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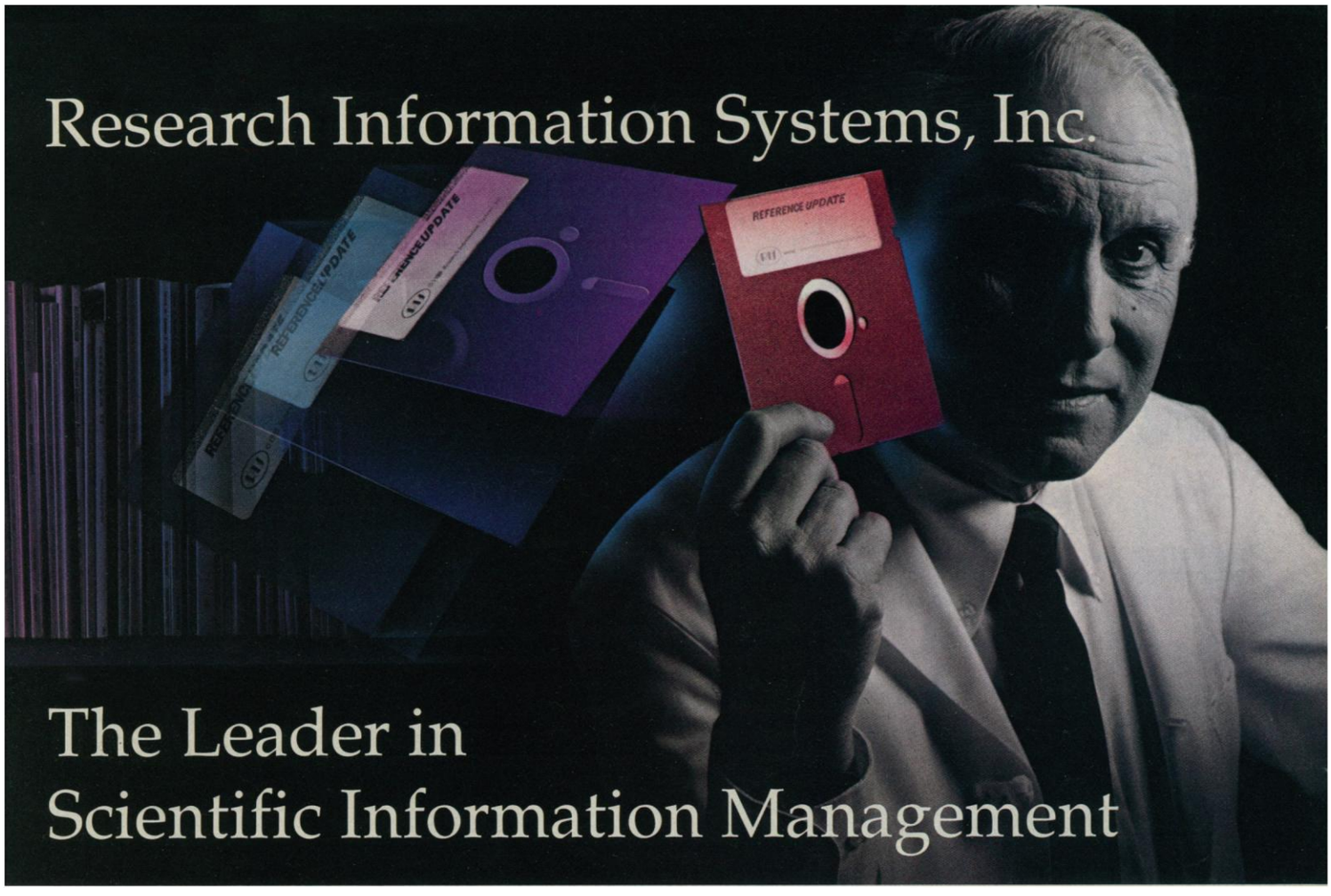

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■ The American Association for the Advancement of Science was founded in 1848 and incorporated in 1874. Its objectives are to further the work of scientists, to facilitate cooperation among them, to foster scientific freedom and responsibility, to improve the effectiveness of science in the promotion of human welfare, to advance education in science, and to increase public understanding and appreciation of the importance and promise of the methods of science in human progress.

