberration is especially troublesome in confocal imaging, a technique which is normally used to achieve increased resolution and narrow depth of field while eliminating out-of-focus light. In confocal systems, the illuminating pinhole is imaged on the specimen and a moving mirror mechanism scans the specimen in a raster pattern. The light emitted from the specimen is rescanned by the same mechanism and reimaged through the pinhole. Since only the light that passes back through the pinhole is imaged, all out-of-focus light is eliminated.

When scanning deep within a specimen using an oil immersion objective, spherical aberration can become so extreme that much of the light coming back from the specimen is out of focus and unable to return through the pinhole.

Water immersion is the solution

This problem can be solved through the use of a water immersion objective. The refractive index of water closely matches that of both physiological solution and living cells, so that the effect of spherical aberration is dramatically reduced when looking deep within a specimen. Water also offers practical advantages because it will not fluoresce or contaminate physiological solution, and is easy to clean up.

Nikon has successfully produced a highly corrected water immersion 60x CFN plan apochromat objective with a 1.2 NA and a 220μm working distance. It has a correction collar that accommodates for cover glasses from 0.15mm to 0.18mm thick. This unique objective not only virtually eliminates spherical aberration, but is also chromatically corrected with high transmission in the near ultraviolet through the red spectrum, making it useful for confocal, fluorescence and DIC microscopy.

For more information on this exciting new technique, call Nikon at (516) 547-8567, fax us at (516) 547-0306, or contact us on the Internet at nikonbio@aol.com.

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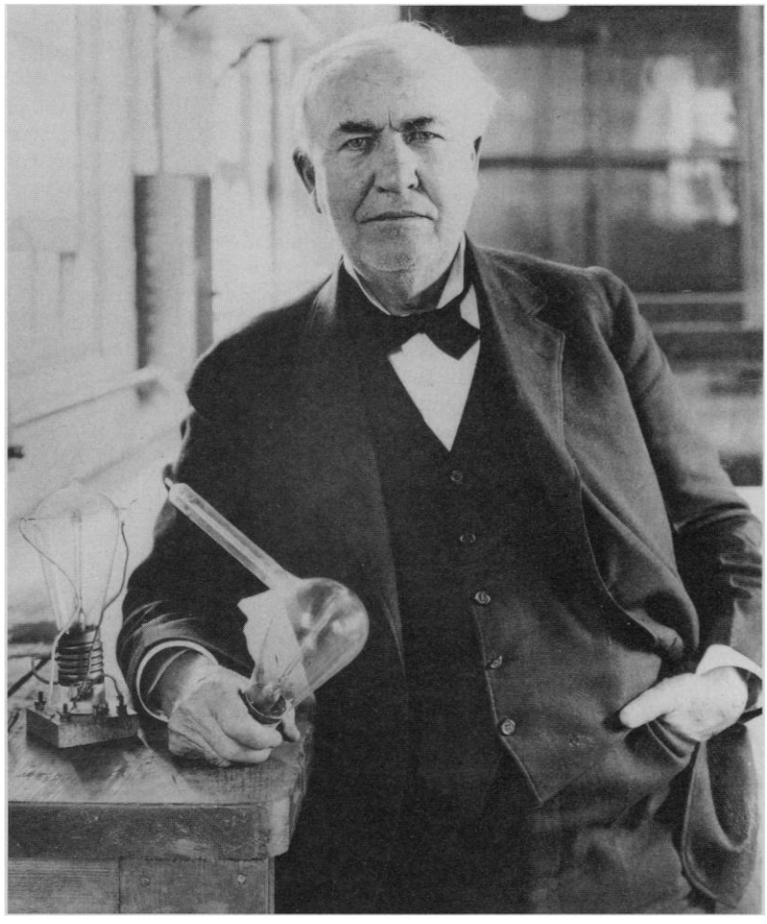

