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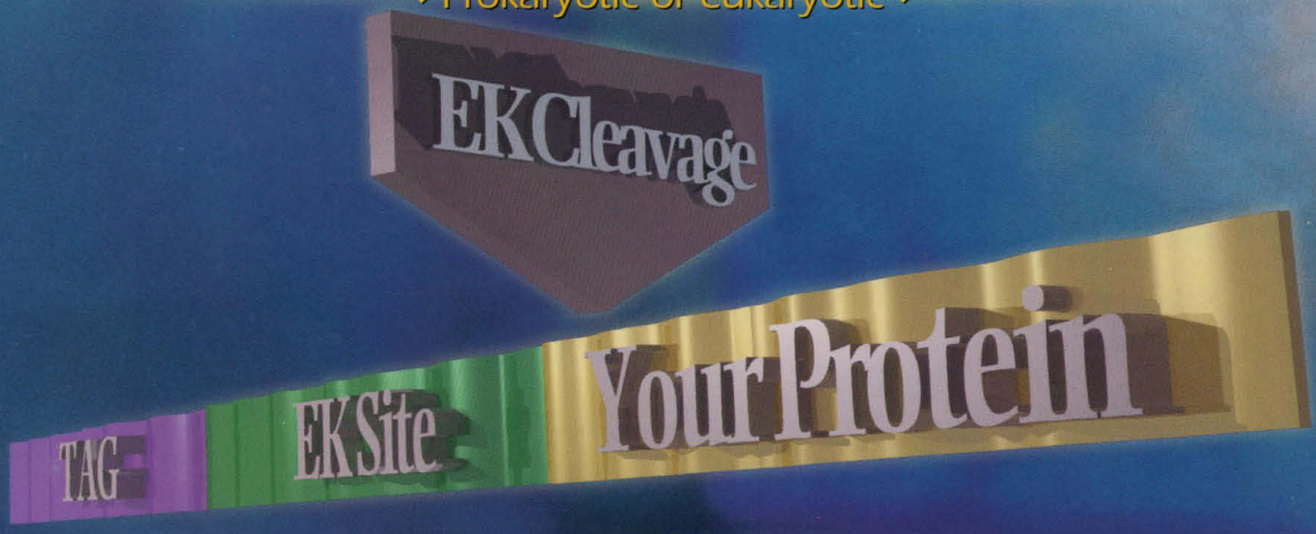

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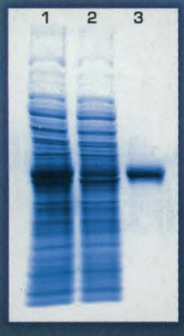

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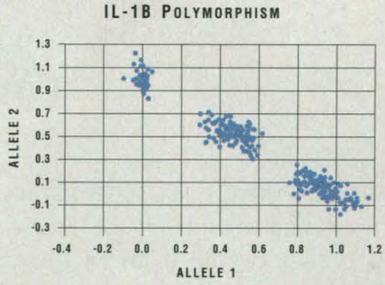

Genotyping of the single nucleotide IL-1B polymorphism: Genotyping of the two alleles of the human Interleukin-1 beta (IL-1B) promoter polymorphism at position −511 was performed using the fluorogenic 5′ nuclease assay. The graph shows genotyping results for 454 individuals. (Results courtesy of Franco di Giovine and Adeel Chaudhray, University of Sheffield, UK.)

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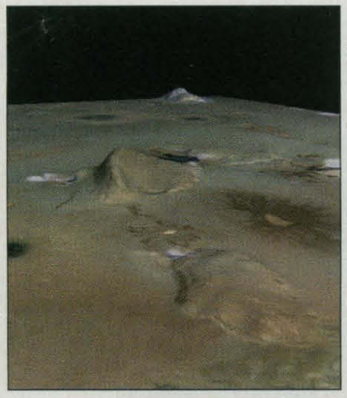

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Io's moving mountains

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Information highway for plants

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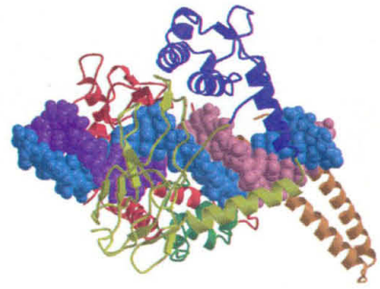
COVER