COVER An Asian cobra. Snake and insect venoms provide experimentalists with proteins for the study of biological action at the membrane surface. Venom phospholipase A_2 from a Chinese cobra, which is closely related to the one shown here, forms crystals of an inhibitor complex, the structure of which reveals the molecular mechanism of interfacial catalysis. See page 1560. [Photograph by Jessie Cohen, courtesy of National Zoological Park, Smithsonian Institution]

Book Reviews

Products & Materials

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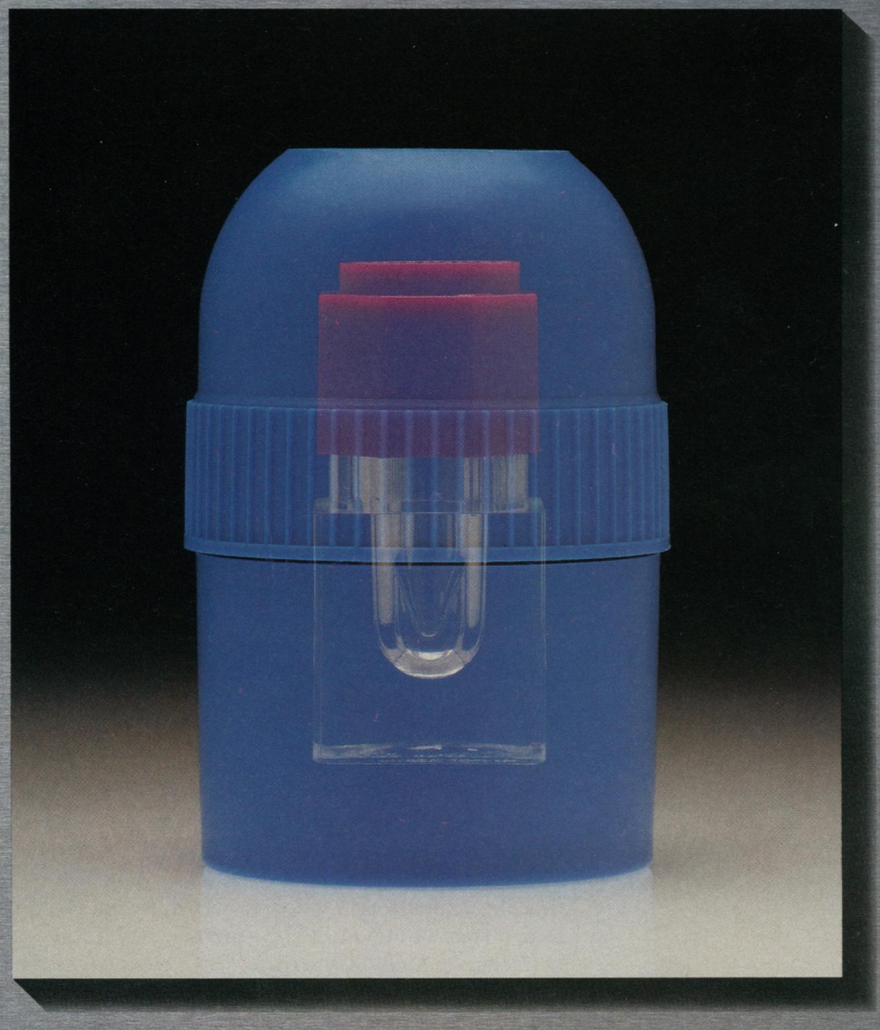

