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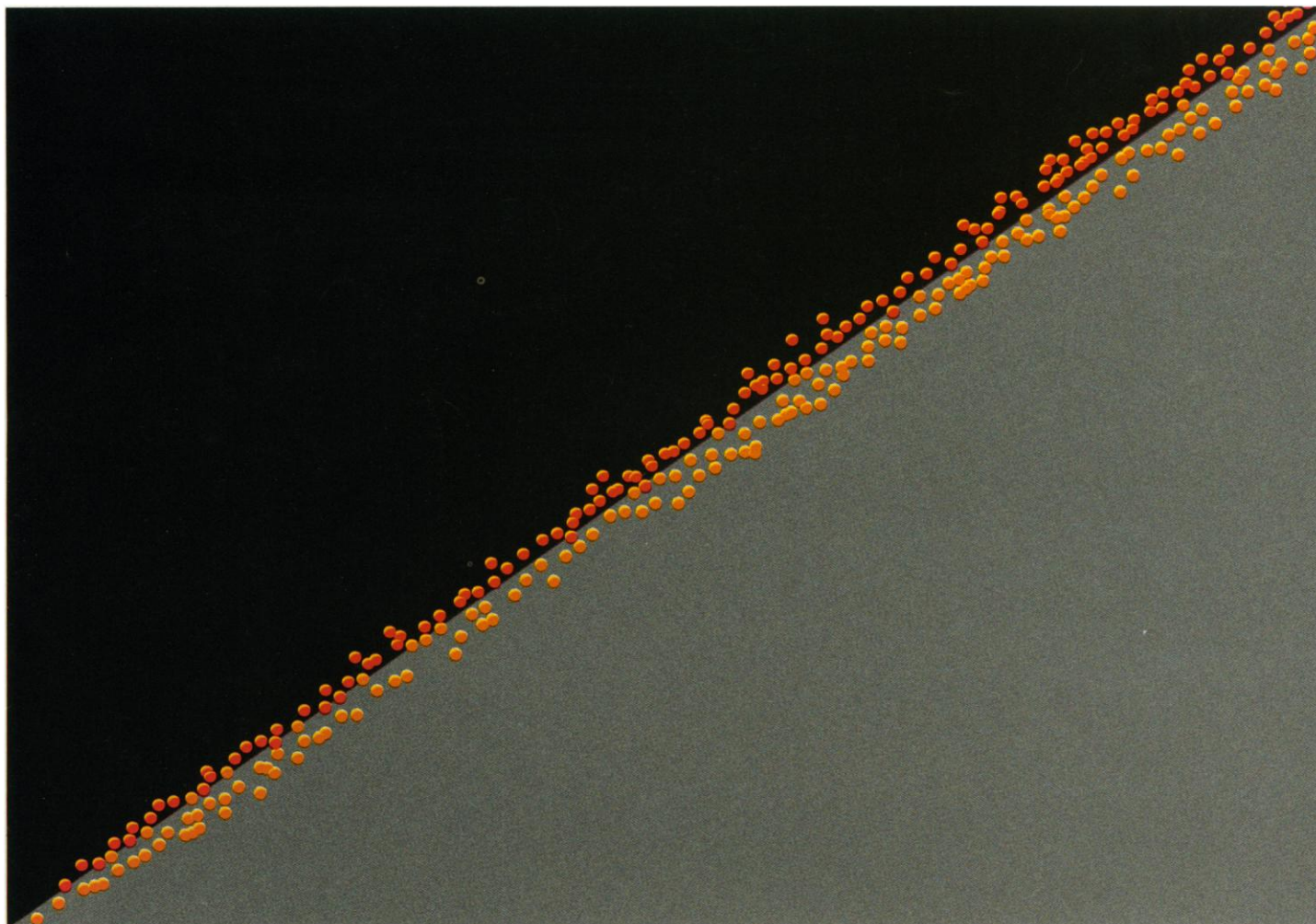
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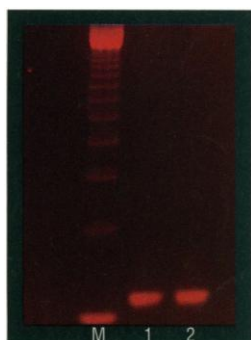