A severe economic downturn has snapped a decade of rapid growth in Southeast Asia and put the region in the international spotlight. That growth had fueled an expansion in the scientific infrastructure of four major countries in the region—Indonesia, Malaysia, the Philippines, and Thailand. A Special News Report, beginning on page 1465, examines what those countries have accomplished and the people behind those achievements, as well as whether that progress can be sustained in light of current conditions. [Montage: C. Faber Smith]



1490, 1504 & 1534

Topoisomerase I unwinds DNA

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edited by PHIL SZUROMI

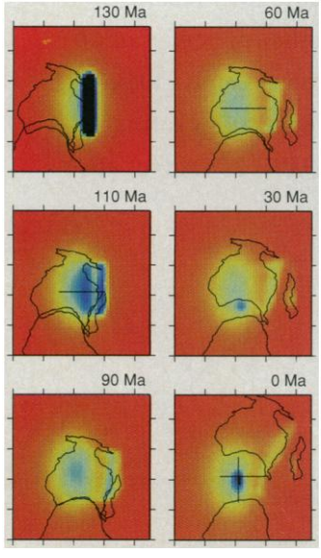
Thermal evolution of Venus

The crust of Venus' surface is dominated by vast volcanic plains, several volcanic rises, and major plateaus. Most of the crust appears to be between 1 billion and 500 million years old. Phillips and Hansen (p. 1492) synthesize recent work on the temporal relations of deformation in these various physiographic units and present a model for the thermal evolution of the planet. The plateaus seem to record early extension in a hot crust; later deformation and volcanism are consistent with cooling and thickening of the crust in the plateaus with time. They suggest that these and other features can be related to initial formation of crustal plateaus above hot mantle plumes, and as the planet cooled with time, a change in the style of convection in the mantle.

■

Uplifting Australia with a downgoing slab

During the Cretaceous, when other continents were inundated by rising seas during the global sea level maximum, the bulk of Australia was left high and dry. To explain this quandary and the anomalous geochemical data, which suggests that the mantle was cold beneath Australia during the Cretaceous, Gurnis *et al.* (p. 1499) modeled mantle convection beneath Australia from the present day to 130 million years ago, along with the inferred motion of the plates at that time. Their model suggests that Australia was uplifted by a subducting slab that passed beneath the continent during the Cretaceous and is presently being drawn up by the Southeast Indian Ridge. The good fit of the observations to the model indicates that mantle-crustal coupling is an important factor for explaining unresolved tectonic anomalies.



■

Recovering their early training

Owls integrate auditory and visual information they receive—interaural time differences and visual receptive field locations—into a spatial map of their environment. It is known that this map can be perturbed in juvenile owls, for example, by fitting their eyes with prisms that shift locations in their receptive field rightward. This particular adaptation is greatly reduced or absent in the adult birds. Knudsen (p. 1531; see the news story by Barinaga, p. 1451) shows that adult owls that were exposed transiently to prisms when they were juveniles appear to retain traces of those events and thus are capable of adapting when subjected to the same prism displacement as an adult. Furthermore, these traces are specific for the early life event because new prisms that produce a leftward shift do not induce plasticity.

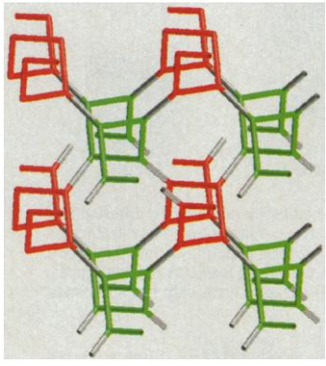
Big slope failure on little Io

Io, the smallest of the Galilean satellites, is noted for its active volcanism. This volcanism provides clues to the crustal surface deformation and its relation to internal dynamics. Schenk and Bulmer (p. 1514; see the news story by Irion, p. 1457) have studied a different structure, a large mass movement at Euboea Montes in the southern hemisphere of Io. This large slumping block of material, located on a smooth undeformed plain, probably represents a landslide related to uplift and compression within the interior of Io beneath this area. The recognition and detailed study of such deformation features will help in the understanding of the dynamic evolution of this small but active moon.

■

Expansion under pressure

Most materials contract in all directions when they are placed under pressure. However, some exceptional materials may expand in one or even two dimensions under pressure. Examples of



materials exhibiting such negative linear compressibility include lanthanum niobate and certain phases of selenium and tellurium. Baughman *et al.* (p. 1522) identify such materials and show that if the material dimensions are chosen appropriately, then the overall surface area may increase even though the overall volume does not. Network materials (such as the helical chain material illustrated) are proposed that exploit this property to achieve no compression or overall expansion under pressure. Negative compressibility effects may also be relevant in muscular hydrostats, such as those found in worms.

