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hNT Neurons

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- elaborate processes typical of mature postmitotic human neurons
- express many neuronal markers¹
- express functional NMDA and non-NMDA glutamate receptor channels²

1. Pleasure, S.J., and Lee, X.M.Y. (1993) J. Neurosci. Res. 35:585-602

2. Pleasure, S.J., et al. (1992) J. Neuroscience 12: 1802-1815

- express and secrete amyloid precursor peptides³
- can be transplanted into rodent brains⁴
- are permissive for HIV infection⁵
- can be transfected

3. Younkin, D.P., et al. (1993) Proc. Natl. Acad. Sci. USA 90: 2174-2178

4. Wertkin, R., et al. (1993) Proc. Natl. Acad. Sci. USA 90: 9513-9517

5. Hirka, G., et al. (1991) J. Virol. 65: 2732-2735

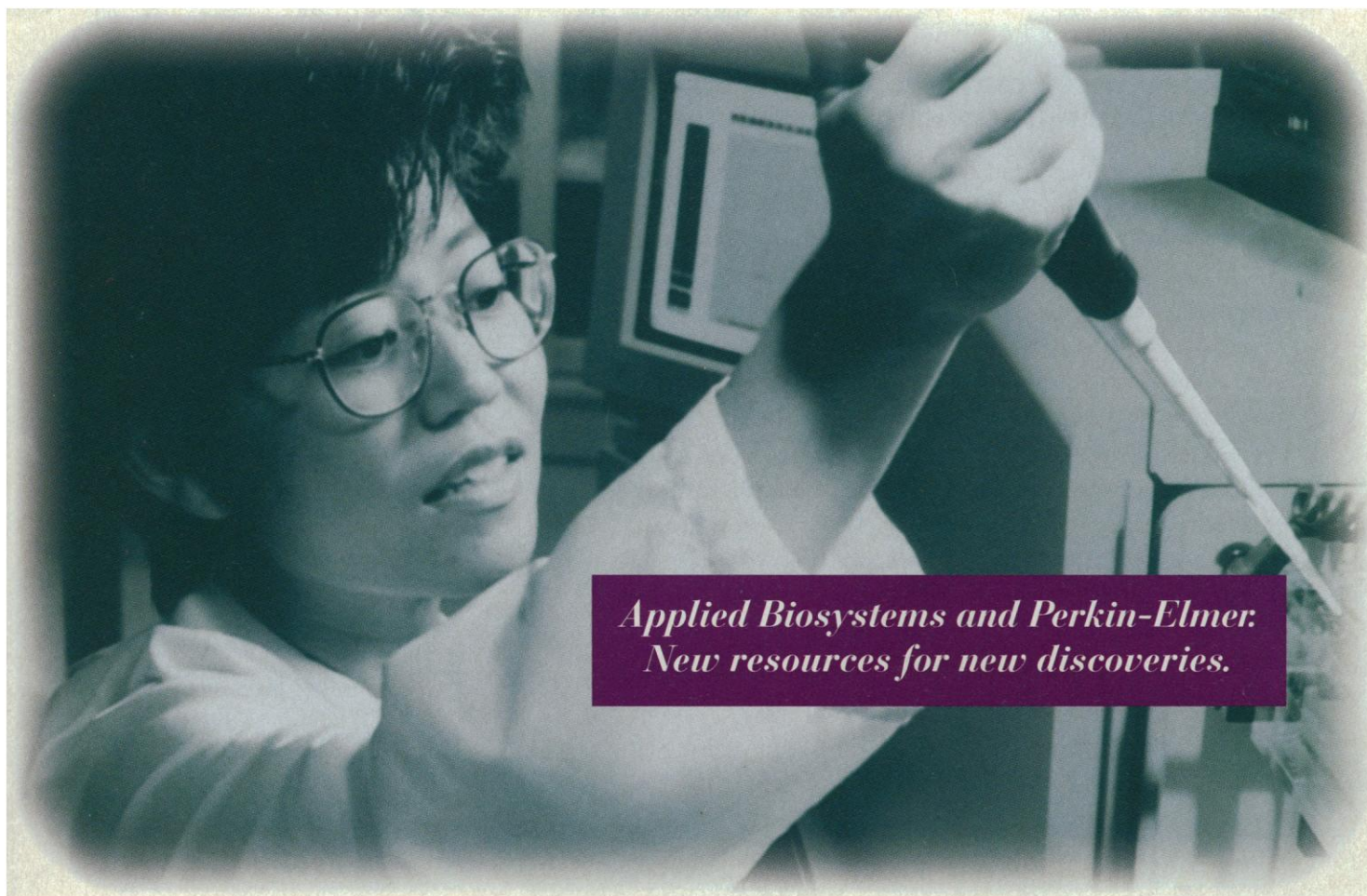
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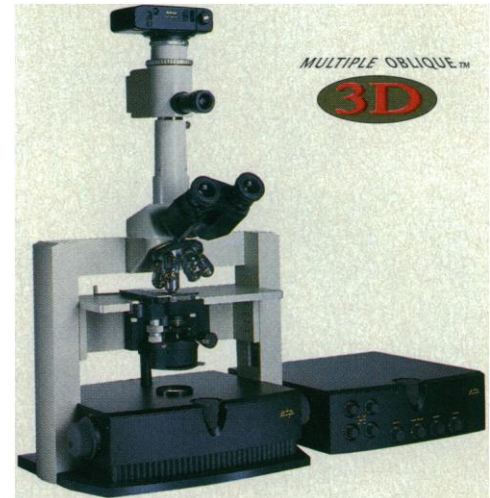
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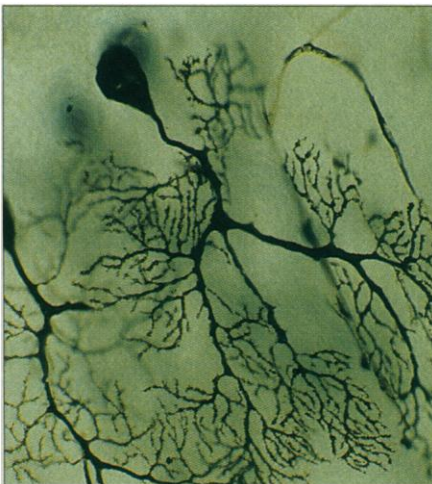


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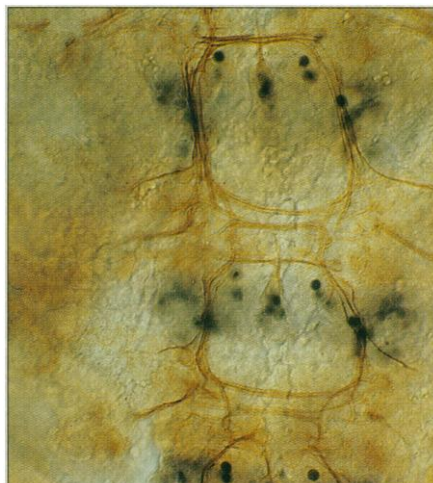
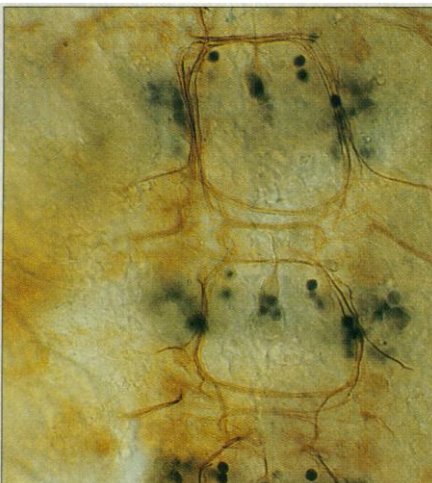
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Specimen: Thick section of cerebellum showing purkinje cells. Approx. 50 -75 μm thick.
Objective: Plan Apochromat 40x dry
Qualities: Extraordinary depth of field with large stereo parallax allows tracing path of dendritic spines. High contrast without loss of resolution brings out fine details in spines.

Gary Greenberg, Ph.D.,
Edge Scientific Instrument Corp.



DEVELOPMENT

Specimen: Grasshopper embryonic ventral nerve cord, stained for axons (brown) and transcription factor engrailed (black). Approx. 80 μm thick.
Objective: Plan Apochromat 20x
Qualities: 3D perspective distinctly separates out the various dorsal and ventral aspects of the nervous system in the developing grasshopper.

