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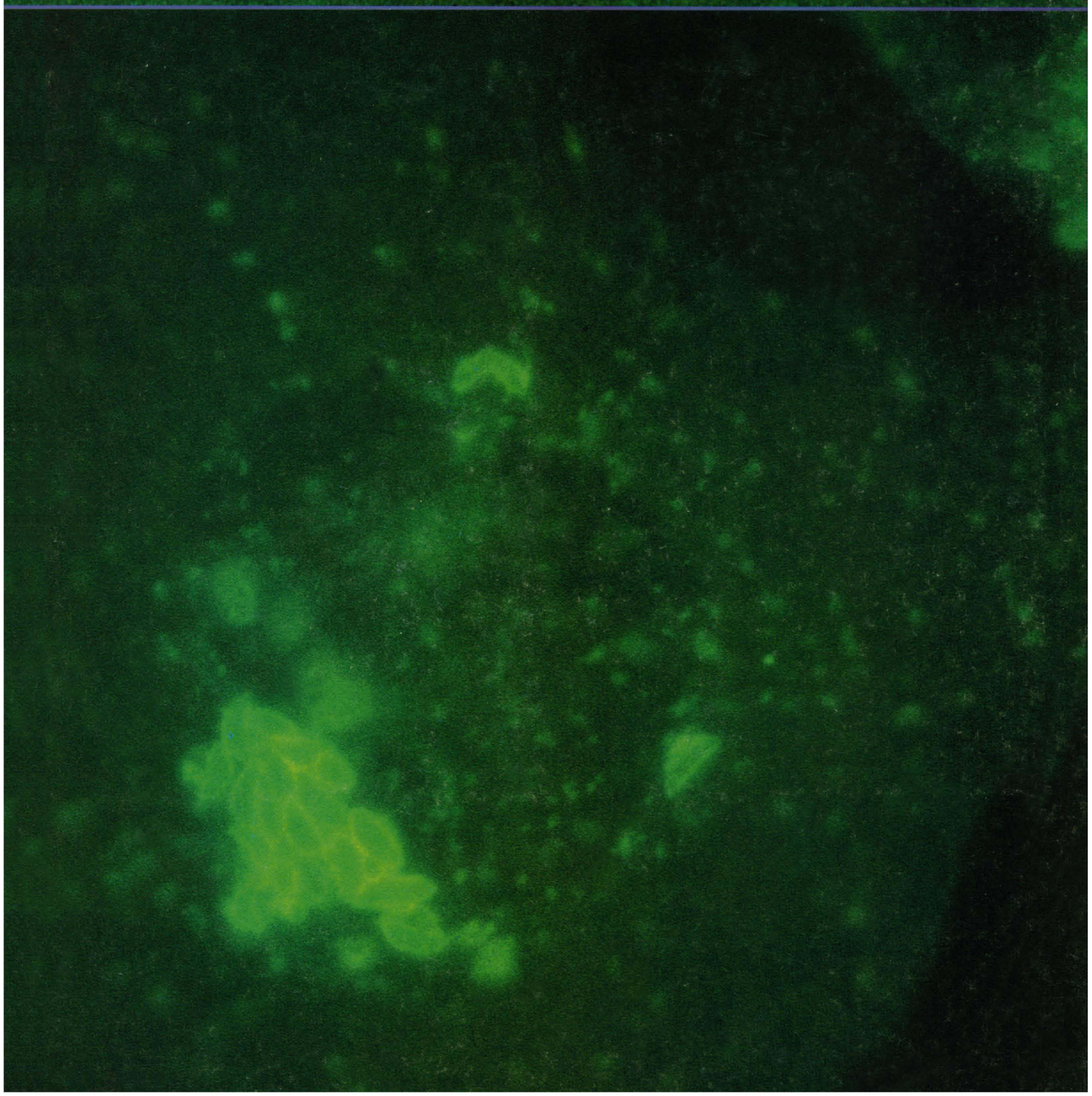