■

Aging clays and rising seas

Sediments derived from the sea floor are usually dated with potassium-argon or rubidium-strontium isotope systems measured on bulk samples of clay minerals. Because the measurements are done on a series of clay minerals that could have formed over a range of time, the recovered ages are variable. Smith *et al.* (p. 1517) developed an argon-40–argon-39 laser probe method to date single pellets of nanometer-sized glauconite grains that yield a more accurate and homogeneous age for a given sediment sample. With this better age resolution, they were able to resolve possible global sea level variations in a sequence of sediments and provide a useful minute tracer of global changes.

■

Change in the weathering

Acid mine drainage is a widespread problem resulting from the oxidation and weathering of sulfide-rich minerals to sulfuric acid. Coal or metal mining has exacerbated the problem, and also the related heavy metal pollution, by concentrating reactive minerals near the surface or exposing ores to ground water. The weathering is greatly enhanced and catalyzed by microorganisms. Typically, it has been thought that the primary bacteria responsible for the weathering is *Thiobacillus ferrooxidans*, and this species has been used in most laboratory studies, but in situ characterization has been difficult. Schrenk *et al.* (p. 1519) used molecular methods to

(*Continued on page 1427*)

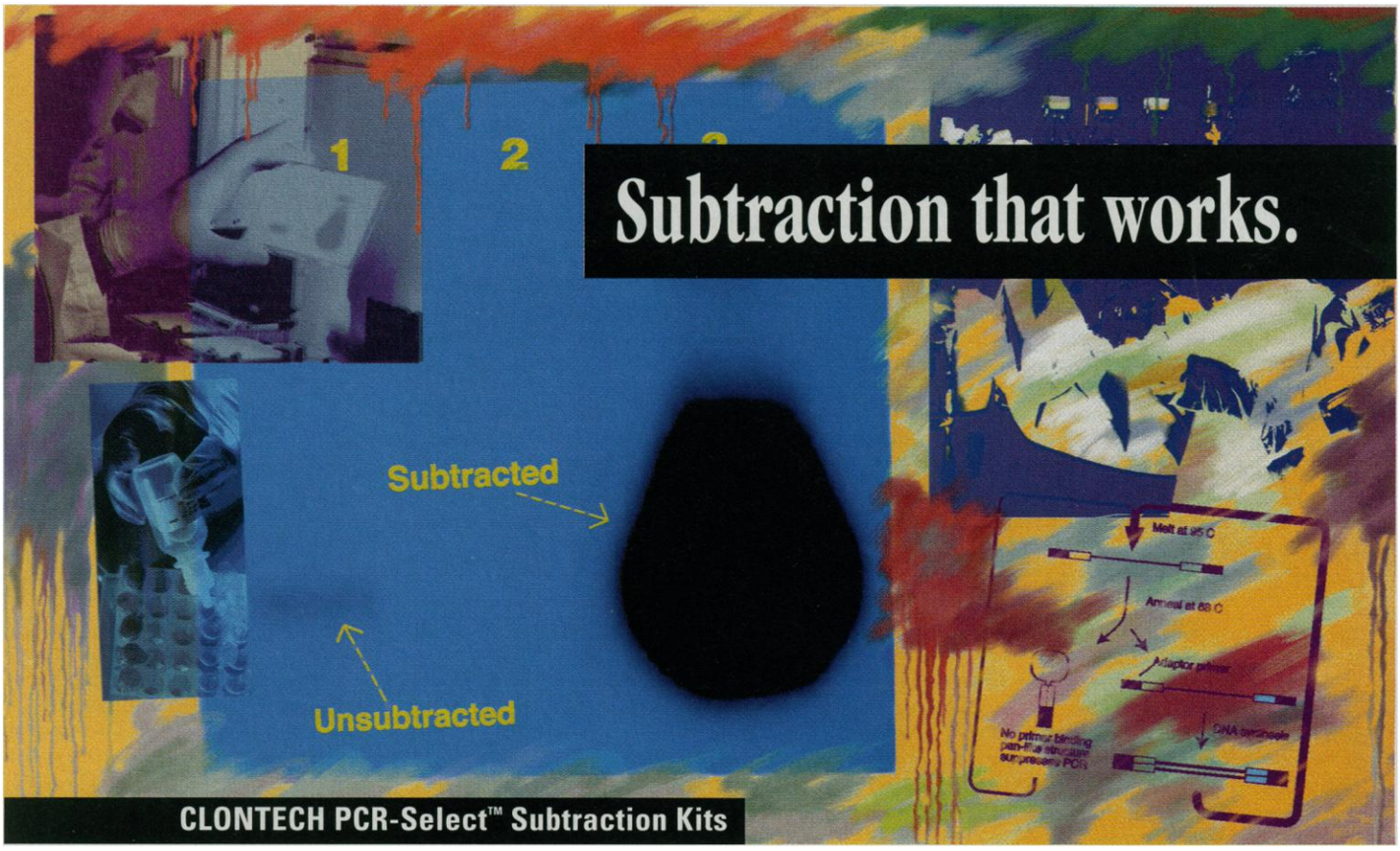
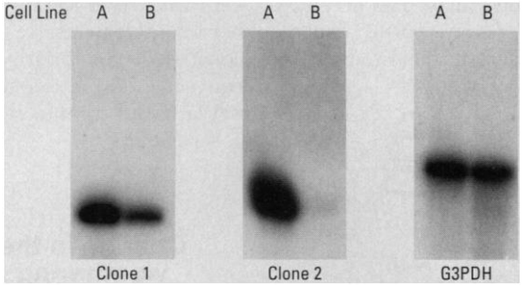


