

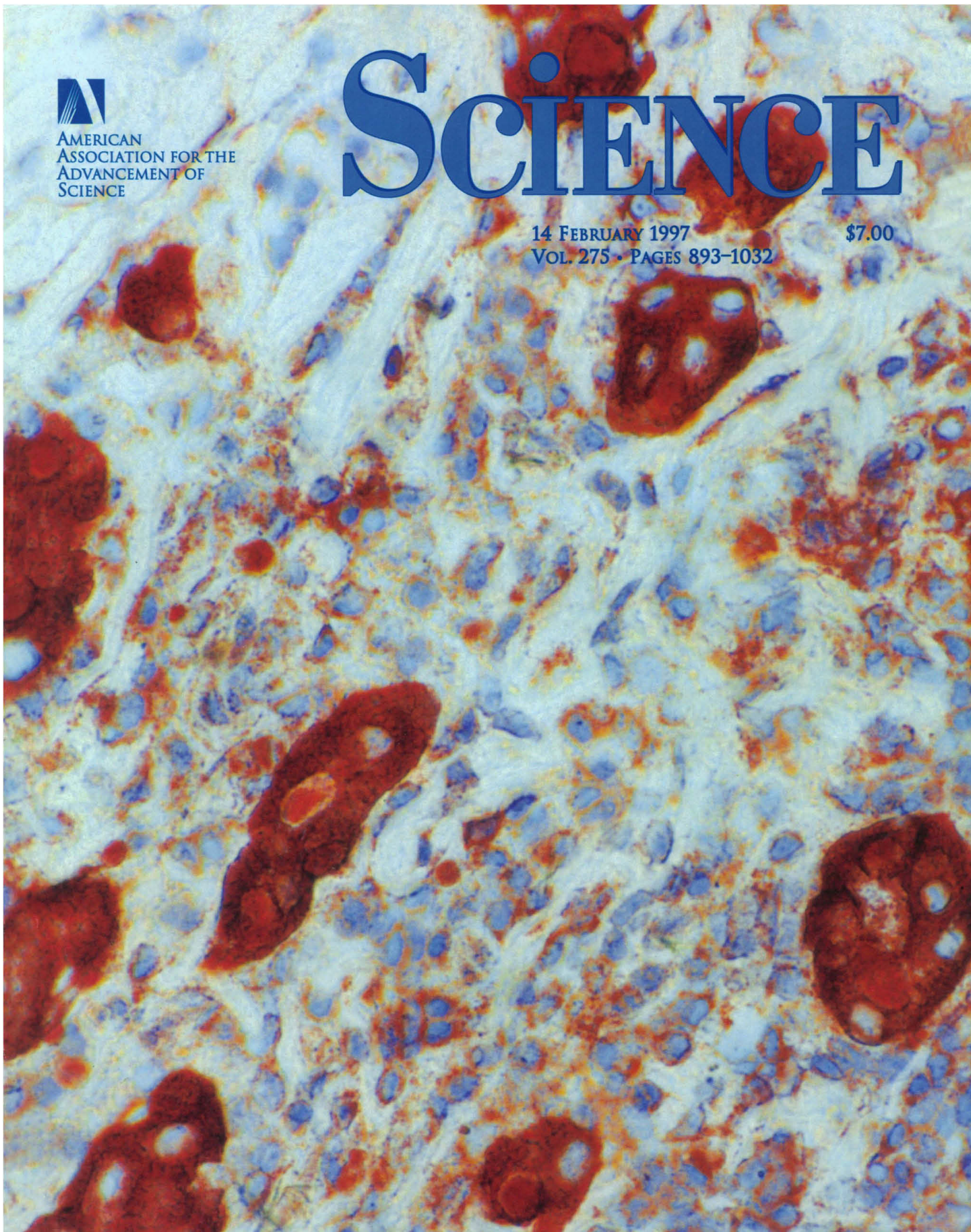


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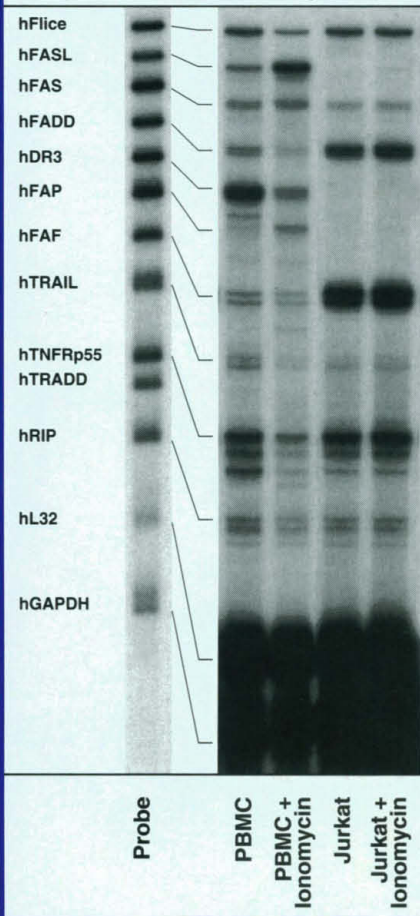
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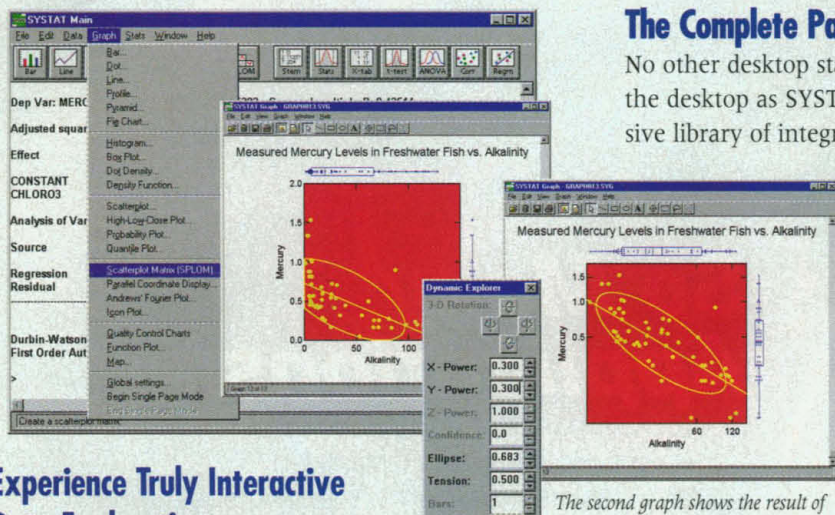
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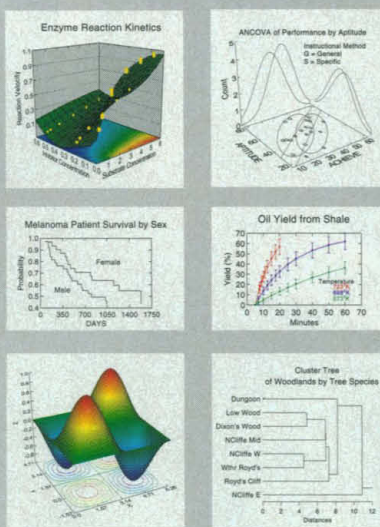
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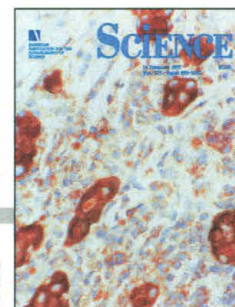
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## COVER

Expression of Fas protein (red) detected by immunohistochemistry on disarrayed thyroid tissue (magnification  $\sim \times 1000$ ) from a patient with Hashimoto's thyroiditis, an autoimmune disorder. Interactions between Fas and its ligand (FasL) control several normal and pathological

processes of cell death. Fas expression induced by interleukin-1 on thyroid cells constitutively expressing FasL triggers thyroid cell death and contributes to the pathogenesis of Hashimoto's thyroiditis. See page 960 and the News story on page 926. [Image: Giorgio Stassi]



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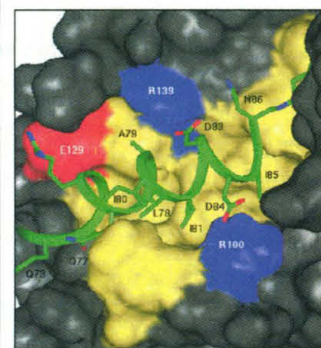
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## On the Web

