

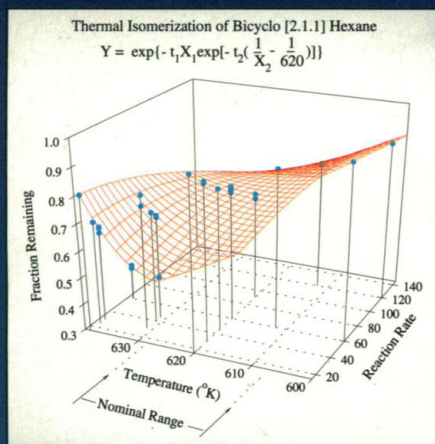
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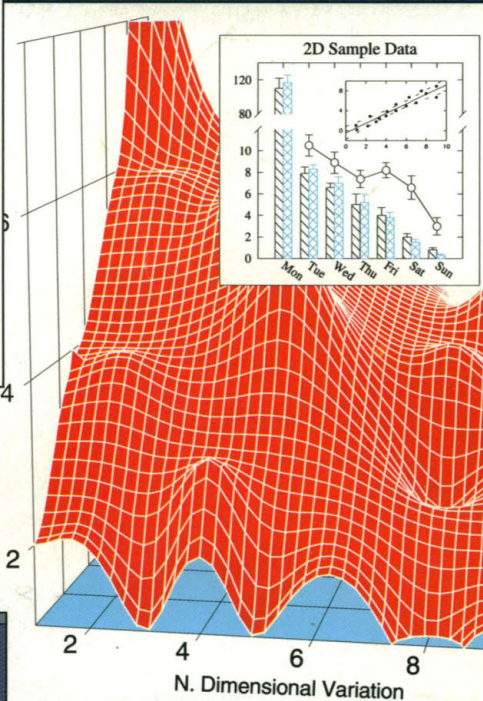
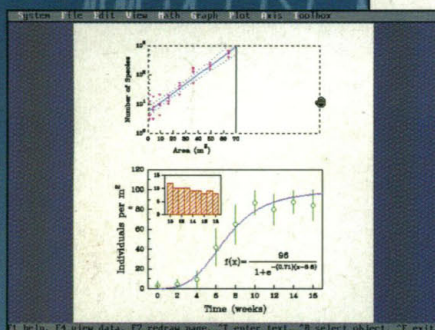
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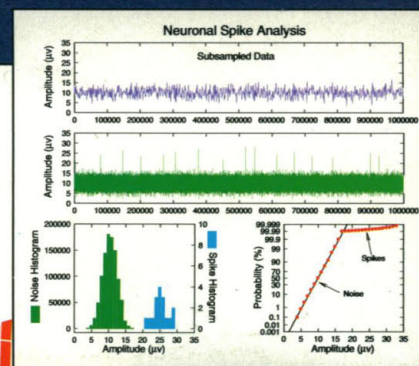