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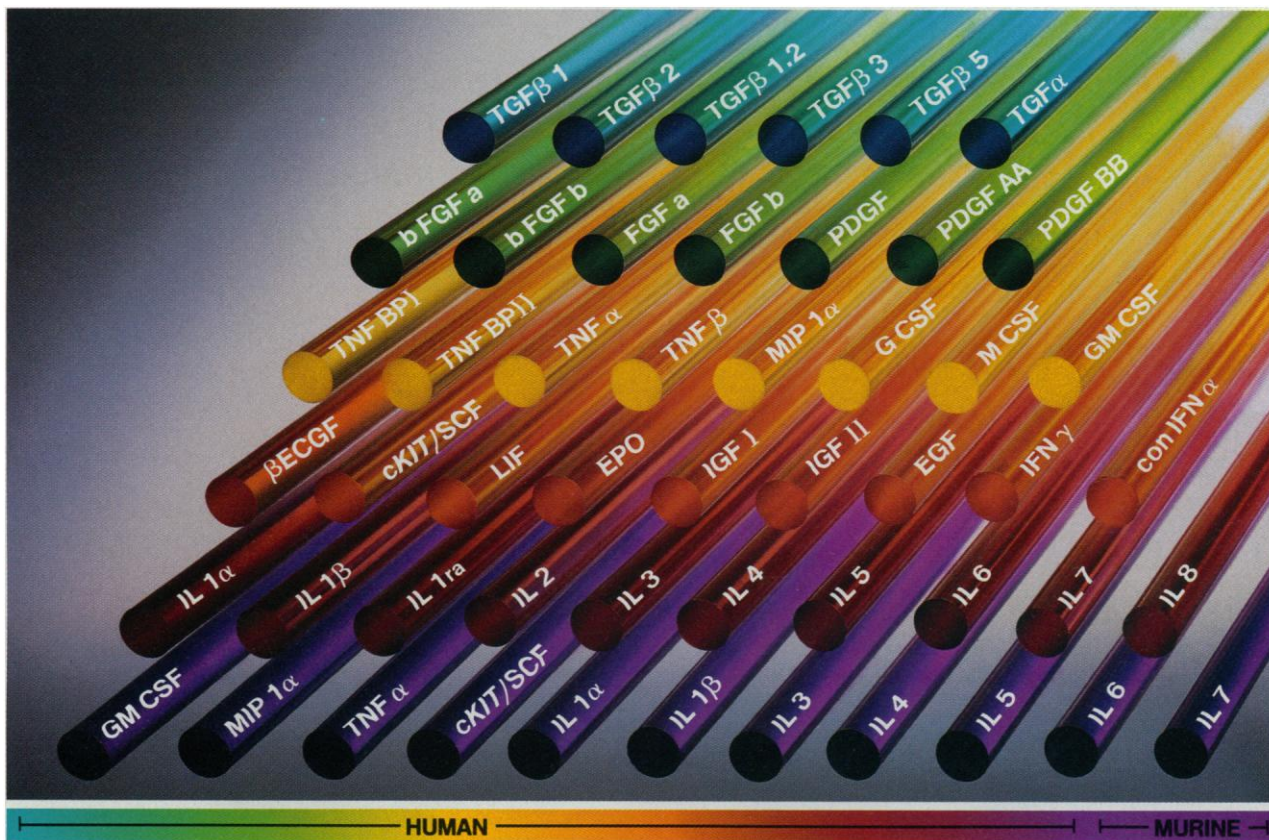
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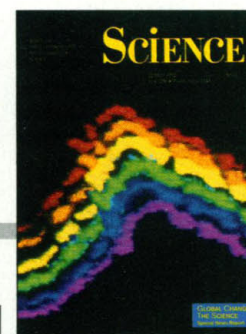
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COVER

Nearly identical high-resolution images of a segment of BlueScript II plasmid DNA scanned in the atomic force microscope. By imaging plasmid DNA on mica in *n*-propanol, reproducible structure along the DNA strand can be revealed; this segment was scanned continu-

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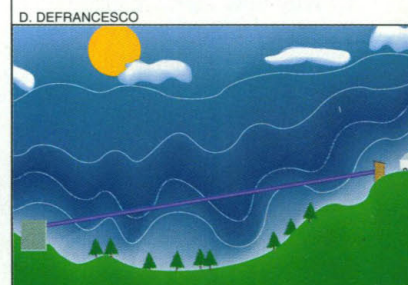
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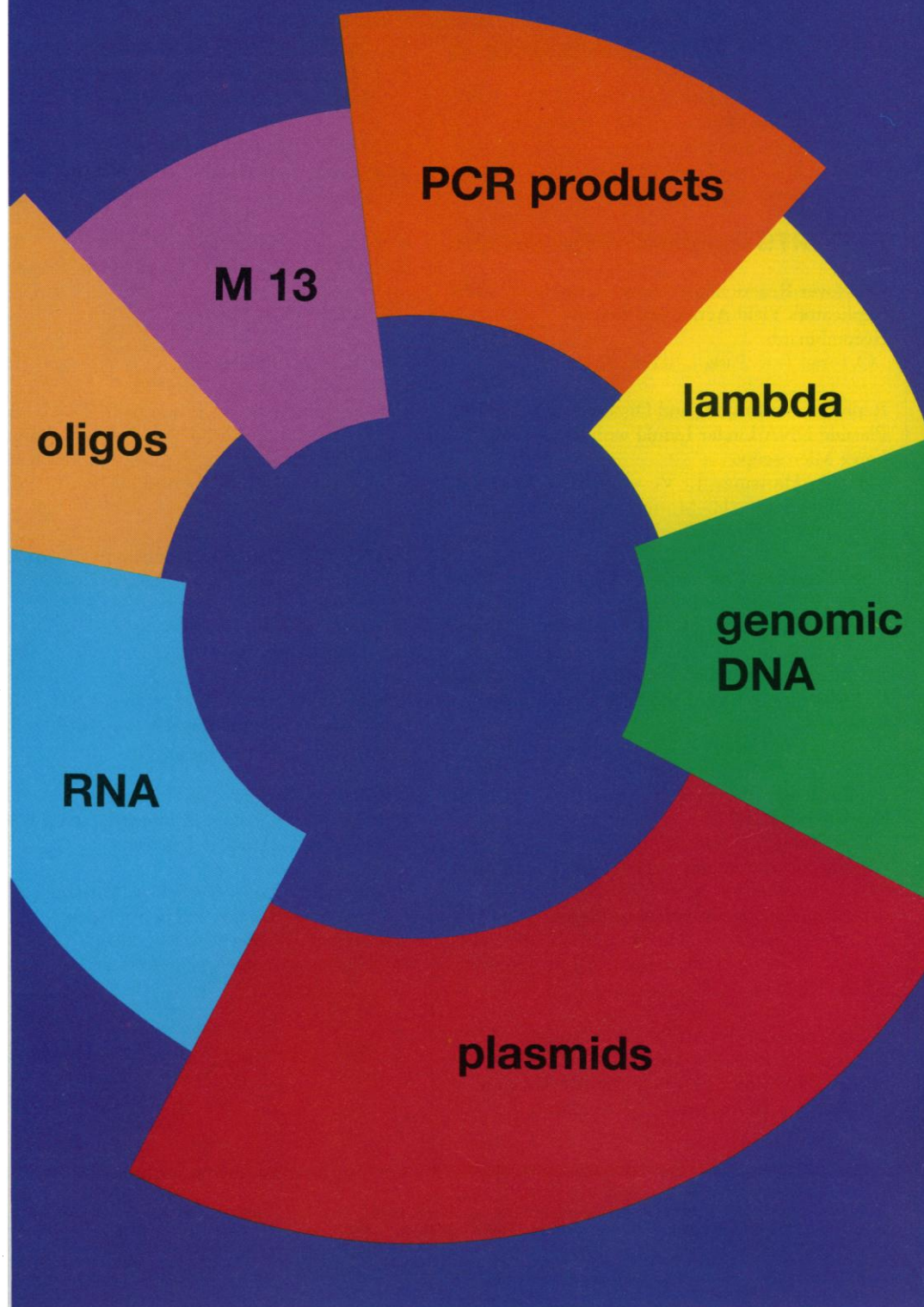
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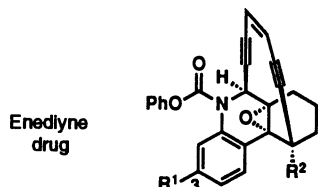
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Drug design

