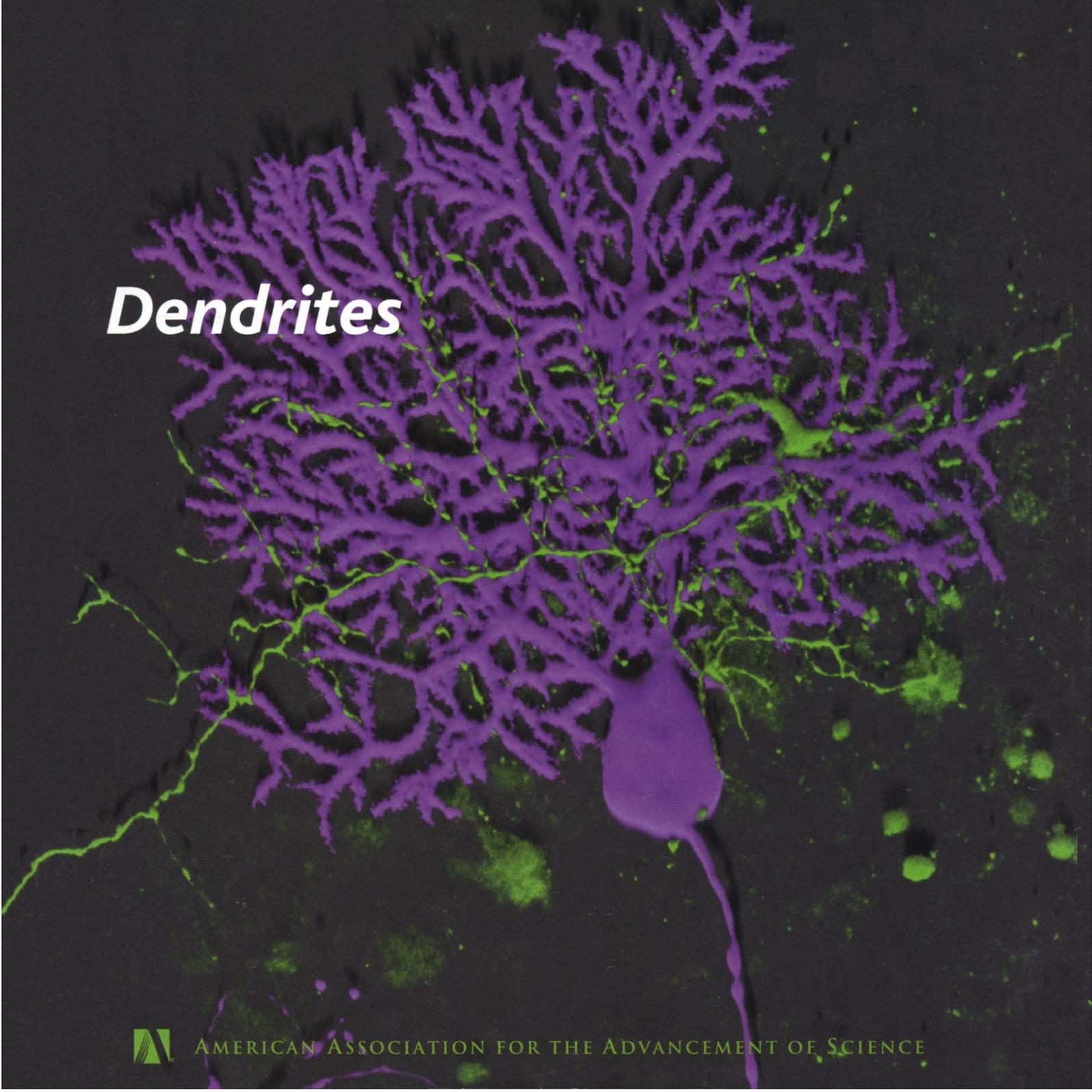


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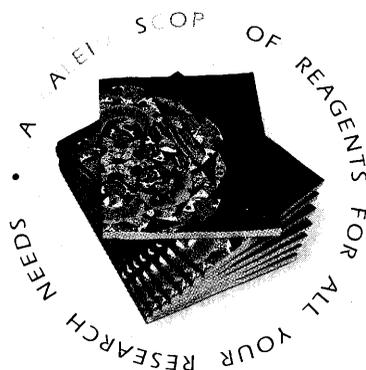
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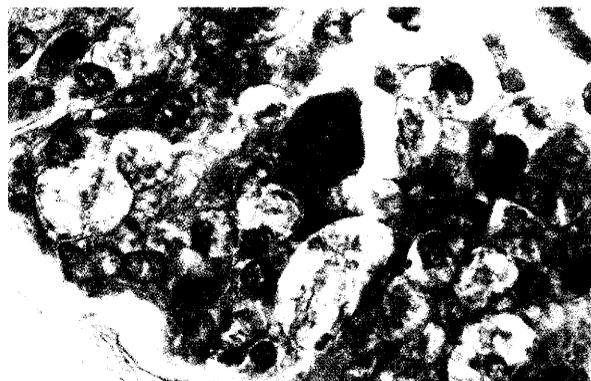


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COVER Dendrites are remarkable branching structures that receive most of the synaptic input to the neuron. A special section starting on page 735 gives an overview of some of the most exciting developments in this field. The image shows a digital reconstruction of the dendritic tree of a cerebellar Purkinje cell (purple, ~140 μm wide) stained with a fluorescent dye, together with an interneuron (green) making synaptic contacts with the Purkinje cell dendrites.

[IMAGE: B. CLARK AND M. HÄUSSER; DIGITAL RECONSTRUCTION, G. GIESE USING IMARIS SOFTWARE]



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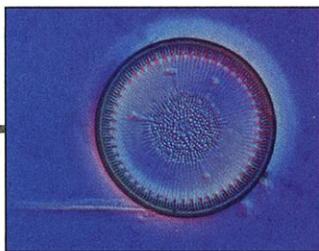
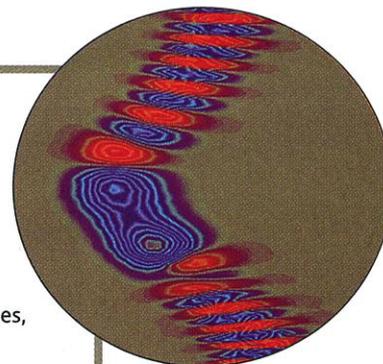
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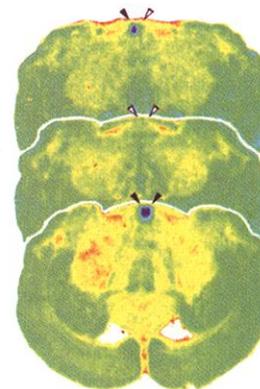
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Image: A computer-generated rendering of Benoit Mandelbrot's infinite fractal formula.



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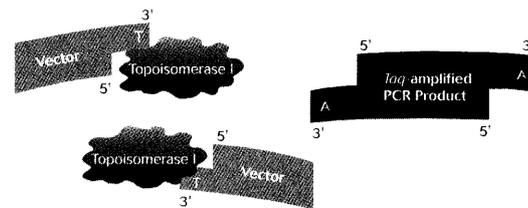


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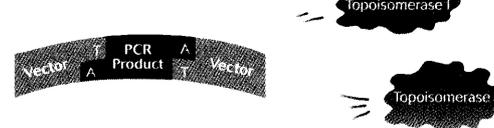
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QUANTUM MECHANICS GETS BIGGER

The general impression we have of quantum mechanics is that it manifests itself on the microscopic scale, and that the quantum-mechanical effects of large-scale objects are so small that they can effectively be ignored. Van der Wal *et al.* (p. 773; see the Perspective by Tesche) report on the quantum superposition of two states of a superconducting loop placed in an applied magnetic field. The superposition consists of clockwise- and anticlockwise-flowing supercurrents established in the ring to counteract the magnetic field. Such large-scale quantum systems have potential applications in quantum computing.

RUNNING RINGS IN SUPERFLUIDS

A particle moving below a critical velocity through a superfluid can do so unhindered, but above the critical velocity a vortex, or a superposition of normal (viscous) and superfluid states, is created. Kivotides *et al.* (p. 777) report model results on the dynamics of the vortex evolution which suggest that the structure may be more complicated than initially thought. A triple-ring structure develops in which the superfluid vortex ring is accompanied by not one, but two normal-fluid vortex rings. This coupled ring structure is coherent and dissipative.

SEEING THROUGH QUANTUM DOTS

With their discrete energy levels and tunable occupancy, quantum dots have been shown to serve as ideal systems for investigating interactions between an individual electronic spin within an environment of conduction electrons. Such an interaction, the Kondo effect, manifests itself as an enhancement in the conductance of the dot. Yang *et al.* (p. 779) used a double-path electron interferometer to measure the phase evolution of the electrons as they traversed the dot to show that the phase provides a sensitive signature of the Kondo regime. The sensitivity of the phase measurement allows them to determine the binding energy of the singlet state.

