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27 April 2001

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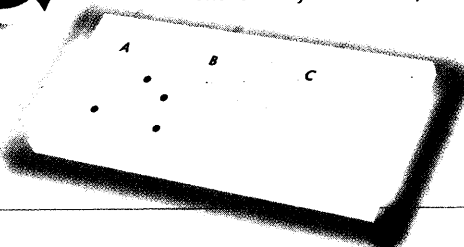
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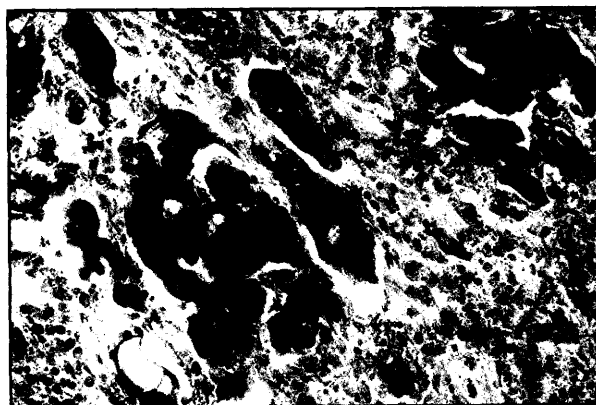
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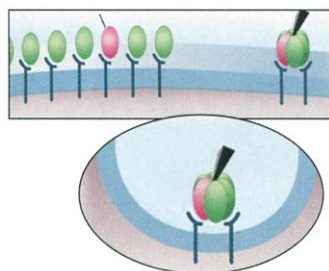
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Rise of New World monumental architecture

Stem cells release insulin **595**

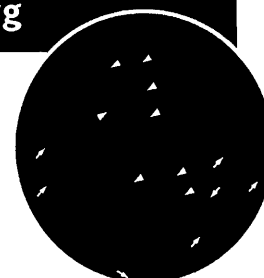
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Fermi Surface Nesting and Nanoscale Fluctuating Charge/Orbital Ordering in Colossal Magnetoresistive Oxides Y.-D. Chuang, A. D. Gromko, D. S. Dessau, T. Kimura, Y. Tokura

PERSPECTIVE: Quasi-Particles Survive—For Now B. Keimer

Extracting the key transport parameters of colossal magnetoresistive materials, using photoemission spectroscopy, reveals formation of a pseudogap.

Evidence for Dust Grain Growth in Young Circumstellar Disks H. B. Throop, J. Bally, L. W. Esposito, M. J. McCaughrean

618 New modeling provides evidence that silicate grains a meter in diameter can form on the inner edge of a circumstellar disk, providing the starting material for forming Earth-size planets around young stars.

Differentiation of Embryonic Stem Cells to Insulin-Secreting Structures Similar to Pancreatic Islets N. Lumelsky, O. Blondel, P. Laeng, I. Velasco, R. Ravin, R. McKay

615 Mouse embryonic stem cells, encouraged by culture conditions to develop into cells that contain and release insulin, hold promise for understanding processes of diabetes.

Autosomal Recessive Hypercholesterolemia Caused by Mutations in a Putative LDL Receptor Adaptor Protein C. K. Garcia *et al.*

Human genetic studies reveal that a putative adaptor protein for the low-density lipoprotein receptor plays an important role in regulating cholesterol levels.

TECHNICAL COMMENTS

Mechanisms Underlying Antigen-Specific CD8⁺ T Cell Homeostasis

Badovinac *et al.* (Reports, 17 Nov. 2000, p. 1354), studying the pattern of antigen-specific CD8⁺ T cell expansion, immunodominance, and death in mice infected with an attenuated strain of *Listeria monocytogenes*, concluded that perforin and interferon- γ (IFN- γ) "regulate distinct elements of CD8⁺ T cell homeostasis independently of their role as antimicrobial effector molecules." Wodarz, in a comment, presents the outline of a mathematical model that, he argues, "shows that, contrary to the arguments of Badovinac *et al.* . . . , their main observations can indeed be explained by the basic mechanisms by which perforin and IFN- γ control infection." Badovinac *et al.* respond that "the Wodarz model is of limited utility because of assumptions that are not consistent with the data and because of its failure to account for the observed results."

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/292/5517/595a

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Germany: Probing the Proteome E. von Ruschkowski

Chemists in Germany uncover a host of opportunities in the rapidly evolving area of proteomic analysis.