Molecules that contain the enediyne group, in which two triple bonds are connected by a double bond, can undergo cyclization reactions that produce radical species. Enediynes can have significant anticancer activity because the radicals formed can damage DNA by



abstracting hydrogen atoms. Nicolaou *et al.* (p. 1172) designed, synthesized, and characterized a number of potent anticancer drugs by mimicking natural enediyne-containing antibiotics such as dynemicin A. Because functional groups involved in delivering, tethering, and activating these compounds have been identified, structure-activity relations can be used to guide the design of new compounds.

Staying in shape

Experiments in which different families of self-replicating molecules have been intermixed show that the hybrid systems can form even better replicators but can also form nonreplicating molecules. Feng *et al.* (p. 1179) synthesized two sets of replicators in which the reaction of two molecules forms a product that is self-complementary; the reactants can then assemble on the surface of the product molecule. Because the two product molecules are held together by relatively weak forces, they can dissociate and thus continue to catalyze the reaction. When the reactant pairs were switched, one pair formed an excellent replicator,

but the second pair was inactive because the shapes of the product molecules did not produce a recognition surface on which new product molecules could assemble.

Metals and buckyballs

Researchers have been able to insert lanthanum, yttrium, and iron into fullerene cages. Now Yannoni *et al.* report the encapsulation of scandium clusters of up to three metal atoms inside C_{82} cages (p. 1191). Electron spin resonance spectroscopy shows that such species can be isolated and stabilized at room temperature. Also in this issue, Xiang *et al.* (p. 1190) report the fabrication of high-quality single-crystal K_3C_{60} . Resistivity measurements show classic metal-like properties in contrast to previous thin-film data. The observed temperature dependence is consistent with an electron-phonon scattering mechanism.

Prolonged activation

The calcium-calmodulin-dependent kinase (CaM kinase) is activated by binding of the calcium-calmodulin complex. The active enzyme then autophosphorylates on a specific threonine residue. Meyer *et al.* (p. 1199) report that the affinity of autophosphorylated CaM kinase for calmodulin is 1000 times greater than that of the unstimulated enzyme. The trapped calmodulin continues to activate CaM kinase even if calcium concentrations are reduced. Their results suggest that CaM kinase may prolong intracellular signaling after a brief increase in the concentration of calcium and that the kinase

Atmosphere oxidation

Oxidation reactions, which primarily involve ozone, hydroxyl radicals (OH), or hydrogen peroxide, can exert control over the lifetimes of many atmospheric gases. Thompson (p. 1157) reviews past changes in the concentrations of these oxidants as well as model predictions for their future trends. Also, Mount and Eisele (p. 1187) present a comparison of measurements of OH, the oxidant that has proved most difficult to measure because of its low ambient concentration. Brune (p. 1154) discusses the implications of this comparison, which yielded values significantly below those predicted by theory.

may respond to the frequency of calcium transients within a cell.

Heregulins

Overexpression of the epidermal growth factor (EGF) receptor or the related protein p185^{erbB2} is associated with certain human cancers. Holmes *et al.* (p. 1205; see news story by Hoffman, p. 1129) have purified and cloned several related proteins called heregulins that bind to p185^{erbB2} and activate its tyrosine kinase activity. The heregulins do not bind to the EGF receptor, but they stimulate proliferation of breast cancer cells in culture. Thus, the heregulins may be the natural ligands for p185^{erbB2}.