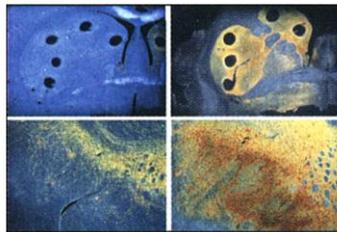
TUNING IN TO ENERGY TRANSFER

The transfer of energy between molecules is an important process in many biological and solid-state systems and can occur via a number of different pathways. For example, when the separation of the molecules is relatively large compared to the wavelength of the light, energy transfer occurs via the emission and absorption of a photon. For small separations, howev-

er, transfer may be nonradiative. Andrew and Barnes (p. 785) show how this nonradiative, or Förster, transfer can be enhanced by limiting the number of photonic modes available to an emitted photon of the donor molecule. The result provides the potential for enhanced photon-harvesting systems and optical networks.

GDNF TO THE RESCUE

The gradual loss of dopamine neurons in the nigrostriatal pathway of the brain causes the motor abnormalities characteristic of Parkinson's disease (PD). Although glial cell line-derived growth factor (GDNF) is known to sustain growth of dopamine neurons in culture, attempts to rescue dopamine nerve cell loss with GDNF in animal models of PD have



proved disappointing. Kordower *et al.* (p. 767; see the Perspective by Olson) present encouraging results with GDNF gene therapy in two primate models of PD: aged rhesus monkeys and monkeys treated with the selective nerve toxin MPTP. GDNF protein was expressed in the nigrostriatal pathway for up to 8 months after delivery of the gene in a lentiviral vector to this area by direct injection. Production of GDNF prevented degeneration of dopamine neurons and prompted some regeneration, which correlated with amelioration of motor deficits, as measured by a hand reach test.

HURRICANE AFTERMATH

Data on the long-term effects of hurricanes on vegetation are being accumulated from a number of sites in the tropics. In a 10-year study, Vandermeer *et al.* (p. 788) evaluated the effects on tree species diversity of Hurricane Joan (1988) in a Nicaraguan rainforest. They found an accumulation of species well beyond the species diversity of nearby undamaged forest in a manner that conforms to the "intermediate disturbance hypothesis" of diversity maintenance. Because of the

large spatial scale of the disturbance, populations of pioneer species are recruitment-limited for a sufficiently long period that other species can gain a foothold and grow into the newly developing canopy.

TRACKING SALMON THAT HAVE SWUM

Salmon abundance has been declining recently in the Pacific Northwest, but the relative contributions of overfishing, degradation of habitat, and climate change have been uncertain, in part because we have lacked a long-term record of salmon abundance. Finney *et al.* (p. 795; see the news story by Brown) have now developed such a record based on nitrogen isotopes and diatom records from sediments in several lakes in southern Alaska that helps resolve these competing effects. The nitrogen isotope signature is dominated by input from spawning salmon that pick up most of their nitrogen in the ocean. When they die after spawning, their nitrogen input in turn fertilizes diatom growth. The record, which extends back about 300 years, reveals large decadal variations in salmon abundance that can be related to climate cycles and a more dramatic decline in the past century that reflects overfishing. The lack of nitrogen input from spawning salmon may be directly impacting ecosystems and further inhibiting the salmon's recovery.

SPLIT CYCLE

Caged hamsters usually run vigorously in their wheels once a day for a few hours, always at the same time, but sometimes this period of activity "splits" and they run twice a day, for shorter times, 12 hours apart. The cause of this splitting behavior has now been clearly visualized by de la Iglesia *et al.* (p. 799), who examined the biological clock located in two symmetrical groups of cells, the suprachiasmatic nuclei, on either side of the midline in the hypothalamus. When their cycles are revealed by staining for messenger RNA of the clock gene *per* in hamsters showing split running behavior, the two halves of the clock are exactly 12 hours out of phase with one another, each hemiclock likely controlling one bout of running per day.

SIGNALING THROUGH AN "AND" GATE

Control of cell shape and motility requires integration of multiple signals that ultimately influence polymerization of the actin cytoskeleton. The WASP protein (for Wiskott-Aldrich syndrome protein, defects in which cause thrombocytopenia, eczema,

CONTINUED ON PAGE 671

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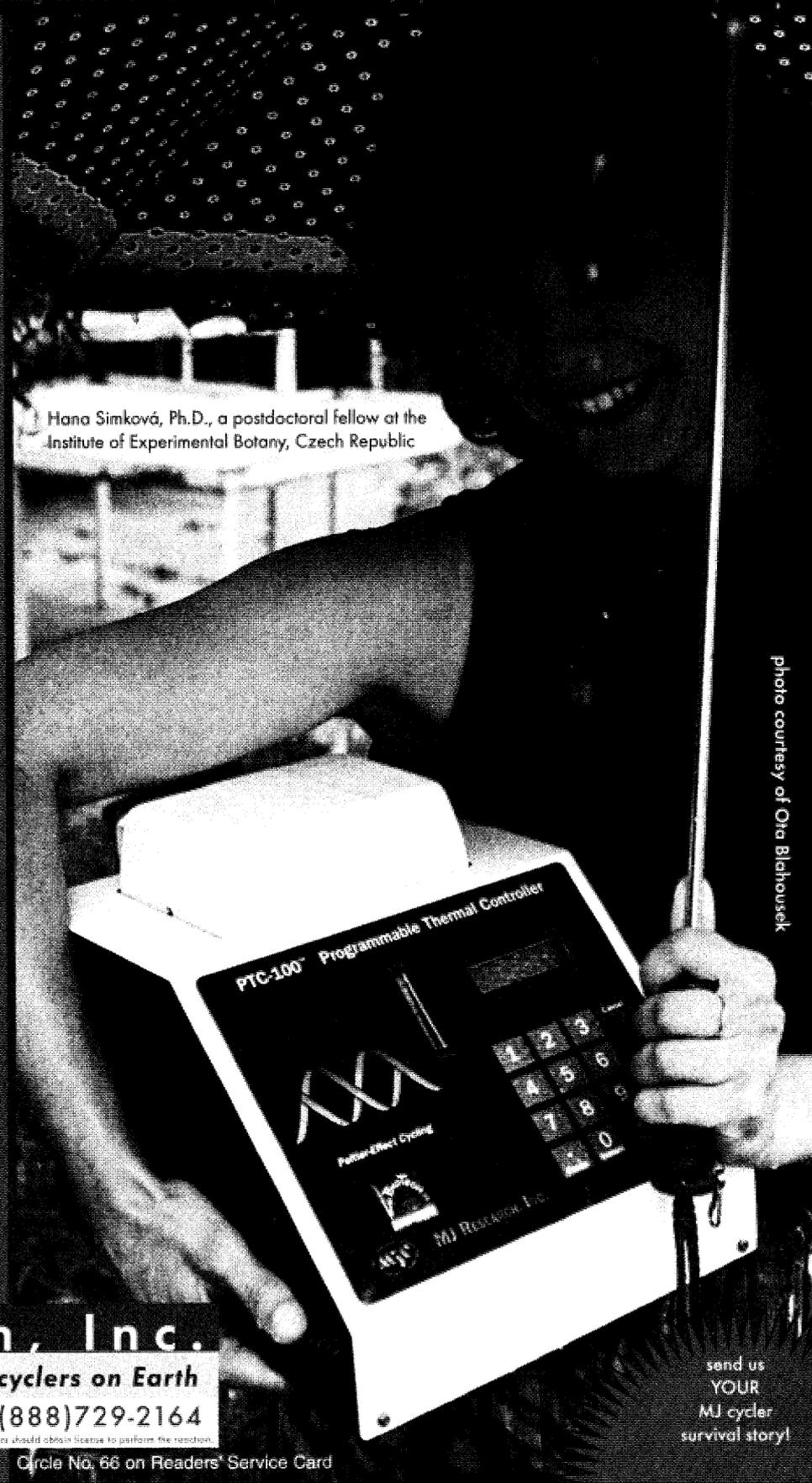


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THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 669

and immunodeficiency in humans) interacts with the small guanosine triphosphatase Cdc42 and phosphatidylinositol 4,5-bisphosphate (PIP₂), which are both mediators of signaling pathways that cause alterations in the actin cytoskeleton. WASP also interacts with the actin-related protein 2/3 (Arp2/3) complex, which stimulates actin nucleation. Prehoda *et al.* (p. 801; see the Perspective by Fawcett and Pawson) examined how the WASP protein processes multiple inputs to coordinate the activity of Arp2/3 and actin polymerization. Their results indicate that N-WASP (neuronal WASP) exists in a "closed" state in which Arp2/3 is bound but inactive and the binding sites for Cdc42 and Arp2/3 are inaccessible. Binding of either Cdc42 or PIP₂ appears to promote an active conformation. Activation by Cdc42 and PIP₂ is highly cooperative, and thus WASP can function as a "coincidence detector" or "logical 'AND' gate" that is highly activated when it receives signals from both Cdc42 and PIP₂.

AS THE WORM TURNS

The availability of the complete genome sequence of the nematode, *Caenorhabditis elegans*, has made it possible for Hill *et al.* (p. 809) to follow gene expression in an entire multicellular organism during the course of development. The authors monitored changes in gene expression on microarrays containing 98% of the open reading frames of the nematode in oocytes, six stages of development, and aged worms. Over the course of development, there is a transition from evolutionarily conserved genes to worm-specific genes.