US: Picking Your Poison M. Sincell

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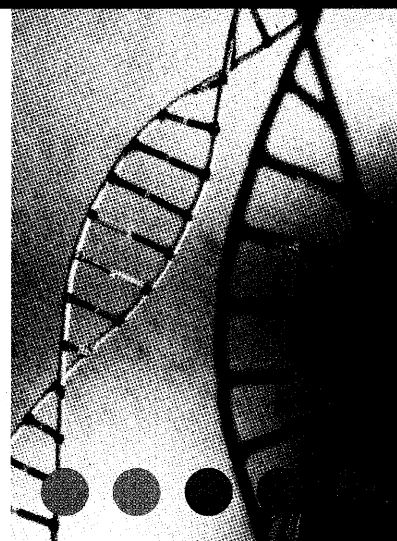
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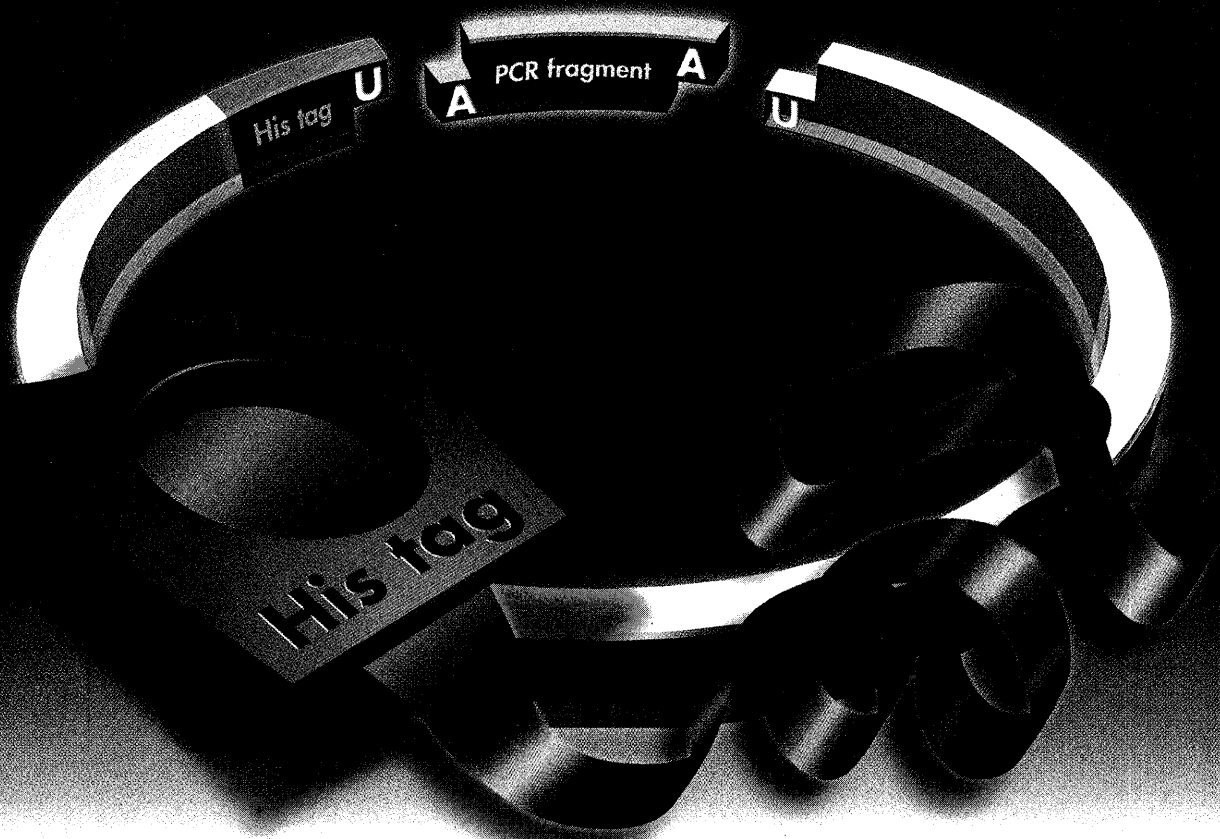
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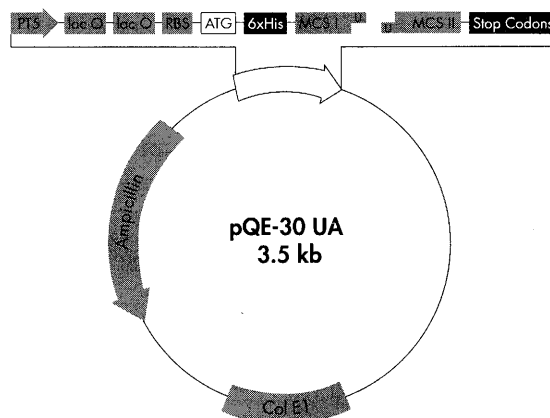


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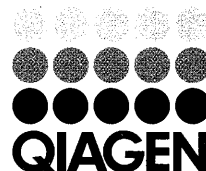
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QIAGEN 03/2001 SWW

THIS WEEK IN Science

edited by Phil Szuromi

Glimpsing Our Galaxy's Halo

The halo of the Milky Way galaxy is thought to be composed mostly of dark matter, which is detected by its gravitational effects on luminous galactic components, but otherwise the nature of this dark matter is unknown. Recent work has suggested that cool white dwarfs—compact, extremely dense stars that no longer produce energy by nuclear fusion and that are now cooling and fading from view—may be one component of the halo. Oppenheimer *et al.* (p. 698; see the 23 March news story by Sincell) surveyed a region near the South Galactic Cap and have now observed a population of extremely faint old white dwarfs with large space velocities that are consistent with these subluminal stars being part of the galaxy's halo. Furthermore, this population accounts for about 2% of the halo's "dark matter." ✕

Mantle Flow in the South Pacific

The volcanic islands of Fiji and Tonga in the southwestern Pacific Ocean are situated above a complex plate boundary. The Pacific plate is being subducted beneath the Indo-Australia plate along the Tonga trench and just west of the trench the Lau backarc basin is opening up. Smith *et al.* (p. 713) used seismic data from local stations on land and the ocean floor to infer the direction of flow in the mantle beneath these islands. The mantle flows north to south from Fiji toward the Lau basin and east to west from Tonga toward the Lau basin. Along the opening of the Lau basin, the mantle flow is coming up because the Samoan hot-spot plume infiltrates the basin.

Selective Bond Breaking with Strong Laser Fields

Bond-selective photochemistry has been a long-sought but elusive goal. One difficulty is that photoexcited states can rapidly redistribute energy in ways that can be difficult to predict. Levis *et al.* (p. 709; see the Perspective by Hurley and Castleman) now report that different reaction outcomes can be selected through a closed-loop feedback algorithm that tailors the phase and amplitude of "strong-field" pulses. For very intense laser pulses (10^{13} watts per square centimeter), the various eigenstates of the molecule can be resonance-ionized by multiphoton adsorption; the states come into resonance through the Stark shifting that occurs in the strong electric fields generated by the laser pulse. By "training" the pulse shape, they can control, for example, whether acetophenone dissociates to form C_6H_5CO and CH_3 or rearrange to form toluene and CO . ✕

695 Anthrax Antidote

Although there is a prophylactic vaccine available for anthrax, the natural rarity of the disease does not warrant widespread use except for military personnel. However, if there were a terrorist incident involving anthrax, a therapeutic vaccine would need to be available for immediate mass use. Sellman *et al.* (p. 695; see the Perspective by Olsnes and Wesche) have developed the raw materials for such a therapeutic by constructing mutants of a key molecule of the multicomponent anthrax toxin. These are dominant-negative mutants, meaning that just one mutant subunit assembling into the seven-subunit component called protective antigen will block the cellular activity of the entire toxin by inhibiting the translocation of the active components across cell membranes. Rats given unadulterated toxin components died within 2 hours, but those given the dominant-negative mutant toxin survived without symptoms until the end of the experiment.

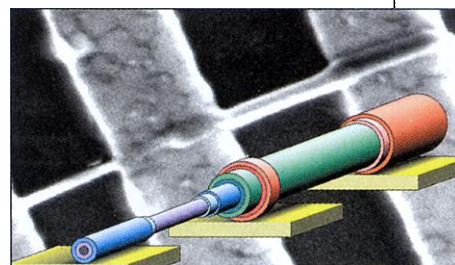
was also inland, and along with more than a dozen other settlements in the Supe Valley, may mark the beginnings of complex society in the Americas.