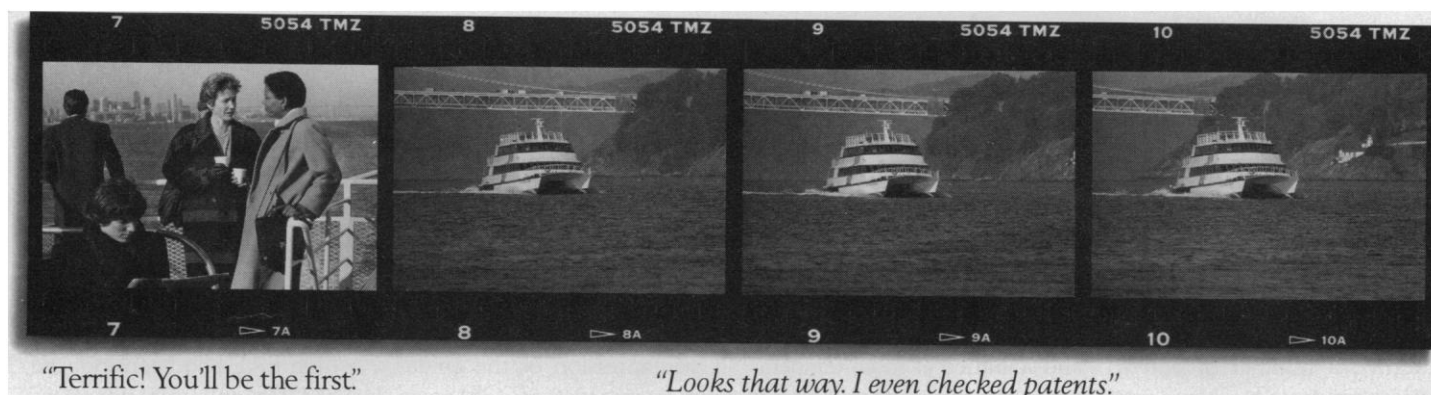
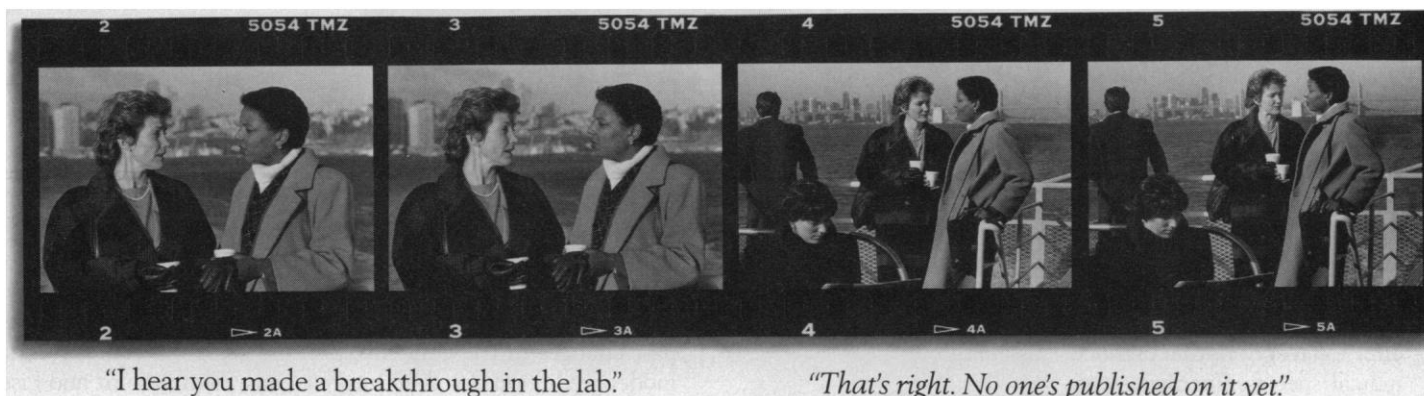
Regulatory CD8⁺ cells

Two animal-model studies of multiple sclerosis that used mice lacking CD8⁺ T cells reveal that these cells, which are normally thought of as effector or killing cells, also have regulatory functions. Koh *et al.* (p. 1210) bred mutant mice that lacked CD8⁺ cytotoxic cells with mice susceptible for the development of experimental allergic encephalomyelitis (EAE), an autoimmune disease. Mortality was lower in these mice (a decrease in the effector response), but

relapse occurred more frequently (indicating that there was less control over the effector response). Jiang *et al.* (p. 1213) used an antibody response to clear CD8⁺ cells from mice in which EAE had been induced. The CD8⁺ cells were not necessary for recovery from the first episode of the disease, but mice lacking these cells were not resistant to a second EAE induction.

Heteromeric NMDA receptor

Like other ligand-gated ion channels, the fully functional N-methyl-D-aspartate (NMDA) receptor has been thought to be composed of heteromeric subunits; the NMDA receptor subunit NR1 shows many of the properties of natural NMDA receptors but conducts only low currents. Monyer *et al.* (p. 1217) cloned three additional subunits of the NMDA receptor from rat brain that are 55 to 70% identical in sequence to one another but that show less than 20% sequence identity to NR1. These NR2 subunits showed typical calcium currents for glutamate and NMDA activation only when they were coexpressed with NR1. The mRNA distributions of NR1 and the NR2s suggest that these heteromeric NMDA receptor subtypes may exist in neurons.