LEARNING WHILE SLEEPING

The songs sung by birds are learned and can be quite complicated. How do birds learn to produce consistent rhythmic patterns of

sounds and to distinguish their own song from those of other birds of the same species and of different species? Dave *et al.* (p. 812) have succeeded in monitoring neuronal activity in the sensory-motor center (robustus archistriatalis) of zebra finches while the birds were singing and while they were asleep. Single unit recording revealed a remarkably similar pattern of action potentials when the bird was hearing its own song played back (auditory response) and when the bird actually sang (premotor activity). The temporal match suggests that these birds have implemented a mechanism for reinforcement learning with delayed reward and, in fact, may be rehearsing their songs in an "off-line" mode in order to become pitch-perfect.

GIVING FORM TO CTLA-4 INTERACTIONS

Signals delivered by cell surface receptor CTLA-4 are critical for ensuring that the T cells do not overstep their mark when responding to antigen. How this is accomplished is not fully understood, but it involves—at least in part—direct inhibitory signals. The efficiency of these signals likely relies on the assembly of inhibitory signaling complexes at the interface between the antigen-presenting cell and the T cell. Ostrov *et al.* (p. 816) have solved the crystal structure of CTLA-4 and in so doing revealed how the organization of this receptor might facilitate the arrangement of such complexes. Their data suggest that CTLA-4 forms dimers that are unlike those made by other members of the immunoglobulin supergene family in that they can interact simultaneously with two of its natural B7 ligands. This organization could help to explain the proficiency of CTLA-4 in regulating the immune responses.

TECHNICAL COMMENT SUMMARIES

Self-Similarity and Clustering in Species Distributions

Condit *et al.* (Reports, 26 May, p. 1414), studying six different tropical forest sites, found that individuals of most tree species in the forests tended to be spatially aggregated rather than randomly distributed. Ostling *et al.*, in a comment, observe that the clustering described by Condit *et al.* "is similar to that expected for a species with a self-similar spatial distribution." They derive an expression for the principal clustering measurement used by Condit *et al.*, relative neighborhood density, in terms of parameters related to self-similarity, and present quantitative comparisons showing a close fit between the species distributions reported by Condit *et al.* and those expected for plots with a self-similar distribution. Condit finds the comment by Ostling *et al.* "elegant and interesting," and agrees that self-similarity underlies the observed patterns—but argues that self-similarity holds at the community level rather than the species level.

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/290/5492/671a

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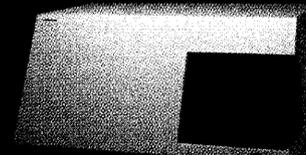


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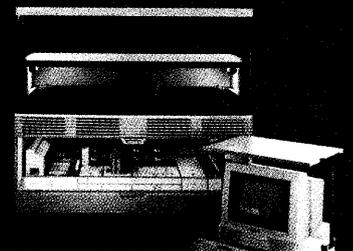
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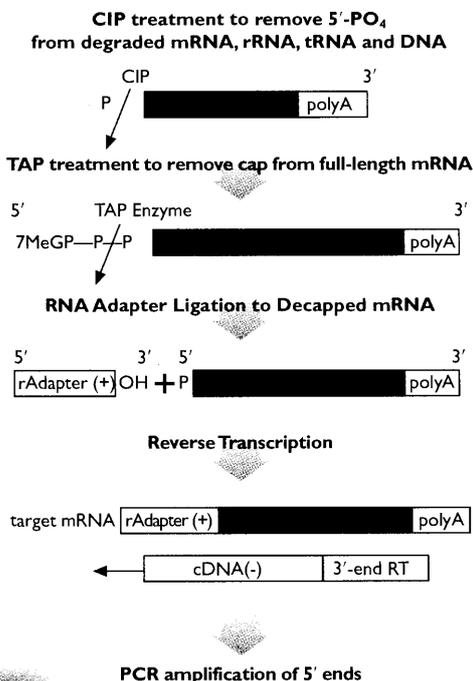
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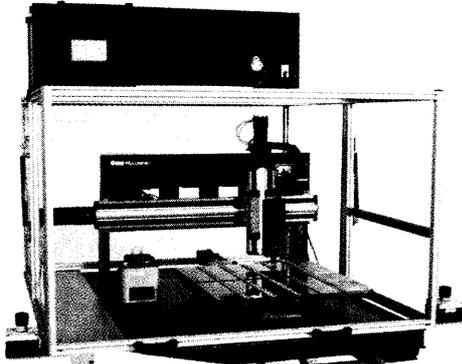
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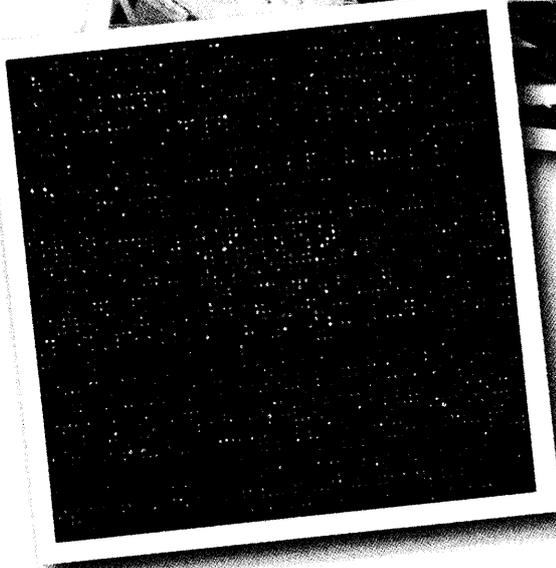
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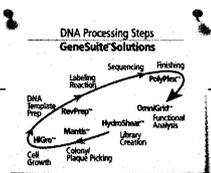
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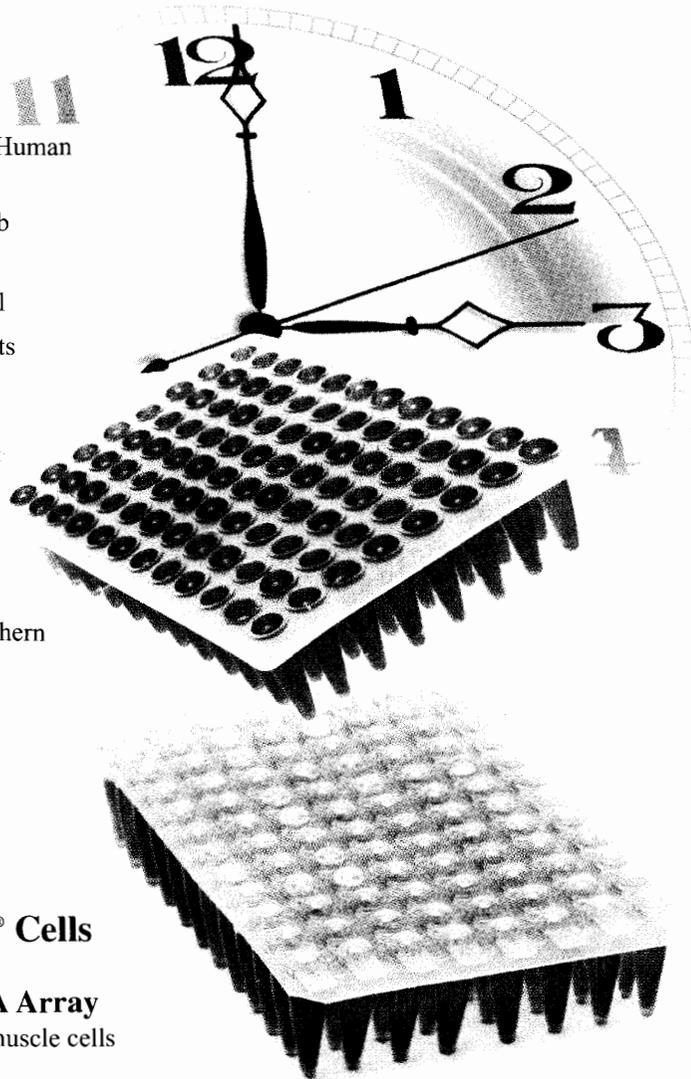
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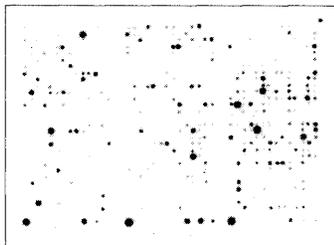
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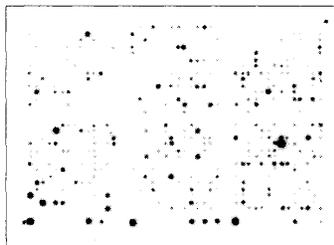
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Human Brain



Human Placenta



The Atlas™ Human 1.2 II Array visualized using chemiluminescent detection. Array hybridization was performed with biotinylated cDNA probes prepared from 2 µg of human brain poly A⁺ RNA or 2 µg of human placental poly A⁺ RNA. Hybridization and detection were performed with the SpotLight™ Chemiluminescent Detection Kit(K1032-1)*. Results were visualized by exposing blots to film for 10 minutes.