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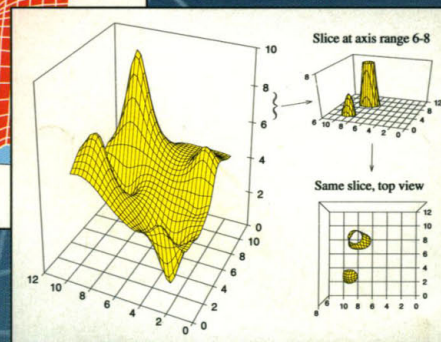
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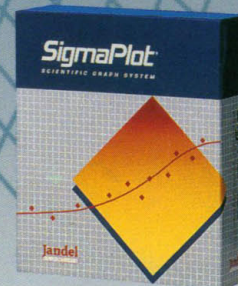
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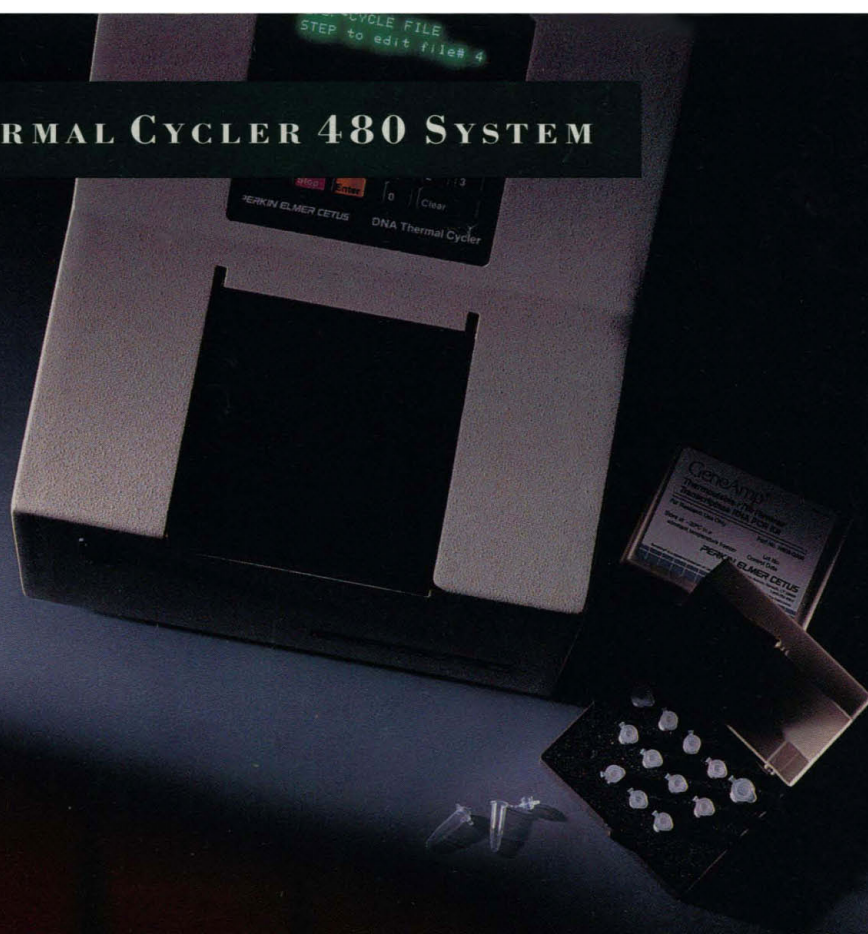


