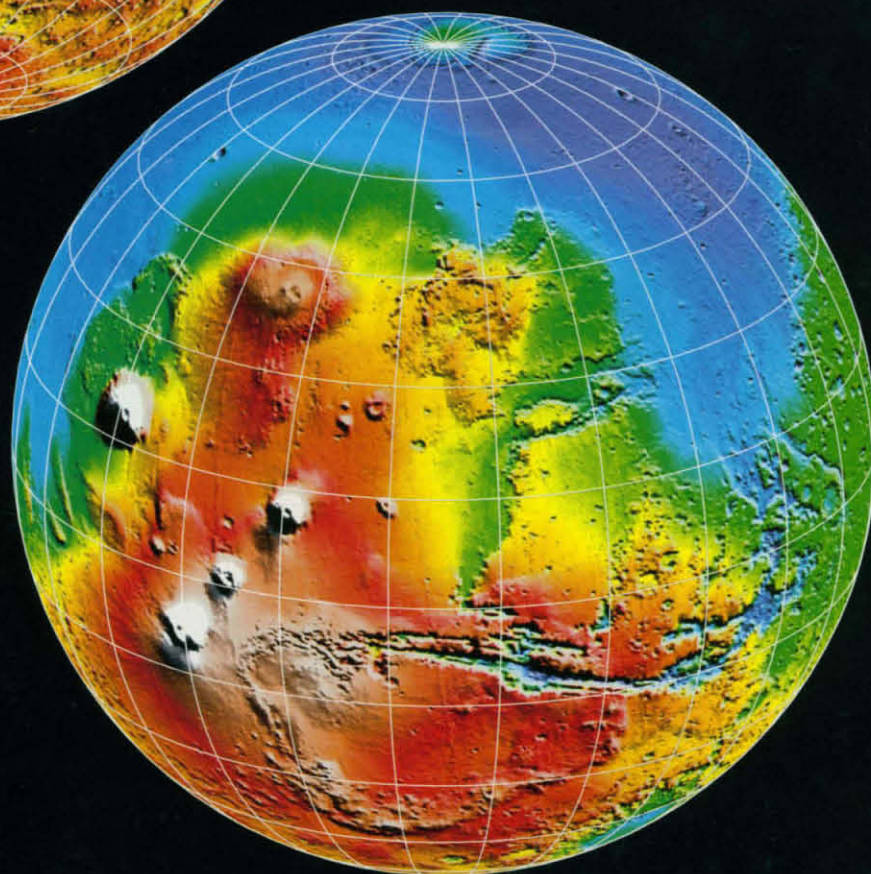
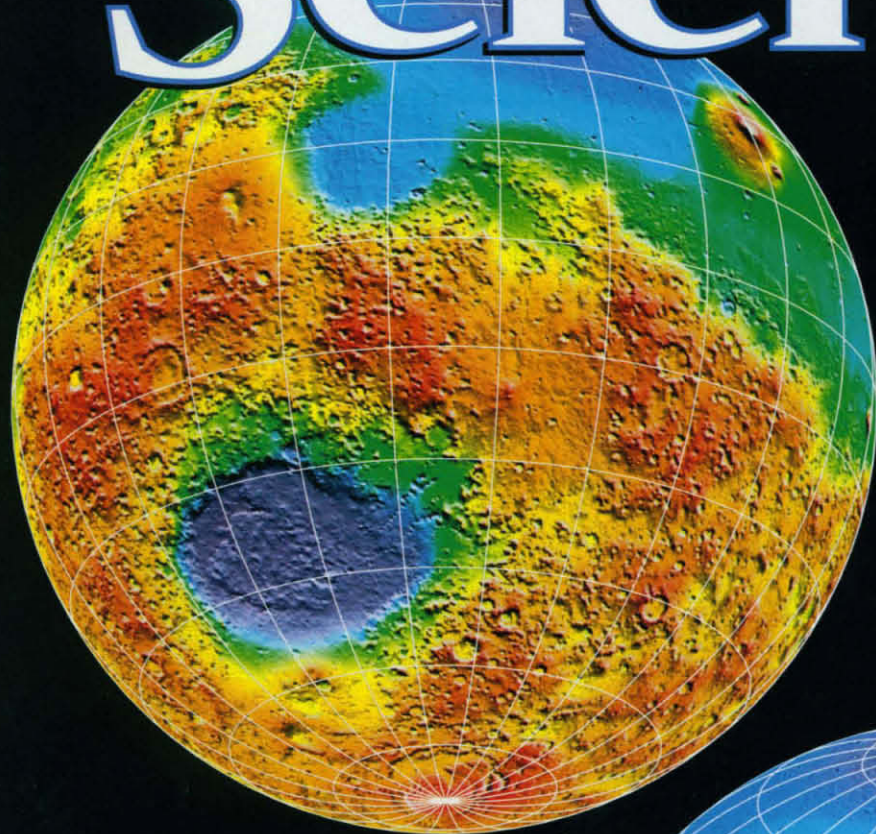