Dr. Barry Condrón, Cal Tech

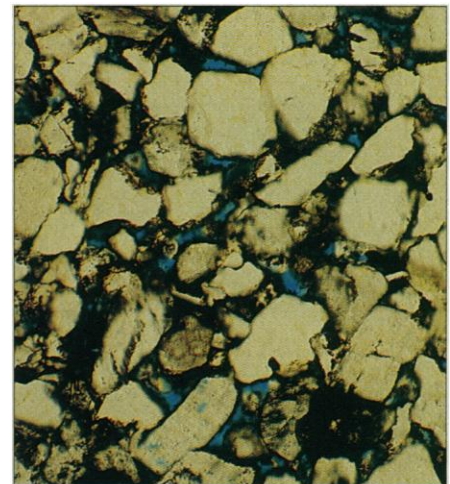
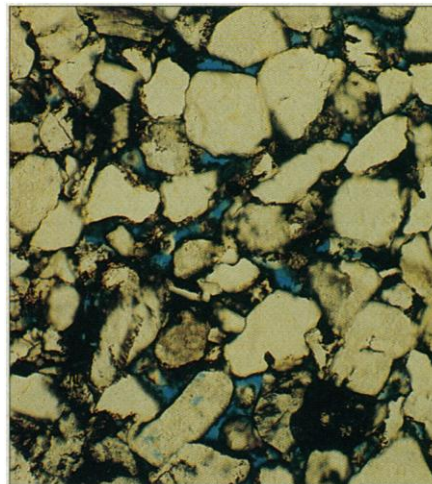
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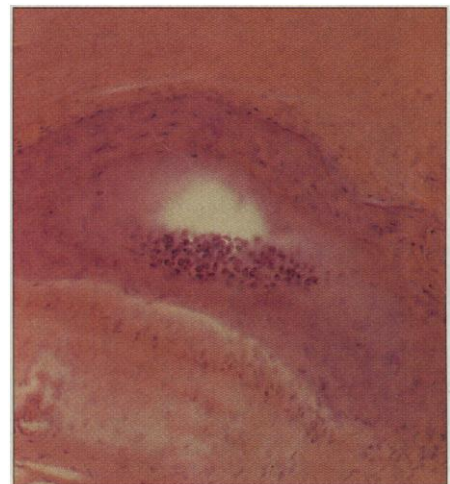
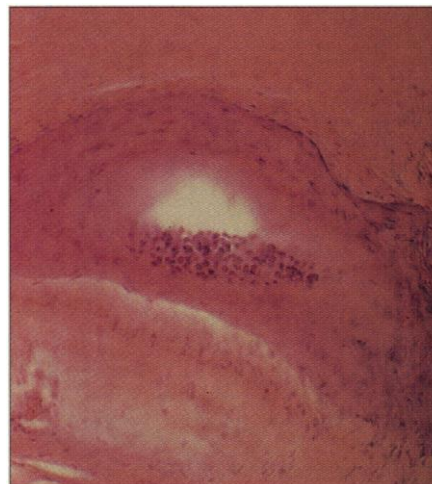
Specimen: Thin section of Jurassic Norphlet Sandstone, offshore Gulf of Mexico, showing quartz grains coated with black pyrobitumens.
Objective: Plan Apochromat 20x
Qualities: 3D perspective permits volume evaluation of infiltrated epoxy (blue).



PATHOLOGY

Specimen: Bone from rat recipient of limb transplant, undergoing lethal graft-versus-host disease. Approx. 40 μ m thick.
Objective: Plan Apochromat 20x
Qualities: 3D perspective reveals fibrous matrix bone spicule and bone canal with infiltrating mononuclear cells.

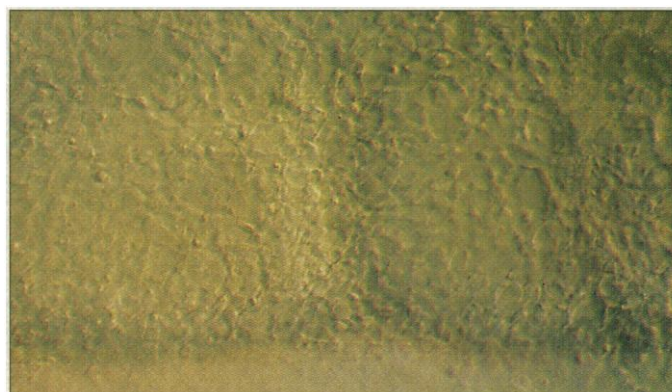
Charles W. Hewitt, Ph.D., UMDNJ –
Robert Wood Johnson Medical School



WHOLE MOUNTS

Specimen: Close up of two somites of living, unstained chick embryo (HH stage 11).
Objective: LWD 40x dry
Qualities: Even with such a thick sample, superb sharpness and high contrast of individual cells is evident.

Gary Greenberg, Ph.D.,
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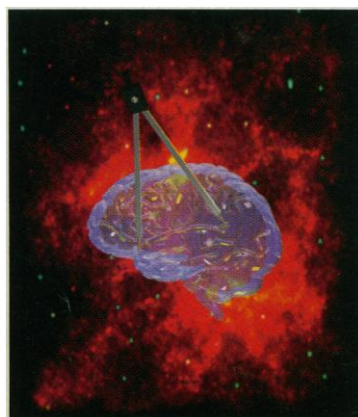
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New Alzheimer's test?



J. HUNTER DOWNS

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Neuroscience enters
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COVER

A male long-tailed manakin. In this species alpha and beta males cooperate in dual-mate courtship displays, but only the alpha partner mates during the partnership, which may last for several years. Long-term field data and genetic analysis of relatedness were used to ex-

clude the two leading explanations for such cooperation—kin selection and reciprocity. Instead, the cooperation is a form of mutualism, with direct but long-delayed benefits to the nonmating beta males. See page 1030. [Photo: Richard LaVal]



Molecular Computation of Solutions to Combinatorial Problems

L. M. Adleman

Efficient Neutralization of Primary Isolates of HIV-1 by a Recombinant Human Monoclonal Antibody

D. R. Burton, J. Pyati, R. Koduri, S. J. Sharp, G. B. Thornton, P. W. H. I. Parren, L. S. W. Sawyer, R. M. Hendry, N. Dunlop, P. L. Nara *et al.*

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Cooperative Display and Relatedness Among Males in a Lek-Mating Bird

D. B. McDonald and W. K. Potts

Molecular Maps of Red Cell Deformation: Hidden Elasticity and in Situ Connectivity

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Interaction of IL-2R β and γ_c Chains with Jak1 and Jak3: Implications for XSCID and XCID

S. M. Russell, J. A. Johnston, M. Noguchi, M. Kawamura, C. M. Bacon, M. Friedmann, M. Berg, D. W. McVicar, B. A. Witthuhn, O. Silvennoinen *et al.*

Functional Activation of Jak1 and Jak3 by Selective Association with IL-2 Receptor Subunits

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Role of TCR ζ Chain in T Cell Development and Selection

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A Potential Noninvasive Neurobiological Test for Alzheimer's Disease

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Coding of Visual Space by Premotor Neurons

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Horizontal Propagation of Excitation in Rat Visual Cortical Slices Revealed by Optical Imaging

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A Molecular Determinant for Submillisecond Desensitization in Glutamate Receptors

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GNDF: A Potent Survival Factor for Motoneurons Present in Peripheral Nerve and Muscle

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Functional Consequences of Posttranslational Isomerization of Ser⁴⁶ in a Calcium Channel Toxin

S. D. Heck, C. J. Siok, K. J. Krapcho, P. R. Kelbaugh, P. F. Thadeio, M. J. Welch, R. D. Williams, A. H. Ganong, M. E. Kelly *et al.*

Spermine and Spermidine as Gating Molecules for Inward Rectifier K⁺ Channels

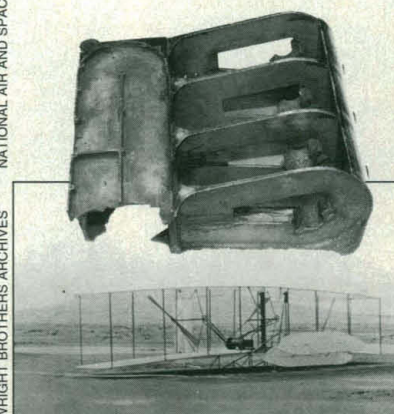
E. Ficker, M. Taglialetela, B. A. Wible, C. M. Henley, A. M. Brown

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Stellar Variability and Global Warming

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The case of the Wrights' engine



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Toxic configurations

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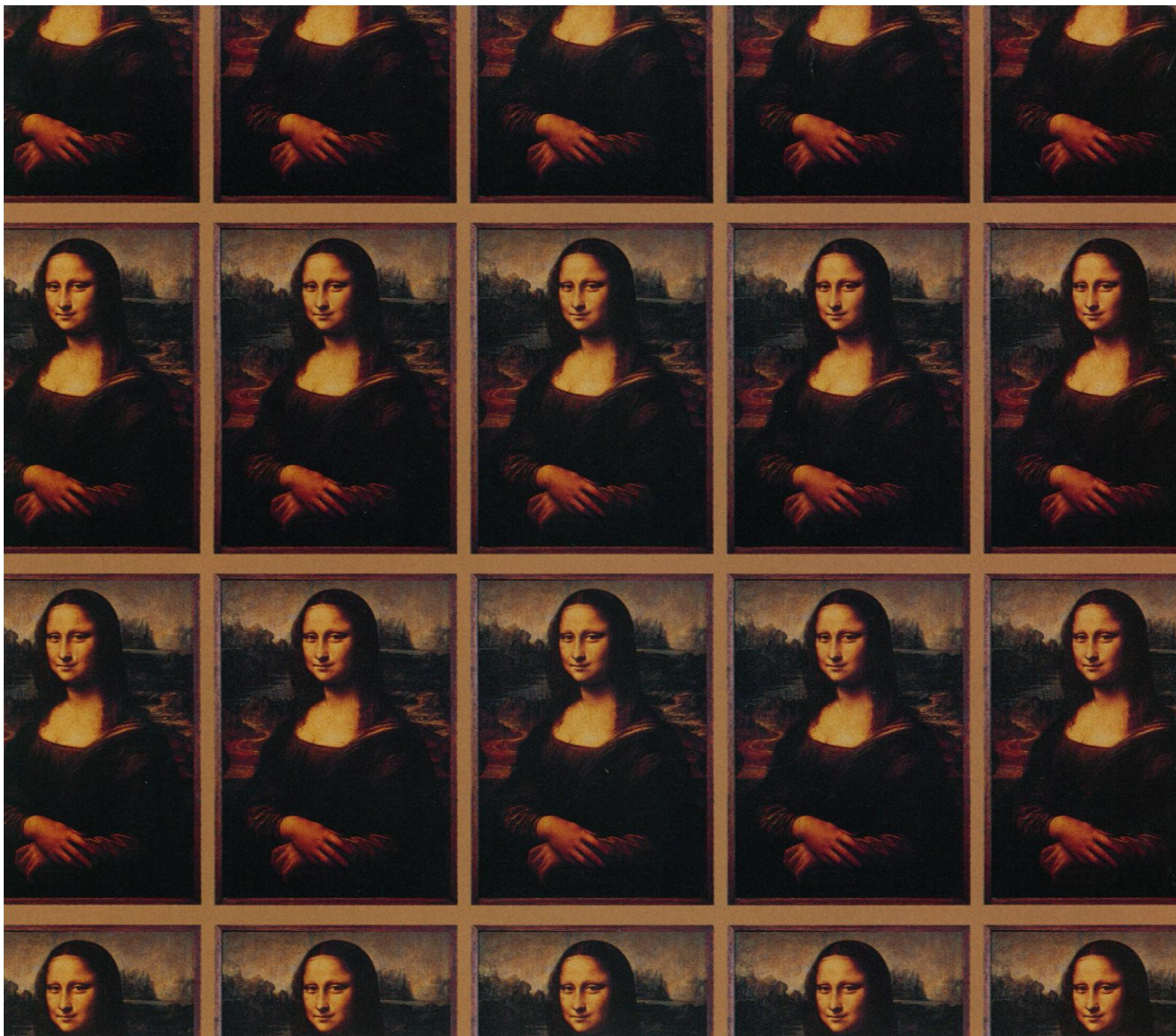
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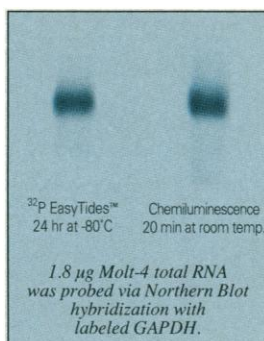
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The Wrights' stuff