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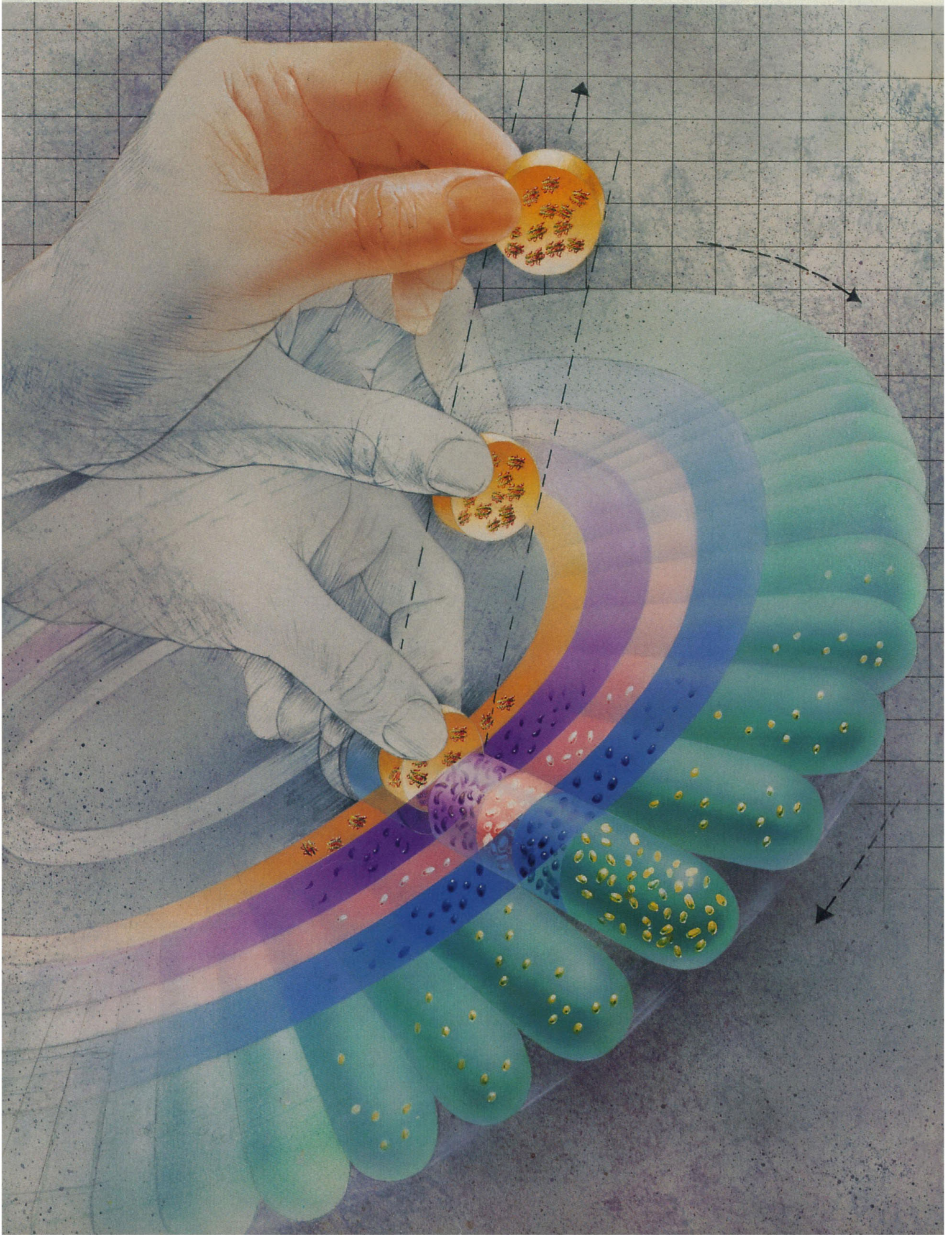
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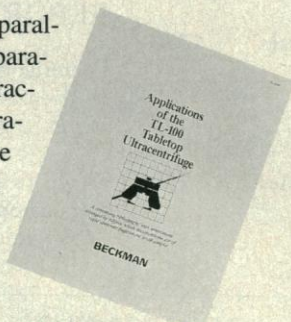
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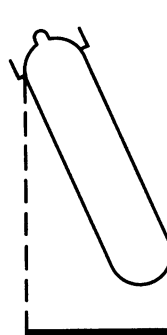
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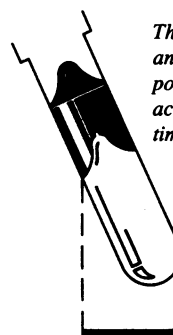
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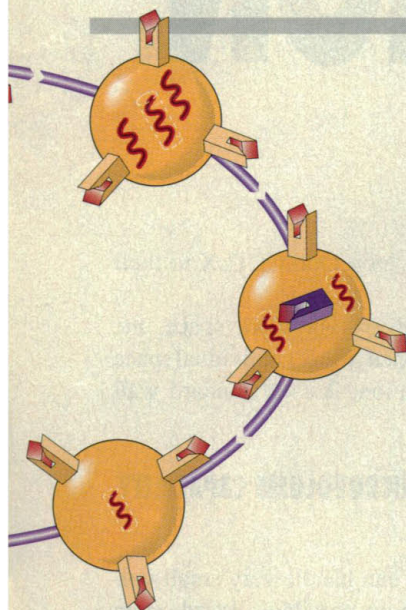
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COVER

Expression of the maize anthocyanin-specific transcriptional activator *R* in tobacco (flowers) and *Arabidopsis thaliana* (stems and leaves) increases anthocyanin (red pigment) biosynthesis in both species and trichome (hair) production in *Arabidopsis*. Wild-type samples

are on the left; those that express *R* are on the right. *R* functions in these heterologous species despite the evolutionary divergence of monocots and dicots and may prove to be a valuable visible marker in many plant species. See page 1773. [Photograph: Ted Preuss]



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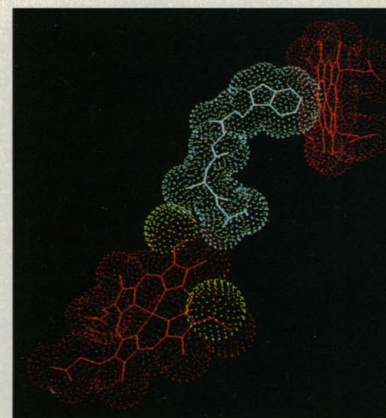
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Hot growth

Hydrothermal vents along ocean spreading centers harbor a variety of interesting organisms. Although some archaeobacteria in this environment grow at temperatures up to 110°C, the important sulfate-reducing eubacteria have been thought to be limited to much lower temperatures. Jørgensen *et al.* (p. 1756) now report evidence for biological sulfate reduction at temperatures up to 110°C in sediment along the Gulf of California spreading center. The yet unidentified bacteria may play a role in the genesis of metal sulfide ores that form in this environment.