Illustration inspired by the art of Robert Rauschenberg (1925).



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(Continued from page 1425)

examine the in situ distribution of microbes at a mine at Iron Mountain, California. The data show that *Leptospirillum ferrooxidans* rather than *T. ferrooxidans* predominates in the acid-forming zone of the mine.

■

At the crossroads

The motion and interaction of dislocations in materials have important influences, for example, on their plasticity, but real-time experimental observation of such processes is difficult because of the complexity of the processes and the speed at which they occur. Mechanisms therefore usually have to be inferred from postmortem information gained, for example, from electron microscopy. Zhou *et al.* (p. 1525; see also commentary by Gumbsch, p. 1489) have performed large-scale molecular dynamics simulations of dislocation intersection processes in copper. A complex series of steps leads from junction formation to unit jog formation. This final state is similar to that observed experimentally.

■

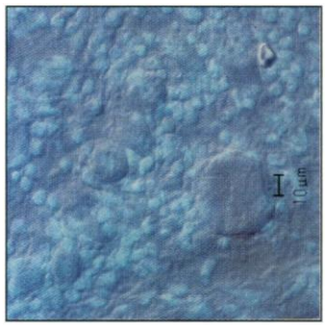
Enzymes that help DNA relieve stress

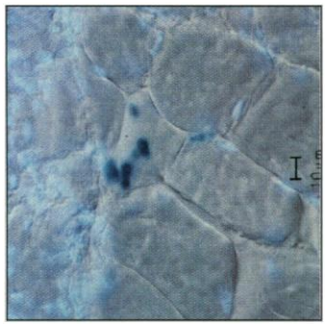
Topoisomerases are enzymes that transiently break DNA strands and thus alter DNA double-helical topology. The type I class of eukaryotic topoisomerases breaks a single strand, which allows any torsional stresses that accumulate during over- or underwinding of the helix to dissipate. These stresses can be introduced during DNA replication, transcription, and chromatin assembly. Redinbo *et al.* (p. 1504) and Stewart *et al.* (p. 1534) present three crystal structures of human topoisomerase I in noncovalent and covalent complexes with DNA that reveal a controlled rotation mechanism for reducing torsional stress and a mode for binding camptothecin, an anticancer drug (see the commentary by Nash, p. 1490).

■

Muscle from bone marrow

One approach to treatment of muscular dystrophies would be to replace the degenerated muscle with new ones. Ferrari *et al.* (p. 1528; see the news story by Pennisi, p. 1456) have found an





accessible source of muscle cell precursors in the bone marrow. Bone marrow cells were genetically marked with an enzyme that was only activated if the cell differentiated along the muscle lineage. They either injected these cells into the degenerated muscle of a mouse where the degeneration had been chemically induced or replaced the bone marrow of these mice with the marked marrow. In both cases, the marked cells differentiated into multinucleated muscle fibers at the site of injury. This result shows that bone marrow contains cells that can differentiate in vivo into mature striated muscle and that genetically modified bone marrow cells can express the genes and survive in the muscle. This approach provides an avenue to explore in the search for therapeutic options for inherited muscle disorders.