The 1903 Wright *Flyer* pioneered not only flight but also the use of a lightweight aluminum-copper alloy for the engine crankcase. In 1909, Wilm showed that the hardness of such alloys could be increased by a thermal treatment that caused some of the copper to precipitate. Gayle and Goodway (p. 1015) present electron micrographs from samples of one of the Wrights' engines, made years before Wilm's demonstration, showing similar "precipitation hardening." This inadvertent achievement resulted, say the authors, from the Wrights' efforts to improve their castings by preheating the molds.

Singles seen

Operating a confocal fluorescence microscope at the optical diffraction and using highly efficient photon detection have allowed Nie *et al.* (p. 1018) to study the diffusion and emission of individual molecules in solution at room temperature. The detection volume and speed and concentration ranges ensured the observation of single molecules. Among the applications presented is an analysis of single-molecule fluorescence.

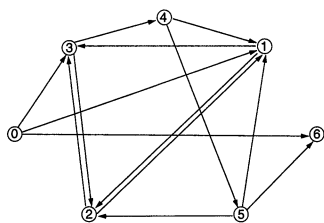
Biomolecular computing

Computational complexity depends on how long an algorithm must run in relation to the size of the problem. For example, the Hamiltonian path problem (given a directed graph, find if there is a path that visits each vertex exactly once) demands impractical amounts of computer time for even modest graphs. Adleman (p. 1021; see the Perspective by Gifford, p.

Getting proteins into chloroplasts

Chloroplast proteins that are synthesized in the cytoplasm but destined to function within the chloroplast require translocation across the inner and outer membranes of the chloroplast. To explore the transport mechanism, Schnell *et al.* (p. 1007) and Kessler *et al.* (p. 1035) isolated proteins from the chloroplast outer membrane that associate with transported proteins as they begin to traverse the outer membrane. One of the associated proteins is similar to the heat shock protein hsp70 and another, a 75-kilodalton protein that appears to be embedded in the outer membrane, could form all or part of a protein-conducting channel. Two guanosine triphosphate-binding proteins were also associated with import intermediates. The authors present a model for how these components might regulate and facilitate protein transport.

993) reports a solution to this kind of problem by means of molecular computing: Vertices of a graph are represented as short DNA sequences. A di-



rected path between two points is represented by an oligonucleotide, so that a full graph could be encoded in longer DNA chains. The "computations" required only standard protocols and reagents.

Jak kinases and T cells

Several signaling steps can influence T cell stimulation; three reports focus on the role of the interleukin-2 receptor (IL-2R) chains and the Jak1 and Jak3 kinases in this process. Bousiotis *et al.* (p. 1039) show that T cells can avoid moving into a state in which they do not respond to antigen (anergy) by signaling through the common γ (γ_c) chain of IL-2R, IL-4R, and IL-7R. Such signaling also caused Jak3 to be tyrosine-phos-

phorylated. Russell *et al.* (p. 1042) show that γ_c mutations that result in severe combined immunodeficiency decreased association between γ_c and Jak3. Miyazaki *et al.* (p. 1045) provide functional evidence that Jak3 is needed for the transduction of an IL-2 signal through the cell.

Primary goal

Developing a vaccine against infection by human immunodeficiency virus-type 1 (HIV-1) has been hampered by the inability of the antibodies that have been raised to neutralize primary isolates of HIV-1. Burton *et al.* (p. 1024) describe a recombinant antibody directed at the CD4 binding region of gp120 that is highly effective at neutralizing a broad spectrum of HIV-1 isolates from infected individuals at concentrations that could be attained in vivo.

Staying connected

The significance of connectivity in the brain can be difficult to assess because experimental techniques usually address neurons singly. Tanifuji *et al.* (p. 1057) used voltage-sensitive

dyes and optical imaging to examine the activity of multiple neurons in slices of visual cortex. Neuronal excitation propagated first in the vertical direction (equivalent to perpendicular to the surface of the brain) through the layers of cortex and then spread horizontally. Vertical cuts through some of the layers eliminated direct horizontal pathways, as expected, but excitation followed a vertical path to an undamaged layer before spreading horizontally, suggesting the potential importance of reciprocal neural connections.

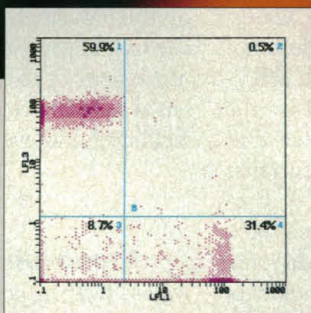
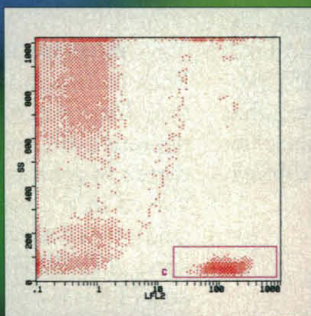
Arm controlled

Both body position and visual stimuli can evoke responses from neurons in the ventral premotor cortex of primates, an area involved in the preparation and guidance of movement. Graziano *et al.* (p. 1054) show that the area of the visual field that can stimulate these neurons depends on the movement of the arm of the monkey rather than on the movement of its eyes. A limb-based coordinate system would facilitate hand-eye coordination.

Removable gate

Inward rectifier potassium channels rectify even in the absence of Mg^{2+} ions, yet excised patches containing these channels lose their time-dependent inward-rectifying response. Ficker *et al.* (p. 1068) show that nanomolar concentrations of the polyamines spermine and spermidine can restore these currents. Such concentrations are well within those found in the *Xenopus* oocytes used in these studies, which suggest that these cations may be acting as voltage-dependent channel blockers.