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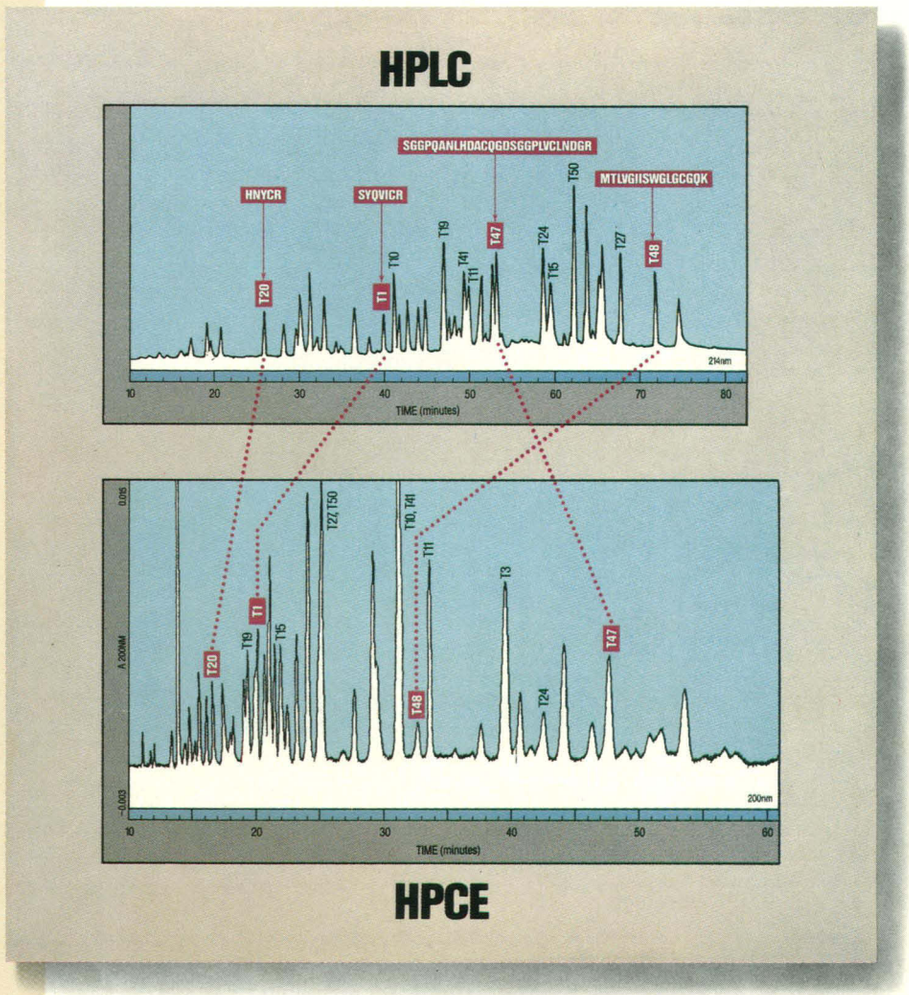