■

Natural CD1d1 ligand

Mouse CD1d1 is a major histocompatibility-like antigen that is the target for a special subset of lymphocytes, the natural killer T cells, but what natural ligand is being presented to the natural killer T cells by CD1d1? Joyce *et al.* (p. 1541) eluted and identified cellular glycosylphosphatidylinositol (GPI) by mass spectrometry. This molecule would fit readily into the hydrophobic pocket that was identified earlier in the crystal structure of CD1. Knowing the ligand may give clues to the maturation of natural killer T cells and their role in immune responses.

■

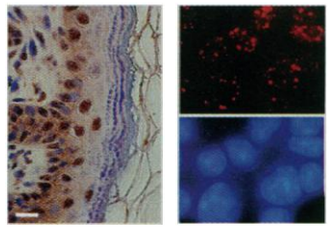
See the light

The biological clock is located in a small primitive nucleus of the brain, the suprachiasmatic nucleus. As days get longer or shorter, the clock is reset by light coming from the retina. Now Morris *et al.* (p. 1544) add a piece to the puzzle of how this resetting occurs. With a complementary DNA subtraction method, they demonstrate that light induces several transcription factors in the suprachiasmatic nucleus—the early response elements c-*fos* and *nur77* and *egr-3*, a zinc finger transcription factor not previously identified in this area of the brain.

■

Partner in crime

Acute promyelocytic leukemia (APL) is frequently associated with a chromosomal translocation that fuses the gene encoding



the retinoic acid receptor α (*RARα*) with *PML*, a gene of unknown function. By studying mice deficient in *PML*, Wang *et al.* (p. 1547) show that this gene regulates the differentiation of hemopoietic cell progenitors and is essential for the growth suppressive- and differentiation-inducing effects of retinoic acid, a naturally occurring regulator of gene expression and an agent used clinically to treat APL. Thus, rather than being an innocuous partner for recombination with the *RARα* gene, *PML* itself appears to play an important role in tumorigenesis.

■

Signaling inside and out

The membrane sphingolipid metabolite sphingosine-1–phosphate (SPP) serves as an intracellular messenger that is generated in response to various extracellular signals and modulates signaling pathways in cells. Lee *et al.* (p. 1552) report that SPP, which is also abundant in serum, is a ligand for the heterotrimeric guanine nucleotide binding protein (G protein)–coupled orphan receptor EDG-1. EDG-1 participates in differentiation of endothelial cells, but its binding partner had been unknown. Activation of EDG-1 by binding of SPP caused increased expression of cadherins and formation of adherens junctional complexes characteristic of differentiated endothelial cells and activated the mitogen-activated protein kinase ERK-2 and the small guanine nucleotide binding protein Rho. Thus, SPP appears to function both as an intracellular and extracellular signaling agent.

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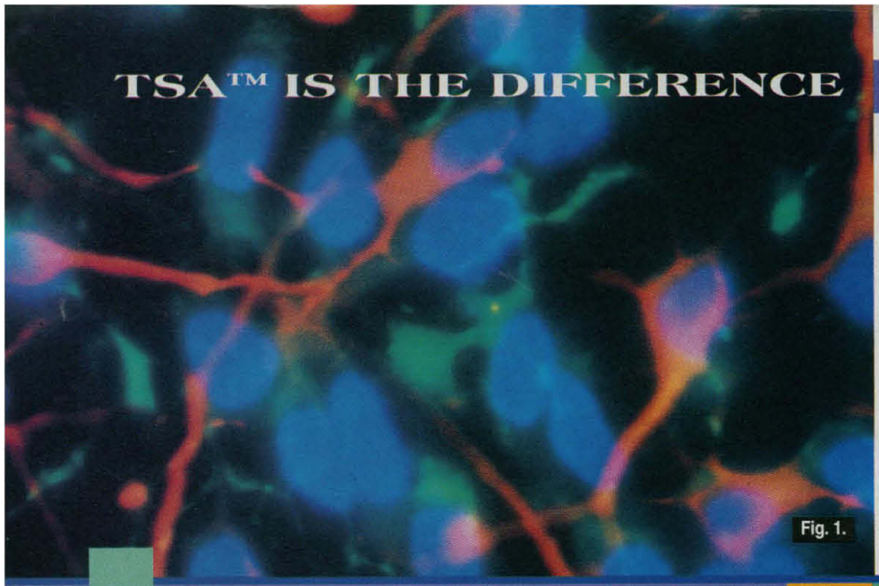

Fig. 1.

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Fig. 1. Multicolor detection using TSA-Direct.
Courtesy of Kevin Roth, M.D., Washington University School of Medicine, St. Louis, Missouri.