For Northern, Southern and other membrane hybridization applications, CLONTECH also offers the SpotLight™ Random Primer Labeling Kit (#K1027-1).

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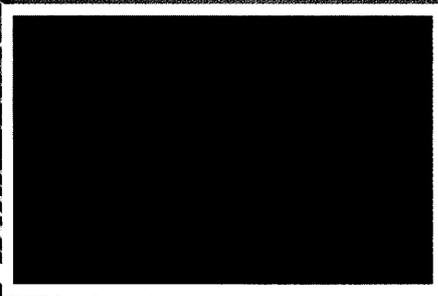
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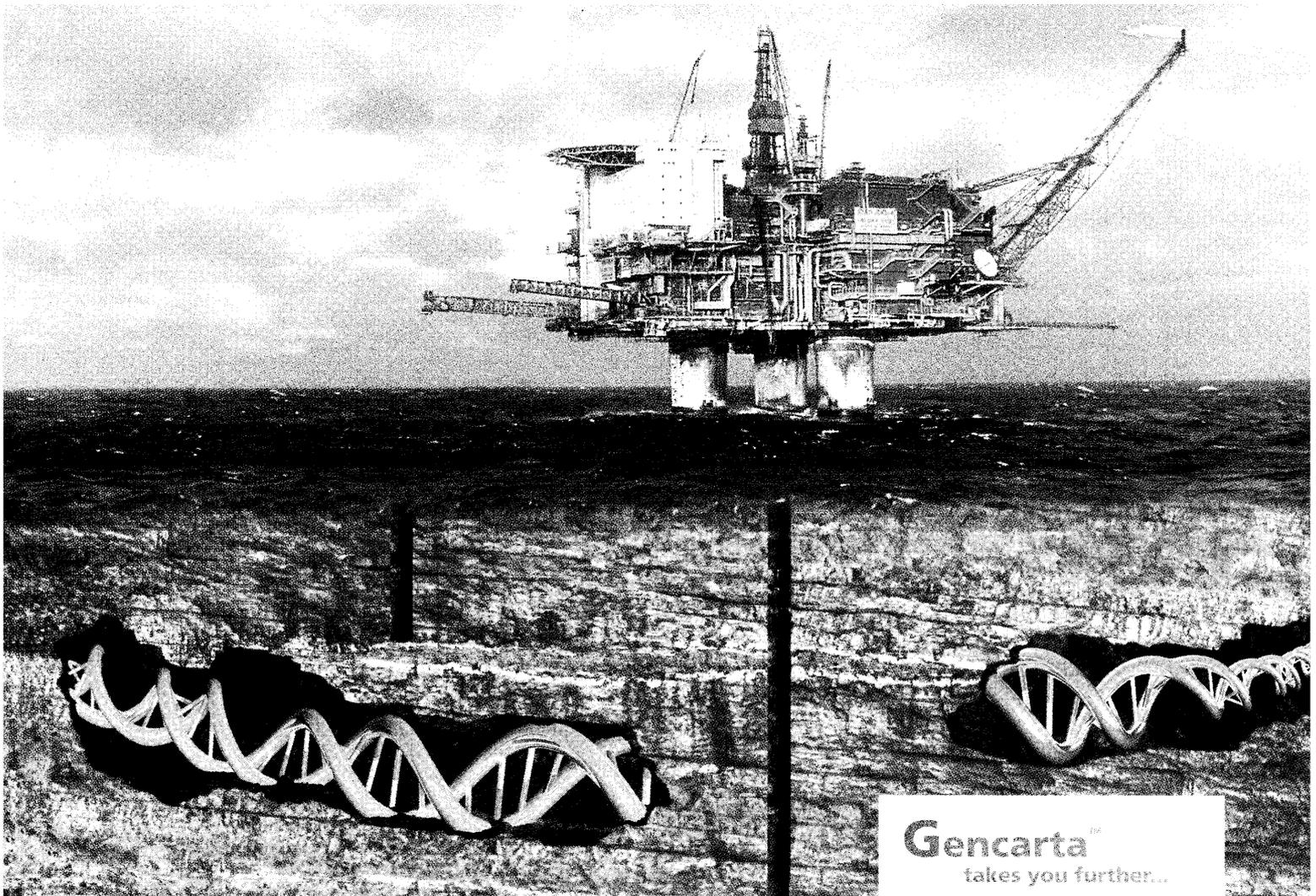
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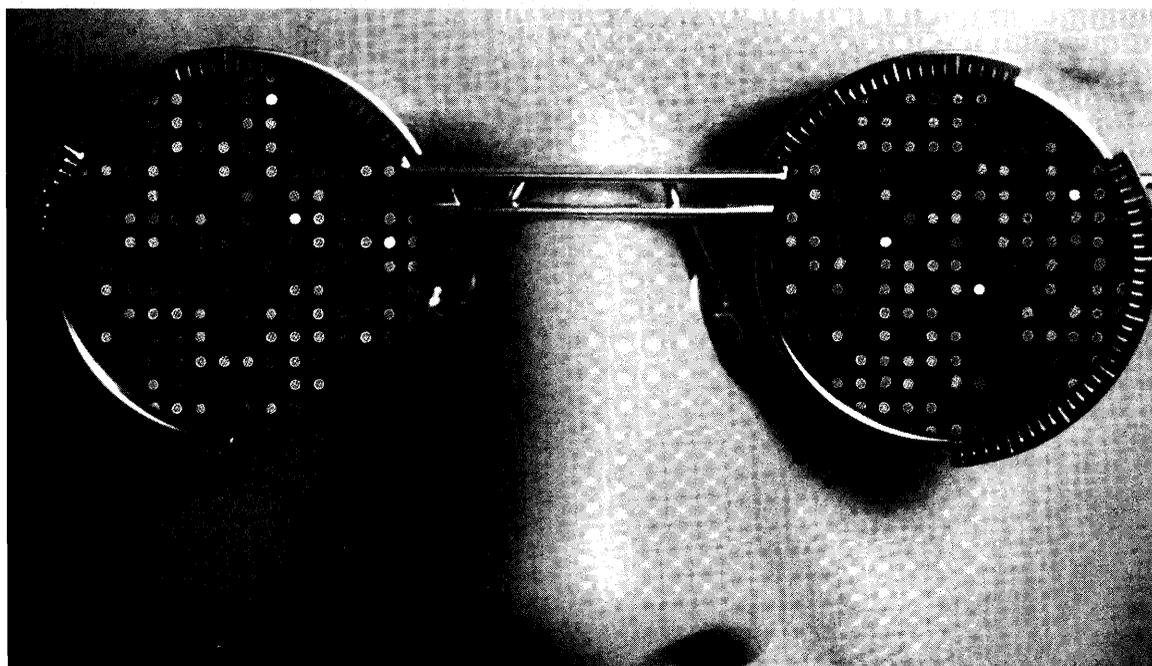
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Hooke: 43 years later, the compound microscope reveals living things are composed of cells.

Leeuwenhoek: invents the first practical microscope and discovers bacteria.

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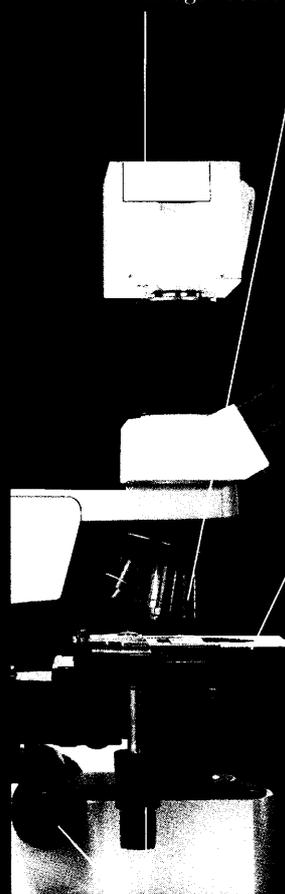
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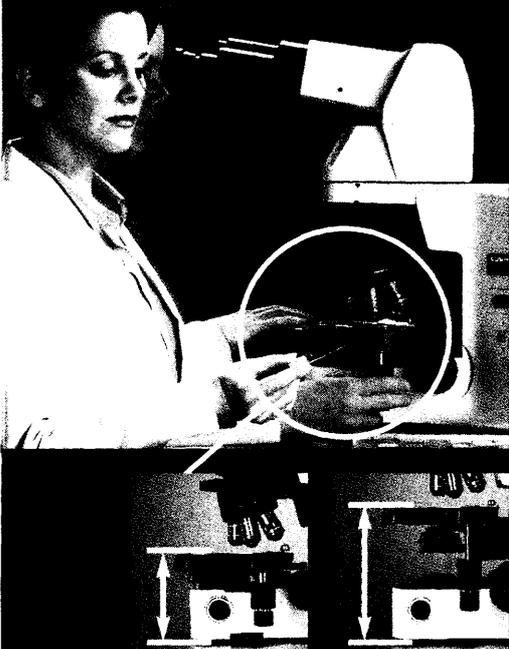
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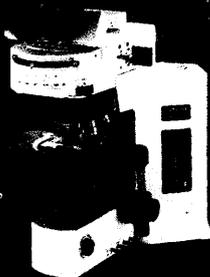
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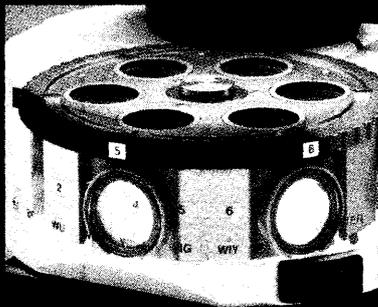