Enhanced Perspective by J. L. Bada on the origins of molecular handedness

<http://www.sciencemag.org/science/content/vol275/issue5302/942.htm>

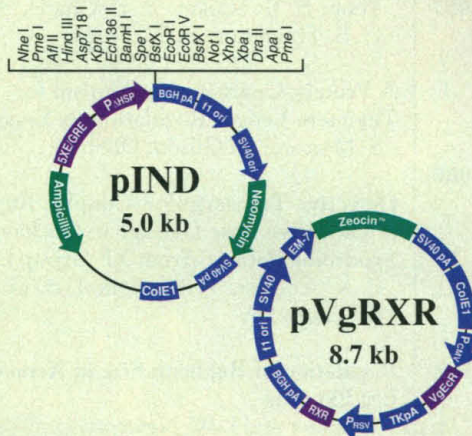


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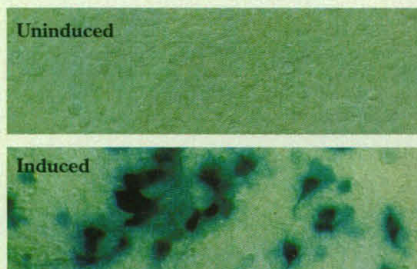
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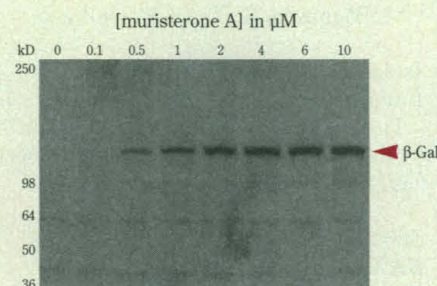
The slides below show a simple colorimetric assay of 293 cells cotransfected with pVgRXR and pIND/lacZ before and after muristerone treatment. This example vividly illustrates the Ecdysone System's tight control and capacity for high inducibility.



Uninduced and induced transiently transfected 293 cells stained with X-gal.

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1. No, D. et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 3346-3351.

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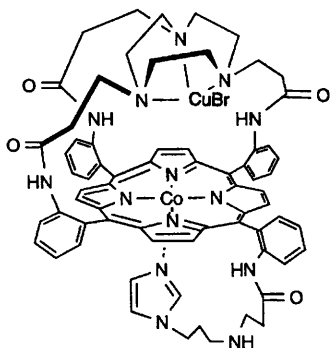
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## Oxidase model

Cytochrome c oxidase in the mitochondria catalyzes a four-electron reduction of  $O_2$  to  $H_2O$  by cytochrome c as part of the cycle that produces adenosine triphosphate. Collman *et al.* (p. 949) have synthesized a model compound that contains a cobalt(II) porphyrin



near a copper(I) atom that can perform this reduction electrochemically through a bridged peroxide intermediate. Like the enzyme, this system operates at physiological pH and does not leak  $H_2O_2$ . This model may prove useful in identifying the rate-determining step of this catalytic process.

## Fas and thyroid disorders

Patients with Hashimoto's thyroiditis (HT), an autoimmune disorder, experience thyroid gland destruction caused by accelerated cell apoptosis. Giordano *et al.* (p. 960; see the news story by Williams, p. 926) found that both normal and HT thyroids express the Fas ligand, FasL, which is also expressed at immune-privileged sites, where it interacts with Fas cell surface molecules to destroy T cells. Unlike normal thyrocytes, HT thyroid cells express Fas, which leads to their death through apoptosis. The authors

## Excess left-handed molecules in a meteorite

Carbonaceous chondrites are assumed to have formed about 4.5 billion years ago and represent a record of early organic chemical evolution. Cronin and Pizzarello (p. 951; see the Perspective by Bada, p. 942) found a small but distinct excess of left-handed amino acids in the Murchison meteorite, which is surprising because most nonbiogenic amino acids are expected to be racemic (containing equal amounts of left- and right-handed enantiomers). Such enantiomeric excesses, which were likely the result of processes in the early interstellar medium, may have influenced prebiotic chemical processes on Earth.

also found that the cytokine interleukin- $1\beta$ , which is expressed during intense inflammation, also induced Fas expression on normal thyrocytes.