Early Cities of Preceramic Peru

The first large settlements in the Americas seem to have developed about 5000 years ago on the coast of Peru. These settlements also marked the development of irrigation and more intensive agriculture, the beginning of the construction of monuments, and the beginning of urban planning. Shady Solis *et al.* (p. 723; see the news story by Pringle) provide new radiocarbon dates for one of the earliest and perhaps the largest known settlement, Caral, in the Supe Valley, Peru. The dates range back to about 4500 years ago. Caral

Sorting Out Carbon Nanotube Conductivity

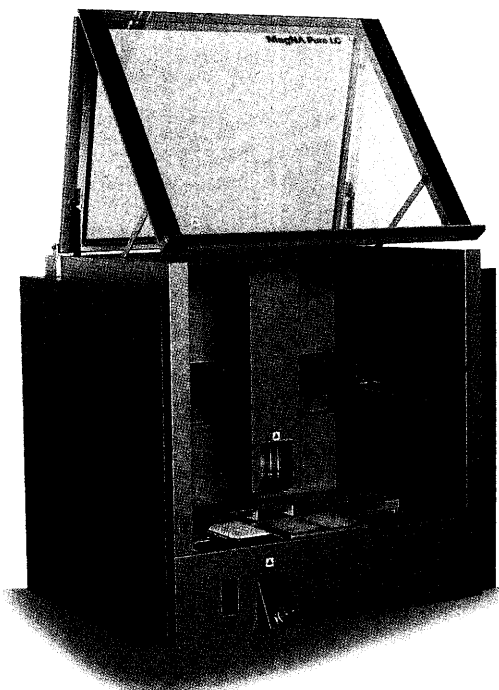
Carbon nanotubes, whether the multiwalled (MWNT) or the single-walled (SWNT) variety, are formed as mixtures of metallic and semiconducting tubes. Two reports examine how structure influences conductivity and how structures can be modified to select for metallic or semiconducting properties (see the Perspective by Dresselhaus). Both the "armchair" and "zigzag" configurations of SWNTs have been thought to be metallic, but recent theoretical work that has considered the distortion in the chemical bonds cast doubt on that perception. Ouyang *et al.* (p. 702) obtained low-temperature scanning tunneling spectra of individual and bundles of armchair and zigzag SWNTs, and clarify that the zigzag types are not true metals but display an energy gap at the Fermi level that depends on the diameter of the tube. Device applications would benefit from ways to control the conductivity of nanotubes that connect electrodes. Collins *et al.* (p. 706) show that an extreme approach—running high currents through the tubes in air—selectively removed the outermost layers of MWNTs or particular tubes from SWNT bundles to create either a metallic or semiconducting contact. Entire arrays of field-effect nanotube transistors were fashioned in this manner.



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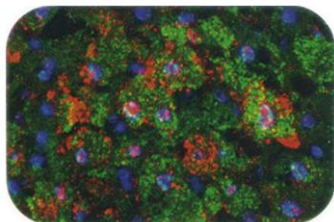
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Managing Mitochondrial Mortality Messages

The proteins BAK and BAX are pro-apoptotic members of the "BH3-domain-only" family of proteins (so-called because they share with the BCL-2 family of proteins only the third of four BCL-2-homology domains). M. C. Wei *et al.* (p. 727) provide evidence that BAK and BAX are essential gatekeepers for apoptotic signals that act through the mitochondria. Signals from death receptors on the cell surface cause activation of tBID (another BH3-domain-only family member), which leads to release of cytochrome c from mitochondria and subsequent cell death. Cells that lacked BAK or BAX alone were still sensitive to tBID, but cells deficient in both proteins did not undergo tBID-induced apoptosis. A broad range of signals from the plasma membrane, nucleus, and endoplasmic reticulum all required the presence of BAK or BAX and thus appear to promote cell death through signals that converge at the mitochondria.



Ripping Up RNA, One Molecule at a Time

Analysis of the folding of single molecules provides insight into the biological forces and folding behavior that are not available through bulk measurements, which are often confounded by the presence of multiple species and multiple folding pathways in solution. In a study of RNA folding, Liphardt *et al.* (p. 733; see the Perspective by Fernandez *et al.*) separately tethered three species of RNA of increasing size and complexity between two polystyrene beads. One bead is caught in an optical trap; the other is linked to a piezoelectric actuator, which is used to rip the RNAs apart. The smallest RNA, a hairpin, unexpectedly comes apart all at once, rather than unzipping slowly, as predicted from bulk measurements, and the two smaller RNAs "hop" repeatedly between the folded and unfolded states when a constant force is applied. Unlike the small RNAs, the largest RNA has a "brittle" structure that is resistant to mechanical deformation but then "fractures" beyond a certain limit.

Turning Somatic Cells into Stem Cells

Stem cells offer great potential for tissue repair in degenerative diseases and in gene therapy, but one limitation has been the need to isolate stem cells from the individual patient. Wakayama *et al.* (p. 740) have taken cloning and stem cell research another step forward. They produced mouse embryonic stem (ES) cells from blastocytes, which were themselves made by somatic cell nuclear transfer. The ntES cells display full developmental potential by differentiating into various cell types, including specialized neurons and gametes. The ntES cell nuclei were then used for nuclear transfer to produce viable clones. This work should enable the generation of ES cell lines from complex genetic mutants and may have significant applications to human medicine.

Creating a Catenated Viral Coat

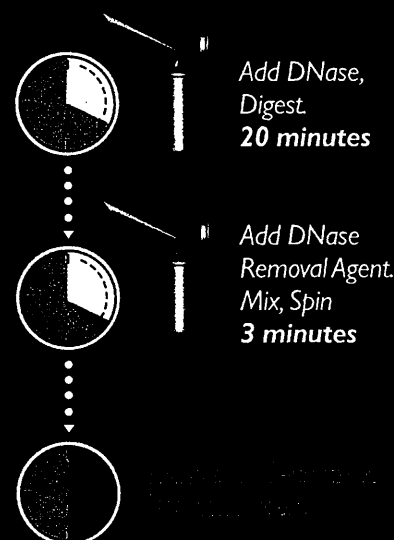
Many viruses undergo conformational changes during maturation. Conway *et al.* (p. 744) now provide a view of the transition from a precursor capsid (Prohead-II) to the mature capsid (Head-II) in bacteriophage HK97. The conformational change is caused mainly by domain rotations with concomitant refolding of two motifs. The expanded and thinner mature capsid is stabilized by an increase in the surface area buried at interfaces and by cross-links that result in a catenated topology. During packaging, repulsion between DNA and the negatively charged inner surface of Prohead II may trigger the transition.