# Science

28 May 1999

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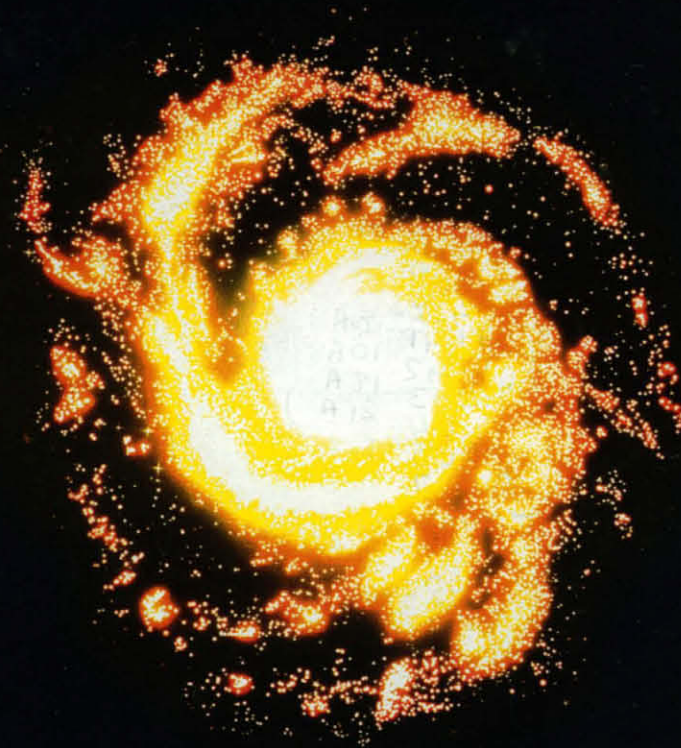
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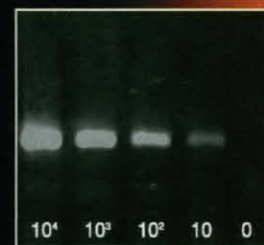
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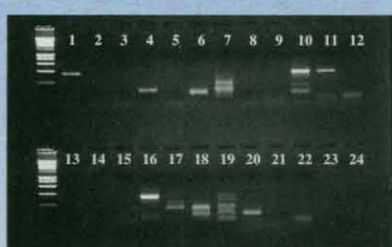
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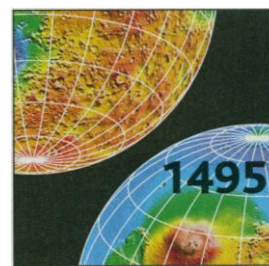
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**COVER** The topography of Mars revealed by Mars Orbiter Laser Altimeter measurements taken through 15 April 1999 from Mars Global Surveyor. Shading was obtained by "illuminating" the topography from the northeast. The upper image shows the Hellas impact basin (dark blue, ~2300 km across), and the lower image shows Tharsis volcanic province and Valles Marineris. [Graphics: G. A. Neumann, Massachusetts Institute of Technology and NASA/Goddard Space Flight Center]



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How the universe  
fell into being

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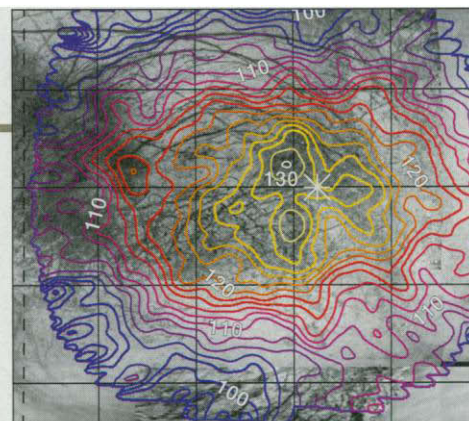
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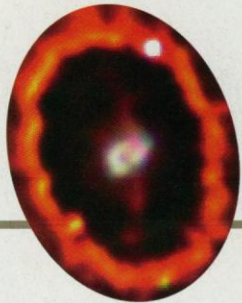


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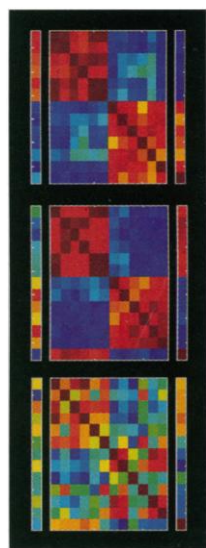
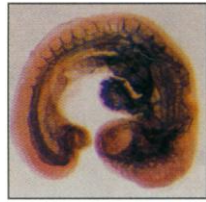
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Correlated brain activity during sensory learning

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## ACCELERATED RACE FOR HUMAN GENOME

### Tetrad Cyclers Have Proven It Can Go the Distance

Over the past year, the genomics community has experienced the scientific equivalent of a seismic shock, for certain private interests have announced plans to sequence the majority of the human genome in advance of the academic participants in the Human Genome Project. This has enormous implications in patent law, because the academics were planning to make the data freely available to all, while private firms may have different agenda.

Thus what was once a methodically scheduled decoding of the human genome has become an all-out race for new sequences. Not ones to throw in the towel early, the academics have instead quickened the pace considerably, announcing plans to publish a "first draft" of the human genome by early 2000. [*Science*, 284 (1999) 406-407, *Nature* 398 (1999) 177]

The academic "champions" in this race are largely the same groups with whom MJ has worked in the development of the Tetrad cyclers. These scientists are proceeding apace—and their work will have substantial implications for the rest of the biological community. With vast quantities of genomic data just around the corner, it might be astute for others to build up their sequencing capacity as well. Many discoveries in functional genomics will no doubt follow the initial data. The Tetrad cycler has a proven ability to handle this sort of cycle sequencing quite well—wouldn't you want to use the same device the big boys (and girls) do?

## Among Robots, Tetrad Has Many Suitors

### Variety of Integrations Available

When the early concepts for the Tetrad cycler were being sketched, easy integration with automated laboratory workstations was a major concern. All sorts of details must be worked out in advance for a cycler to function properly in the robotic milieu—for example, where will the airflow be routed? How will the plates be sealed? More importantly—how will the robot communicate with the thermal cycler?

Thank goodness, these details have already been addressed by MJ, in collaboration with several robot manufacturers. Existing integrations can be purchased for many applications from such well-known suppliers as Beckman-Coulter, CRS Robotics, Packard, and Rosys-Anthos. Most of the necessary engineering has already been done, which can save

## The MJ Tetrad™ Thermal Cycler of Choice for Genomic Sequencing



A Tetrad™ cycler with manual heated lids

### Tetrad Cyclers Offer Many Useful Features

The "marching orders" given by the collaborating genome centers directed development of a cycler with huge capacity and great speed—and the Tetrad cycler expresses both these traits in abundance. In addition, its modular design allows fitting of *eight* different designs of block (to fit any vessel), while powerful network interfaces and optional motorized lids allow easy integration into automated systems.



### Canada Direct!

MJ Research now sells and supports its instruments in Canada directly. Now Canadian scientists can get the same great factory service and experienced support that US scientists enjoy.

## GENOME CENTERS WANTED MORE

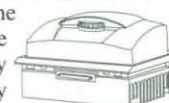
### Ultra-high Capacity for Rapid Workflow in Cycle Sequencing

WALTHAM, Mass. — In 1994, MJ Research introduced the mid-sized DNA Engine™ thermal cycler. Scientists at various genome centers loved the product—but they wanted vastly greater capacity. Sequencing entire genomes requires a huge number of DNA amplification reactions, and the centers simply didn't have space for dozens and dozens of cyclers.