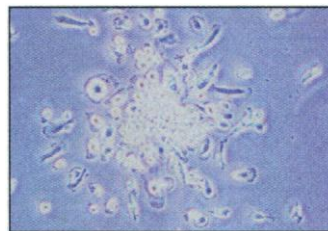
## Allergic response and IL-4

The natural killer (NK)-like T cells can secrete interleukin-4, a cytokine required for the differentiation of T cells into the type 2 helper ( $T_H2$ ) cells that mount the allergic response. Smiley *et al.* (p. 977) show that mice that lack CD1 and hence the NK-like T cells could not produce the initial burst of IL-4. However, the mice could still mount an allergic response by producing immunoglobulin E antibodies in response to antibodies to immunoglobulin D.

## Blood vessel progenitor cells?

Production of new blood vessels in adults has been thought to occur through proliferation and remodeling of endothelial cells (ECs) from existing vessels. Asahara *et al.* (p. 964) isolated putative EC progenitor cells from human peripheral blood and showed that they differentiate into ECs in vitro. The cells also migrate to sites of active

angiogenesis in several animal models, a behavior which suggests that they may be useful for



targeted delivery of therapeutic agents that stimulate or inhibit angiogenesis.

## Setting the pace

The nematode gene *clk-1*, which controls the rate of development and life-span, as well as the period of rhythmic behaviors such as swimming and defecation, has been identified and cloned. Ewbank *et al.* (p. 980; see the Perspective by Guarente, p. 943) show that the sequence of the CLK-1 protein is highly conserved in eukaryotes and is similar to the yeast metabolic regulator Cat5p. These results suggest a link between cellular metabolism and longevity.

## Replicon size

Initiation of DNA replication occurs at more genomic sites in embryonic cells than in somatic

cells. Walter and Newport (p. 993) have found that altering the nucleo-cytoplasmic ratio in *Xenopus* egg extracts can change the size of replicons in the added sperm chromatin, mimicking the natural shift in replicon size that occurs at the time of the mid-blastula transition. The amounts of origin recognition complex bound did not change, implicating a still unknown factor in controlling replicon size.

## Lassoing catalytic antibodies

A strategy has been developed to screen catalytic antibodies directly for their desired reactivity. Janda *et al.* (p. 945) attached the substrate for a particular catalytic reaction to a functional group that would become activated during catalysis. This activated group, which is also attached to a polymer support, then binds to the antibody. Catalytically active antibodies from a library will be immobilized while retaining their activity, and inactive antibodies can be rinsed away.

## Life's instabilities

A subset of human colon cancers are characterized by genetic instability at nucleotide repeat sequences. Rampino *et al.* (p. 967) show that this instability frequently affects a repeat sequence in BAX, a gene that normally promotes cell death, in a way predicted to functionally inactivate the encoded BAX protein. Colon cancer cells with BAX mutations might be selected during colon tumorigenesis because these mutations would enable the cancer cells to escape death.