Submitting to DNA Testing

The oral polio vaccine (OPV) developed by the Wistar Institute was administered to more than 1 million people in Central Africa. There have been claims that the vaccine was grown in chimpanzee kidneys contaminated with a simian immunodeficiency virus, thus giving rise to the AIDS pandemic. Poinar *et al.* (p. 743; see the news story by Cohen) used the polymerase chain reaction to test for the presence of chimpanzee DNA in samples provided by the Wistar Institute. Their results identify the primate source for the vaccine as macaque monkeys and provide no evidence to support the OPV hypothesis for the origin of AIDS.

CREDIT: M. C. WEI ET AL.

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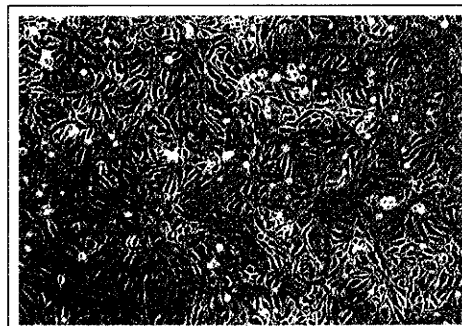
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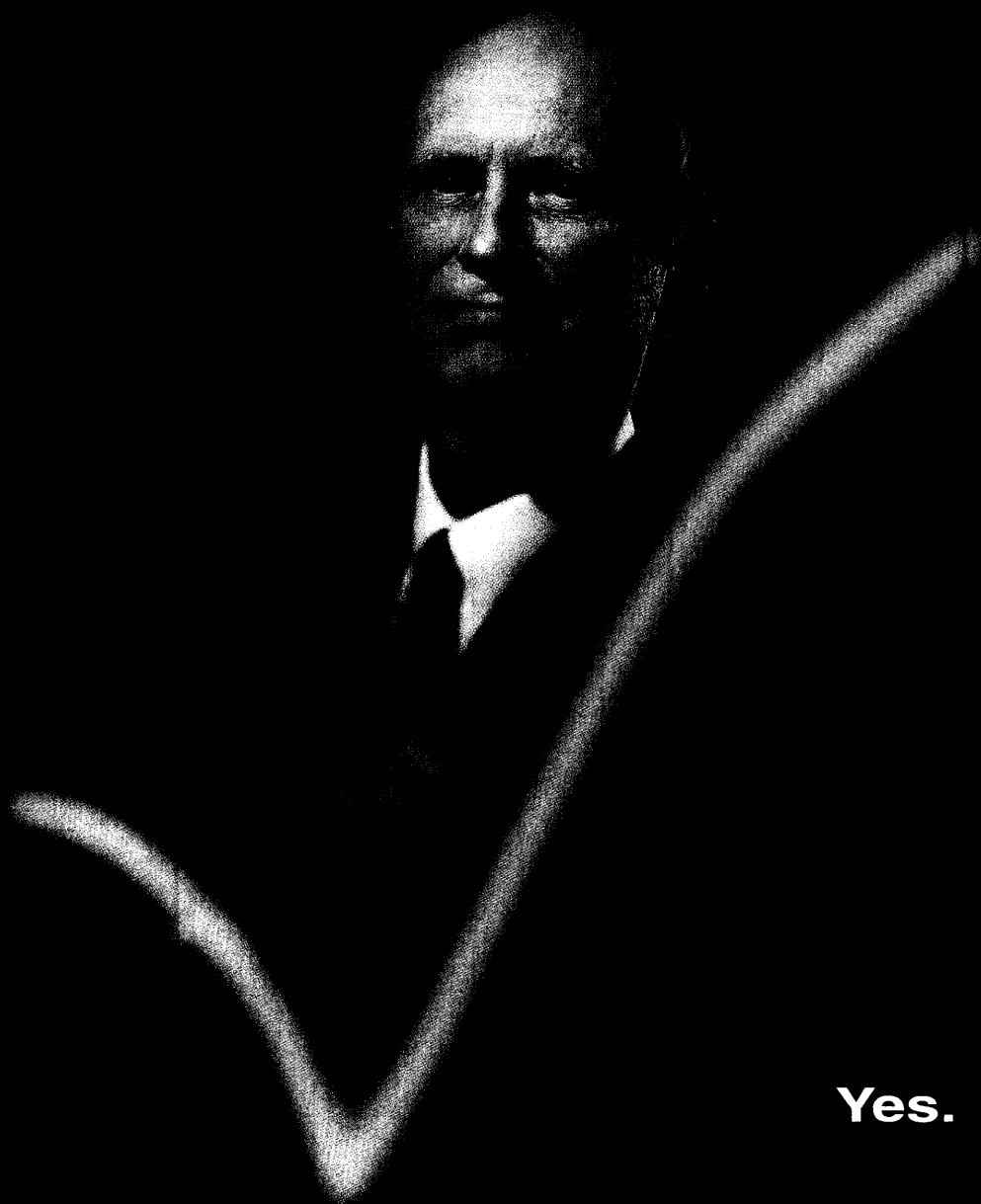
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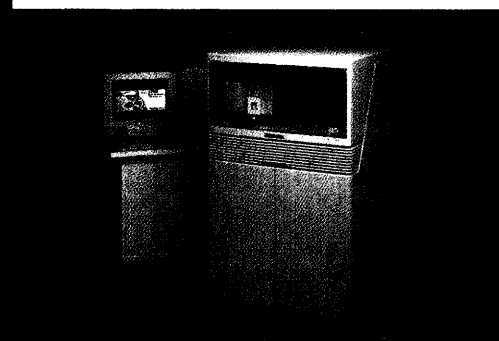
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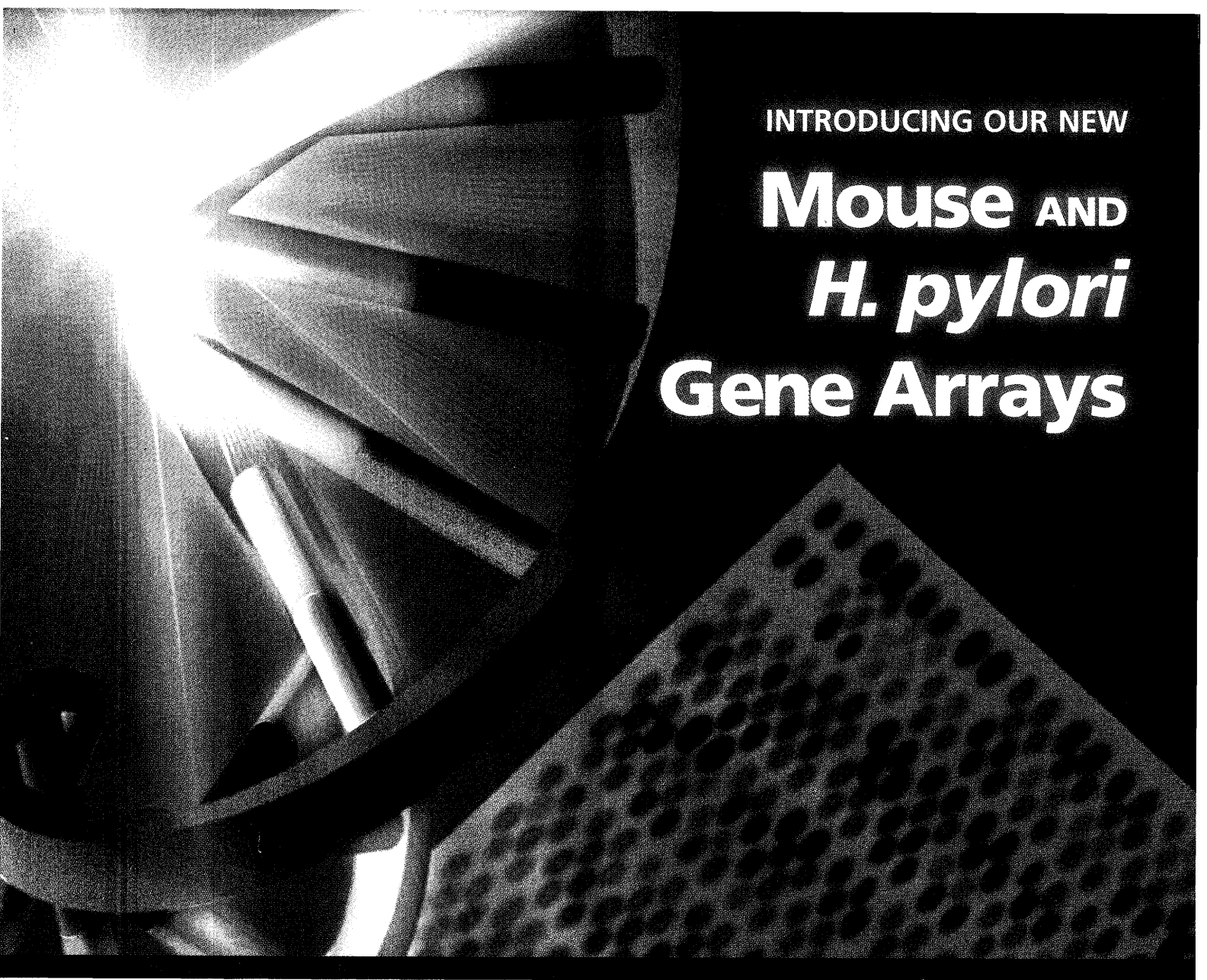
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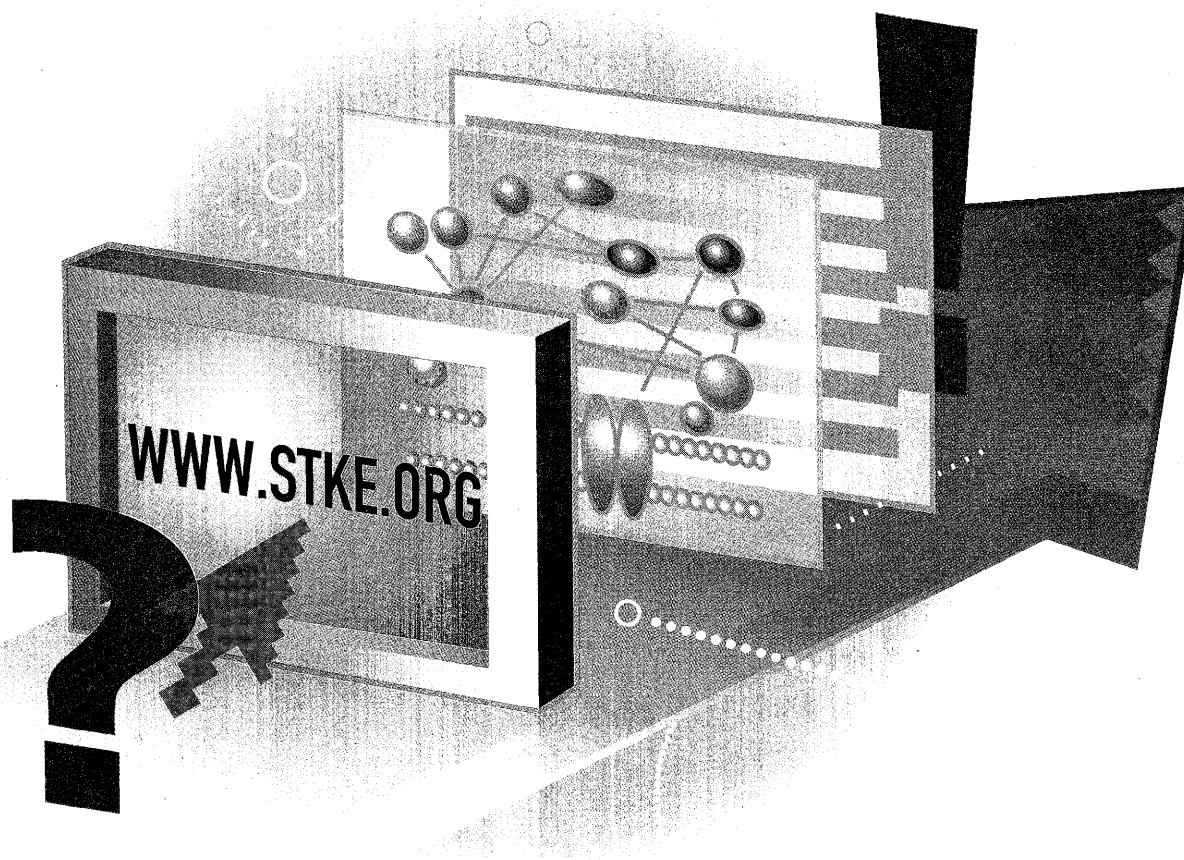