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Catalytic mechanism

PHOSPHOLIPASES are lytic enzymes that cleave aggregated phospholipids at membrane surfaces. They are abundant in mammalian pancreatic juice and in the venom of snakes and insects. Because the catalytic activities of phospholipases result in the release of substances that trigger inflammatory reactions, insights into how these enzymes work might clarify the nature of destructive inflammatory responses and lead to the development of inhibitory pharmaceuticals. Furthermore, the actions of phospholipases may be much like those of other enzymes that act at interfaces. Three papers this week by Sigler, Scott, White, and colleagues provide new data on the structure and likely mode of action of phospholipase A_2 molecules (pages 1541, 1560, and 1563). Crystal structures were solved for bee venom phospholipase A_2 in a complex with a transition state analog and for snake venom phospholipase A_2 in a similar complex or uninhibited. Although the snake and bee phospholipases are different, their catalytic surfaces and interactions with the analogs and with calcium ions were virtually identical. On the basis of the stereochemical observations, mechanisms are proposed to explain how the substrate enters the enzyme's active site and how its cleavage is accomplished.

Nuclear waste repository

A site in the Yucca Mountains of southern Nevada has been selected as a possible burial place for nuclear waste. How suitable a choice is it? Specifically, how likely is it that in the foreseeable future the underlying water table (currently about 250 meters below the proposed site) will rise to the level of the repository and transport radioactive materials to discharge points? Studies by Quade and Cerling indicate that the level of the regional water table remained below the elevation of the proposed repository for at least the last 300,000 years (page 1549). Carbon and oxygen isotopes in layered carbonates at Trench 14, which is near the site, matched those associated with modern desert soil carbonates (which formed independent of ground water) rather than those of nearby springs. If radioactive wastes are eventually buried at the Yucca Mountain site, it appears that they will remain where they are interred.

Balanced sex ratio

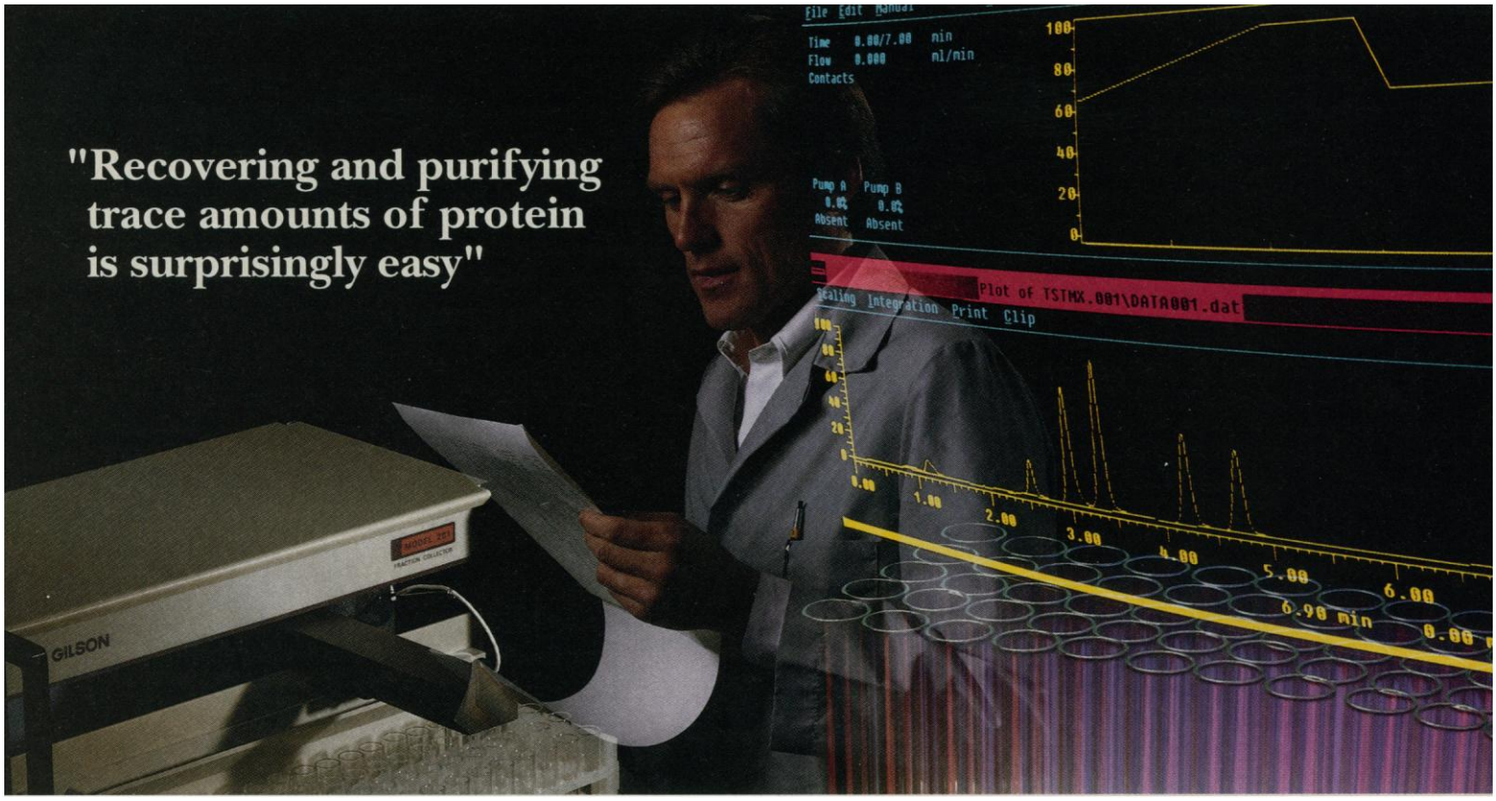
WHY do so many species of organisms produce approximately equal numbers of male and female progeny? Does the balanced sex ratio reflect a selection process that leads to equal numbers of males and females or is it merely a nonadaptive consequence of a genetic sex-determining mechanism (equal numbers of male and female sex chromosomes)? Conover and Van Vorhees have studied sex-ratio determination in populations of Atlantic silversides whose sex is determined both by an environmental factor (water temperature) and by genetics (sex-determining genes) (page 1556). The larvae that develop when the water temperature is cold become females; those that develop in warmer water become males. Once sex is determined it is irreversible. When the silversides were grown in tanks of sea water held at constant extreme temperatures, sex ratios were highly skewed; with time, frequency-dependent selection of the minority sex drove the sex ratio back to 1:1. The results provide experimental support for a 60-year-old theory that the balance is adaptive. They also suggest that, despite dramatic changes in the environment, the ratio can return to 1:1 even in species whose sex ratio normally is under the influence of environmental factors. Therefore, extinction in the face of a changed environment would not be inevitable.