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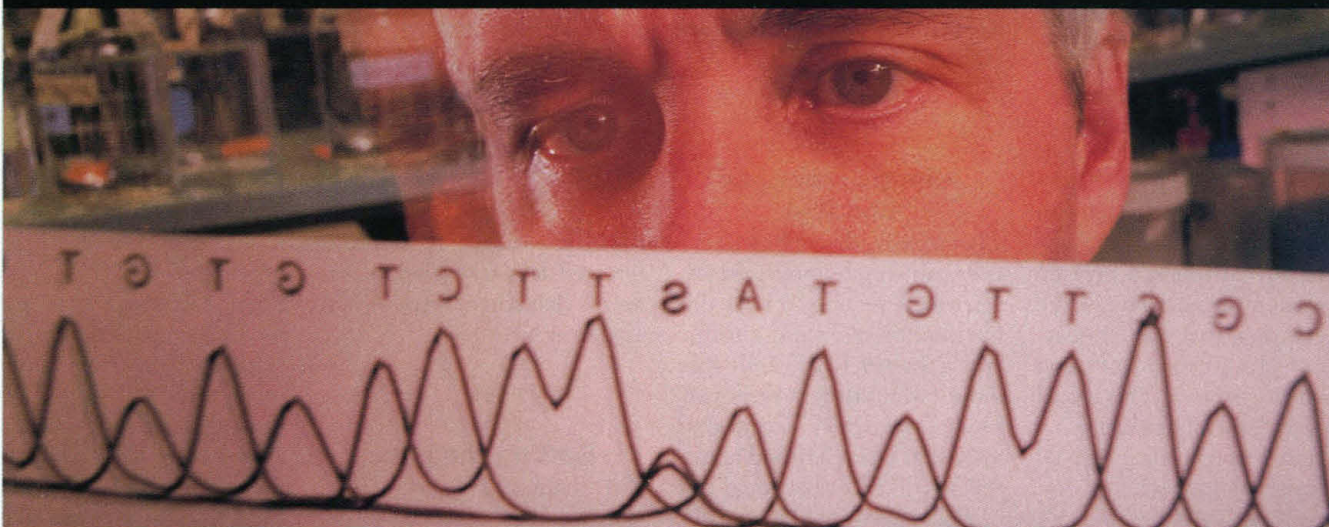
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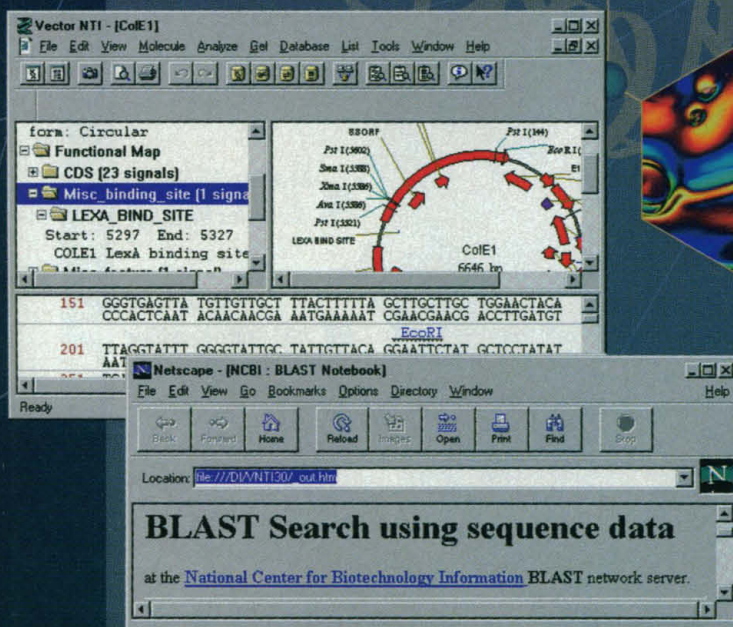
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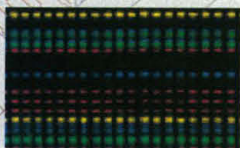
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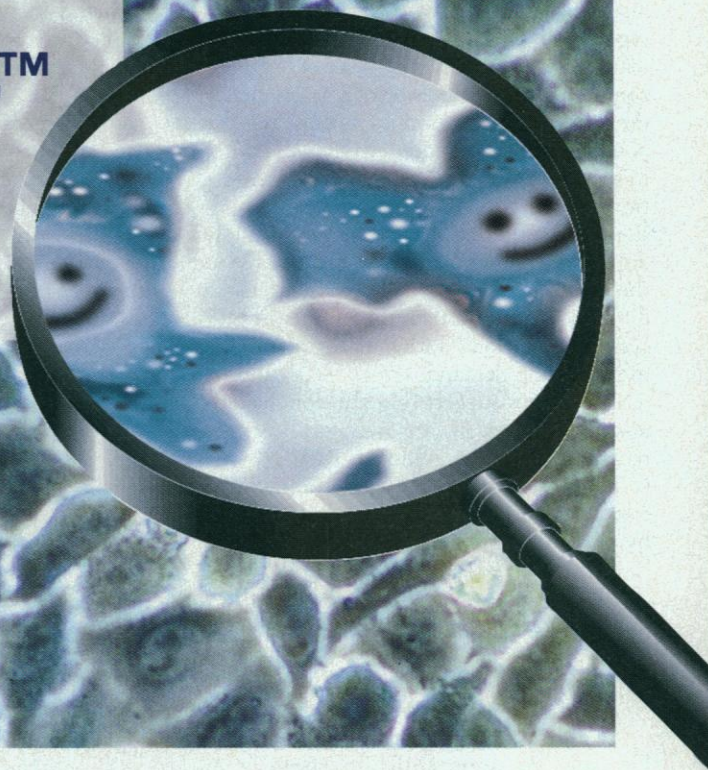
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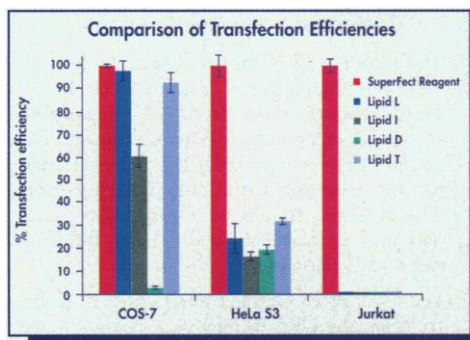
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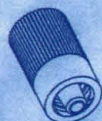
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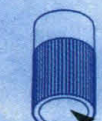
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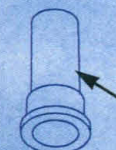