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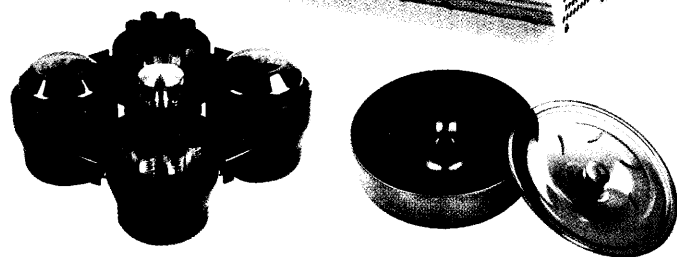
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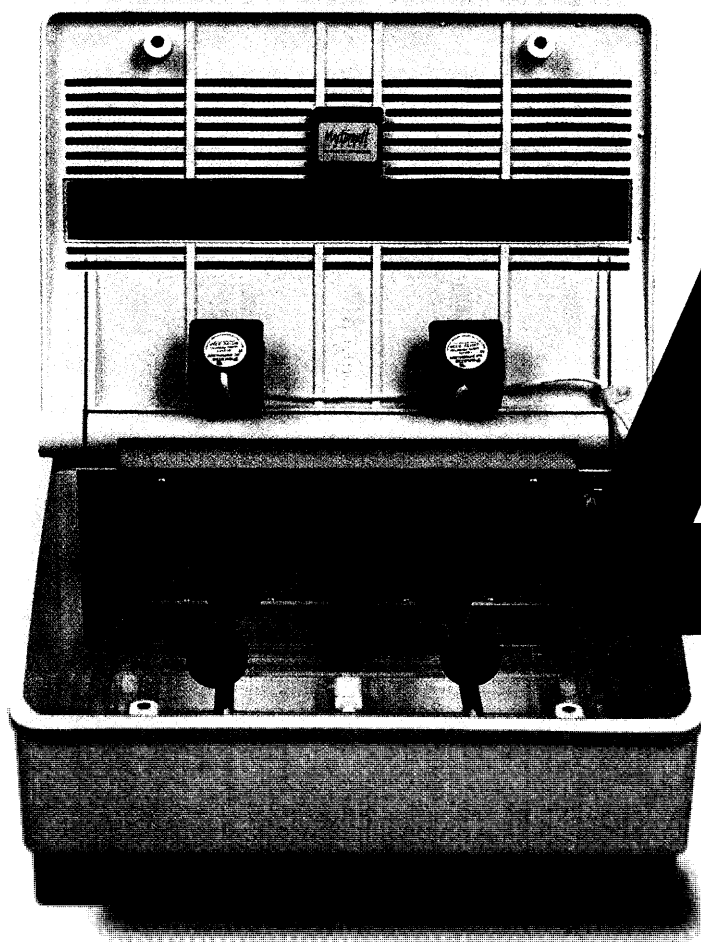
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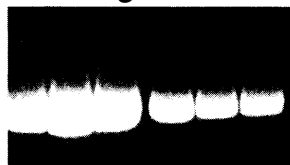
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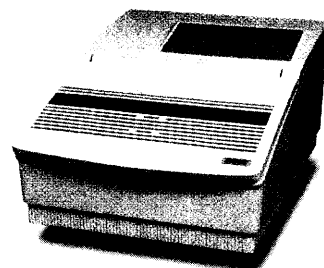
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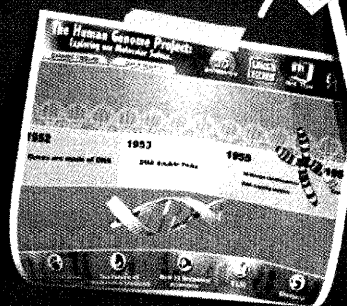
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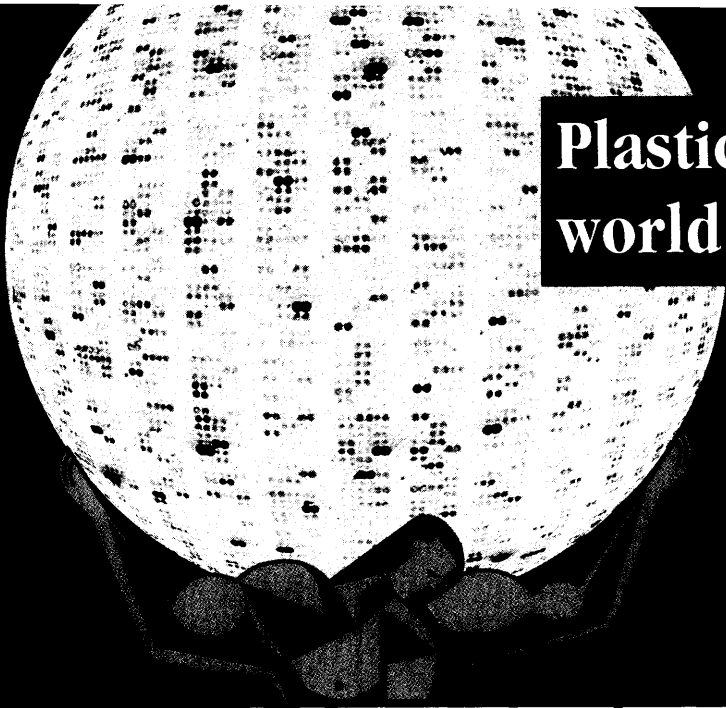