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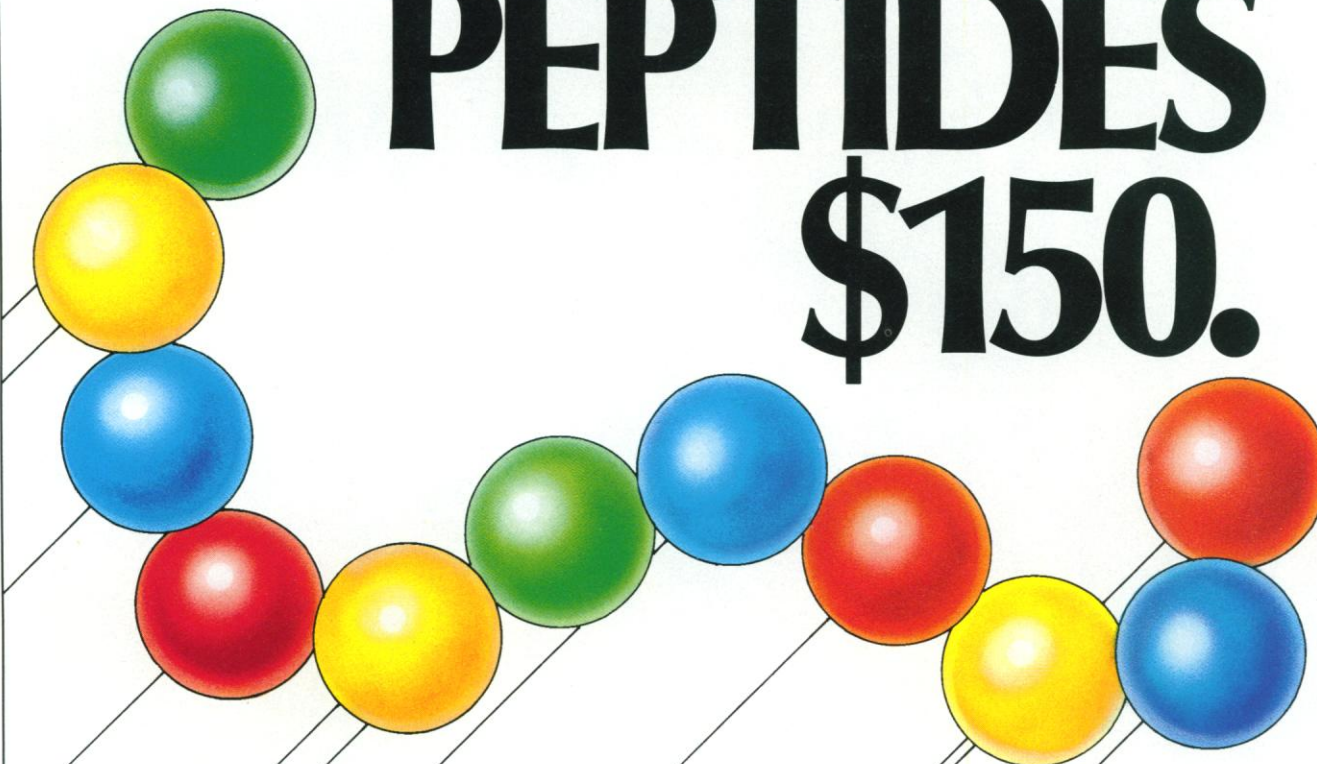
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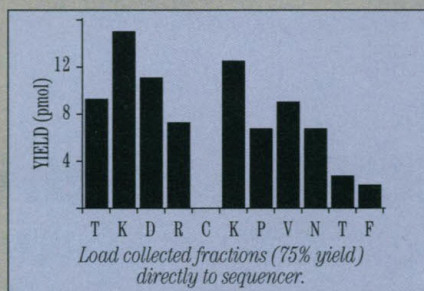
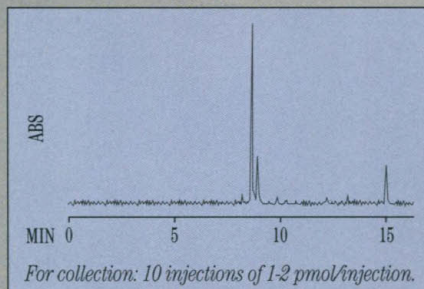
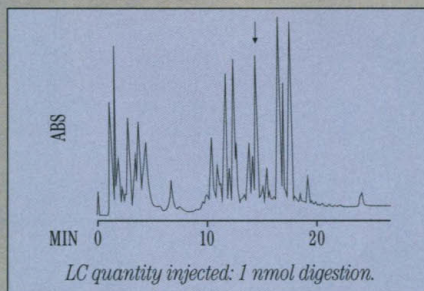