Manipulative moves

Surfaces of metal single crystals often represent a simple termination of the bulk structure, but in some cases, such as the (111) surface of gold, the surface atoms rearrange to compensate for the reduced number of bonds that they can form. Hasegawa and Avouris (p. 1763) show that the scanning tunneling microscope can be used to modify the $22 \times \sqrt{3}$ reconstruction of Au(111), which comprises domains of close-packed atoms connected by dislocation lines. The tip can be used to transfer atoms from one location to produce a hole. When these holes are made in the dislocation lines, the pattern of the surface reconstruction rearranges.

Opening material

Open framework compounds based on polymeric selenium anions have been synthesized at relatively low temperatures (200°C) by Dhingra and Kanatzidis (p. 1769). The compound $(\text{Ph}_4\text{P})_2\text{Se}_5$ (where Ph is a phenyl group)

and excess selenium react in molten form with gallium, indium, or thallium to produce red crystalline $(\text{Ph}_4\text{P})[\text{M}(\text{Se}_6)_2]$, where M is the metal atom. The tetrahedral metal centers and the bridging Se_6^{2-} ligands form an open network of channels that contain the PPh_4^+ counterion. Such open framework metal chalcogenides could have interesting electrical, optical, or catalytic properties.

Trans-splicing keys

In nematodes, trans-splicing reactions produce a subset of messenger RNA that contains a common 5' end of 22 nucleotides called the spliced leader. Hannon *et al.* (p. 1775) identified regions of the donor RNA that are required for trans-splicing. When transferred to a heterologous RNA, these regions permit the hybrid RNA to participate in trans-splicing. Cross-linking studies suggest that one of the regions required for trans-splicing may base pair with U6 snRNA, an essential U snRNA for cis- and trans-splicing.

Opening genes

The transcriptional activation of many genes is associated with

disruption of the nucleosome arrays at enhancer and promoter sequences. Workman and Kingston (p. 1780) have examined whether DNA binding by a transcription factor can directly destabilize nucleosomes. They found that in vitro the DNA binding domain of the GAL4 transcription factor can displace nucleosome cores in a defined chromatin system. Such displacement of nucleosomes from enhancers and promoters by some transcription factors may make these DNA regions accessible to other regulatory factors necessary for transcription.

Weak signals

Animals with cancer frequently have impaired function of the immune system. However, the cause of the reduction in cytolytic activity of CD8^+ T cells from such animals is not known. Mizoguchi *et al.* (p. 1795) found that CD8^+ T cells from tumor-bearing mice had defects in signaling from the T cell antigen receptor (TCR). The TCRs from these mice with tumors lacked certain protein components but contained a subunit of the Fc receptor, which binds to antibodies. These alterations in the TCR and the signals it generates may account for some

of the weakened immune response in animals with tumors. See also a News story by Travis (p. 1732).

Processing pathways

Peptides bind to class II major histocompatibility complex (MHC) molecules in an endosomal compartment. Sette *et al.* (p. 1801) studied peptide binding to a class II MHC molecule transfected into human B lymphoblastoid cell lines that are defective in antigen processing. The transfected cells produced normal amounts of class II, but the molecules were unstable and dissociated into monomers. Most of the peptides bound to the class II were long fragments of the class II-associated invariant chain. This result suggests that a third processing pathway may operate in addition to endosomal processing and the cytosolic processing of some viral peptides.