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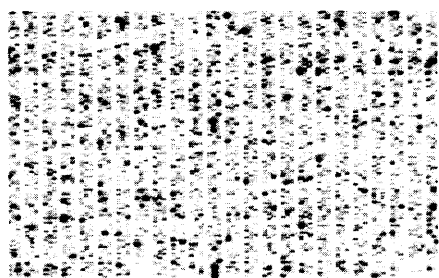
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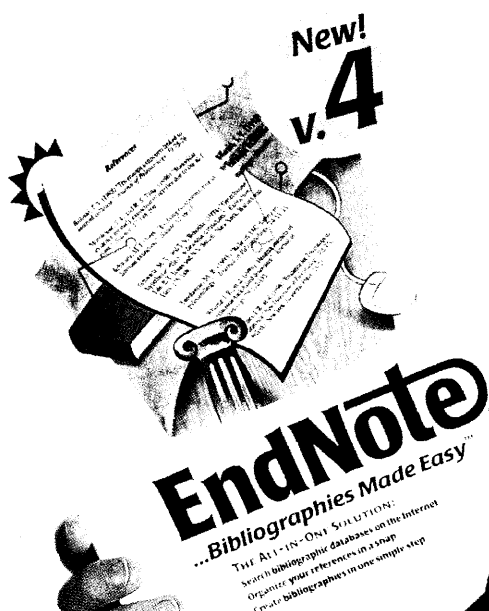
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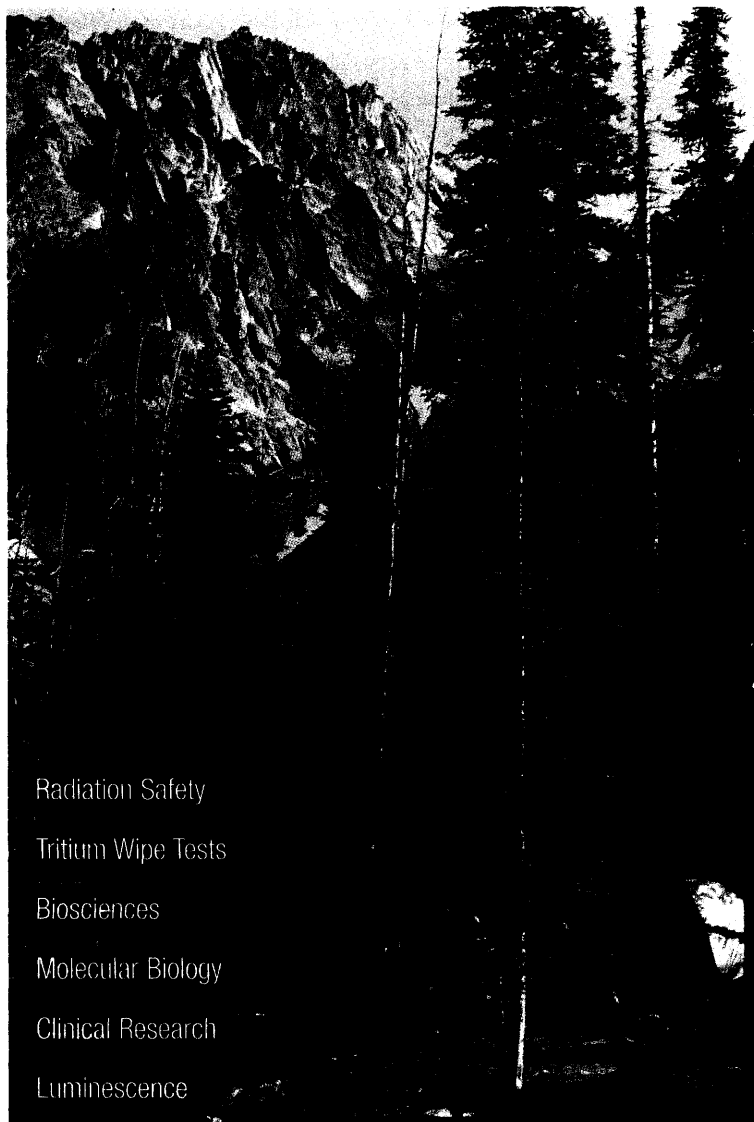
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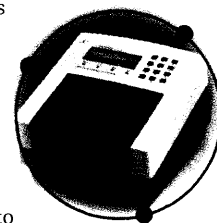
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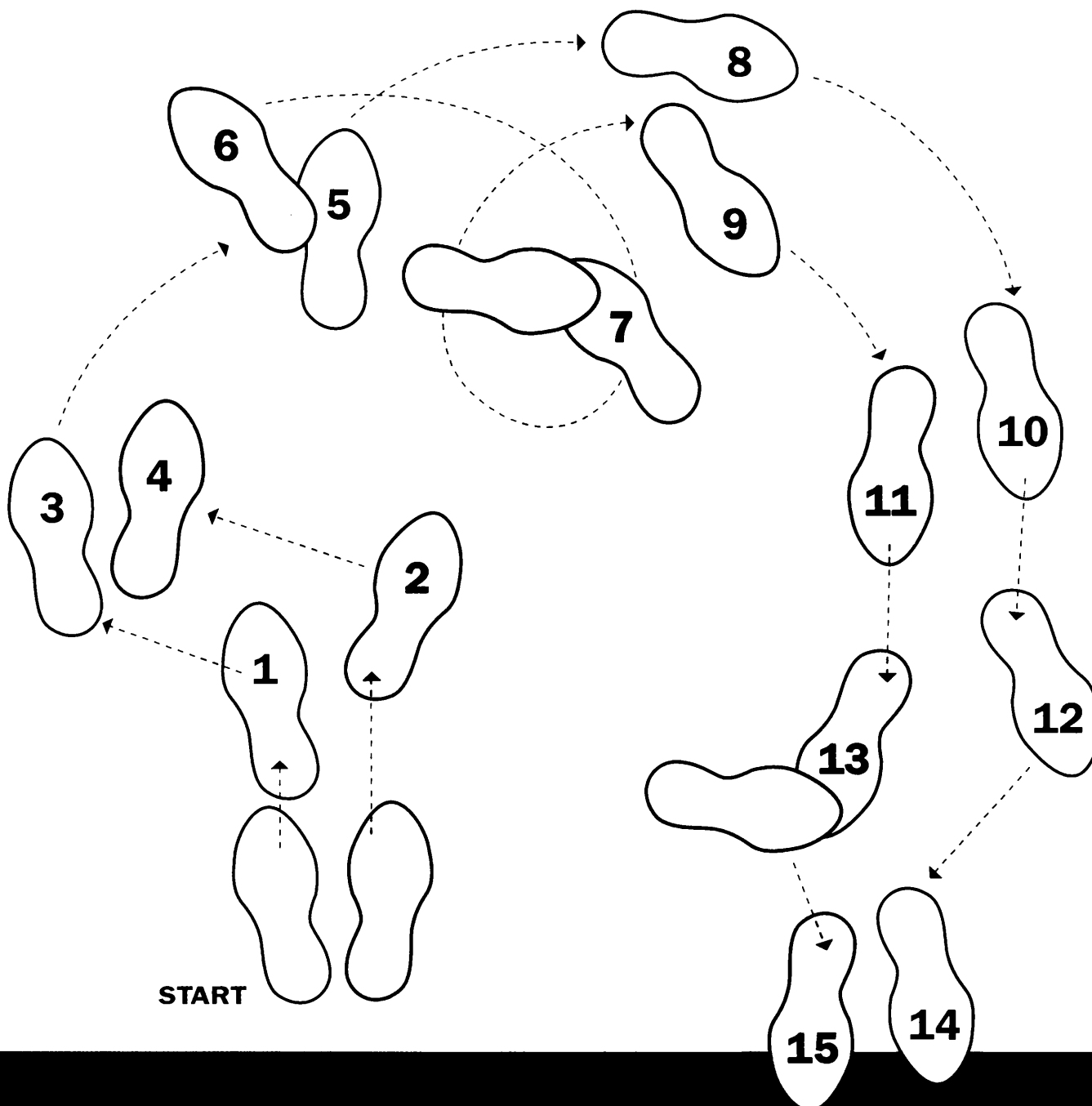
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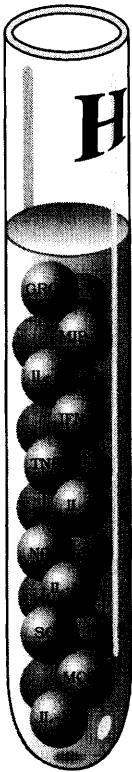