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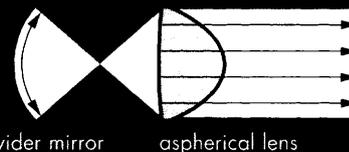
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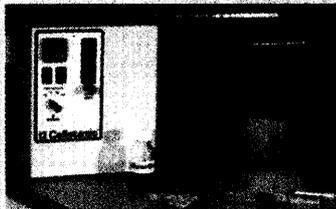
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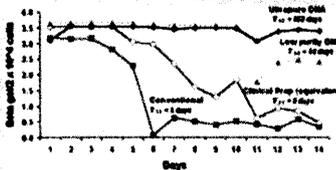


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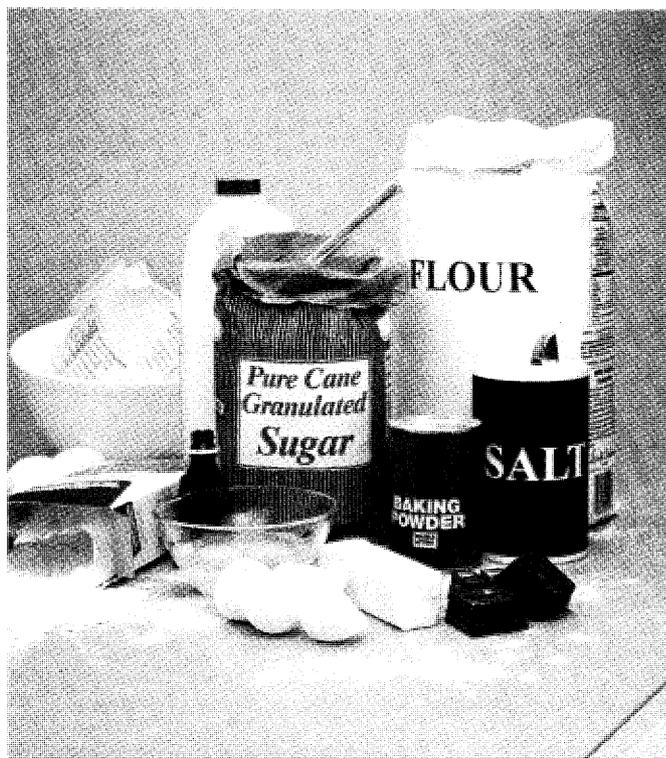
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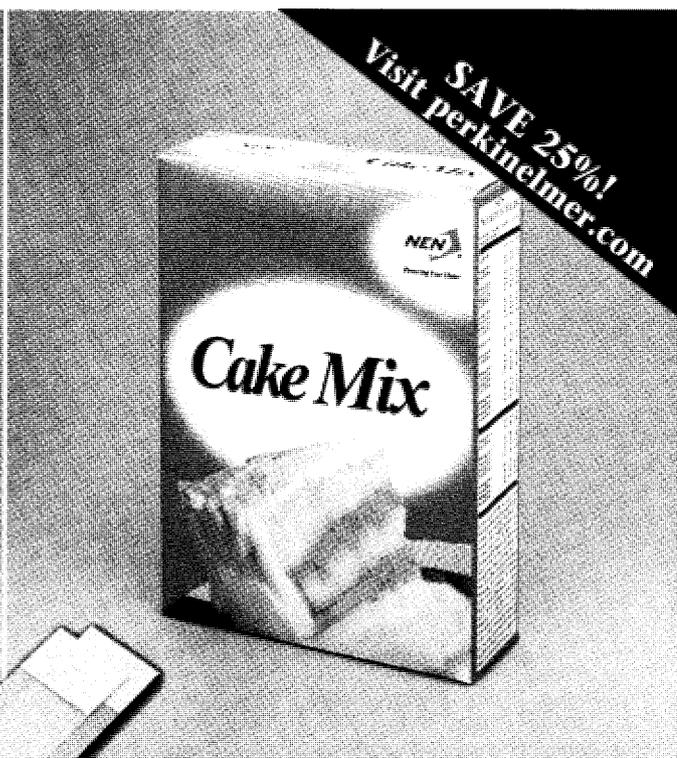
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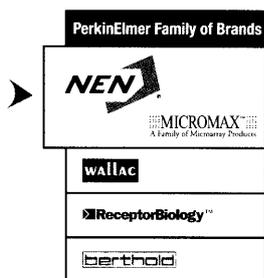


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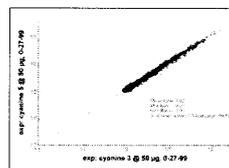
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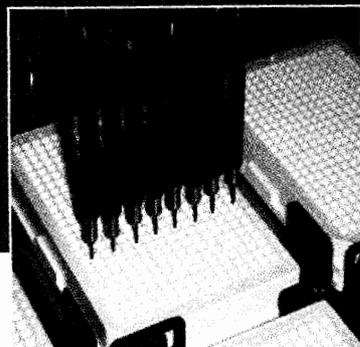
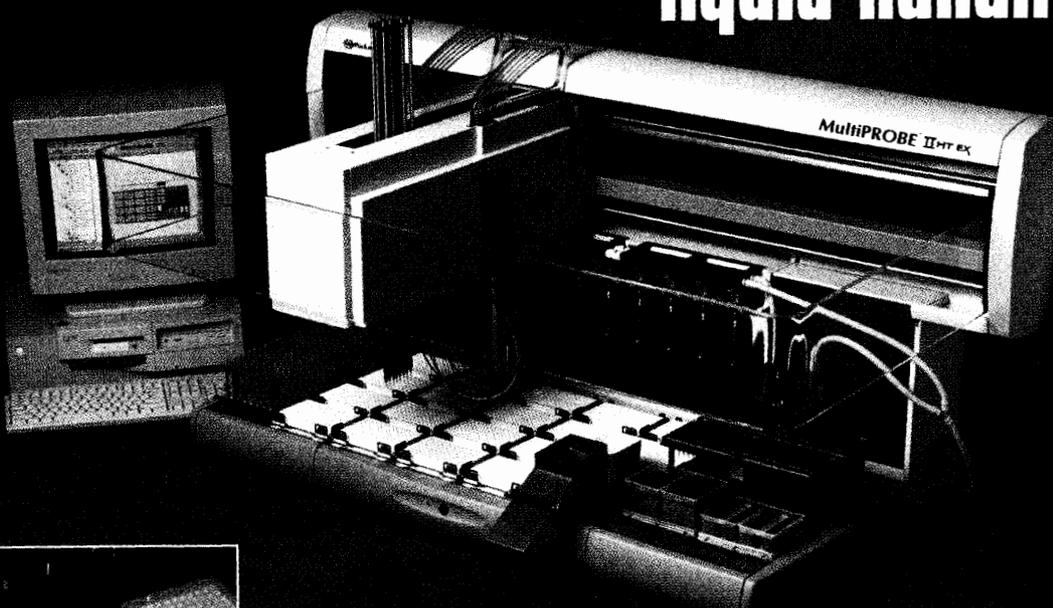