Mixed signals

Binding of peptide ligands to their receptors causes increased transcription of specific sets of genes. Interferon- α can activate a transcription complex composed of three tyrosine phosphorylated proteins (one of which is 91 kD) and a fourth 48-kD protein that binds to DNA. Shuai *et al.* (p. 1808) report that the structurally unrelated cytokine interferon- γ caused tyrosine phosphorylation of the same 91-kD protein. Also, that protein alone was transported to the nucleus where it bound DNA. Thus the activation of specific genes in response to these cytokines results from activation of different combinations of latent cytoplasmic transcription factors.

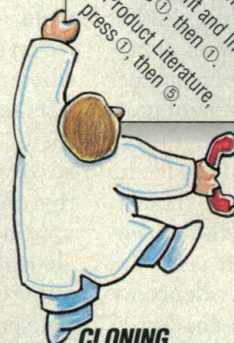
HIV-1 expression in neurons

One complication associated with HIV-1 infection is AIDS dementia complex (ADC), which is associated with neuronal loss in the central nervous system (CNS). Corboy *et al.* (p. 1804) constructed transgenic mice that contained the long terminal repeats (LTRs) from HIV-1 strains isolated from the cerebrospinal fluid and frontal lobe of an ADC patient. Neuronal expression in the CNS of a β -galactosidase marker directed by the LTRs was observed for these strains. Although earlier studies with HIV-1_{IIIIB/LAV} showed no expression or replication in neurons, the U3 regions of these different strains contain more than 27 base differences. Neurons apparently contain transcription factors that can activate gene expression from the LTRs of particular HIV-1 strains.

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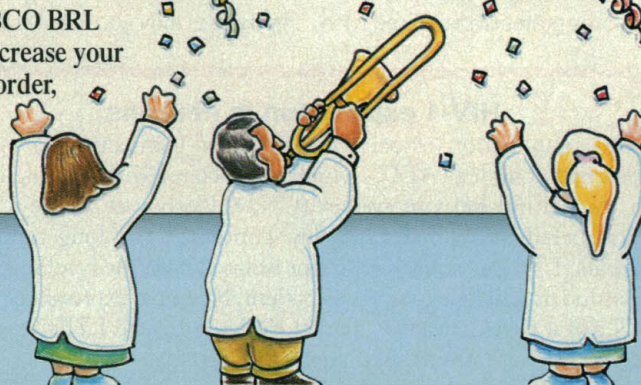
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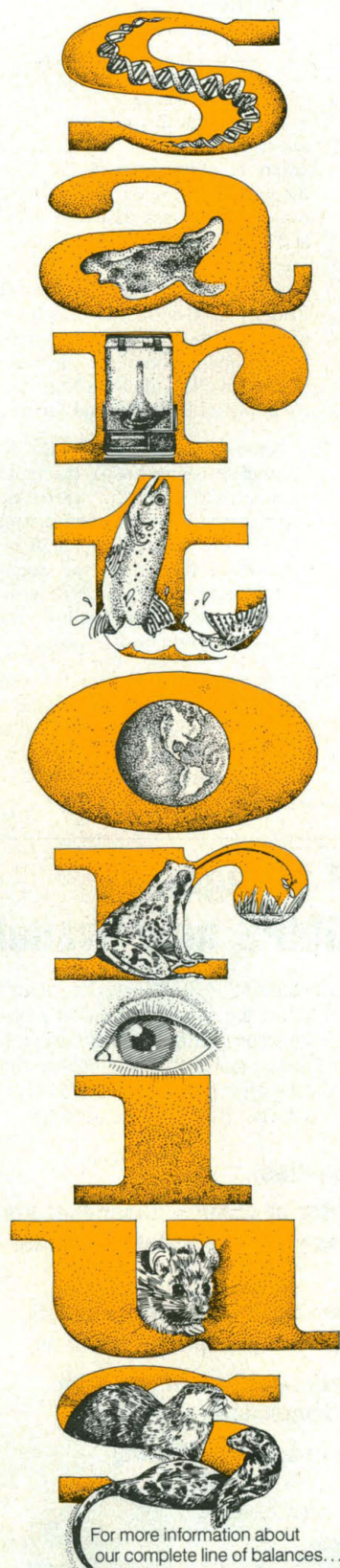
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Understanding Neurodegenerative Diseases: Alzheimer's Disease

Sunday, 14 February, 8:30 am–11:15 am

Session Chair: **Joseph B. Martin**, *Univ of Calif-San Francisco*

Joseph B. Martin, *Univ of Calif-San Francisco*

Introduction—The human brain mapping initiative

Leonard Berg, *Washington Univ School of Med*

Alzheimer's disease: The clinical and pathological syndrome

Kenneth S. Kosik, *Harvard Med School*
From the amyloid precursor protein to the plaques and tangles: Where does it go wrong?