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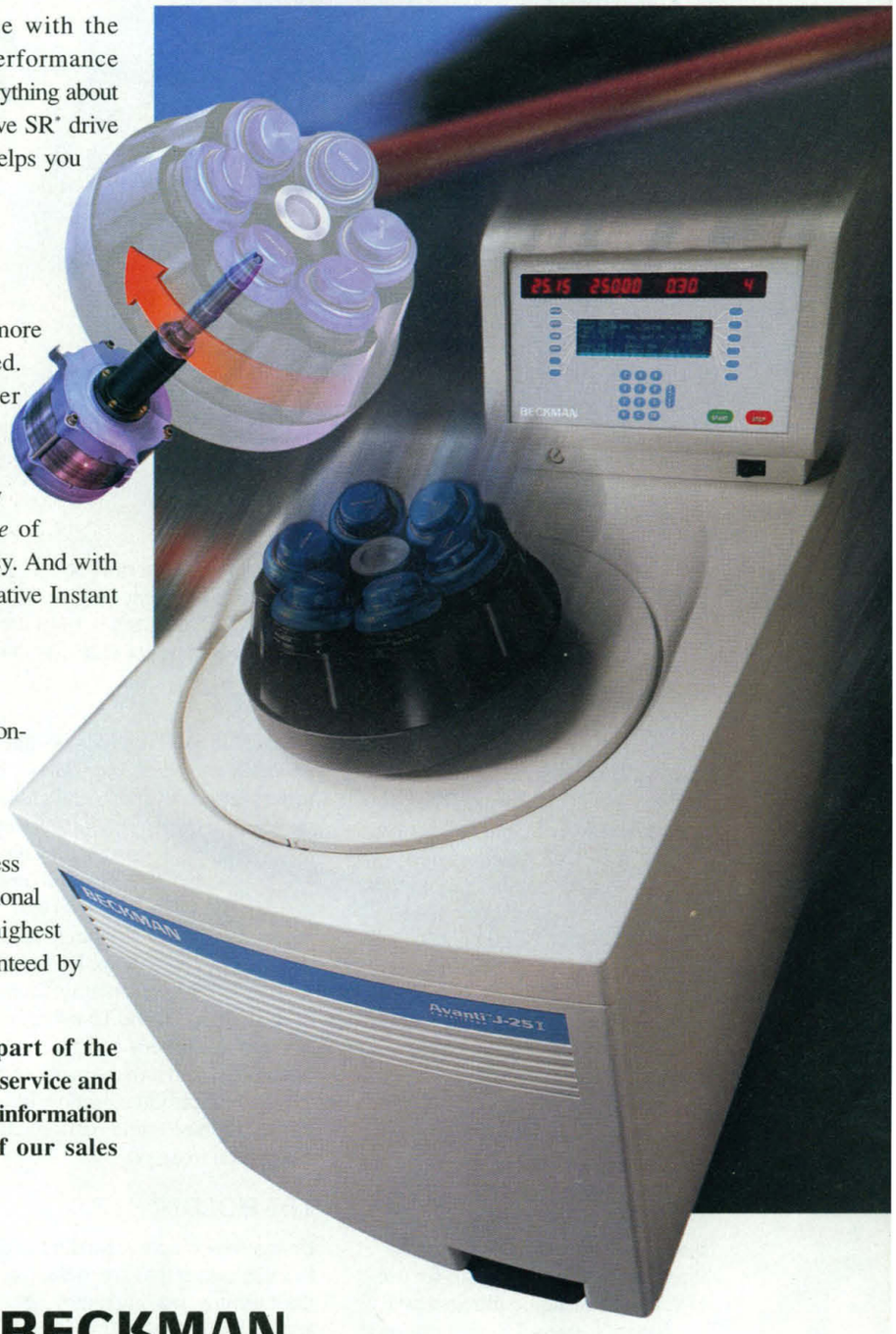