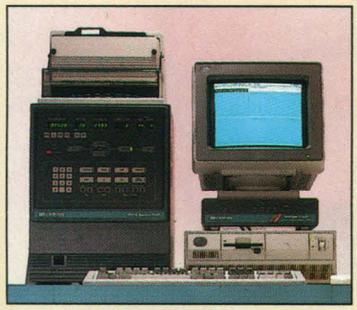

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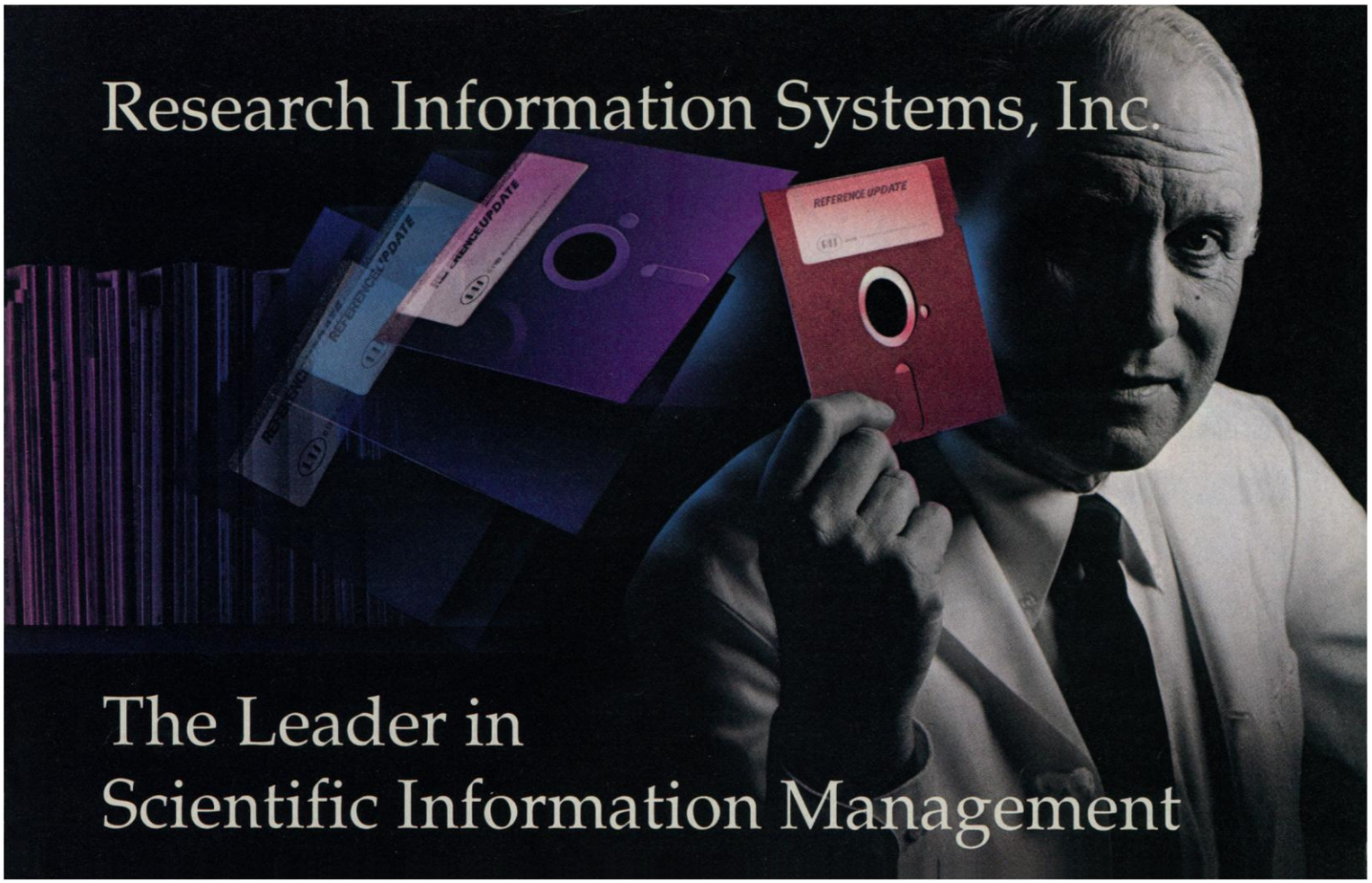
Chromatogram of a tryptic digest of recombinant tissue plasminogen activator by reversed-phase HPLC in phosphate-acetonitrile buffer.

Electropherogram of the same tryptic digest (35 nl; 250 μg/mL) in 100 mM phosphate with pH 2.5.