Targeted gene insertions

PARASITIC protozoa cause tremendous morbidity and mortality worldwide, both in animals and in humans. There is, therefore, keen interest in understanding their biology and in preparing vaccines from live attenuated organisms (those that reproduce and induce immunity but are not pathologic). One approach to both of these goals is to disrupt or alter the functioning of the parasite's own genes or to insert new genes into the parasite's chromosomes. Lee and Van der Ploeg describe methods for targeting genes to specific sites on the chromosomes of *Trypanosoma brucei*, the parasite that causes sleeping sickness in humans (page 1583). They confirmed that the genes were stably integrated into the chromosome and properly expressed. Successful integration was achieved through recombination between homologous regions on the plasmid that carried the new genes and on the target site of the chromosome. Because the majority of the integration events occurred by homologous recombination, detailed analyses of these protozoal genomes should now be possible.

AIDS neurologic damage

THE AIDS virus can have devastating effects on the nervous system of an infected individual. In the worst cases, paralysis, seizures, and global dementia can result. In vitro studies suggest that the neurologic damage may be induced by toxic substances that are secreted by HIV-1–infected mononuclear phagocytic cells (page 1593). Cells in this lineage reside in the brain (microglia) or invade the brain (macrophages and multinucleated macrophage-like giant cells) and, when activated by the infection, may chronically release their poisons. Partial characterization of the secreted toxin suggested that it was unlike any known HIV-1 protein or previously characterized toxic substance secreted by activated macrophages. It acted through the neuronal NMDA receptors, which have been implicated in a variety of neuropathologic conditions. Giulian *et al.* propose that the neurologic consequences of HIV-1 infections might be reduced by suppressing macrophage activation, blocking synthesis of the neurotoxin, or blocking the NMDA receptors. ■ RUTH LEVY GUYER



Chromatographers speak out about the Gilson Auto-Preparative HPLC system

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A pharmaceutical QC lab supervisor likes the capacity and reliability of the system. A multi-mode fraction collector with 120- or 540-tube capacity is the key. The collector—either the Gilson 201 or 202—has a stationary rack design. Unlike collectors with carousel racks, it won't jam. The collector acts as a system controller, and multicycle capability allows collection of fractions from the repetitive runs into the same set of tubes for automated sample purification.