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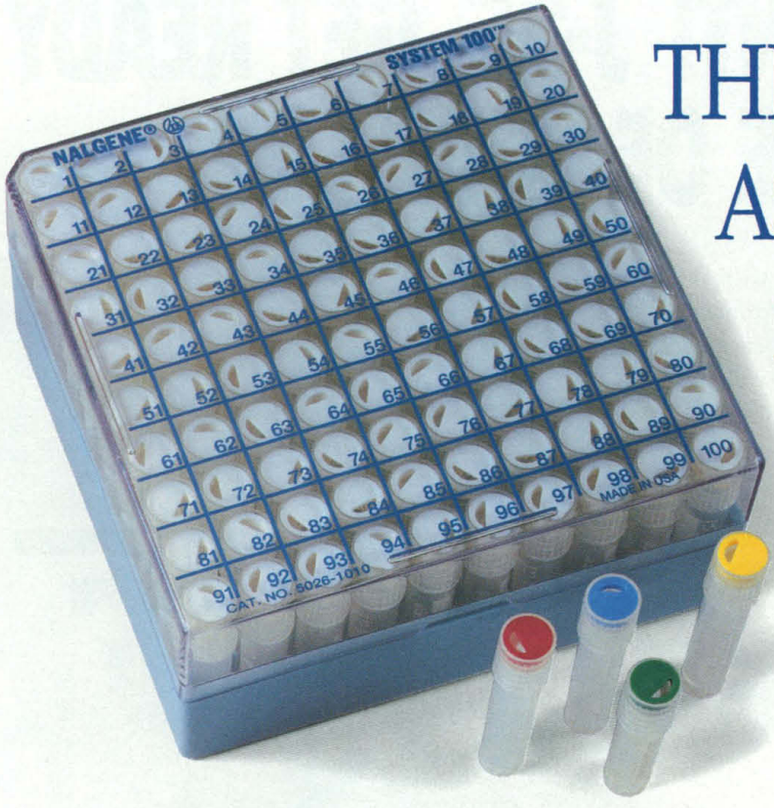

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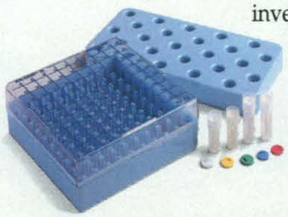

Look at it as getting 23% greater freezer capacity without the cost of additional freezers.

THE CRYOBOX

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*Compared to typical 81-vial capacity storage boxes.

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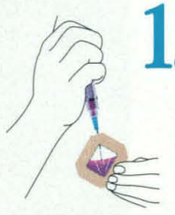

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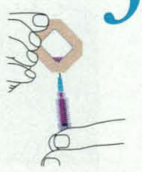

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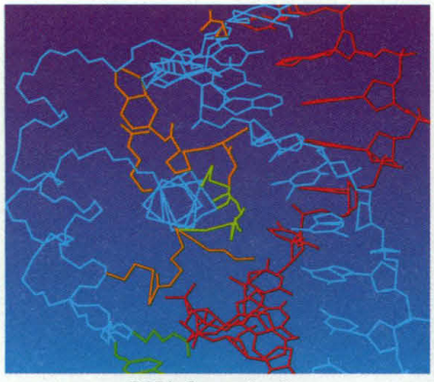
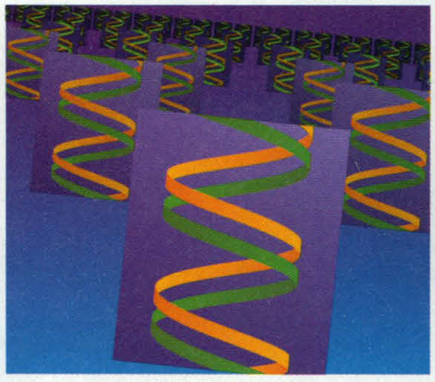
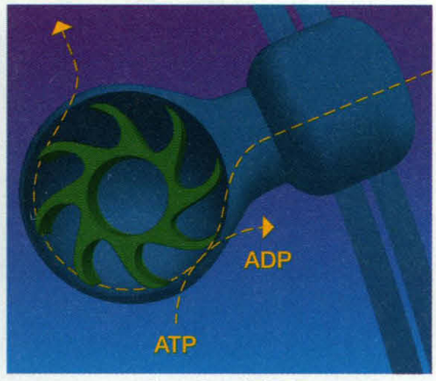