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COVER Immunofluorescence photomicrograph of vacuoles containing the parasite *Toxoplasma gondii* inside a Chinese hamster ovary cell stably transfected with murine Fc receptors. Infected cells were stained with an antibody to a lysosomal glycoprotein (lgp). Only parasites coated with antibody before internalization reside in lgp-stained vacuoles, indicating that route of parasite entry determines fusion competence of the vacuole. See page 641. [Photograph by Philippe Male, Yale University]

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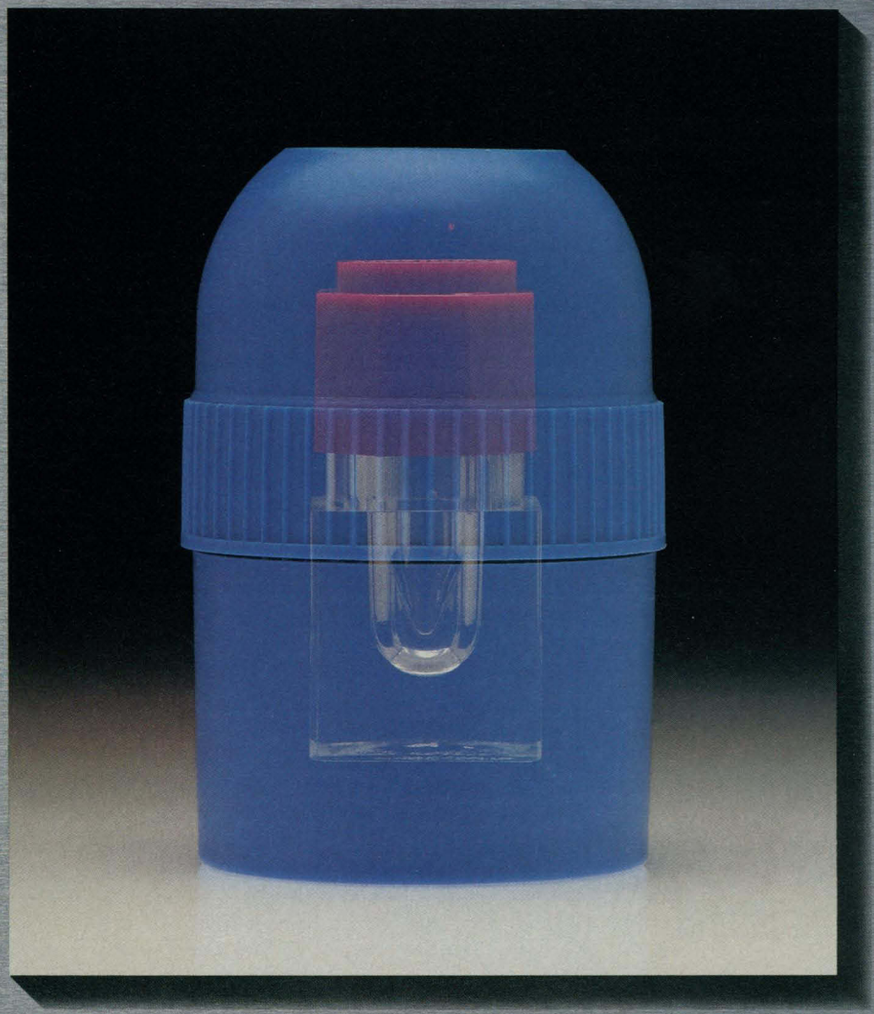

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Ice

A new ice age is dawning. Ice is a methamphetamine; its name comes from its physical form—sheet-like transparent crystals. In Hawaii ice has already surpassed cocaine in popularity, and its use is growing in the western United States. The ice habit is hard to kick, and its effects are devastating. The drug is typically smoked because more of it gets to the brain faster through inhalation than through injections. A high from ice may last many hours; after the initial flash users can become violent or psychotic; later, they sleep for long periods and then wake up depressed and start smoking again. Already a $3-billion expanding industry has developed in the United States around the manufacture and sale of ice; because this is a synthetic drug, it could in theory be made in limitless amounts. Cho provides an overview of the ice story—the history of its use, the neurophysiologic and biochemical processes that account for its effects, how it is metabolized by the body, and how it compares with cocaine (page 631). Much is already known about the drug but the big question is how to stop its use and spread.