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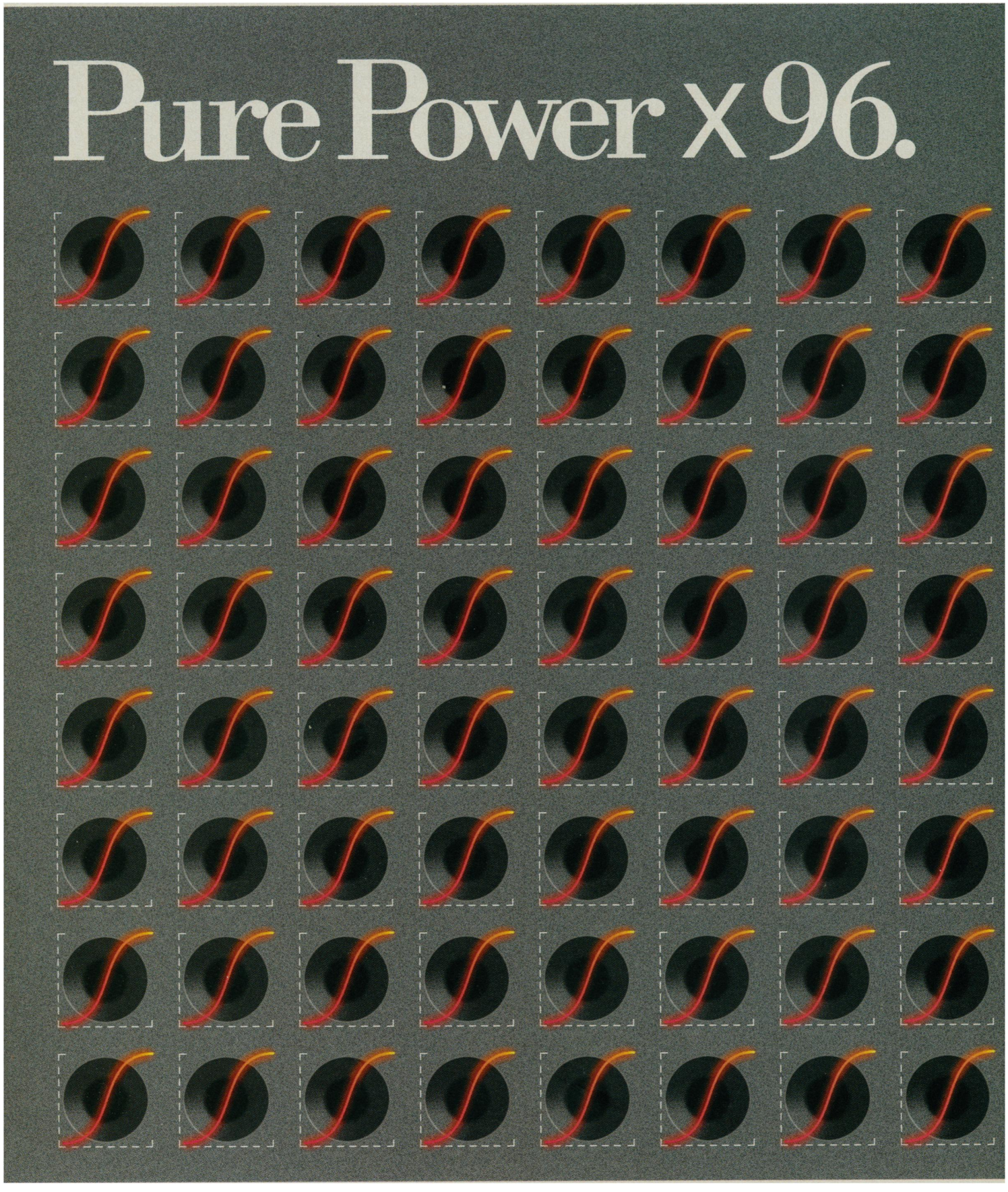