The DNA Engine had been built with a modular block format, and a design concept was that this format allowed the possibility of multi-block units. At the time, it was thought that the market for high-capacity cyclers would be relatively small—confined primarily to genome centers—but MJ had always found that the needs and desires of genome centers anticipate future trends in molecular biology in general.

Thus in 1995, MJ developed the Tetrad™ cycler, with four independent blocks. The genome centers were genuinely enthusiastic, and they began snapping up all the Tetrad cyclers MJ could produce. Much to the surprise of many at MJ, numerous other customers wanted Tetrad cyclers too. Genomics/high-throughput work was growing at a rate far beyond what most had anticipated, and soon the company was backordered for many months.

Simultaneously, automated sequencers were improving in quality and capacity. Sequencing data began pouring out of the labs and into Genbank (as well as into private databases...) Due to its unparalleled ability to cycle 1536 samples at high speeds, the Tetrad cycler has served as the industry-standard workhorse for feeding these sequencers with amplified DNA. New developments allow the use of fantastically small reactions (down to 2µl), and other exciting advancements are on the horizon.



Modular "Alpha" block



The Sagian™ Core System of Beckman-Coulter many months of agonizing delay when trying to set up a high-throughput operation in a hurry.

In a nutshell, communication with the cycler is two-way via a RS-232 or an IEEE-488 port. Sealing is with film or reusable pads, over 96-well or 384-well plates, with pressure being applied by motorized Power Bonnet™ lids.

PCR is covered by patents owned by Hoffmann-La Roche, Inc. & F. Hoffmann-La Roche Ltd. Users should obtain license to perform the reaction.

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## PUTTING THE SQUEEZE ON SILICA

The most common form of silica is quartz. With increasing pressure, quartz eventually transforms to stishovite, which has been identified in highly shocked rocks and has been thought to be important in Earth's lower mantle. The occurrence of phases at higher pressure has been suggested; Sharp *et al.* (p. 1511) have now found such a phase in a highly shocked meteorite from Mars. Electron diffraction data imply that the phase has a structure similar to that of lead oxide. The new phase may be the stable silica phase in Earth's lower mantle and may have been missed in other highly shocked rocks because of its conversion at lower pressures to other phases.

## SUPERCONDUCTING NANOTUBES

Carbon single-walled nanotubes, depending on their diameter and helicity, can be semiconducting or metallic, and those that are only about 10 nanometers in diameter are expected to behave as one-dimensional conductors. Kasumov *et al.* (p. 1508) now show that individual carbon nanotubes about 1 nanometer in diameter (as well as bundles of about 100 of these nanotubes) can carry supercurrents. The nanotubes are connected between two superconducting electrodes; at the low temperatures used to make the electrodes superconducting (1 kelvin), they find that if the resistance of the nanotube is sufficiently low, a supercurrent can flow through it.

## EUROPAN NIGHTS

The Galileo spacecraft has a photopolarimeter-radiometer (PPR) that maps the thermal radiation from the surface of a satellite. Spencer *et al.* (p. 1514) derived a map of the nighttime surface temperatures of Europa from PPR data and found that the temperatures vary with latitude, in some regions by as much as 5 kelvin. An explanation for these temperature variations remains to be determined, but the intriguing possibilities include either a change in the thermal inertia of the ice, which would be related to the changes in temperatures between daytime and nighttime, or an unresolved heat source from within Europa.

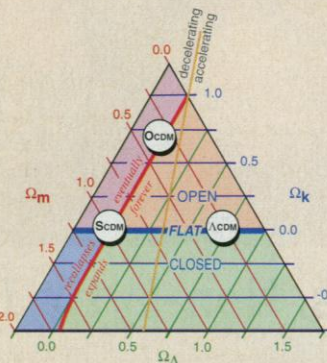
## THE HIGHS AND LOWS OF MARS

The topography of a planet can reveal much about its evolution. Smith *et al.* (p. 1495; see the cover and the news story by Wuethrich) have obtained a high-resolution global view of the topography of Mars from Mars Global Surveyor. The data con-

firm that the high elevations of the southern hemisphere reflect internal processes and show that a widespread deposit from an impact crater forms much of the high elevations. Surface water over much of the planet would have drained into a large basin in the northern hemisphere.

## YOUNGER, FASTER, LIGHTER

The universe developed rapidly in the first second after the Big Bang, and so has the pace of results that are helping astrophysicists understand the structure and evolution of the universe (see the news story by Glanz). Bahcall *et al.* (p. 1481) review the latest theoretical and observational results and simplify the description of the universe to three characteristics, the density of matter, the expansion rate, and the shape,



which they represent with a "cosmic triangle." Their review suggests that the universe is lightweight, accelerating, and flat. In a related research article, Lineweaver (p. 1503; see the news story by Finkbeiner) synthesizes similar recent data related to the "cosmic triangle" and calculates a best estimate for the age of the universe. He gets a youthful 13.4 billion years old, about 1 billion years younger than some previous estimates, but still old enough to allow the creation of galaxies like our own.

## SAVING FISHERIES

There are two approaches to ensuring the sustainability and biodiversity of fisheries: One is the use of catch limits, as is currently practiced, and the other is the setting up of marine reserves to protect stocks. The introduction of reserves has been hampered by a lack of information of relative yields from the two systems. Hastings and Botsford (p. 1537) used a

simplifying set of assumptions to show that yields are similar and that, under some circumstances, marine reserves offer significant advantages over catch quotas.

## A GRACEFUL EXIT

Many viruses kill the cell in which they reproduced by lysing the cell wall, but filamentous phage f1 exits *Escherichia coli* without killing the bacterium. Marciano *et al.* (p. 1516; see the Perspective by Zimmerberg) have purified a bacteriophage-encoded protein, pIV, and showed that it acts as a channel for f1 to exit its bacterial host. Differences between mutant and wild-type protein activity indicate that pIV is a gated channel and that changes in channel properties could affect sensitivity to the antibiotic vancomycin. Protein pIV is a member of a family of proteins involved in secretion of virulence factors from Gram-negative bacterial pathogens.