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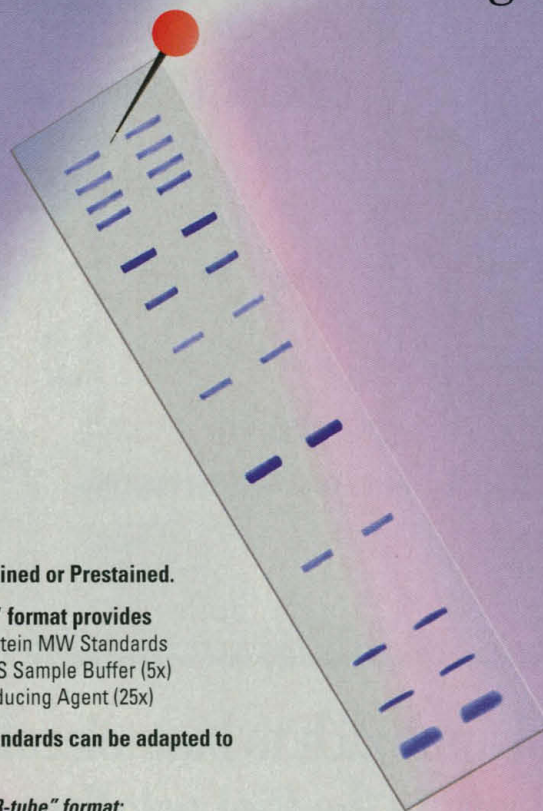
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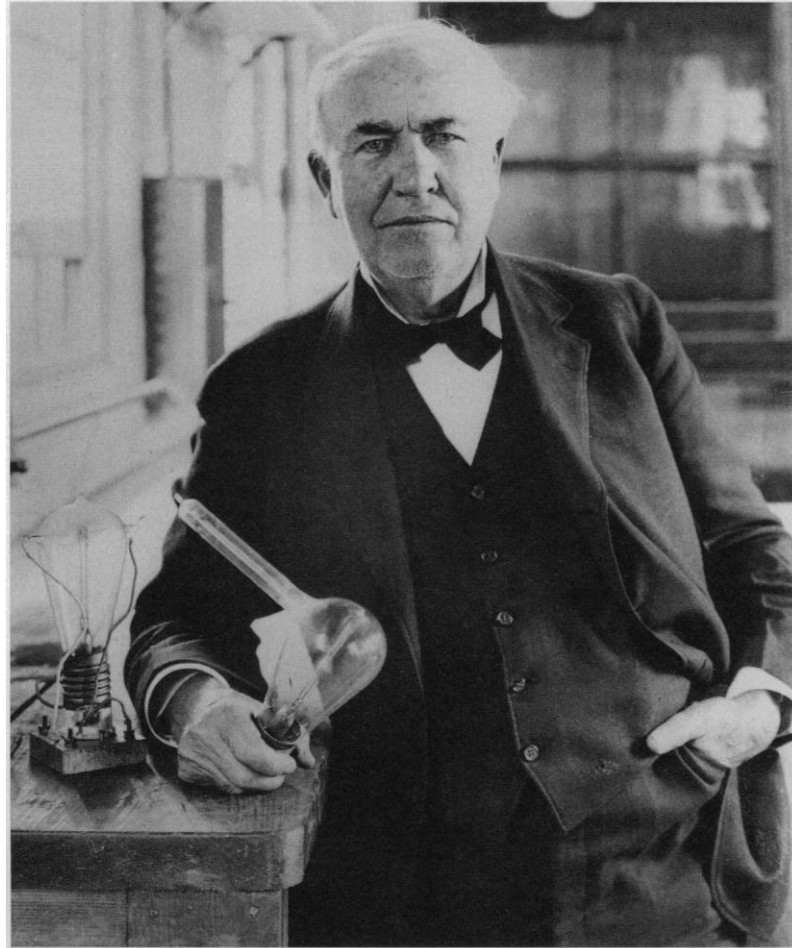
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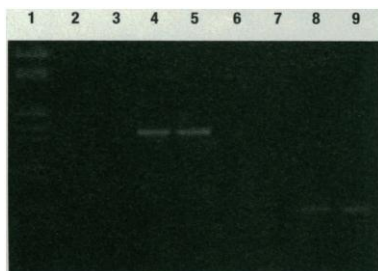
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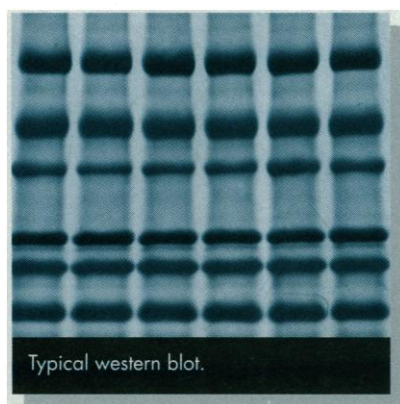


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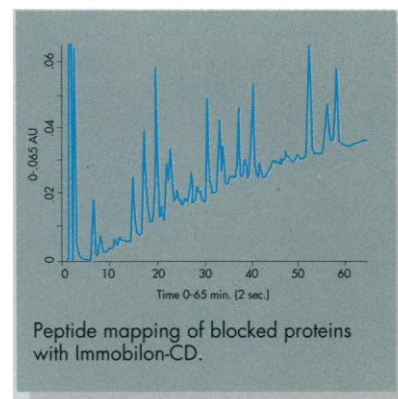
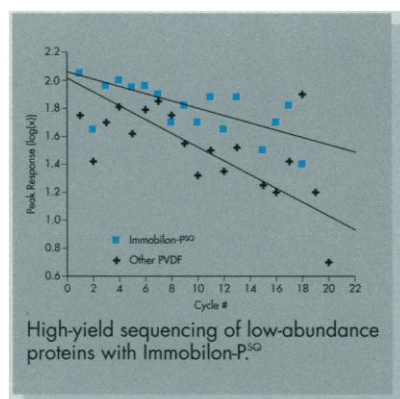
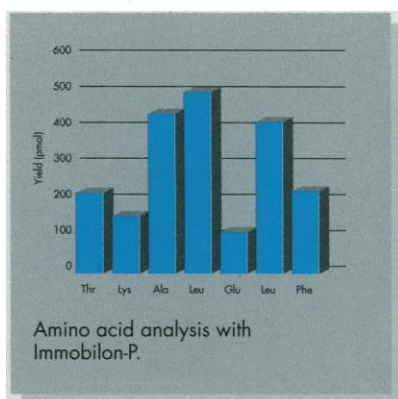
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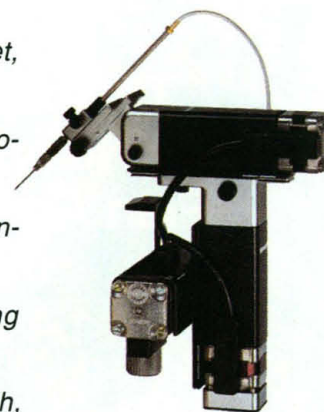
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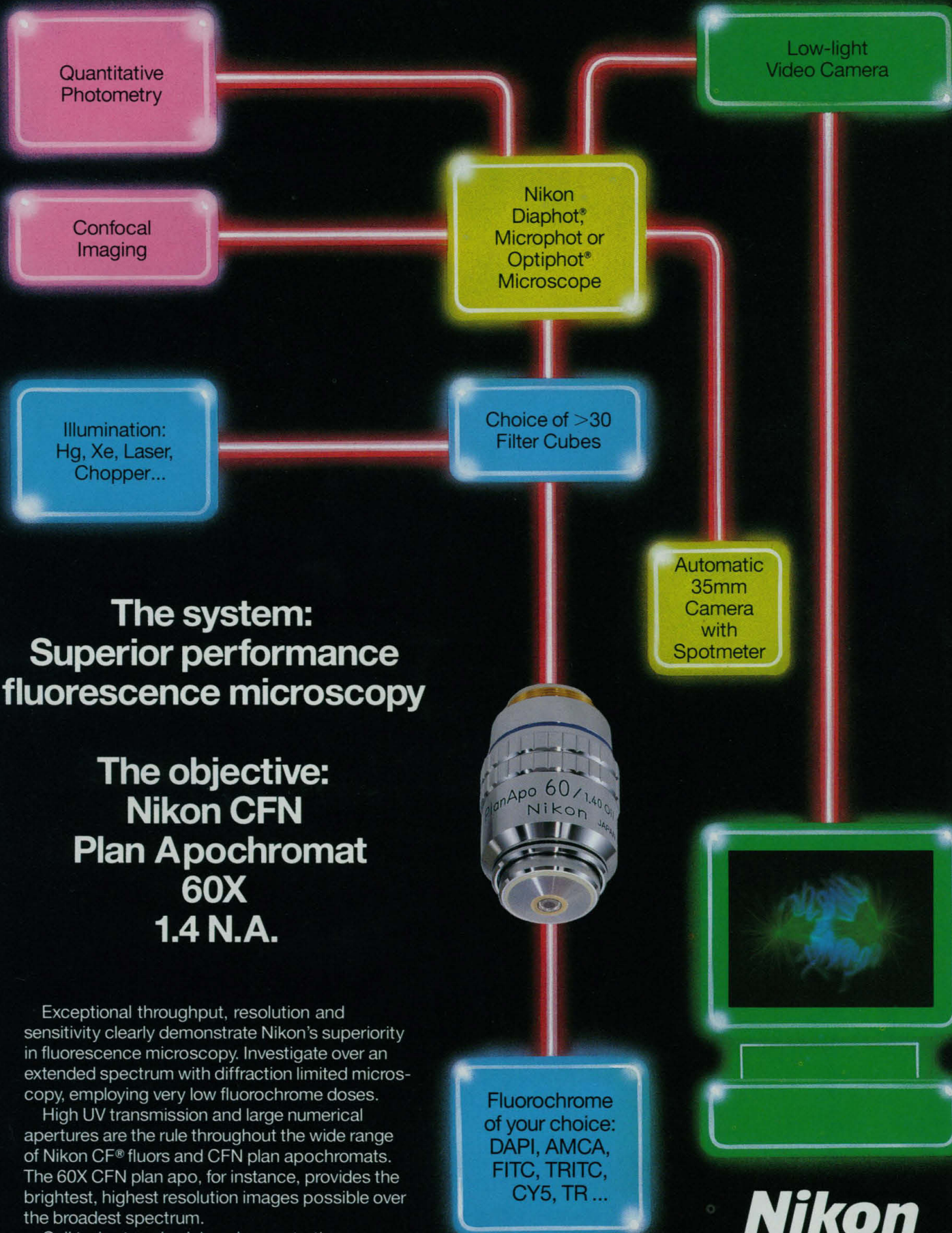
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References

1. Fodde, R., and Loosekoot, M., *Human Mutation*, 3, 83, (1994).
2. Fischer, S.G. and Lerman, L.S., *Proc. Natl. Acad. Sci., U.S.A.*, 80, 1579 (1983).
3. Borresen, A. L., et al., *Proc. Natl. Acad. Sci., U.S.A.*, 88, 8405 (1991).