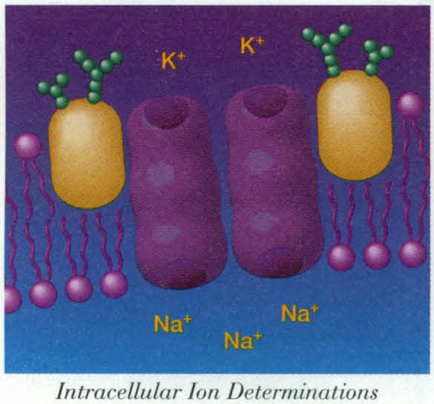
DNA Quantitation



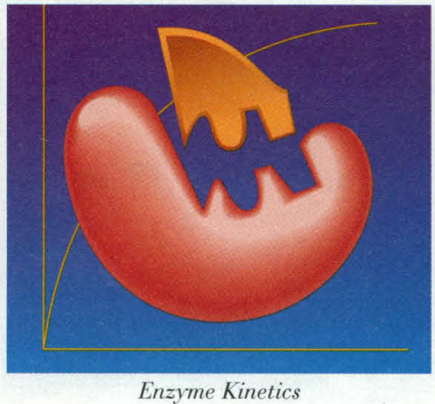
PCR Detection



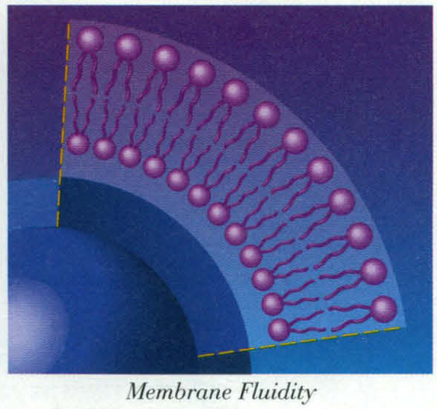
Low Level ATP



Intracellular Ion Determinations



Enzyme Kinetics



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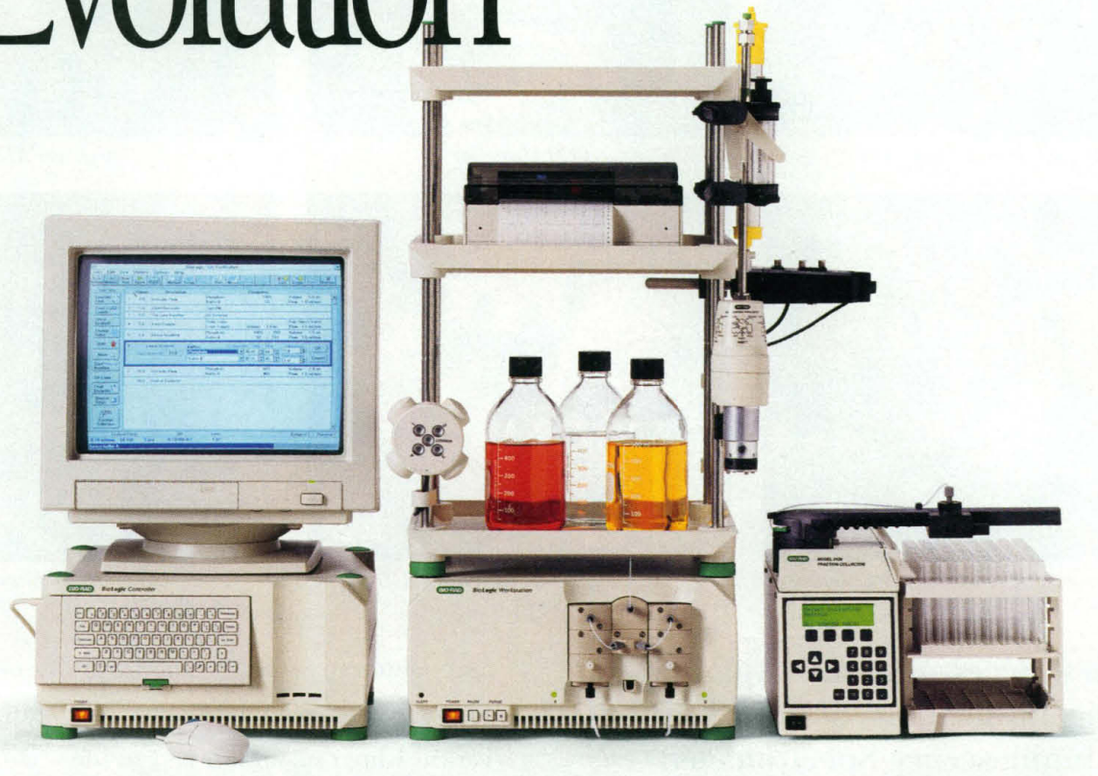