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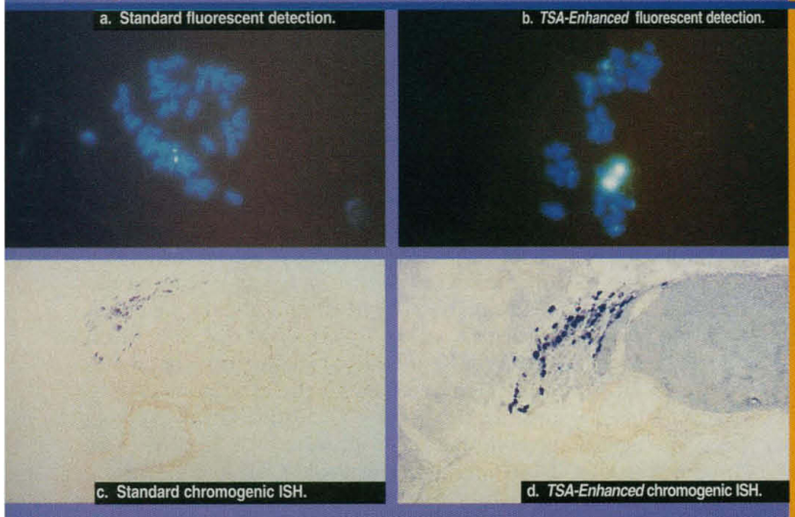
Fig. 2



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Figs. 2 a-b. Fluorescent detection of chromosome centromere probes in metaphase spreads.
Figs. 2 c-d. In situ chromogenic detection of oxytocin in rat brain tissue sections.

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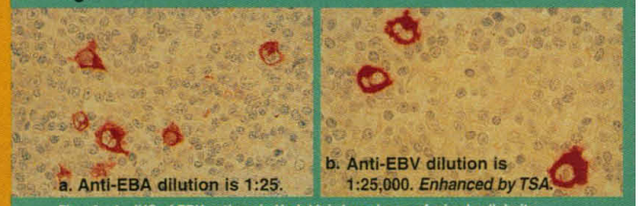
Fig. 3



Figs. 3 a-b. IHC of EBV antigen in Hodgkin's Lymphoma of mixed cellularity.
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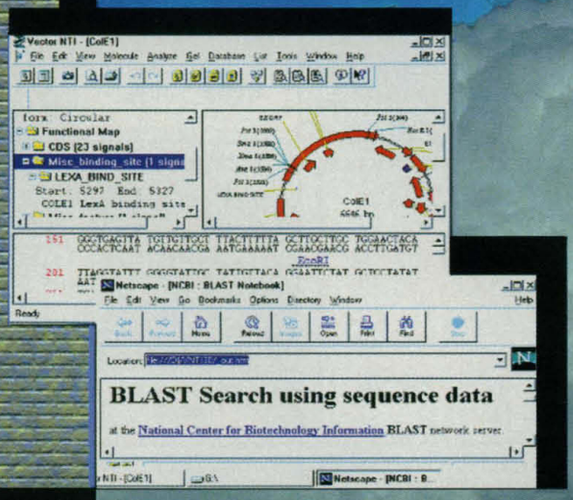

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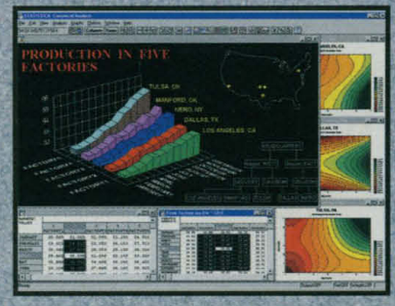