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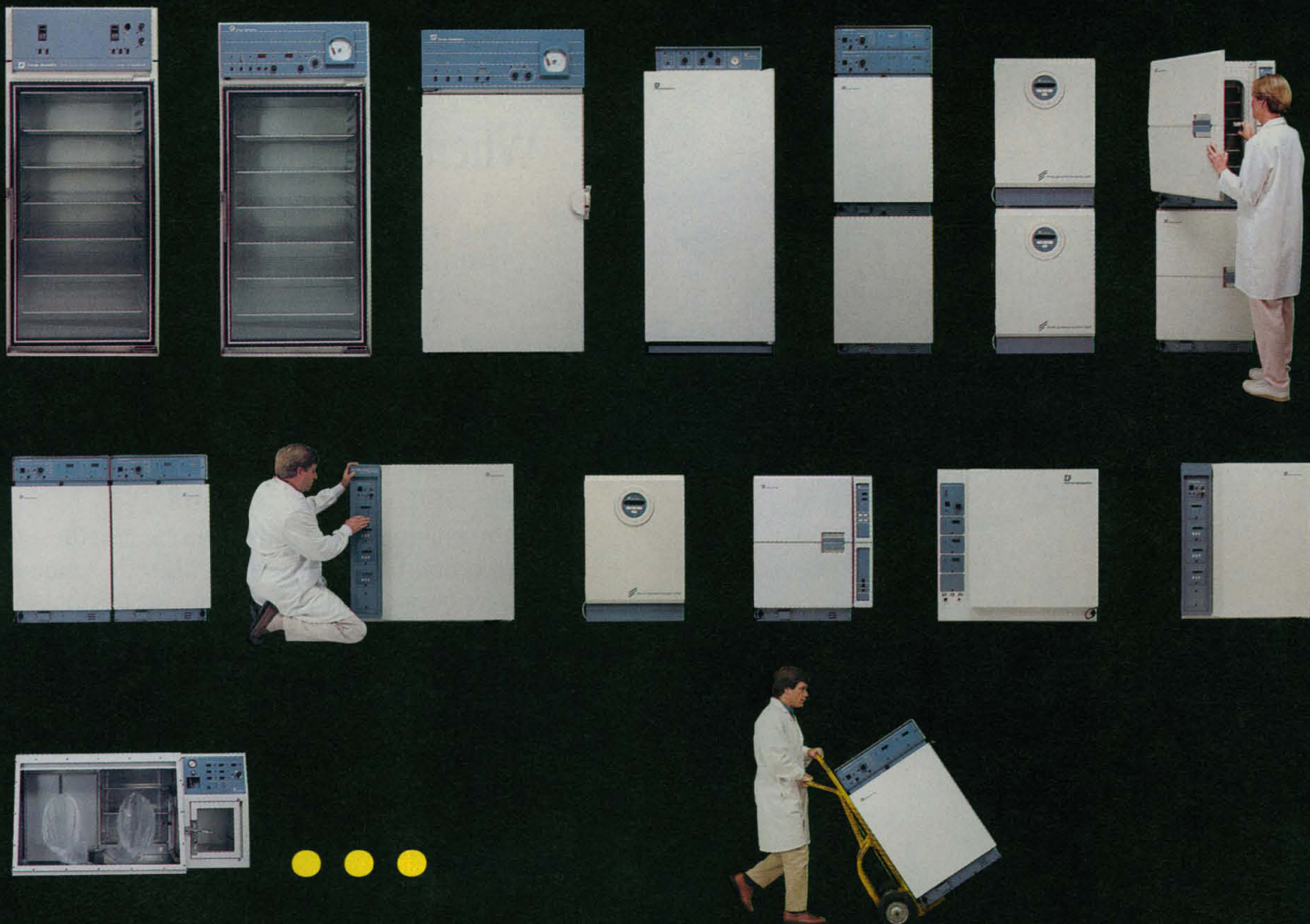
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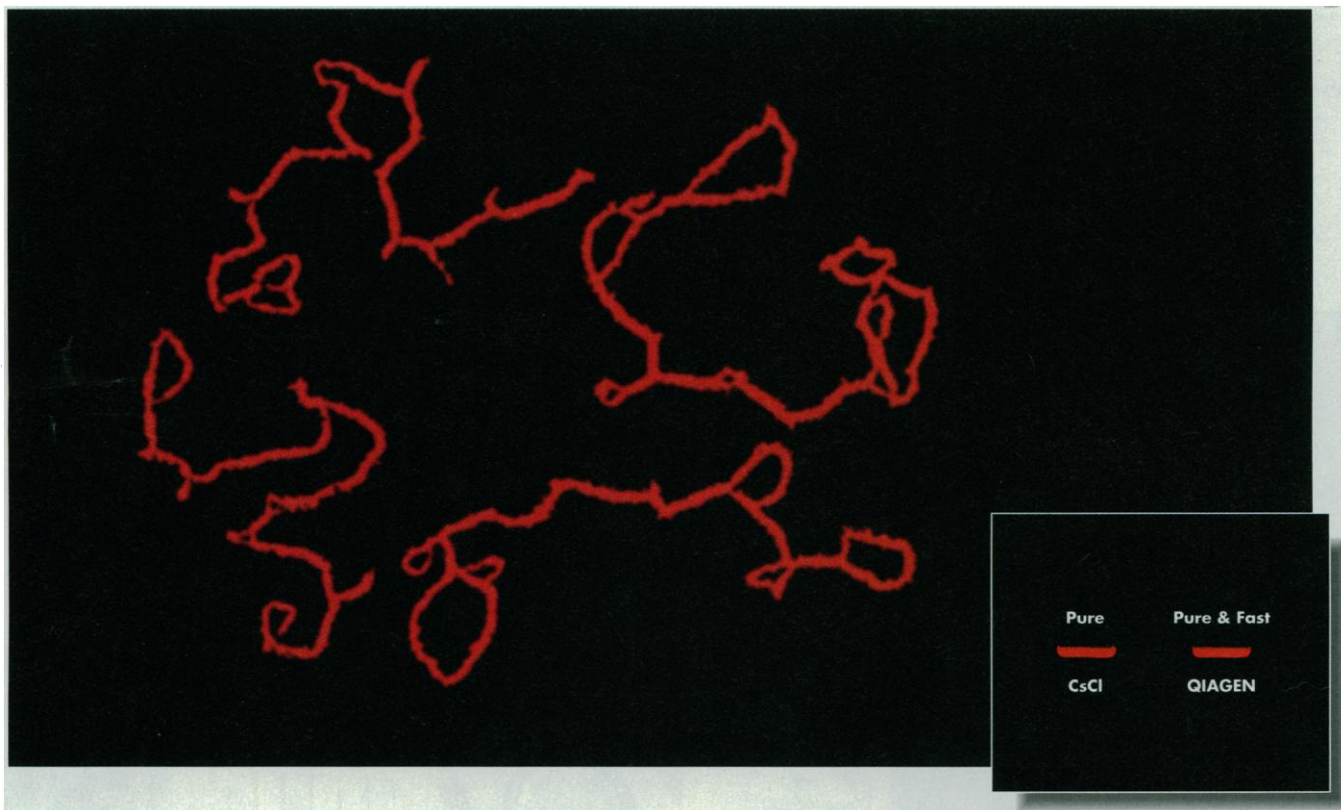
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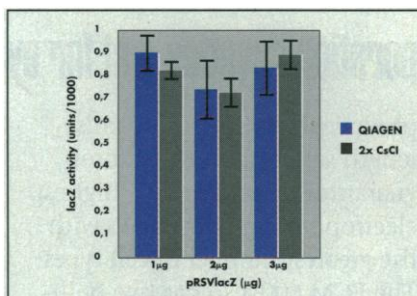