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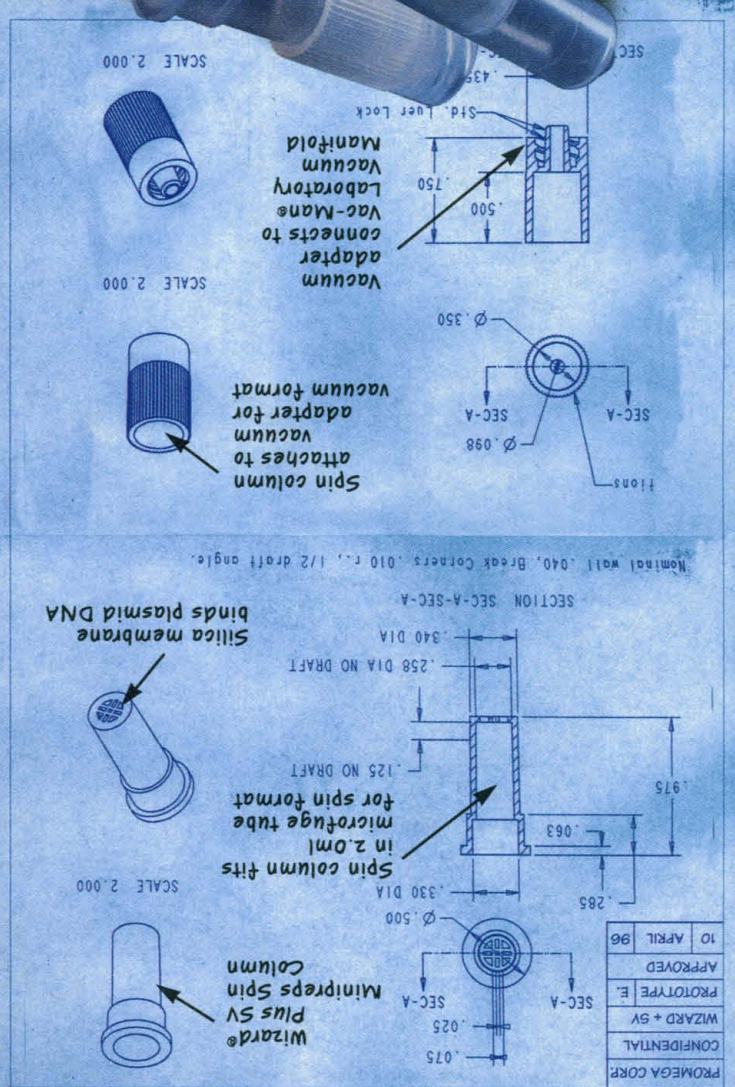
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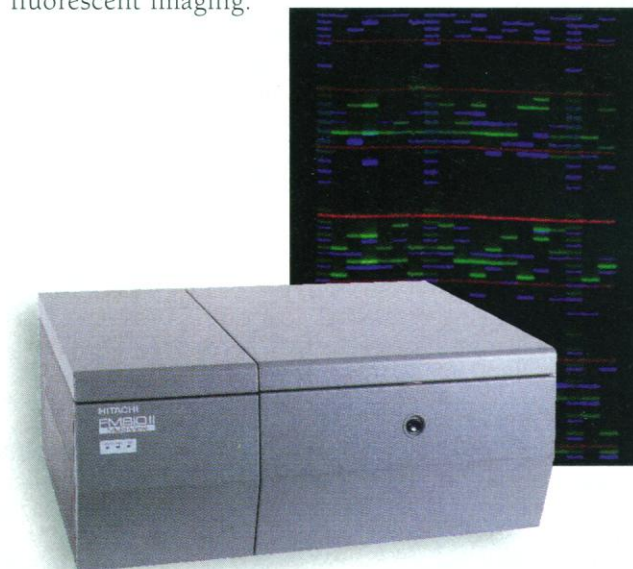
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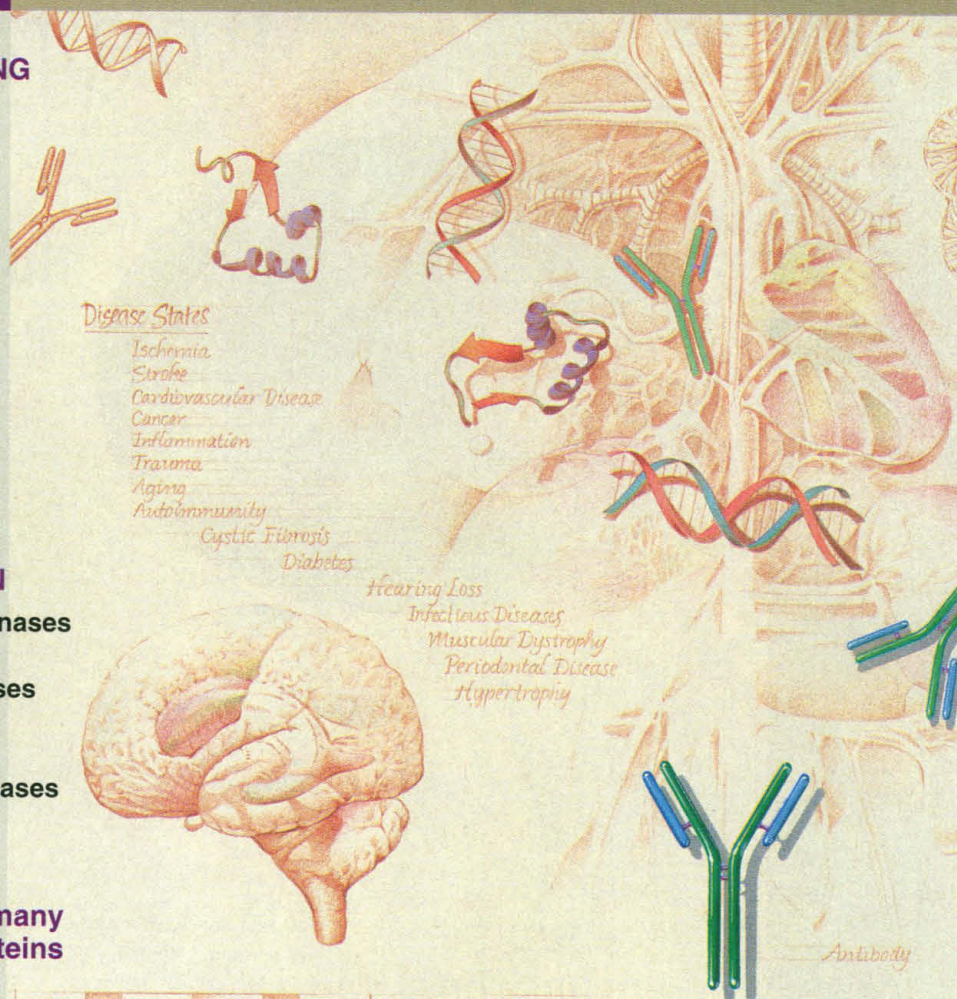
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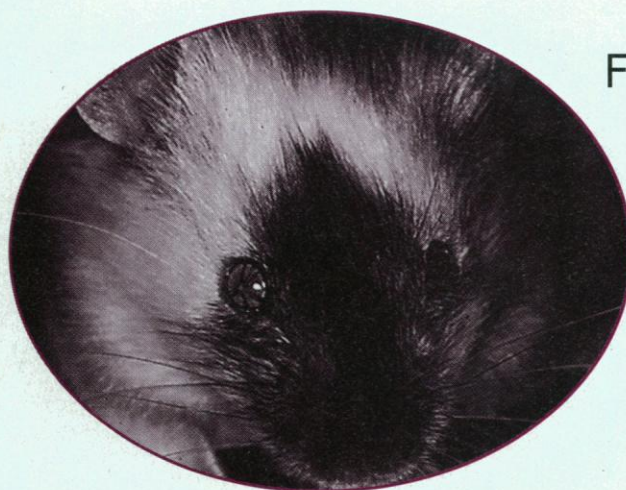