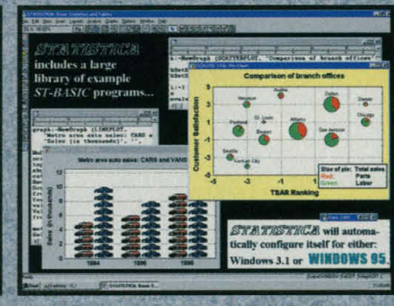

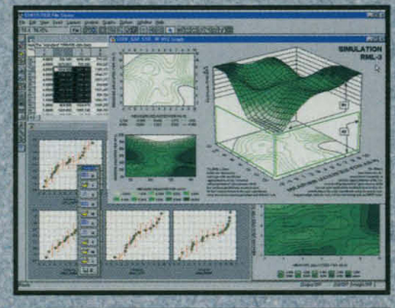

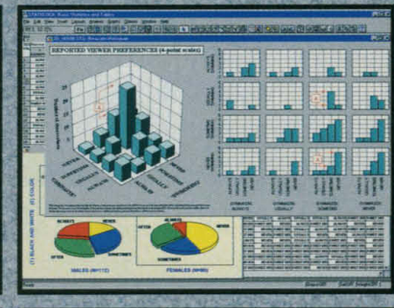

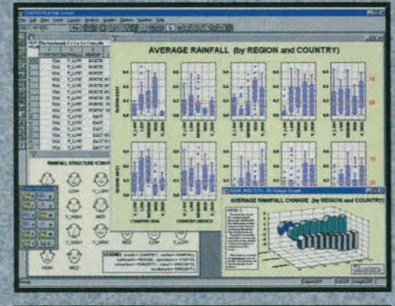

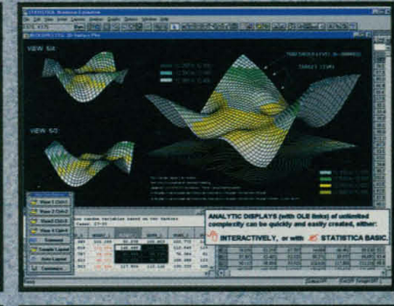

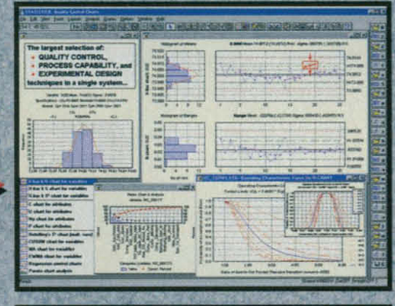

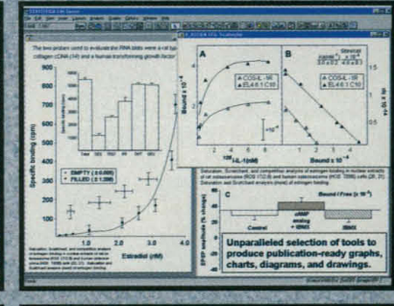

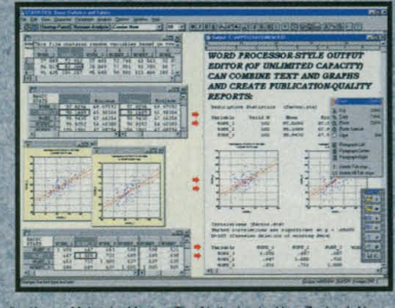

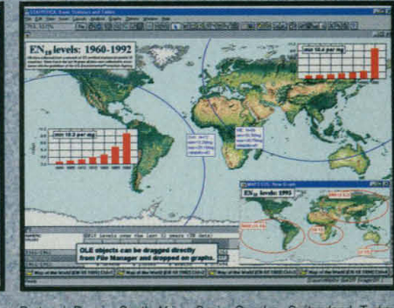

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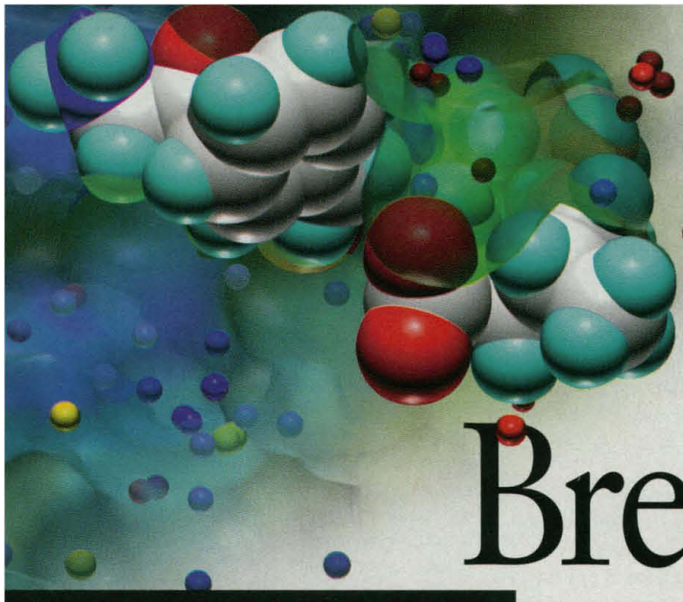