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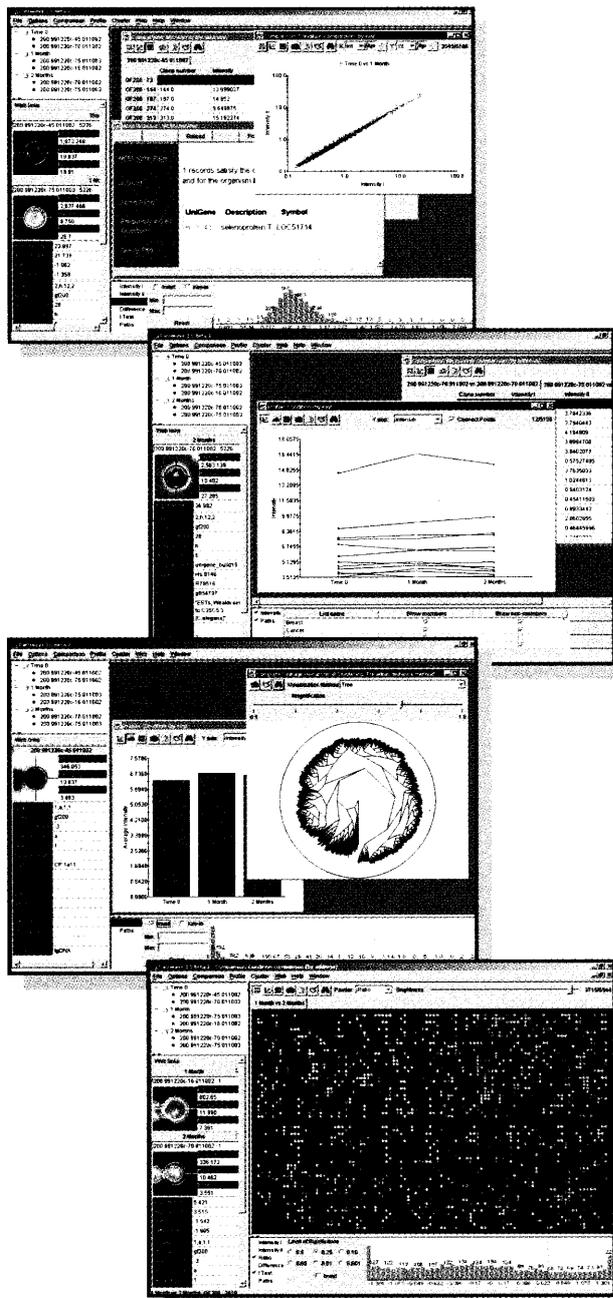
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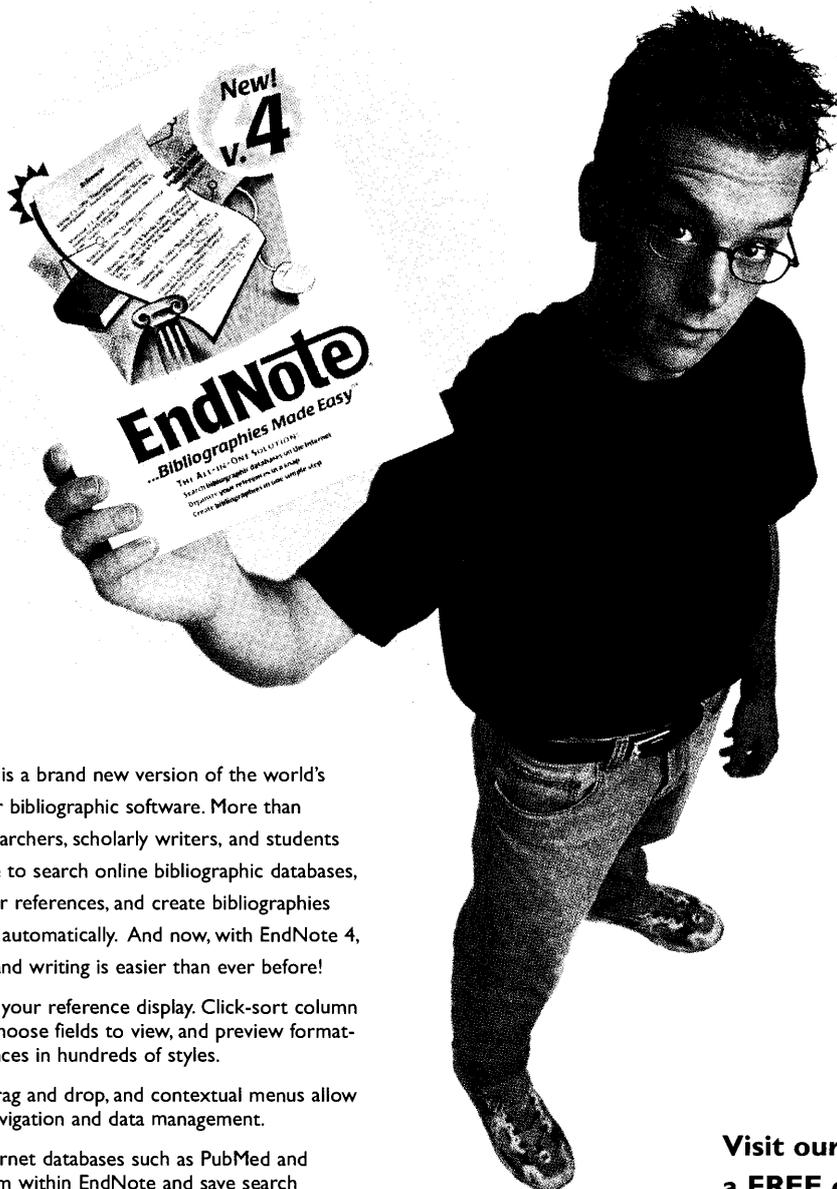
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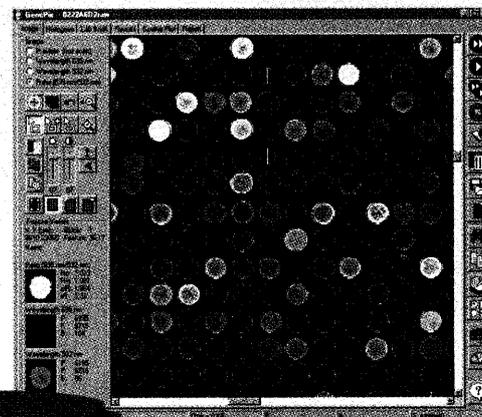
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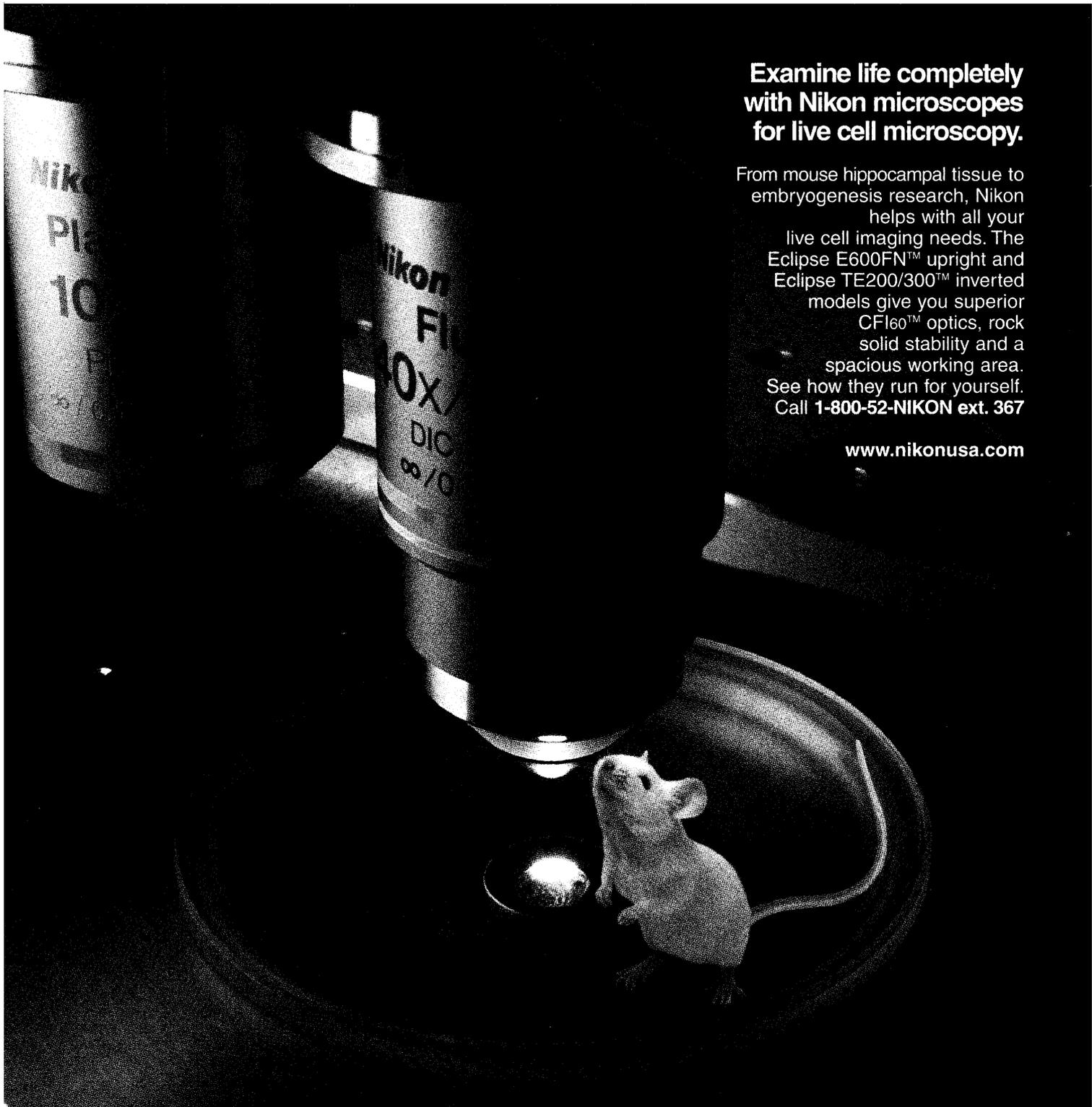
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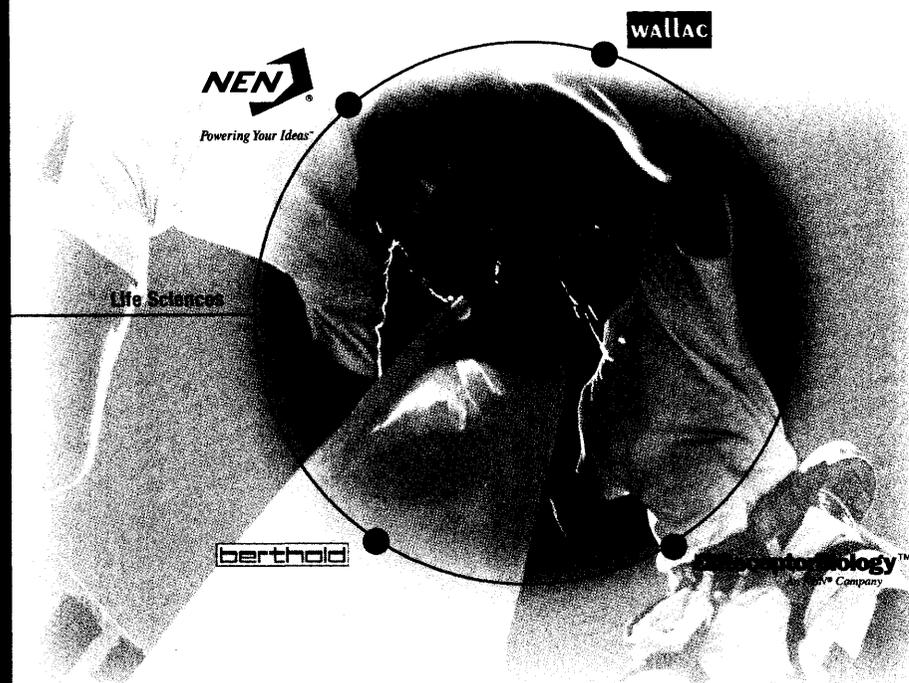
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Fig. 2