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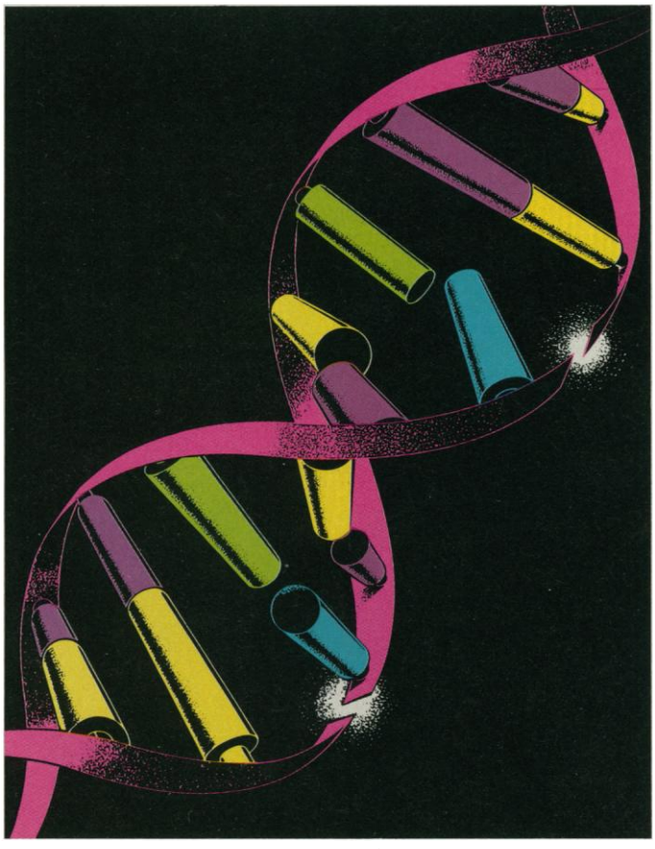

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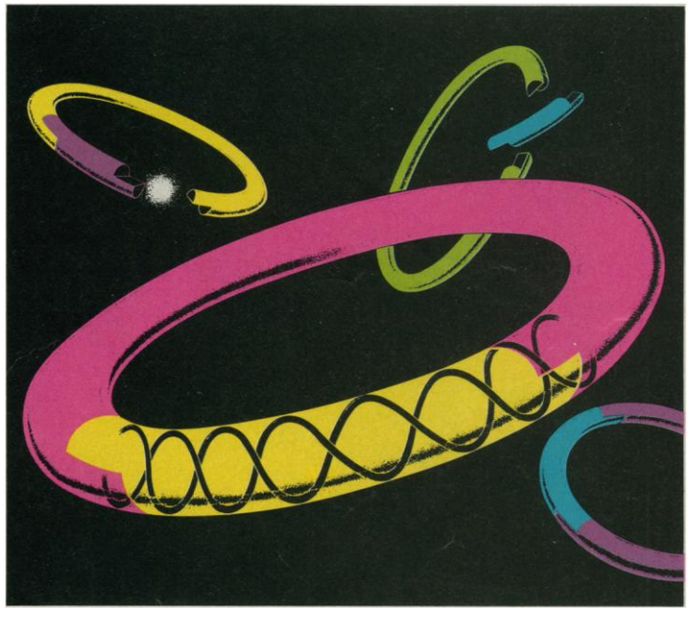