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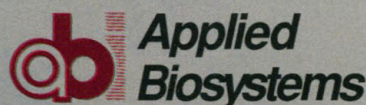
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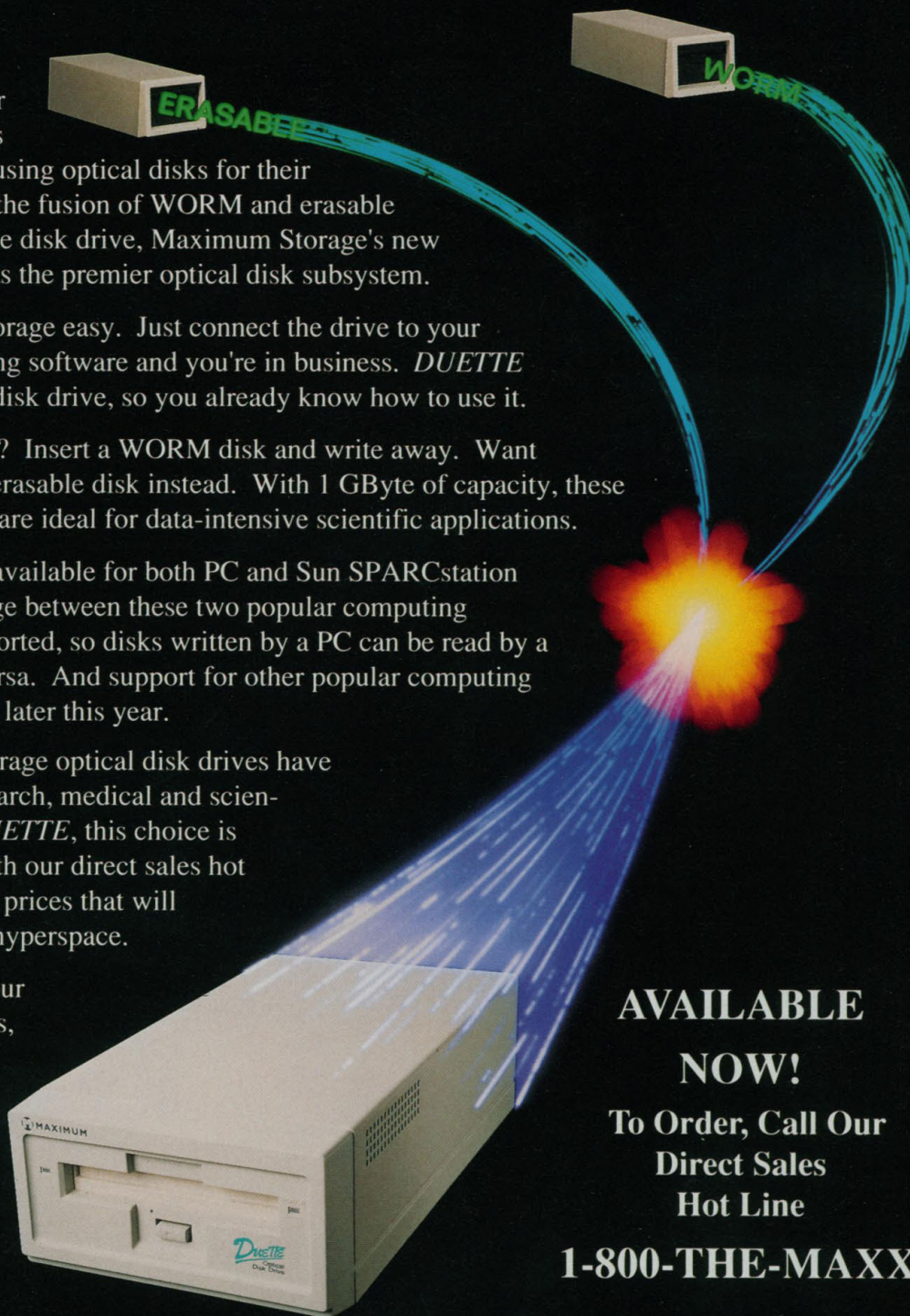
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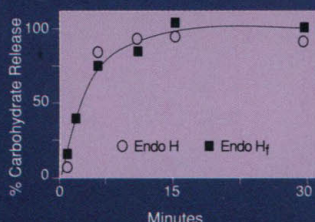