Inhibiting vacuole fusion

THE protozoan *Toxoplasma gondii* is an intracellular parasite that lives in vacuoles (phagosomes) inside host macrophages and other nucleated cells (cover). Vacuoles that contain these organisms do not fuse with lysosomes (sacs of digestive enzymes) and therefore the parasites are not destroyed. Why is membrane fusion inhibited? Joiner *et al.* conclude that, at the time that the tachyzoite (the invasive stage of the parasite) is ingested, some irreversible change is made in the phagosome membrane such that it is incapable of fusing with other membranes (page 641). Perhaps the phagosome fails to make or display membrane signals needed for communicating with other vacuoles. (In contrast, if the parasites are coated with antibodies and enter the cell through antibody receptors, fusion with other vacuoles occurs.) The block to fusion is permanent; even if the tachyzoites die in the phagosomes, vacuole fusion does not occur. This system is ideal for analyzing necessary and sufficient components of membrane recognition and fusion and may lead to new therapeutic approaches for treating toxoplasmosis and related parasitic diseases.

Memory glass

WHEN a crystal of $AlPO_4$ berlinite is put under high pressure (18 gigapascals) it turns into an amorphous glassy substance; when the pressure is then released below 5 gigapascals, the material reverts to its original crystal structure with its original crystallographic orientation. Kruger and Jeanloz call this material memory glass because the disordered state—the glass has no diffraction pattern—quite surprisingly retains a memory of the structure it had when orderly (page 647). They suggest that the high-pressure conditions ablate the crystal's long-range order; but, unlike ions in glasses that have been formed at high temperatures, the ions in the memory glass have moved only minute distances from their positions in the original crystal, constrained from greater movement by the low (300 K) reaction temperatures. As pressure is released, the ions slip back into the state of lowest free energy, which happens to put them back where they were in the original single crystal.

Clue to cellular senescence

THE retinoblastoma gene, which is associated with eye tumors and several other types of cancers, may have a direct role in the senescence of human cells. Senescent fibroblasts are arrested in the G_1 phase of the cell cycle and even with stimulation by serum they can no longer enter the synthetic (S) phase of the cycle and go on to proliferate (page 666). Quiescent young cells are also arrested in G_1, but exposure to serum stimulates them to enter S. In both cell types the retinoblastoma protein $p110^{RB}$ is unphosphorylated; it gets phosphorylated by serum in the quiescent cells but not in those that are senescent. Stein *et al.* propose that a causal relationship may exist between failure to phosphorylate $p110^{RB}$ and failure to enter S. Results from other studies indicate that certain viral oncogenes are able to bind unphosphorylated $p110^{RB}$ in senescent cells and push them into S; these oncogenes therefore can inactivate the inhibitory function of the retinoblastoma protein in senescent cells (and in quiescent cells) much as phosphorylation does in quiescent ones.

Making binocular connections

CONNECTIONS in the nervous system are plastic during periods in development called "critical periods." For example, the critical period for establishing binocular vision in the frog stretches from the late tadpole stage to the early juvenile stage; during this time external stimuli affect the patterns of connections that can be made. In each tectal lobe of the midbrain, projections from the two eyes get aligned to produce a binocular optic map. If the two are not in register (a condition that can be brought about experimentally by rotating one eye), axons from the ipsilateral eye (the one on the same side as the tectum) adjust. After the critical period, such adjustments are no longer possible. Udin and Scherer provide evidence that decreased functioning of glutamate receptors may contribute to the loss of axon plasticity after the critical period (page 669). They find that ipsilateral axons can be made plastic again by exposure to a substance (NMDA) that stimulates these receptors. A model is presented that shows how glutamate, new visual input, and stabilization of axons may be linked to each other.