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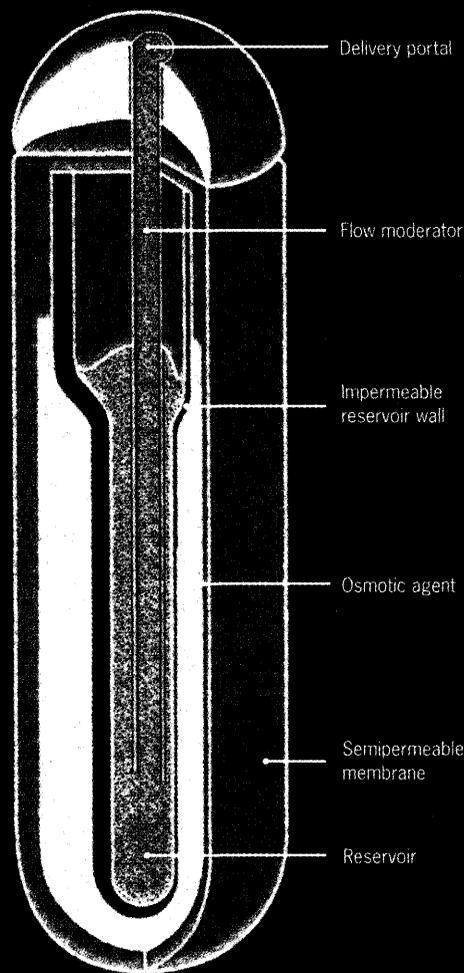
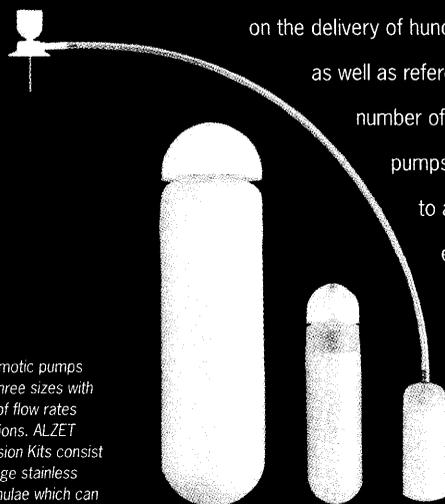
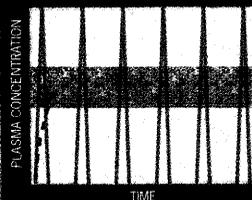


Fig. 1

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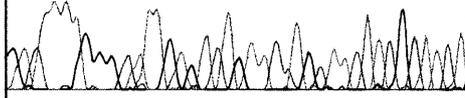
when you can
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Fig. 1. Fluorescent sequencing results of a 100 bp pUC18 PCR fragment sequenced with a -20 Fwd primer using the DYEnamic ET Terminator Cycle Sequencing Kit (Amersham Pharmacia Biotech). Data generated for USB by Cleveland Genomics (clevelandgenomics.com), a research service company. PCR clean-up performed with: (a) ExoSAP-IT; (b) a column designed for PCR clean-up. Base miscalls in (b) are due to inherently low yields of short PCR products when using columns.

Fig. 2. Autoradiograms of a 20.7 kb Lambda PCR fragment sequenced with MBL202 Fwd primer using USB's Thermo Sequenase Radiolabeled Terminator Cycle Sequencing Kit. PCR clean-up performed with: (a) ExoSAP-IT; (b) a column designed for PCR clean-up.

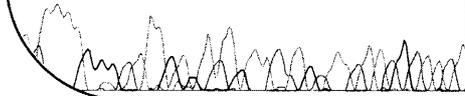
GATCCCCGGGTTACCGAGCTTCGAATTCGTAAATCATGTCAATA

Fig. 1(a)



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Fig. 1(b)



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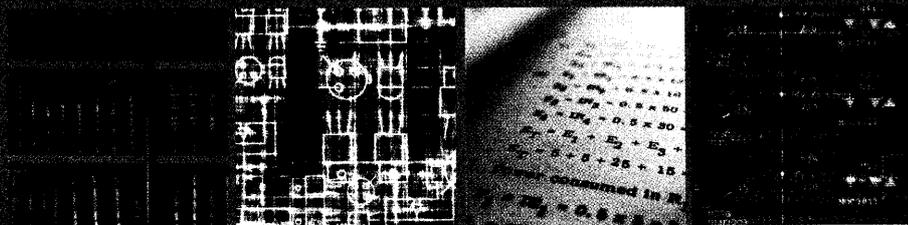
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[†]The Polymerase Chain Reaction (PCR) is covered by patents owned by Roche Molecular Systems and F. Hoffmann-La Roche Ltd. [‡]Patent pending on product. The method of use is covered by the following patents: 5,756,285 and 5,741,676

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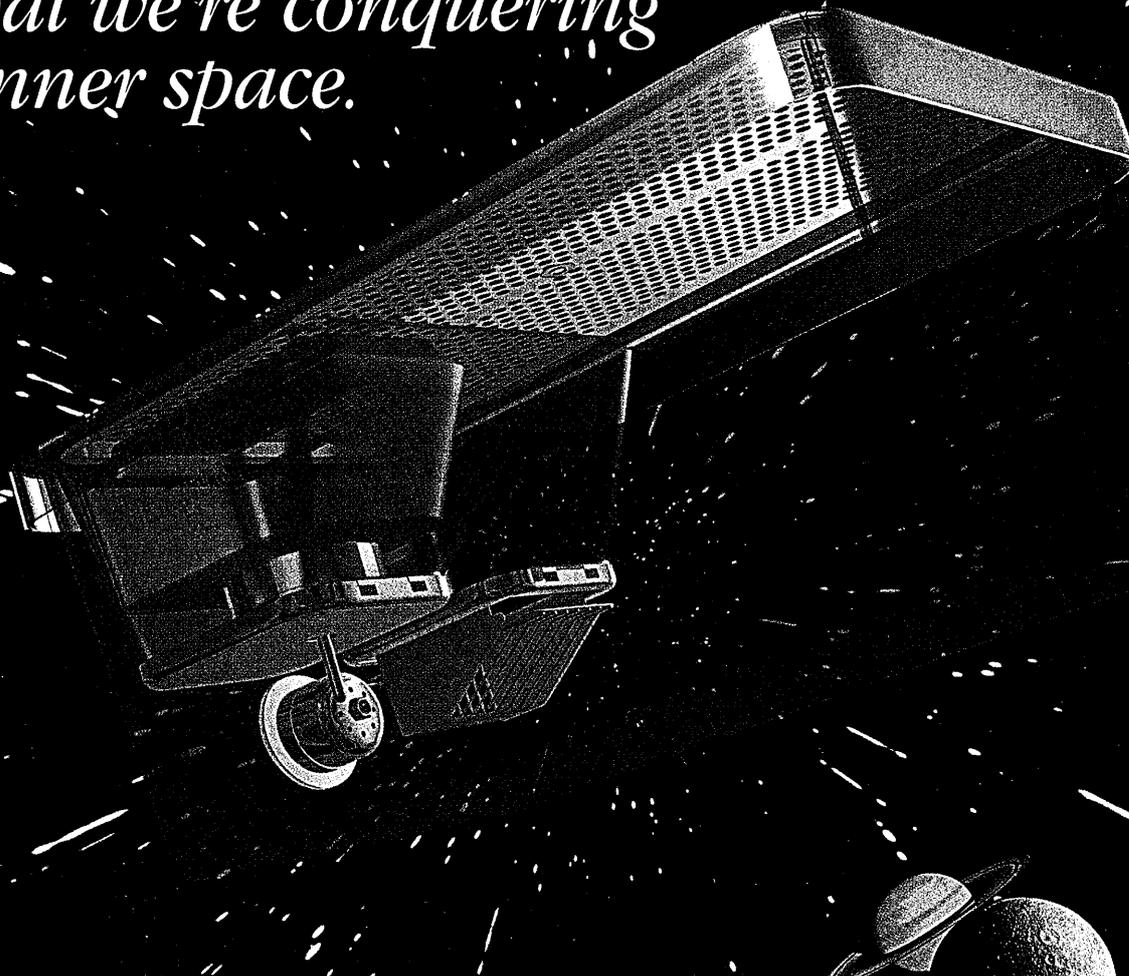
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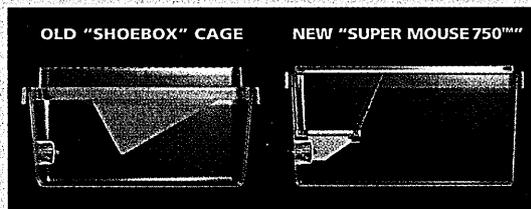
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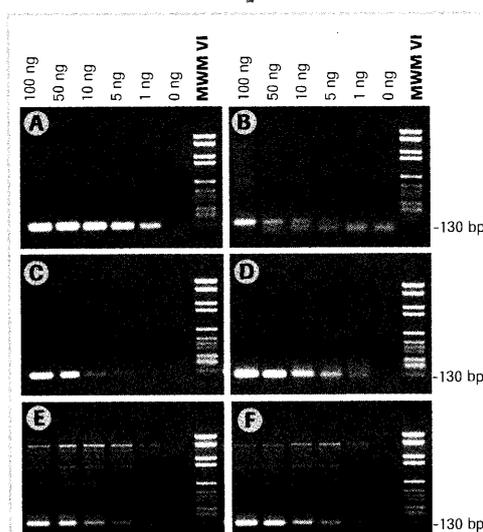