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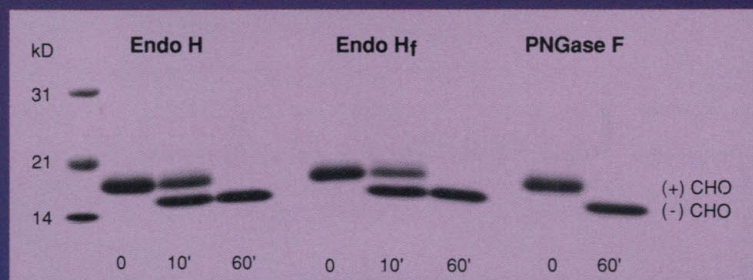
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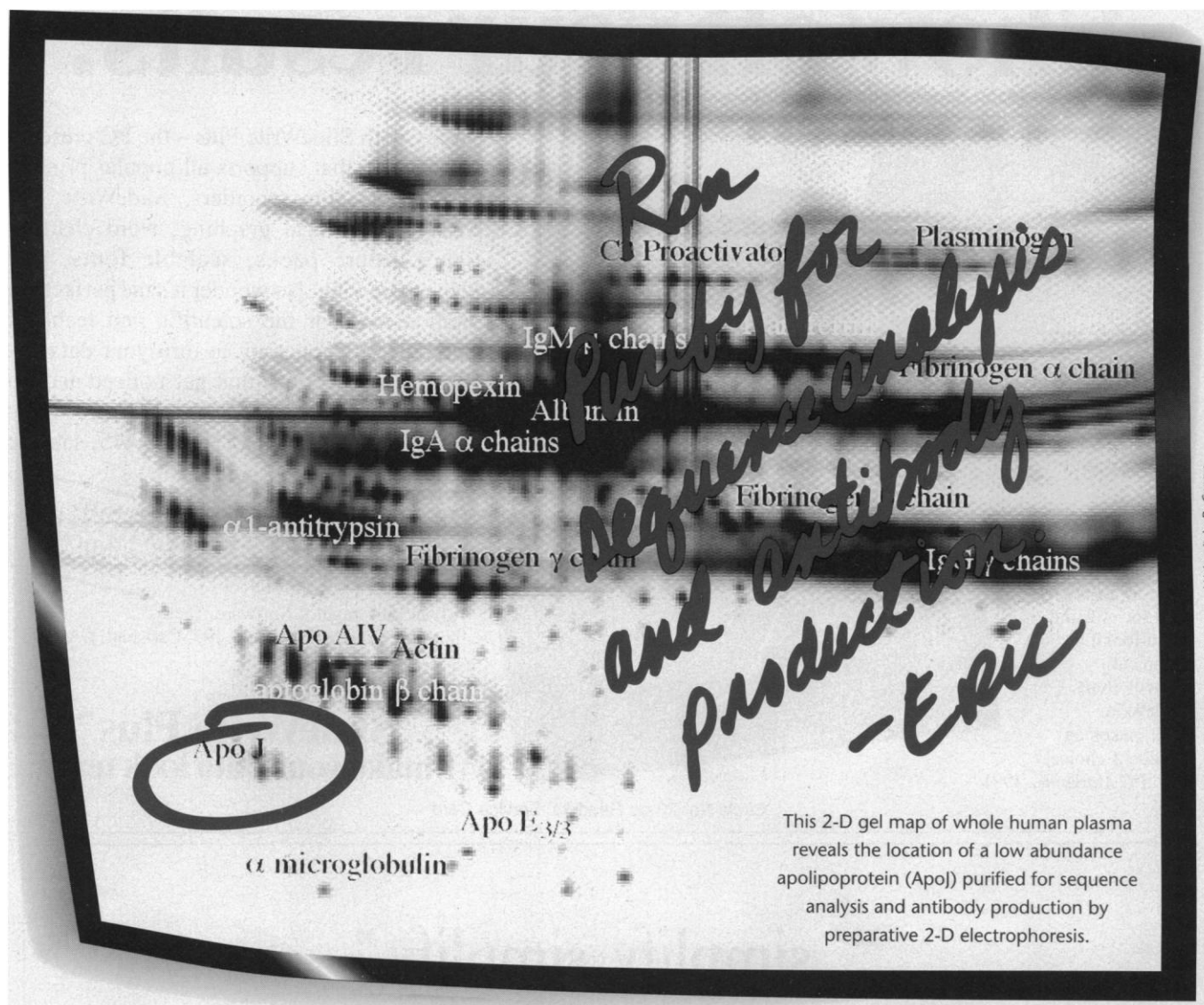
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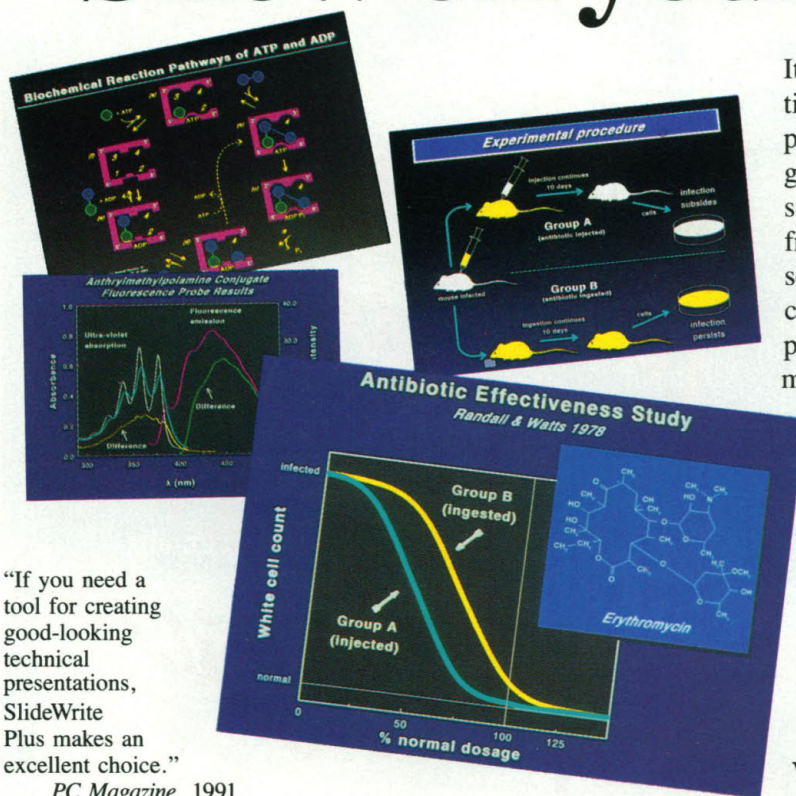