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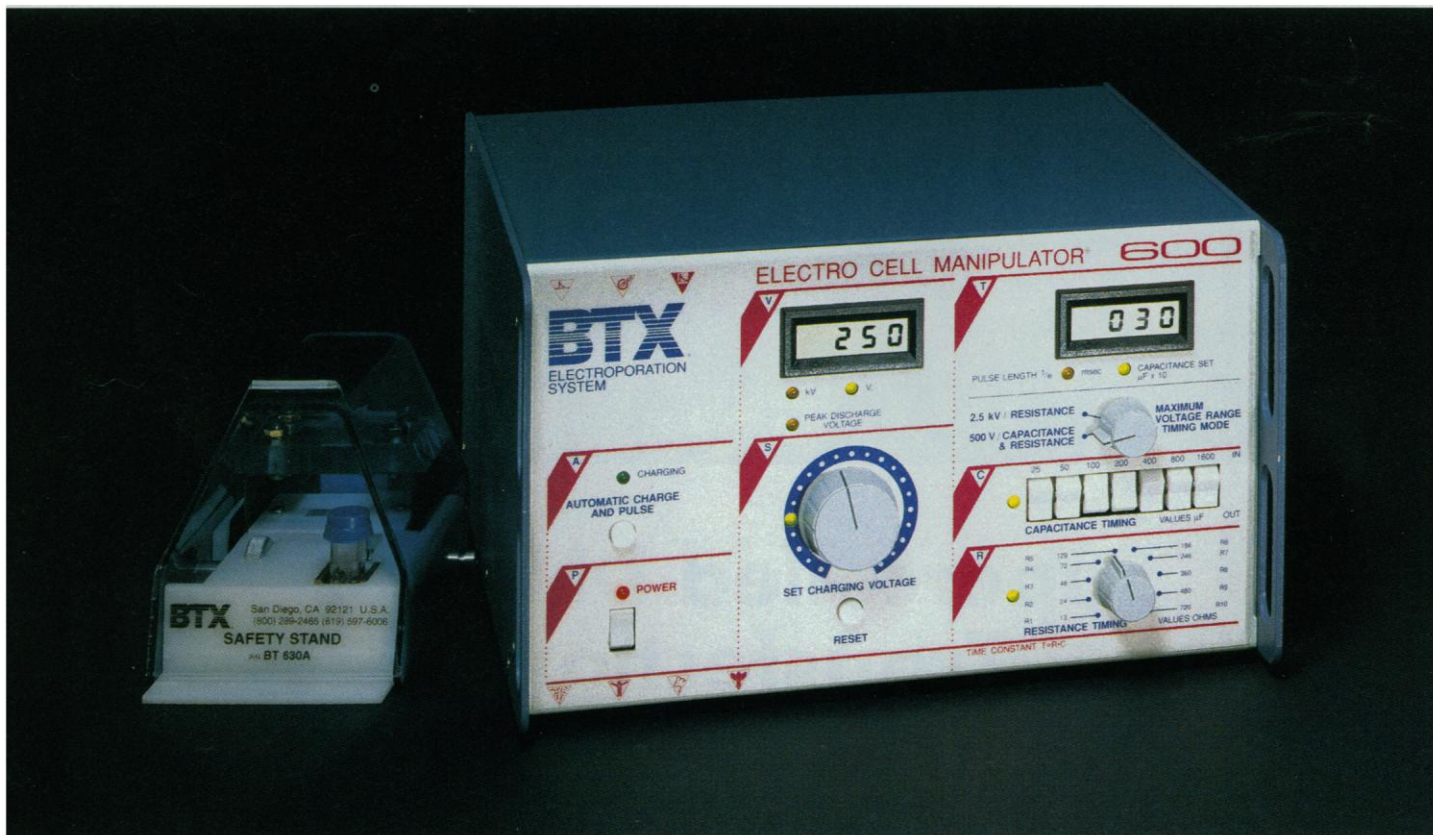
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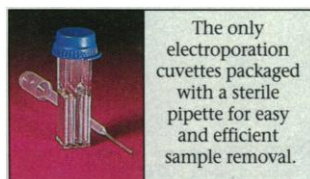
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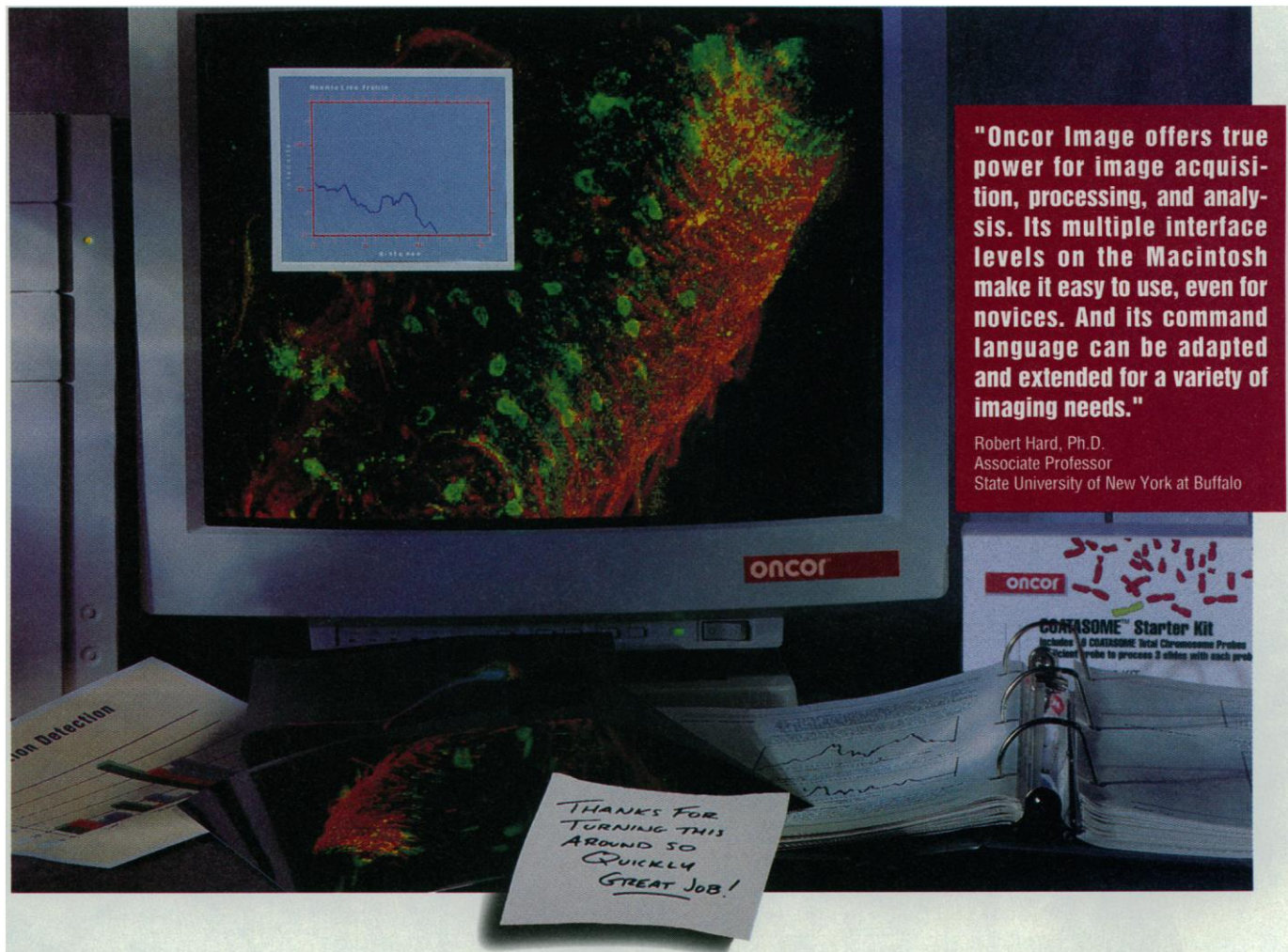
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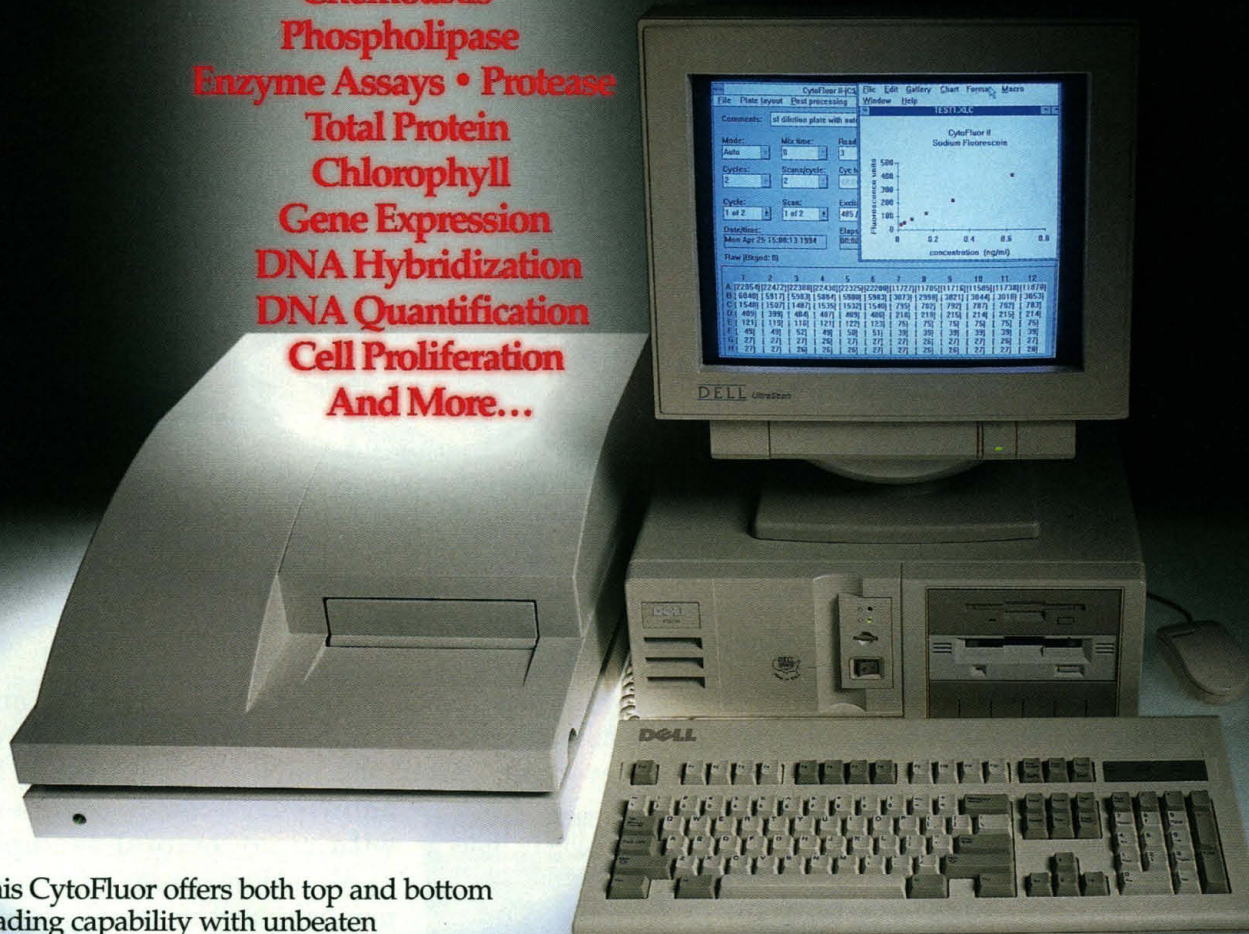
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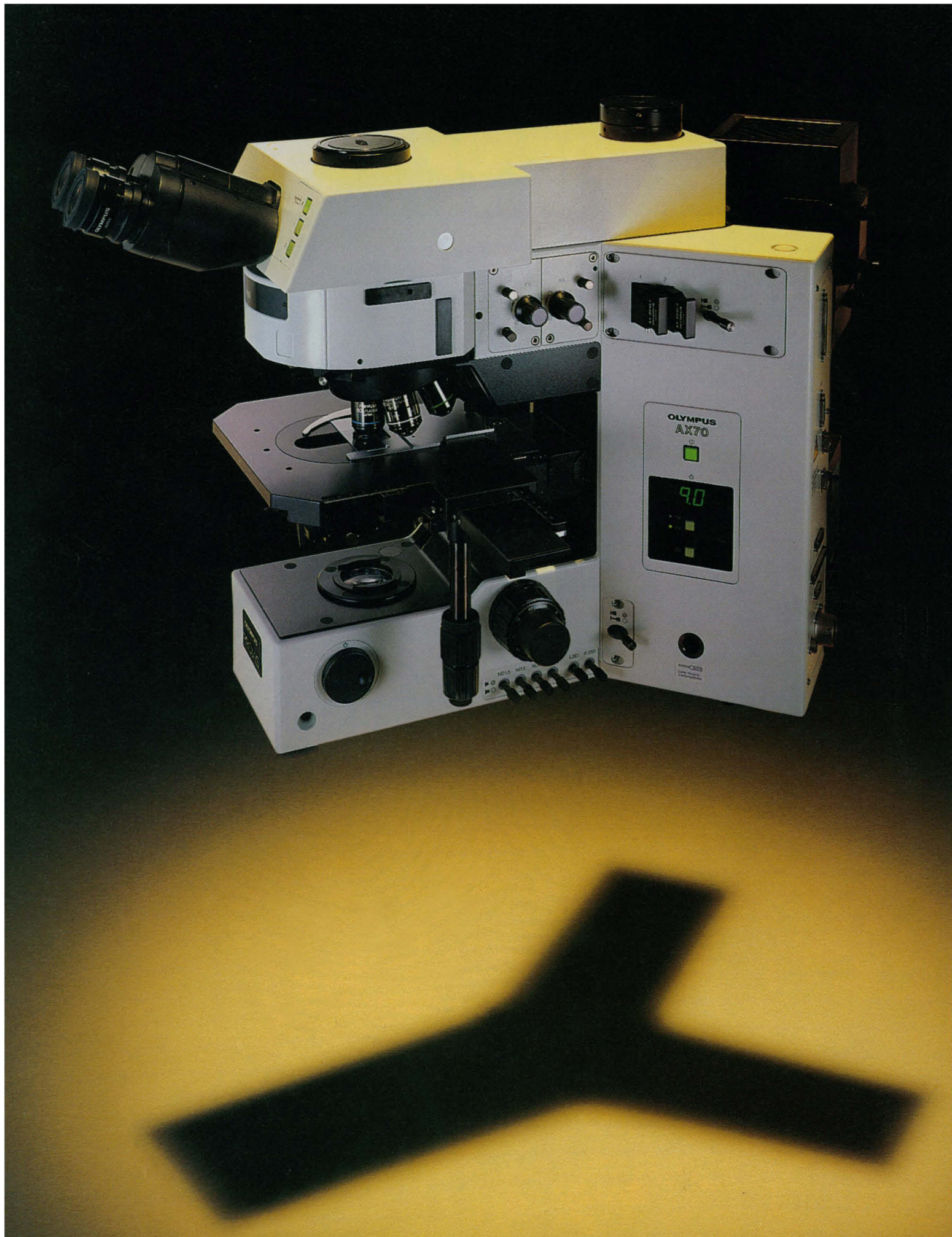