Alison Goate, *Washington Univ School of Med*

Mutations in the amyloid precursor protein gene in Alzheimer's disease

Brad Hyman*, *Massachusetts General Hospital*

An analysis of the memory deficit in Alzheimer's disease

Donald L. Price, *Johns Hopkins Univ School of Med*

The biology of Alzheimer's disease: Lessons from studies of model systems

Keynote Address

Sunday, 14 February, 1:15 pm–2:15 pm

Eric R. Kandel, *Columbia Univ College of Physicians and Surgeons/HHMI*
Cell and molecular mechanisms of memory storage

Perceiving the World: An Exploration of the Senses

Sunday, 14 February, 2:30 pm–5:00 pm

Session Chair: **David C. Van Essen**,
Washington Univ School of Medicine

Randel Reed*, *Johns Hopkins Univ*
Genes involved in visual processing

John E. Dowling, *Harvard Univ*
Retinal processing of visual information

David C. Van Essen, *Washington Univ School of Med*
Mapping the visual cortex: From monkeys to humans

John S. Kauer, *New England Med Center/ Tufts Med School*
Distributed representation of odor information: A paradigm for parallel neuronal processing

Stephen G. Lisberger, *Univ of Calif-San Francisco*
Sensory-motor processing for smooth eye movements

Memory and Learning: Lessons from Models

Monday, 15 February, 8:30 am–11:30 am

Session Chair: **Marcus Raichle***,
Washington Univ School of Med

Larry R. Squire, *VA Medical Ctr/Univ of Calif-San Diego*
Brain systems and the structure of memory

Gary Lynch, *Univ of Calif-Irvine*
Biological origins and computational features of memory in brain networks

Marcus Raichle*, *Washington Univ School of Med*
Contributions of brain imaging to an understanding of brain areas involved in memory and learning

Endel Tulving, *Rotman Res Inst of Baycrest Center, Toronto*

How do we think about memory?

Panel discussion: Sharing the data involved in dissecting brain functions

Keynote Address

Monday, 15 February, 1:15 pm–2:15 pm

Floyd E. Bloom*, *Scripps Res Inst*
Experience with brain mapping

Mapping Strategies

Monday, 15 February, 2:30 pm–5:30 pm

Session Chairs: **Constance M. Pechura**,
Inst of Med; **Joseph B. Martin**, *Univ of Calif-San Francisco*

Robert Langridge*, *Univ of Calif-San Francisco*

Mapping molecules: Computations in time and space

Bruce R. Schatz, *Univ of Arizona*
Mapping organisms: From a worm genome to a human brain

Joseph Coyle, *Harvard Med School*
A neuroscientist's view of the brain

Vinton G. Cerf, *Corporation for National Research Initiatives*
A computer scientist's view of the brain map

Alan I. Leshner, *Natl Inst of Mental Health*
The Human Brain Project: The federal role