## UNDERSTANDING AN OLD VACCINE

The Bacille Calmette-Guérin (BCG) family of vaccines against tuberculosis was derived serendipitously after continuous passage of bovine tubercle bacilli in guinea pigs in 1921. However, as a result of the passage history, current strains are different from the original progenitor strain, which may explain the vaccine's variable efficacy in different parts of the world. Behr *et al.* (p. 1520; see the Perspective by Young and Robertson) compared the genomes of BCG strains with that of *Mycobacterium tuberculosis* and *M. bovis* by microarray assay and fluorescent in situ hybridization and found a series of deletions in BCG strains that made it possible to follow their evolution. These results should help in the efforts to design new tuberculosis vaccines.

## SENDING SUGARS AGAINST STAPH INFECTIONS

Bacterial pathogens keep a set of genes in reserve that are only activated when they enter their hosts. Because these genes are thought to be particularly useful for bacterial survival and infection promotion, they may make ideal vaccine targets. Not only would the vaccine be specific for the microbe, but it may interfere with a virulence system crucial for the bacteria's survival. McKenney *et al.* (p. 1523) report the primarily in vivo expression of a surface polysaccharide called PNSG during *Staphylococcus aureus* infection. Purified PNSG protected mice from lethal *S. au-*

CONTINUED ON PAGE 1431

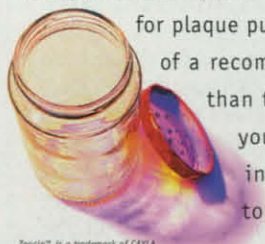




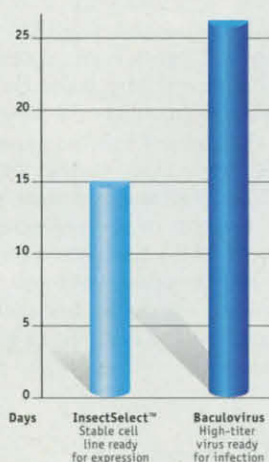
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# THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 1429

*reus* infections by inducing an antibody response. Because of the growing prevalence of antibiotic-resistant *S. aureus* strains, a preventative strategy may provide a needed alternative approach.

## IN SYNC

Some extracellular signaling molecules bind to their cell surface receptors and trigger a release of calcium ( $\text{Ca}^{2+}$ ) from intracellular stores through inositol 1,4,5-trisphosphate ( $\text{IP}_3$ )-gated  $\text{Ca}^{2+}$  release channels. The freed  $\text{Ca}^{2+}$  is then available to regulate various cellular responses such as secretion, proliferation, and gene expression. Hirose *et al.* (p. 1527) used a probe tagged with green fluorescent protein to monitor  $\text{IP}_3$  concentration and show that in a single cell, the mobilization of  $\text{Ca}^{2+}$  into oscillations or propagating waves occurs in synchrony with changes in  $\text{IP}_3$  concentration and localization. The concurrence of these events in space and time indicates that  $\text{IP}_3$  dynamics support  $\text{Ca}^{2+}$  signaling patterns.

## PAYING ATTENTION?

Learning with awareness utilizes different brain structures than learning without awareness. Although the prefrontal cortex has been shown to play a crucial role for the awareness of associations, a competing hypothesis is that awareness needs the interaction of multiple separate brain

regions within a large-scale neuronal system. McIntosh *et al.* (p. 1531) asked people to perform a visual discrimination task while simultaneously presenting tones to them. After some time, one group consciously noticed an association between the tones and the visual stimuli. Subjects who became aware not only scored better in the test, but showed different patterns of brain activity during positron emission tomography scans. Although the left prefrontal cortex showed the highest level of activity, there were several other regions that also showed an increase that could be correlated with awareness.

## LOSING MUSCLE

Patients with hereditary hemorrhagic telangiectasia, a disease characterized by disruptions of the vascular system, have mutations in the gene encoding endoglin, a protein that binds to transforming growth factor- $\beta$  (TGF- $\beta$ ). Li *et al.* (p. 1534) investigated the role of endoglin in vascular development by studying endoglin-deficient mice. Although the early stages of vasculogenesis occurred normally, the mice died in utero because the endothelial tubes were not remodeled into mature blood vessels. This remodeling defect was caused by a failure in vascular smooth muscle development, a finding that may in part explain the pathogenesis of the human disease.

## TECHNICAL COMMENT SUMMARIES

### Polymorphisms Not Found in the IL-13 Gene Promoter

The full text of these comments can be seen at [www.sciencemag.org/cgi/content/full/284/5419/1431a](http://www.sciencemag.org/cgi/content/full/284/5419/1431a)

M. Wills-Karp *et al.* (Reports, 18 Dec., p. 2258) studied the role of the type 2 cytokine interleukin-13 (IL-13) in a mouse model of asthma. They concluded that IL-13 "was necessary and sufficient for the expression of allergic asthma."

K. L. Anderson *et al.* "examined the IL-13 promoter region" on the human genome "in 129 individuals from a population in the United Kingdom." They found "an absence of polymorphisms" in the subset of asthma patients, leading them to "doubt the significance of the IL-13 promoter as a susceptibility locus for atopy or any of the associated conditions...."

In response, Wills-Karp and L. L. Rosenwasser state that they have also found "no significant population-based polymorphisms in this region" of the genome, but that other "possible mechanisms" may exist that involve "polymorphisms in downstream receptor and signaling molecules."

### Fas, p53, and Apoptosis

The full text of these comments can be seen at [www.sciencemag.org/cgi/content/full/284/5419/1431b](http://www.sciencemag.org/cgi/content/full/284/5419/1431b)

M. Bennett *et al.* (Reports, 9 Oct., p. 290) studied the gene p53, which "acts as a tumor suppressor by inducing both growth arrest and apoptosis." They concluded that "p53 can mediate apoptosis through [tumor necrosis factor] Fas transport from cytoplasmic stores."