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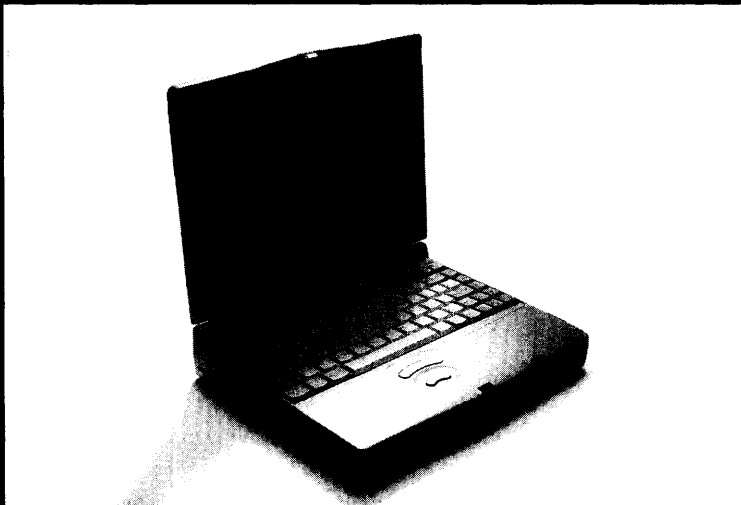
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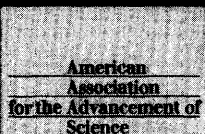
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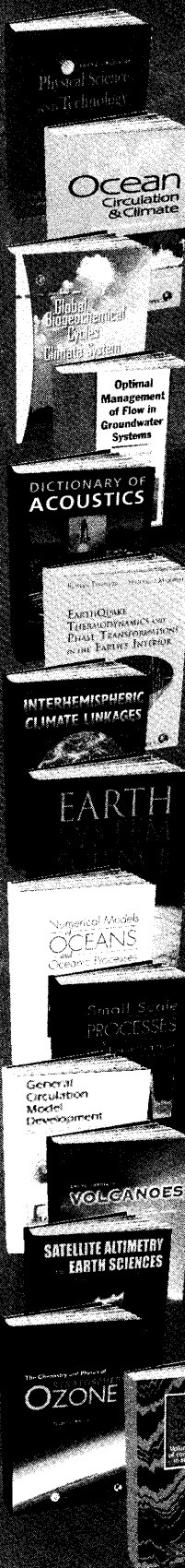
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GeneOrder 2.0, which runs partly on a server and partly as a Java applet on a user's computer, goes partway toward a comparison of gene order and clustering. Users enter GenBank accession numbers for both the query and reference genomic sequences, and the program compares the protein products of the two. Each translated gene in the query sequence is compared against all of the gene products from a reference sequence, using BLASTP. The output of the comparison is a two-dimensional plot of points, similar to a dot plot. These correspond to the sequential (not map) position of each gene along one genome that matches with a gene in the other genome. For two closely related organisms, the plot shows mainly a central diagonal of points, each point designating a gene with a protein homolog and similar sequential position in both genomes. Thus, the plot identifies genes in each that are in the same order on the genome. A table accompanying the plot allows one to hyperlink to National Center for Biotechnology Information data records that identify the gene sequences.

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GeneOrder warns users to limit the size of the genome sequences to less than 250 kb (or 250 proteins), which is, unfortunately, quite small. GeneOrder works reasonably well when comparing the gene order of relatively short genomic sequences of related viruses, a purpose for which the program appears to have been written originally.

—R. L. Bernstein and J. B. Spalding

National Biotechnology Information Facility, New Mexico State University, Las Cruces, NM 88003-8002, USA. E-mail: rbernste@sfsu.edu (R.L.B.); spalding@psl.nmsu.edu (J.B.S.)

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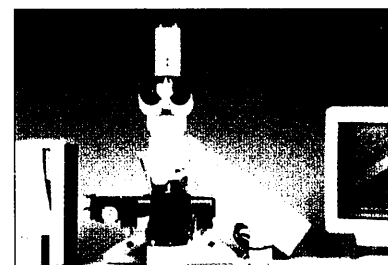
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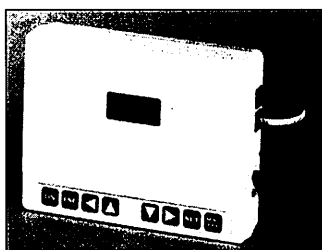
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