Panel discussion and concluding remarks

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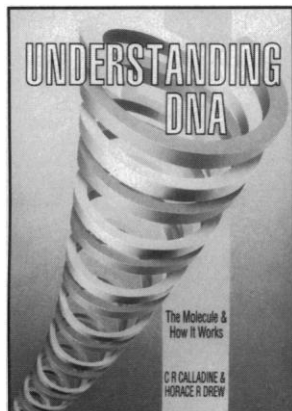
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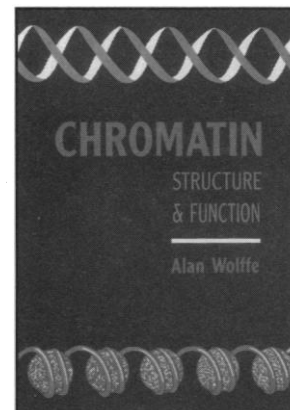
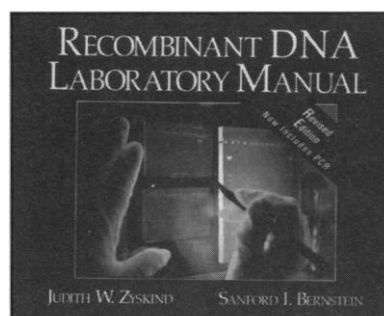
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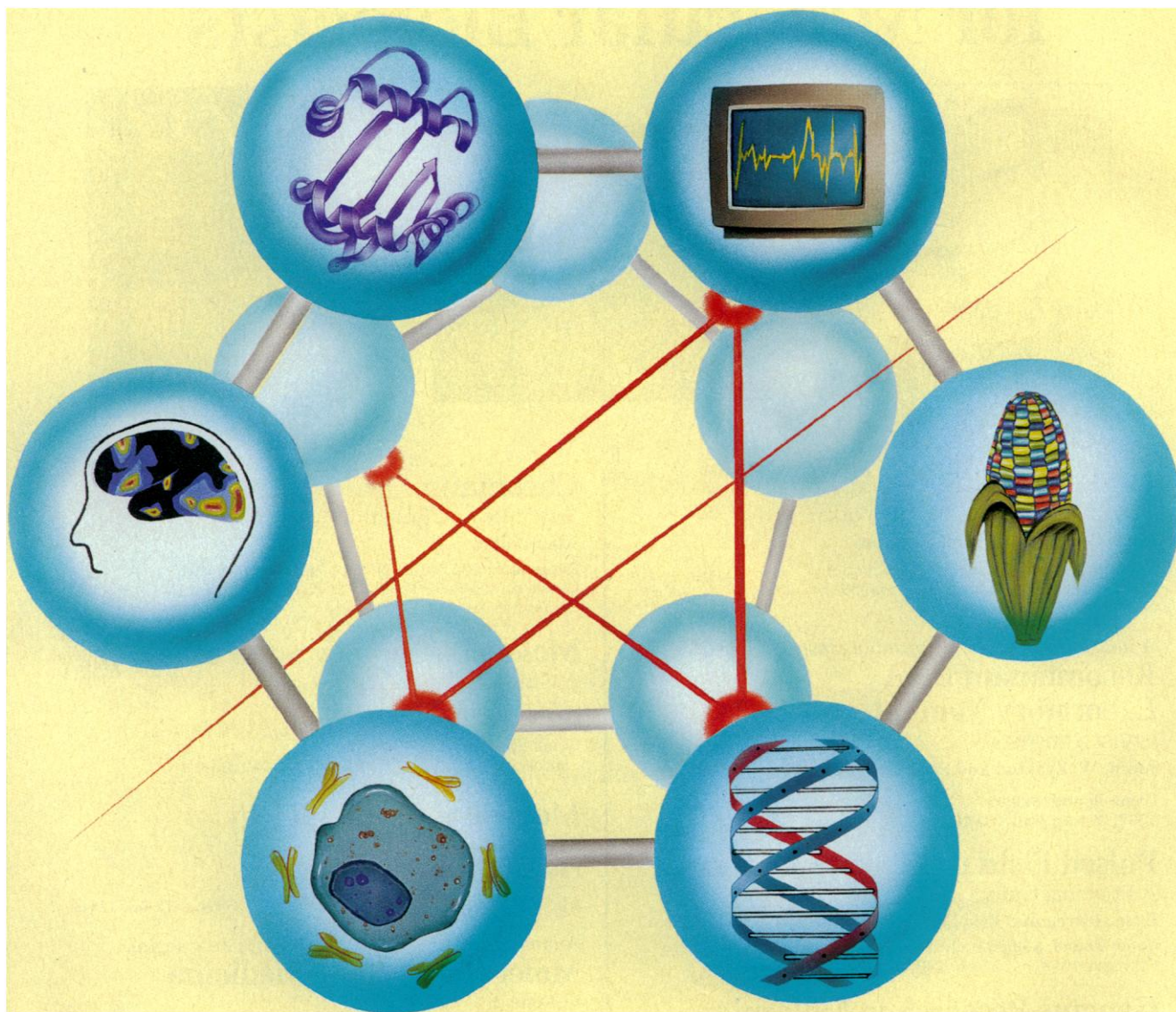
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