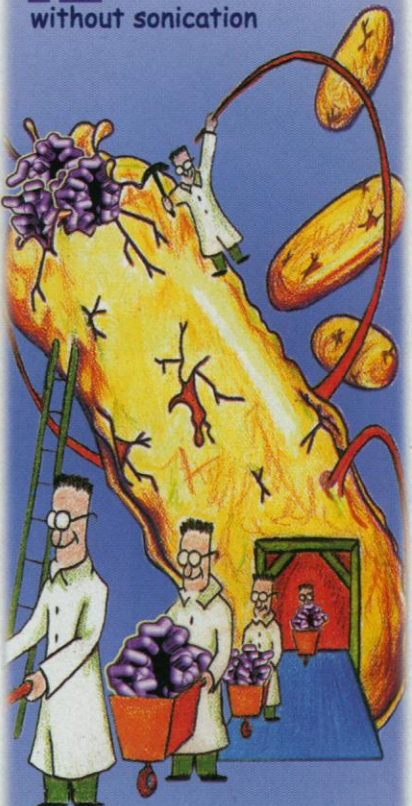
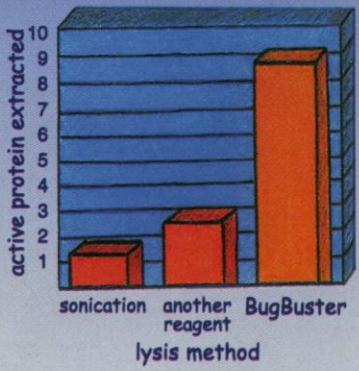
L. O'Connor and A. Strasser comment that they "and others have established that Fas is not required for p53-activated cell death..." and "that p53 is not required for Fas-induced apoptosis...."

In response, Bennett *et al.* state that these studies "are not directly comparable. Evidently, p53 and Fas may interact at multiple levels to induce apoptosis in many different cell types."

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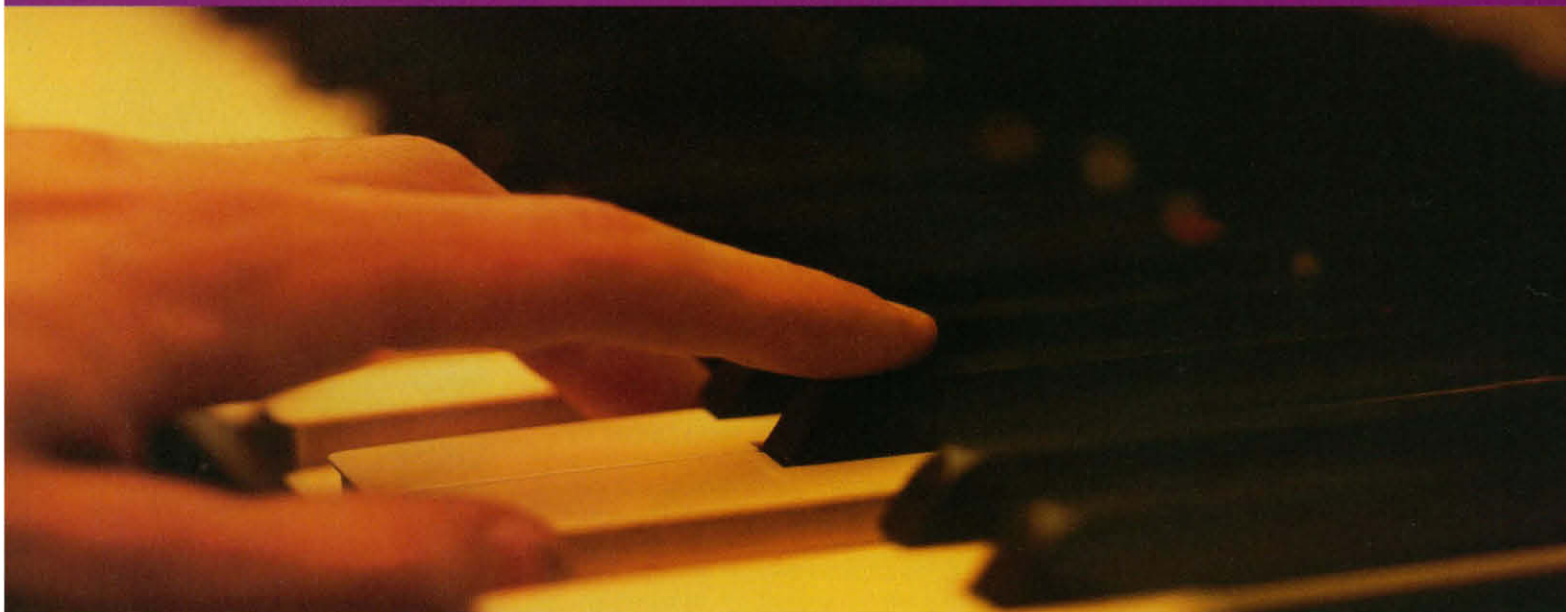