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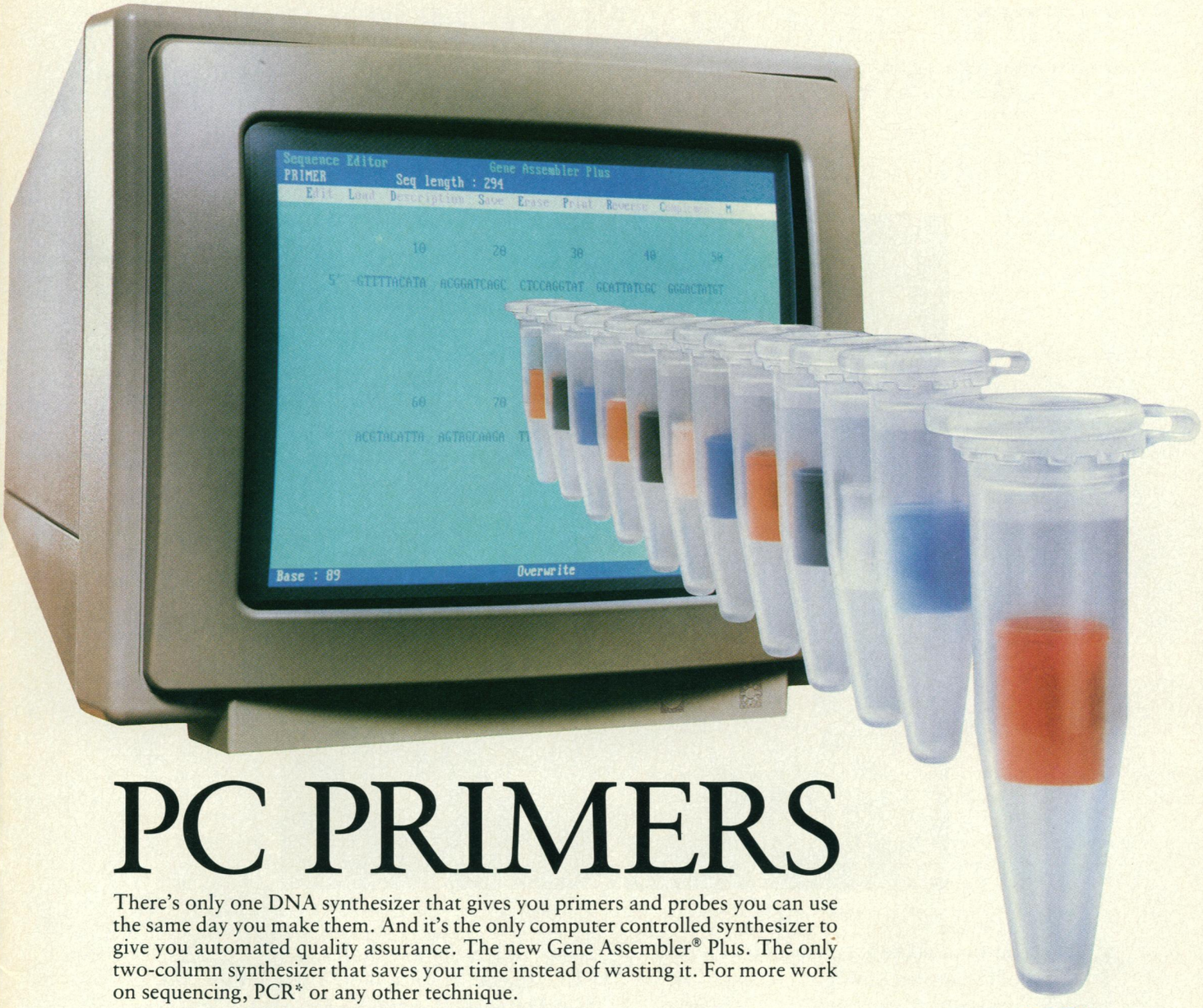

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