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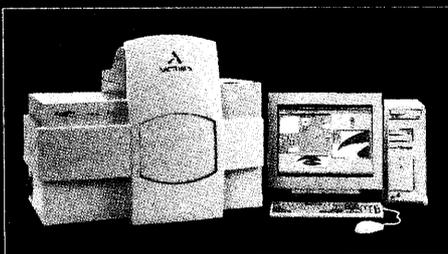
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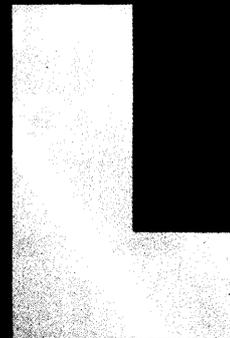


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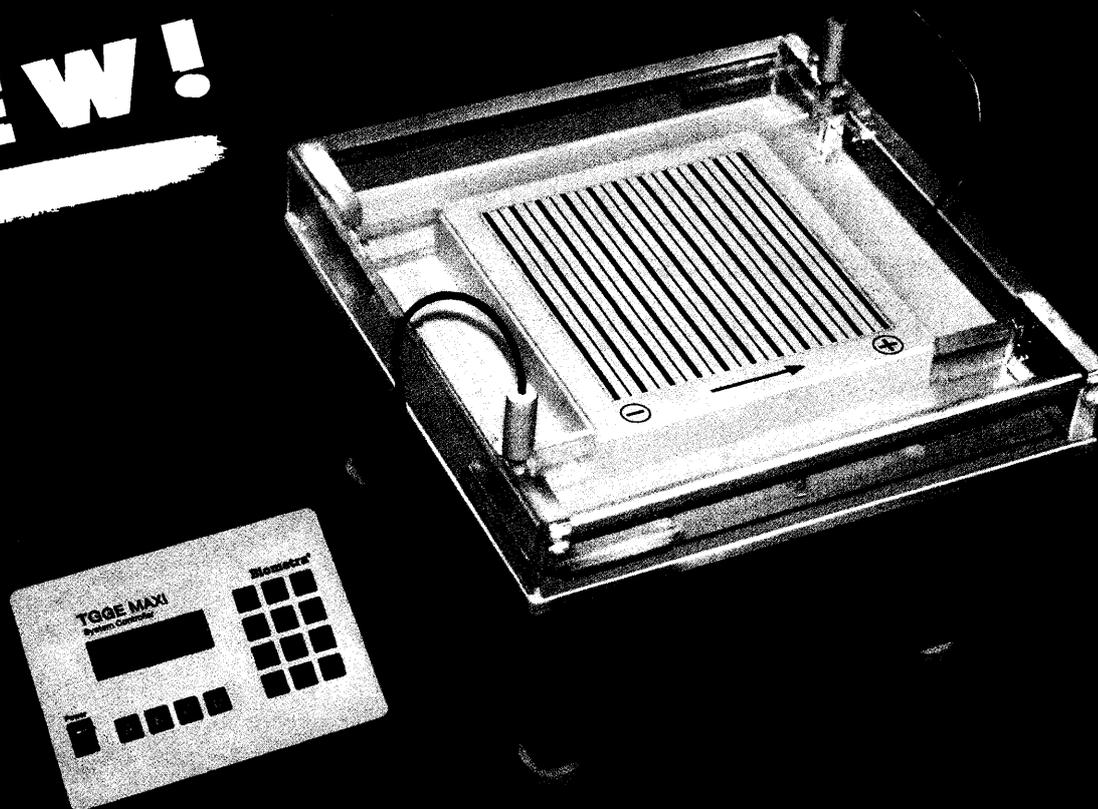
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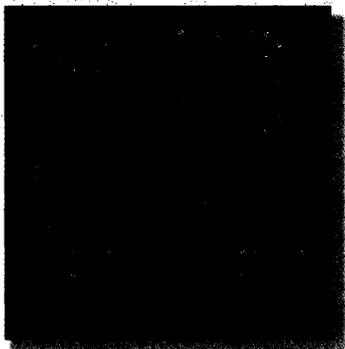
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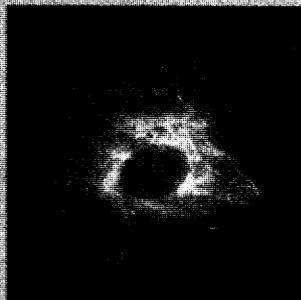
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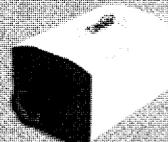
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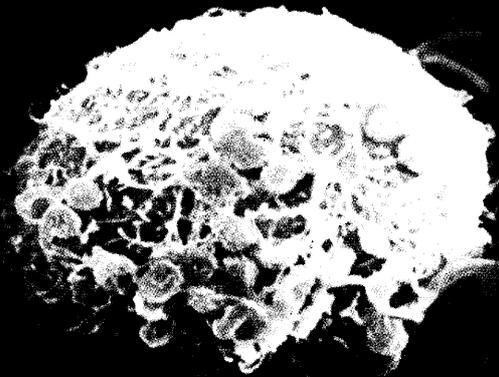
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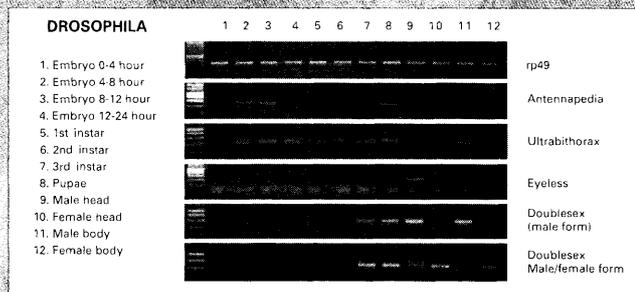
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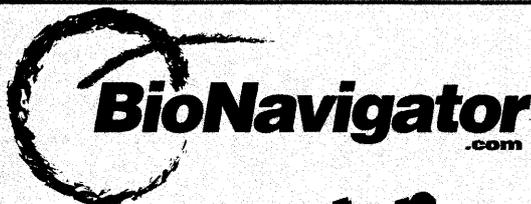
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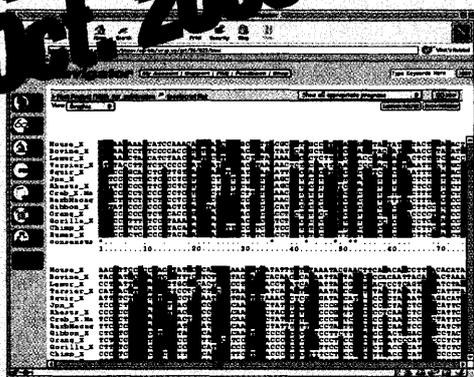
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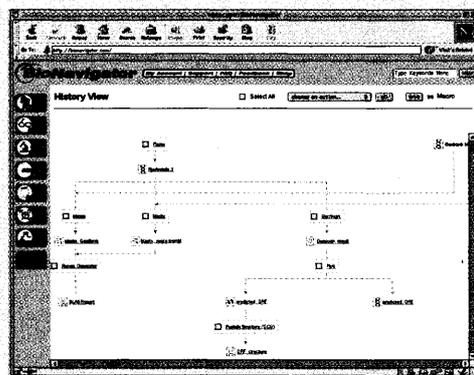


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