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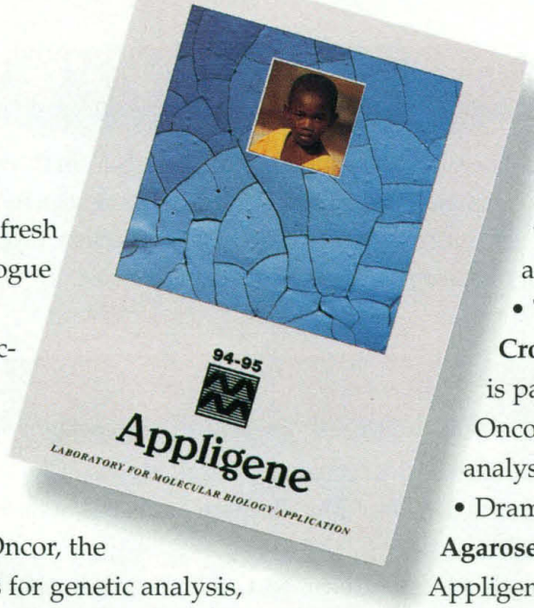

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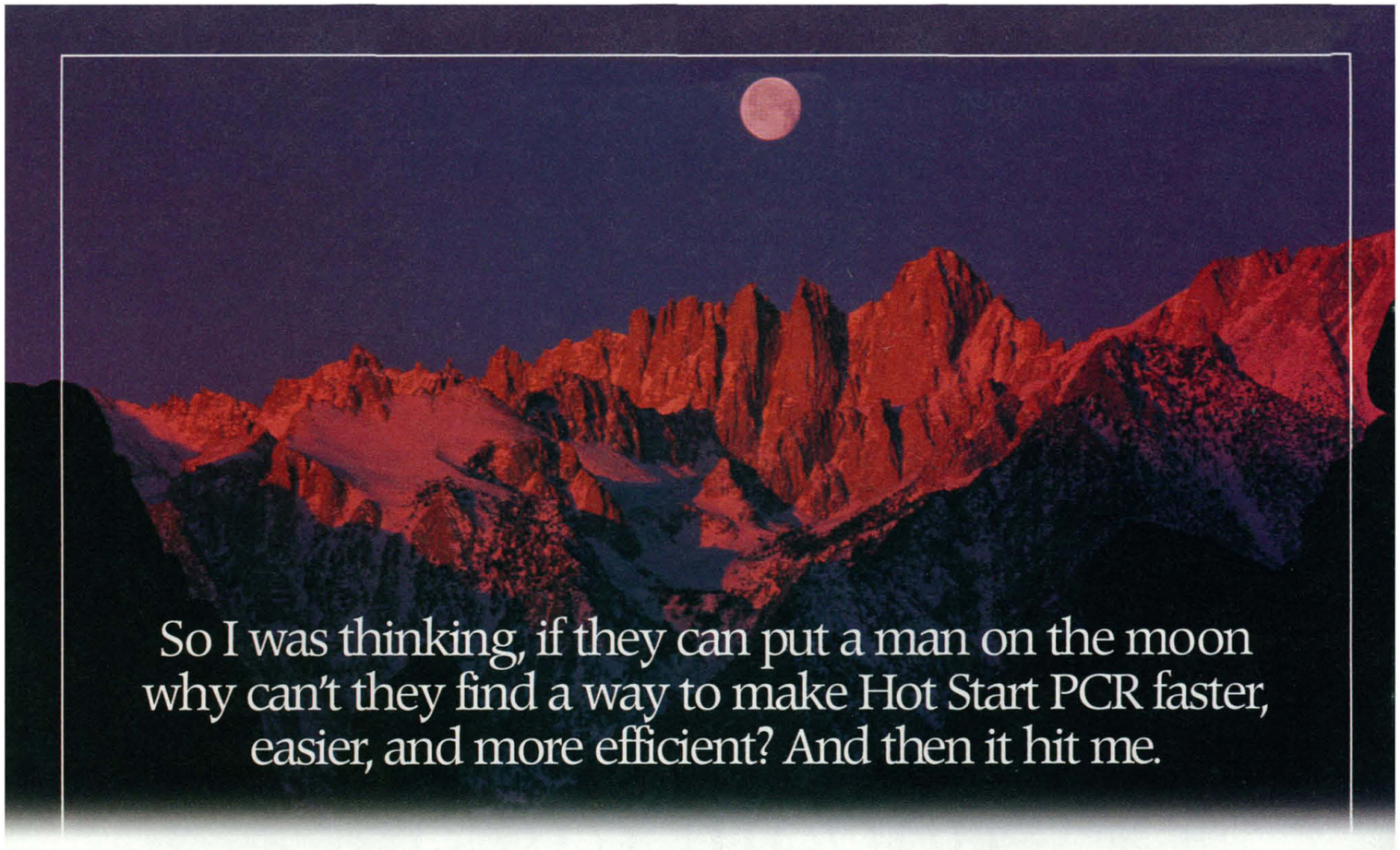