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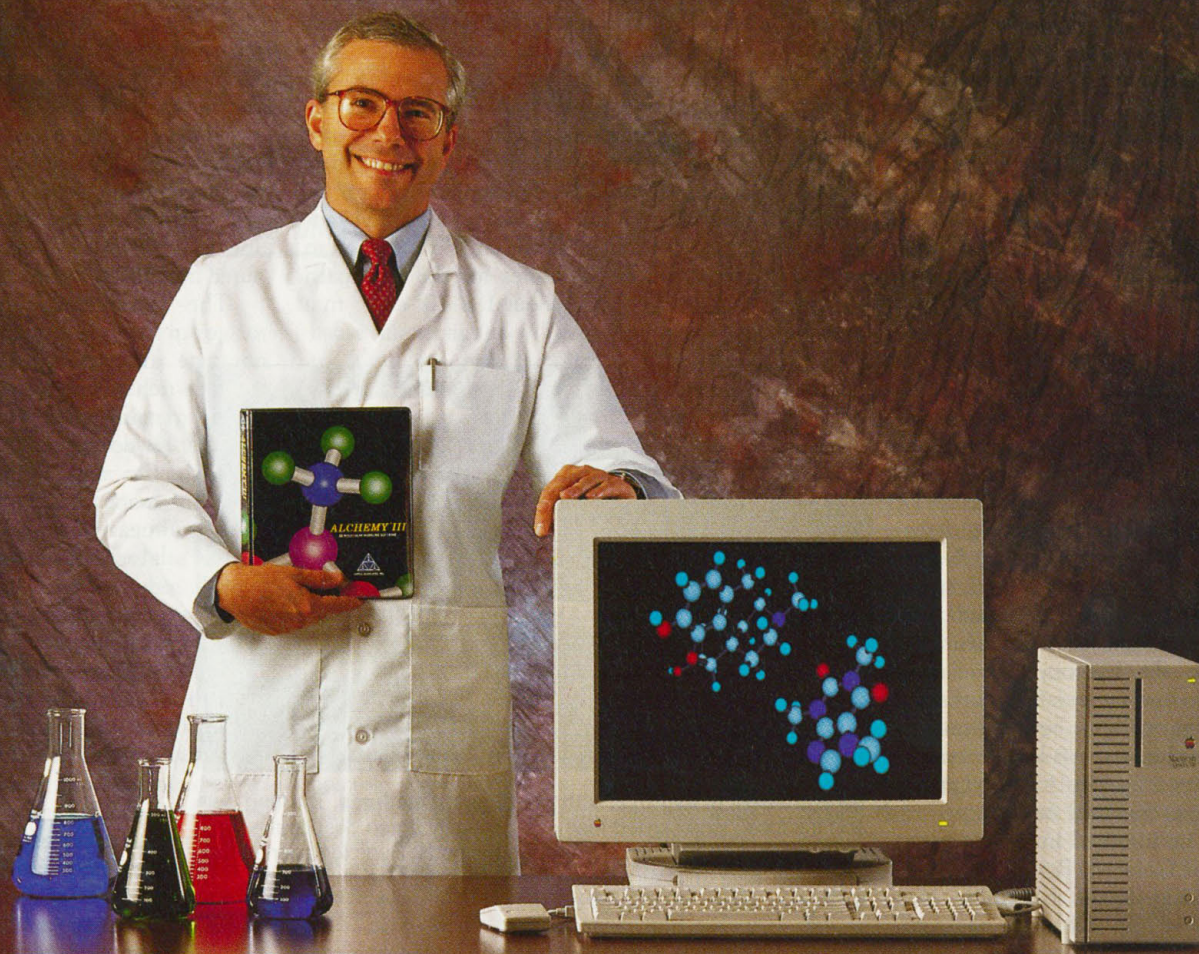
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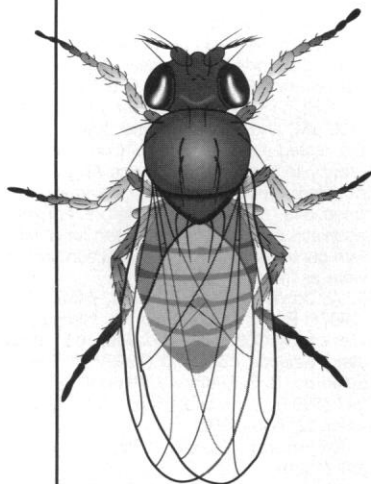
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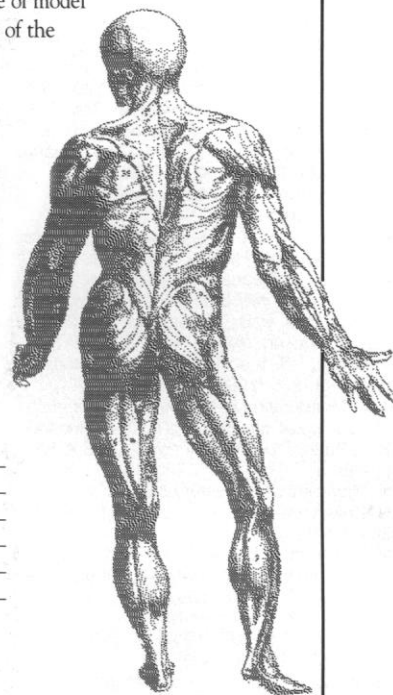
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