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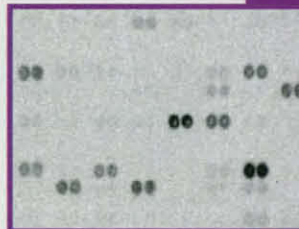
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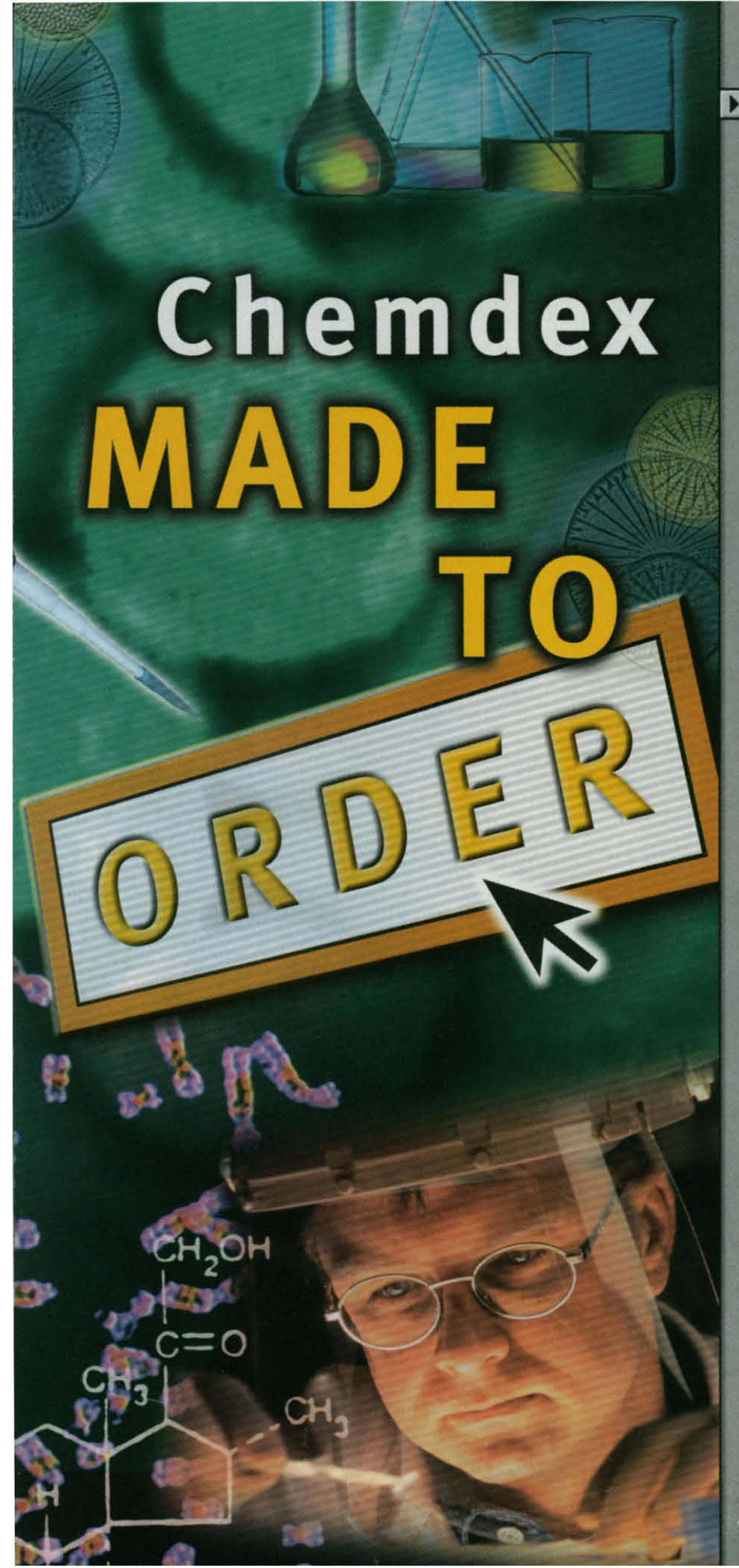
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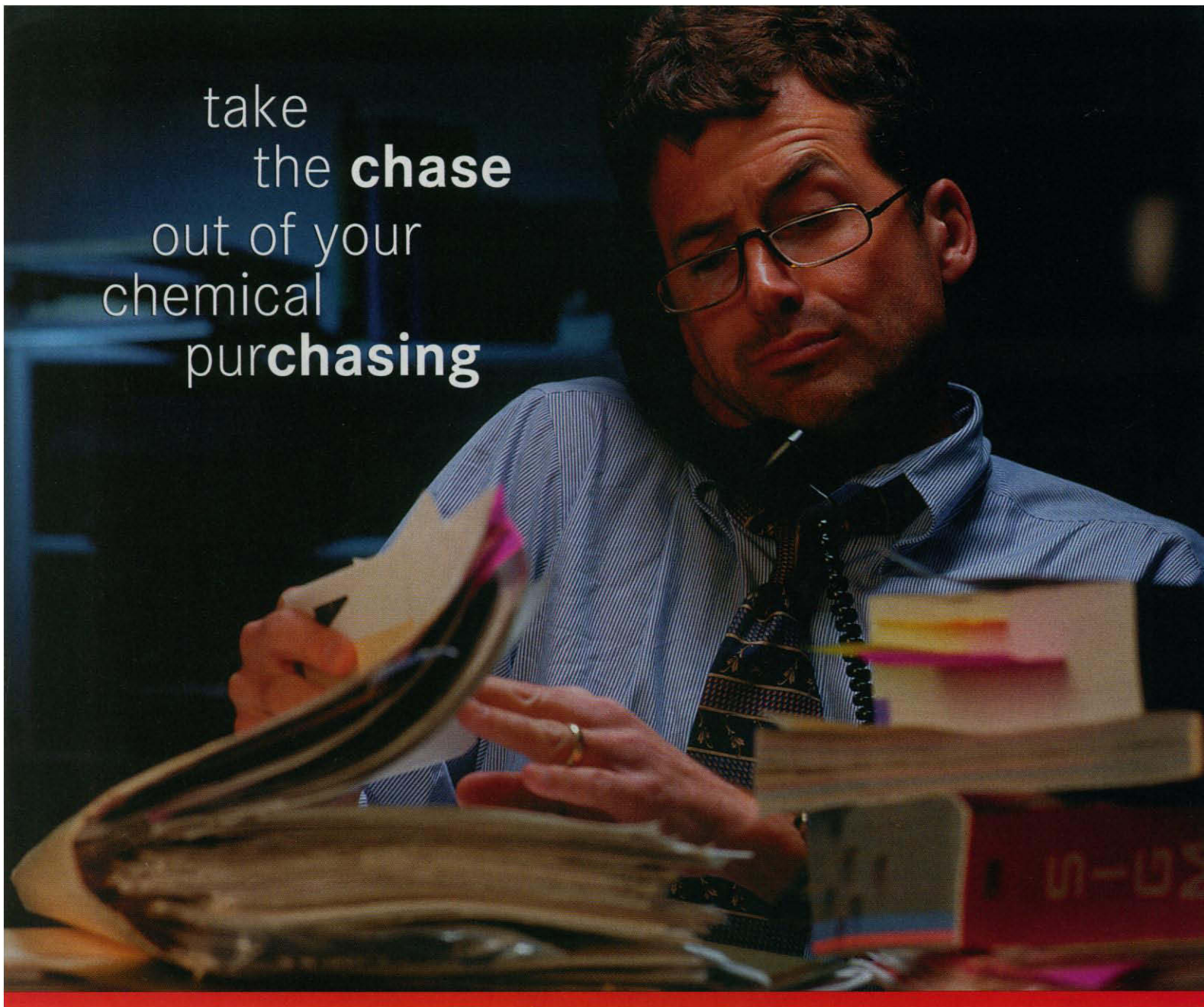
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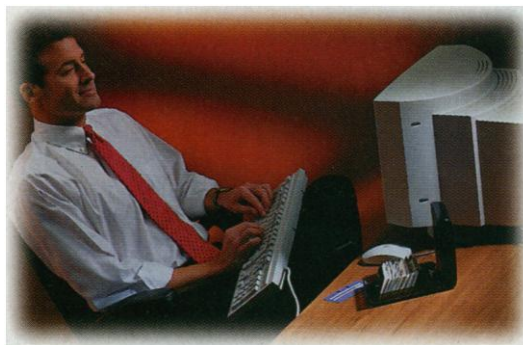
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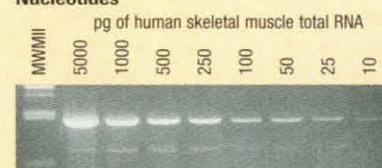
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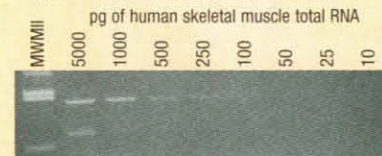
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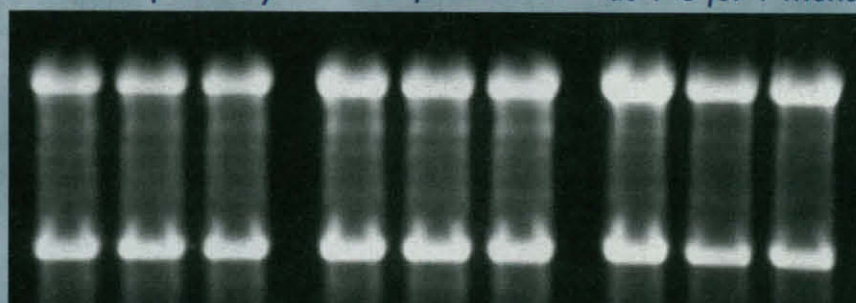
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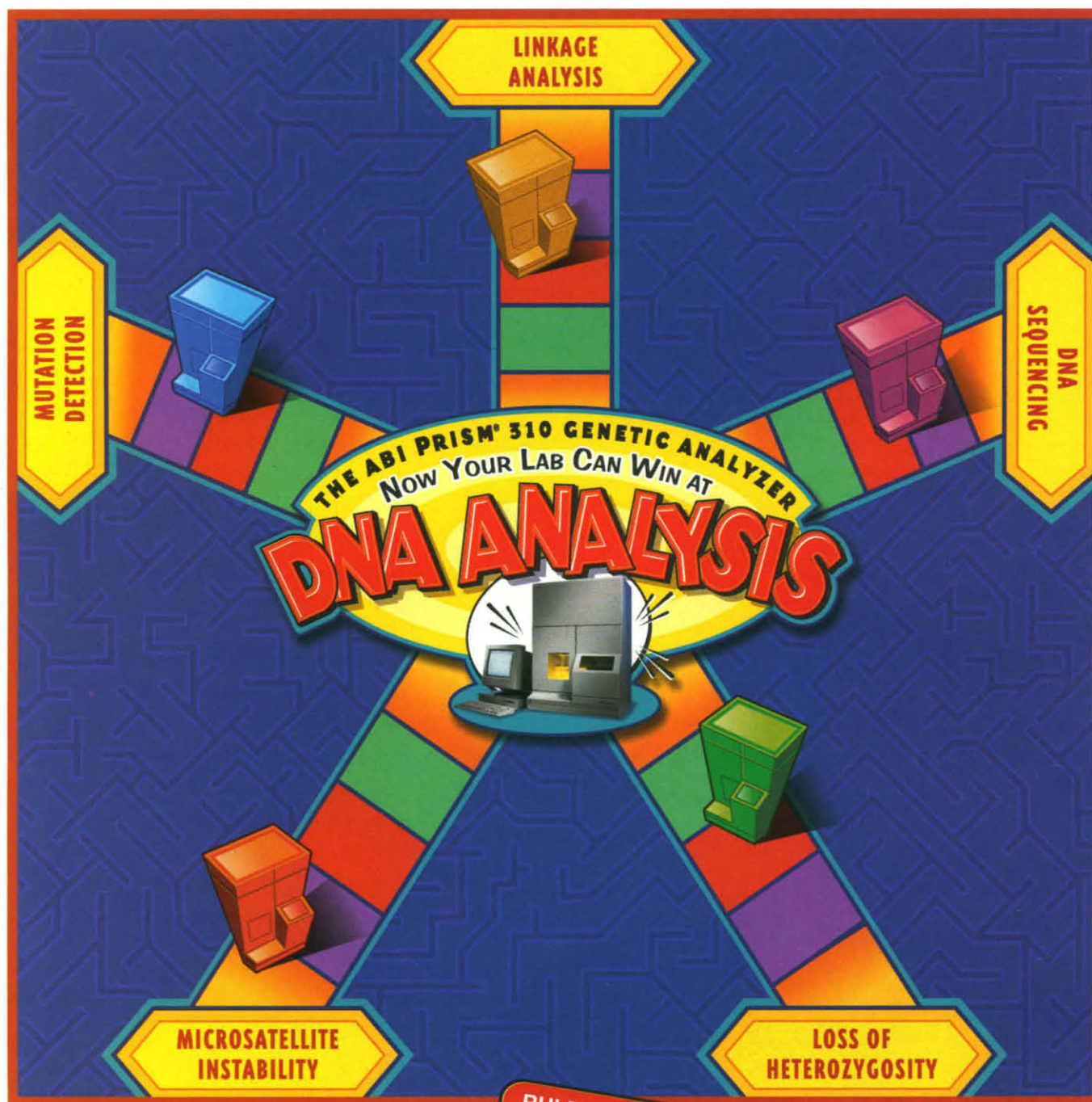
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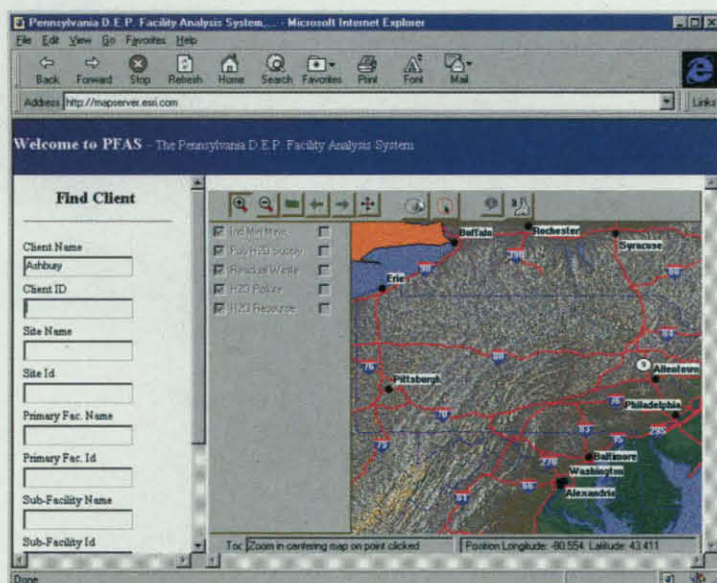