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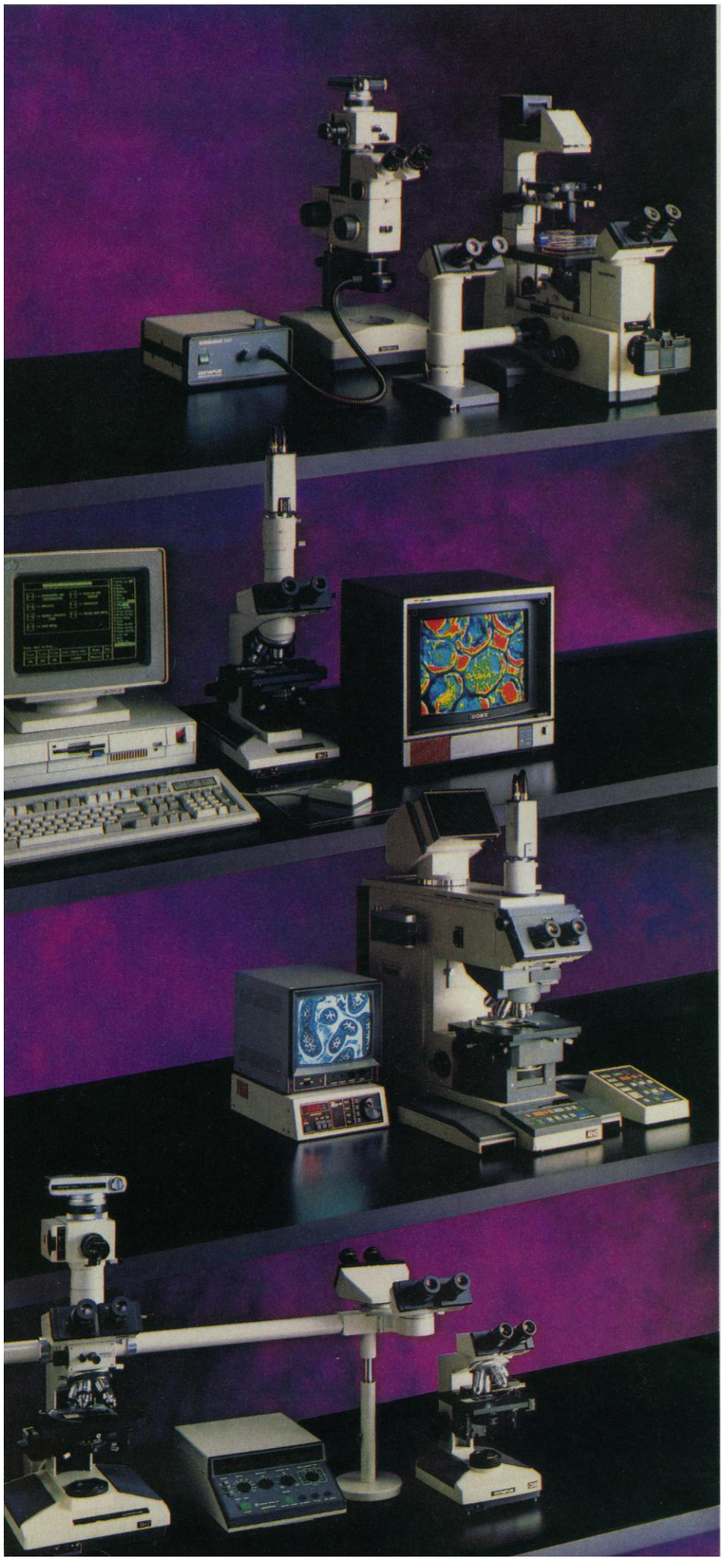

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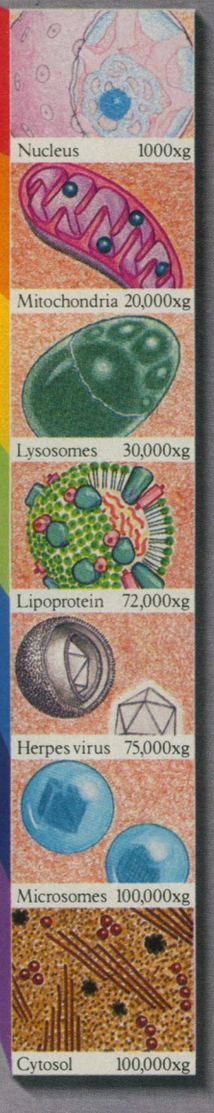

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