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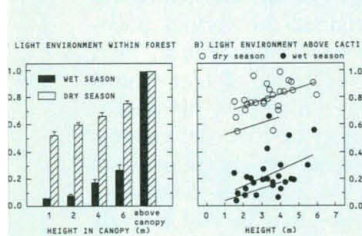
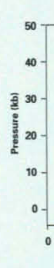
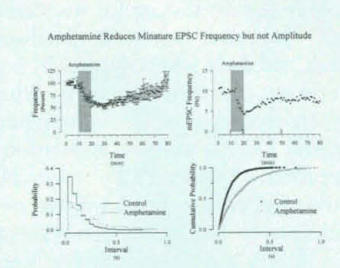
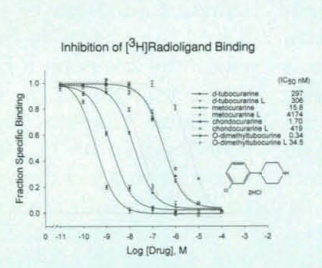
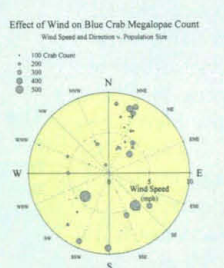
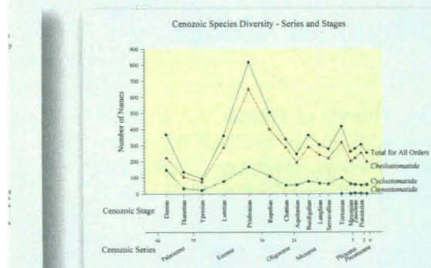
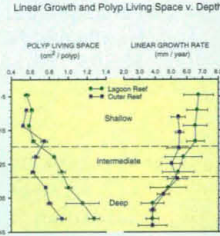
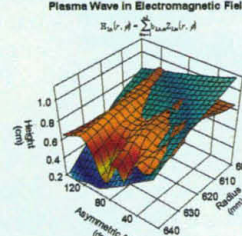
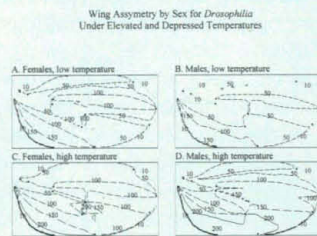
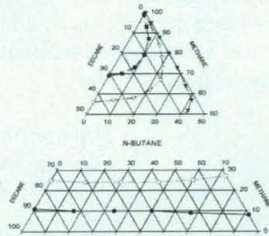
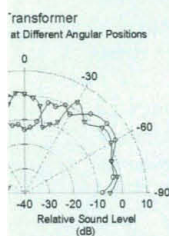


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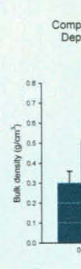
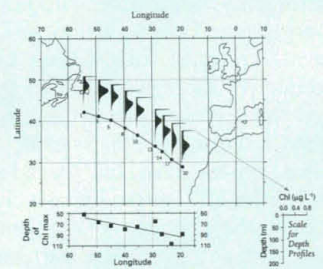
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