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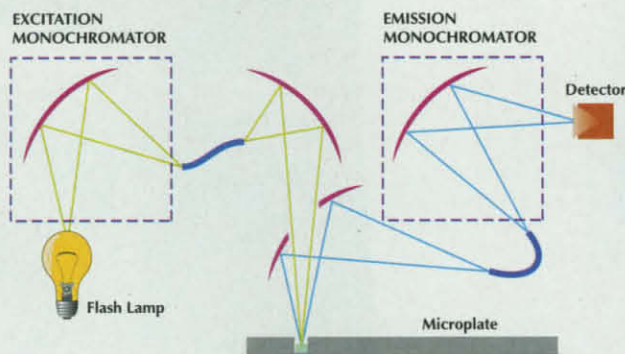
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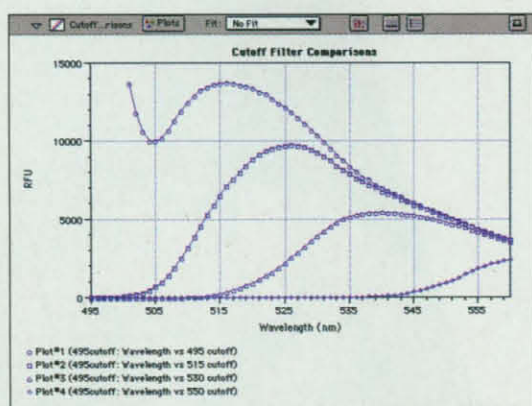
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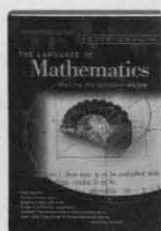
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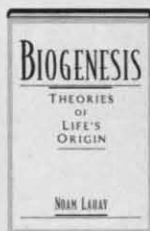
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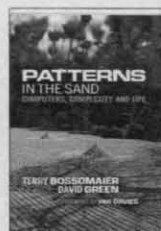
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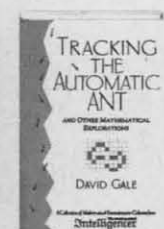
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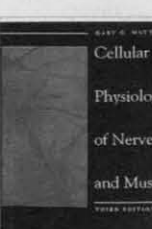
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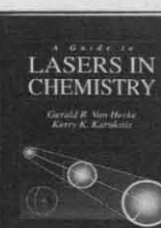
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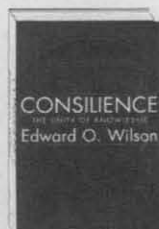
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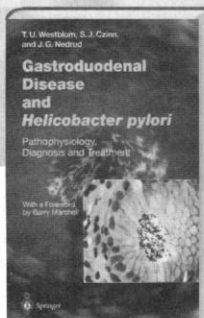
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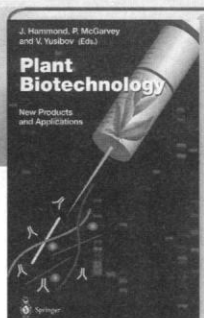
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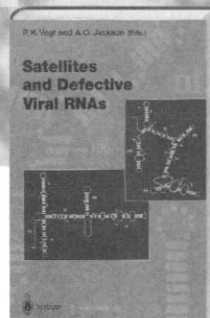
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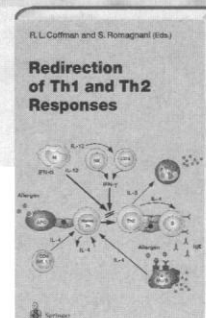