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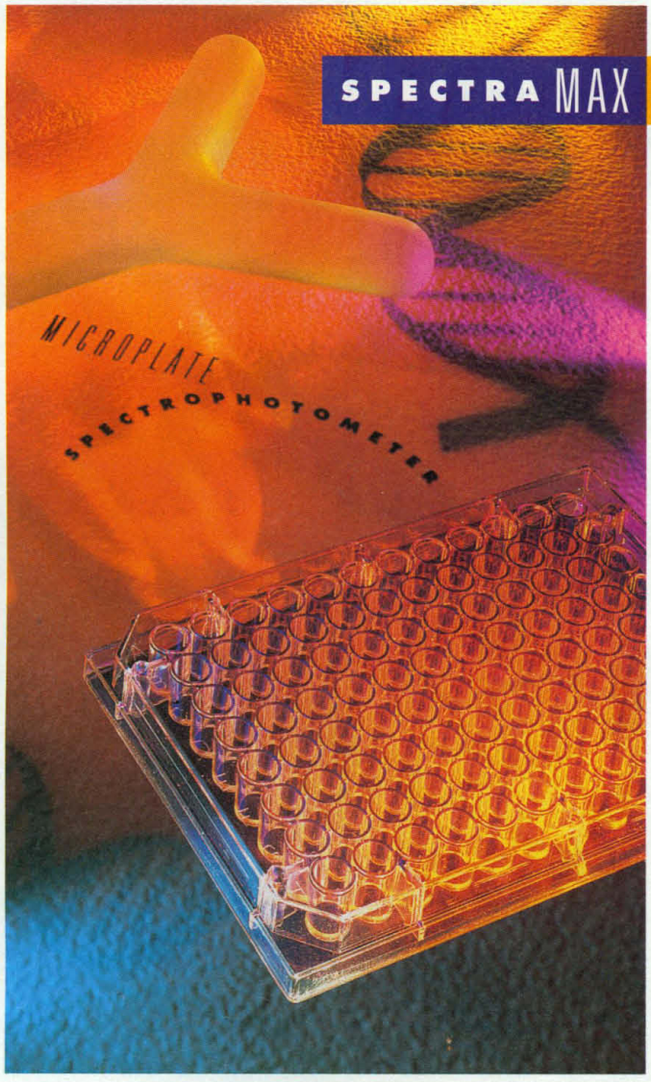