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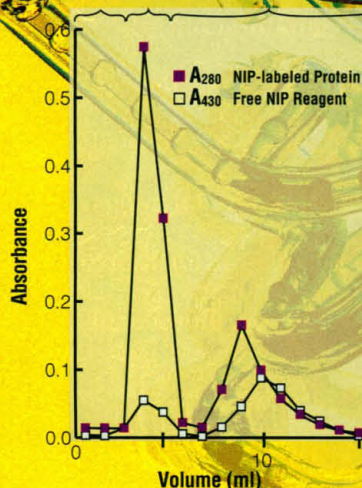
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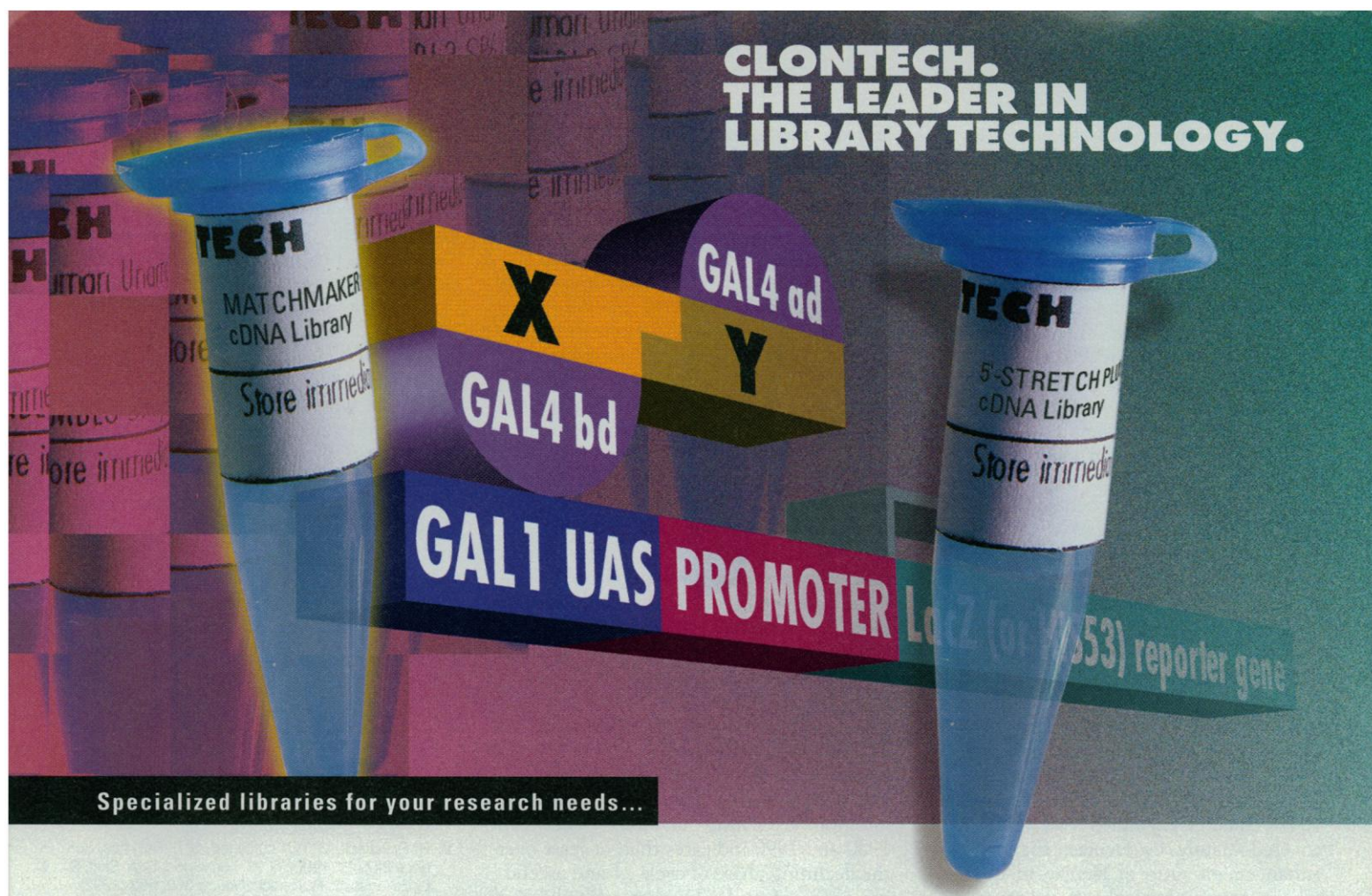
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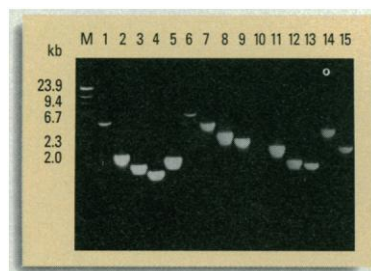
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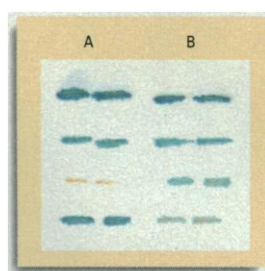