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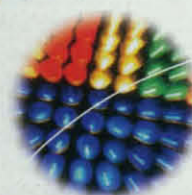


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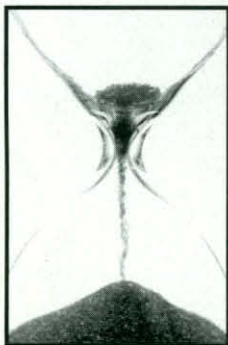
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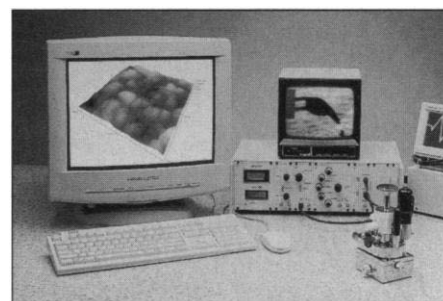
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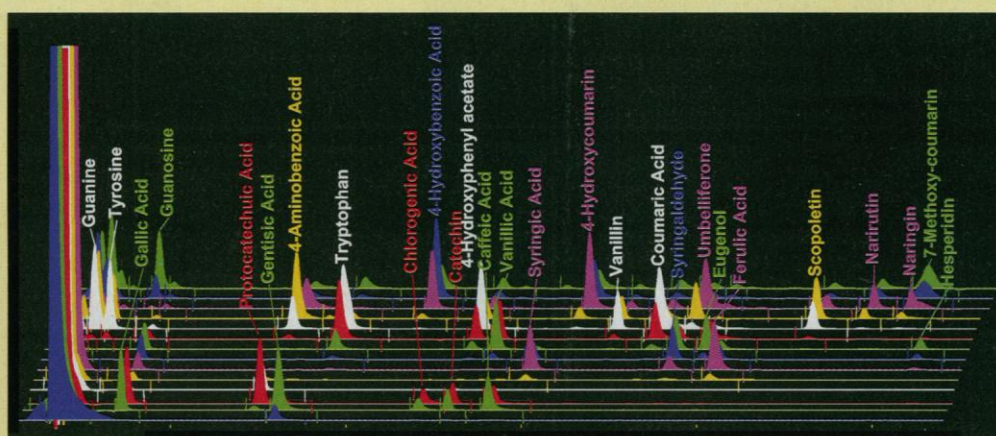
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