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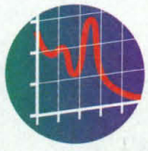
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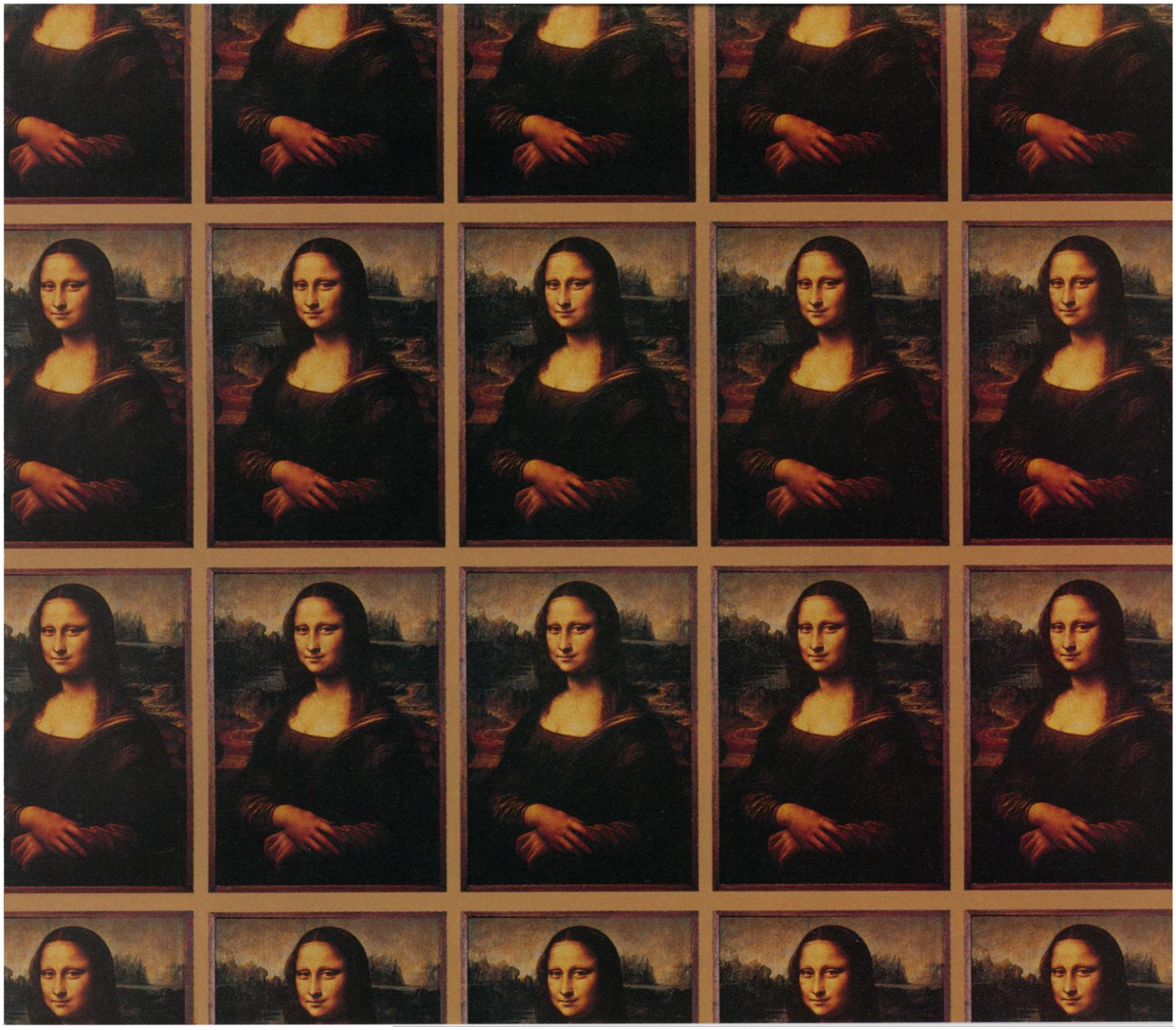

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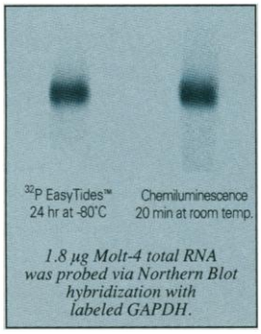

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