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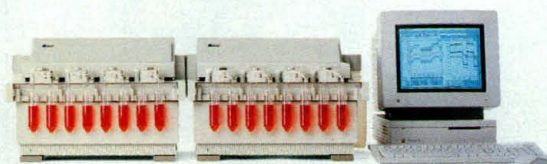
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1. *Science* 257, 1906-1912, (1992) 2. *J. NIH Research* 5, 69, (1993)

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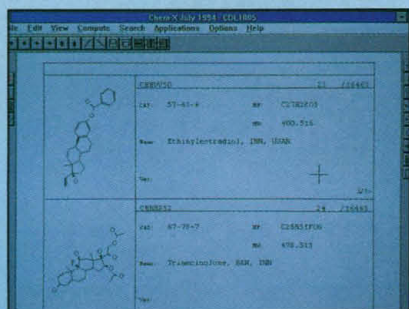
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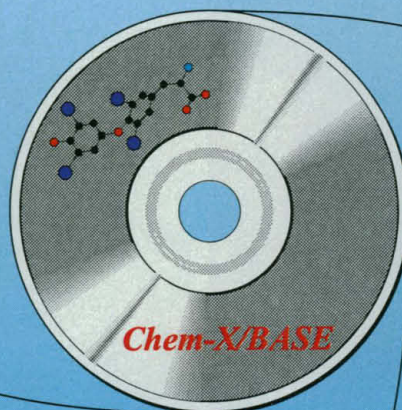
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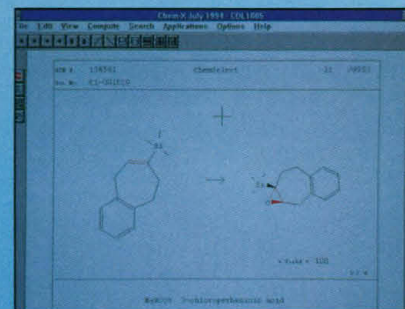
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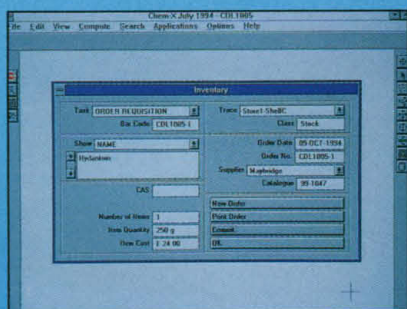
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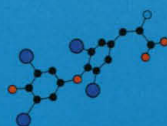
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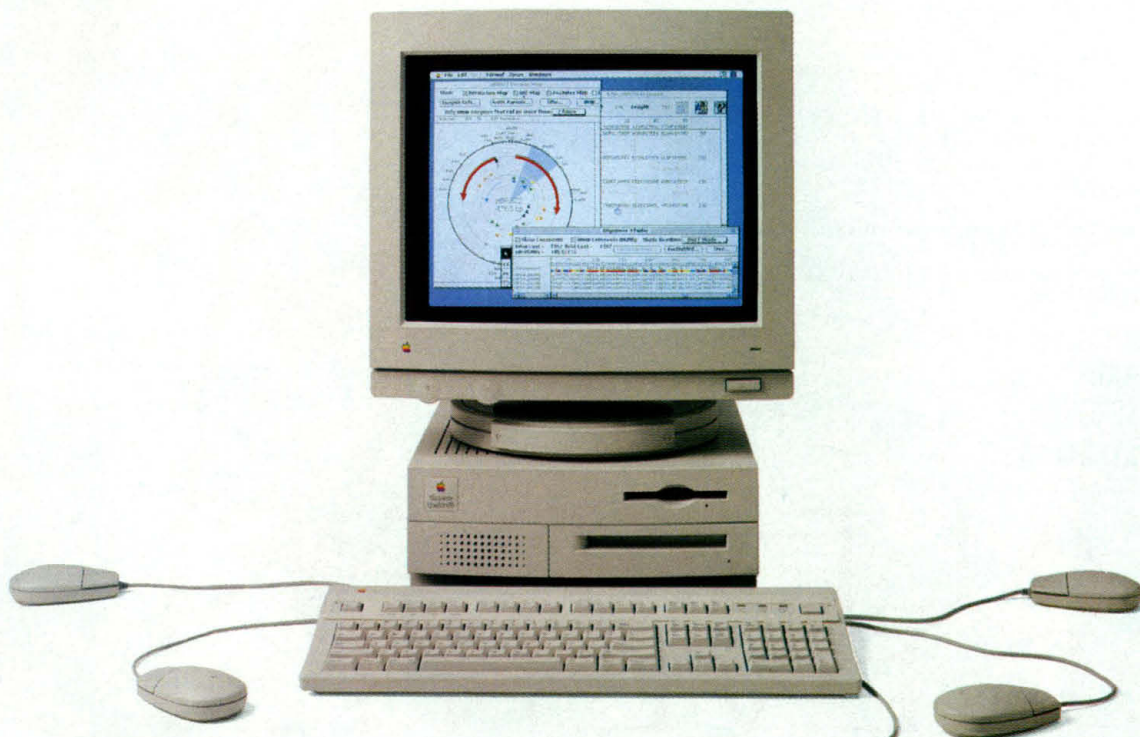
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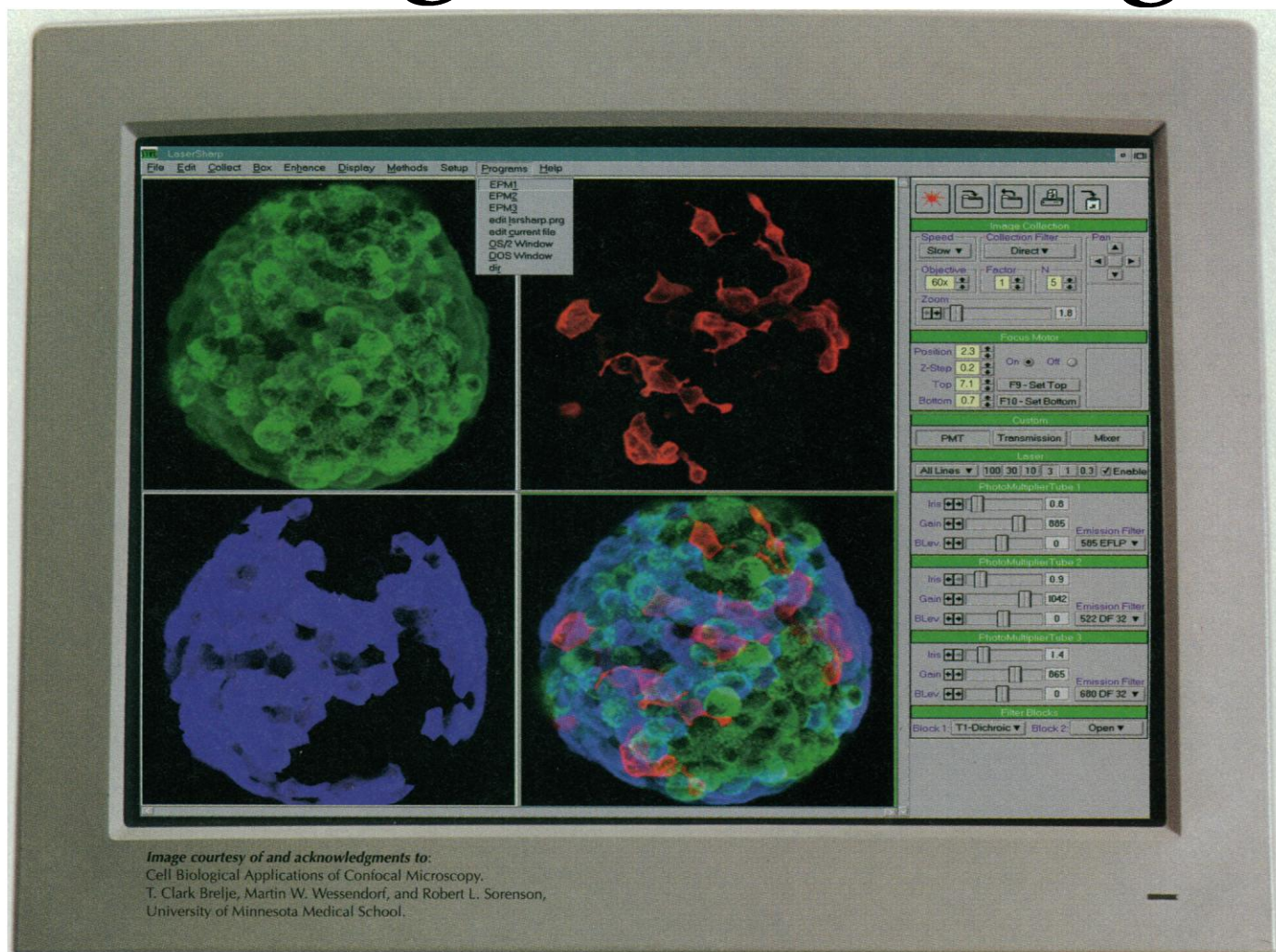
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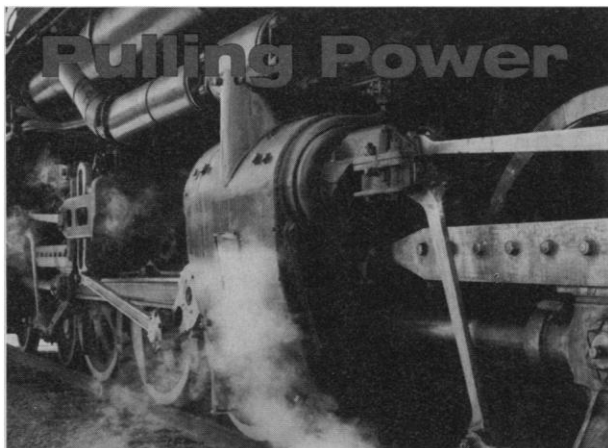
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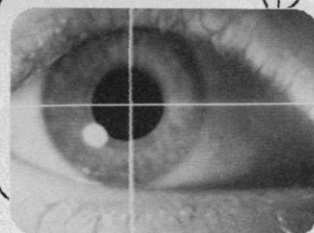
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Mutation detection

a ACGT
G A

b ACGT
A/G A

PAH codon 1: met → ile

Elken, H.G. et al., Human Mutation 1992; 1: 388-391

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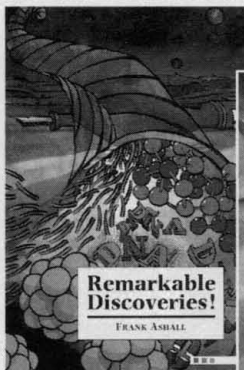
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