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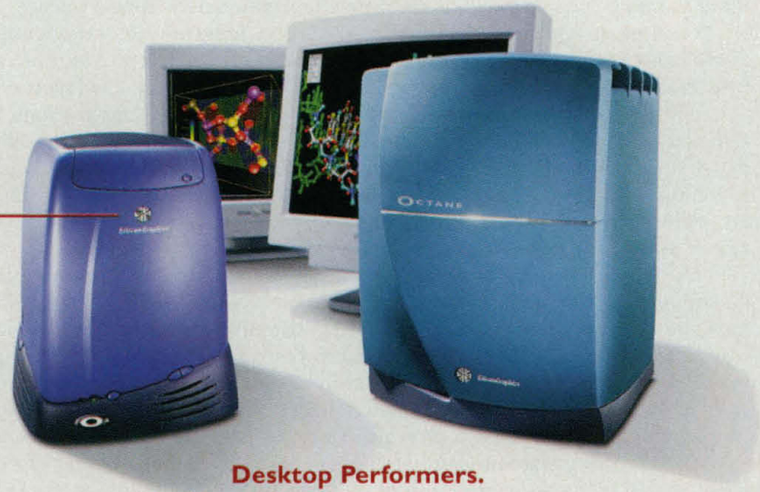

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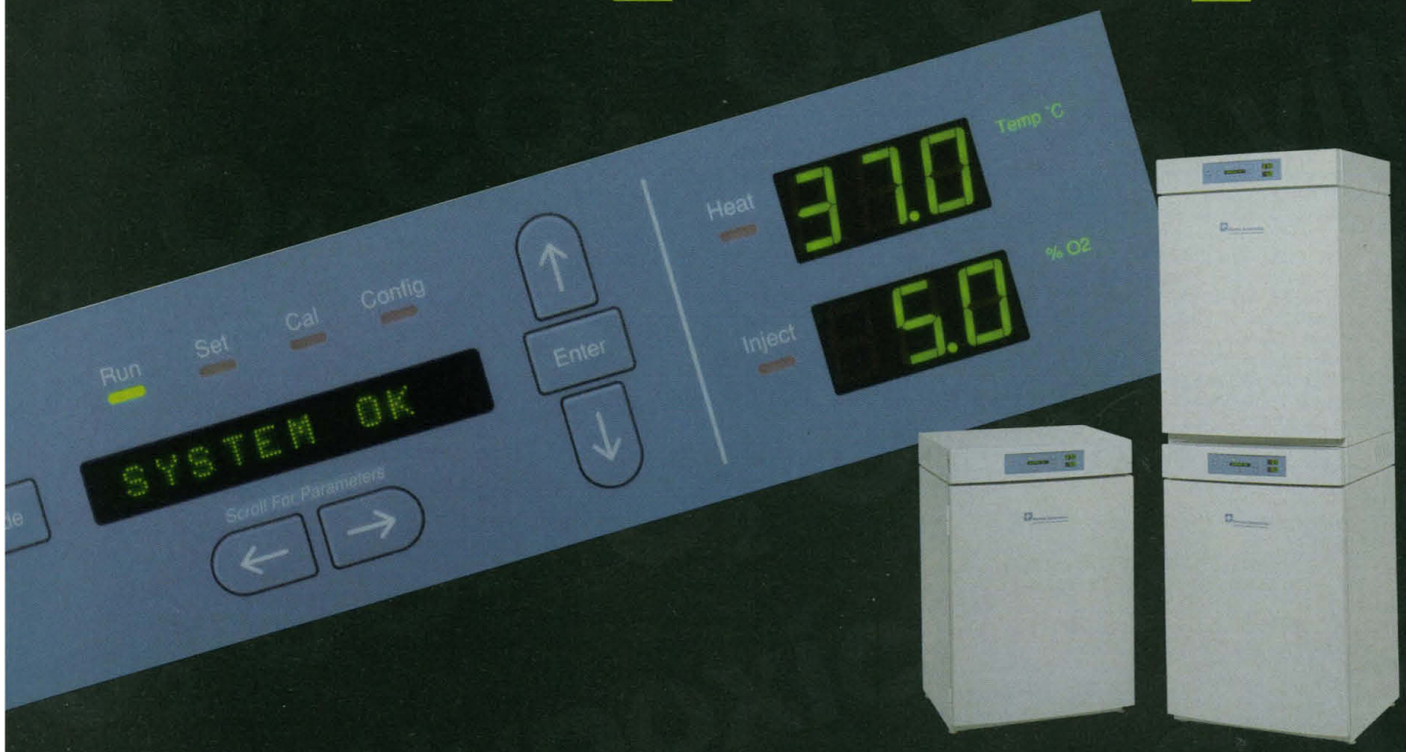

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