

Science

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of the Year

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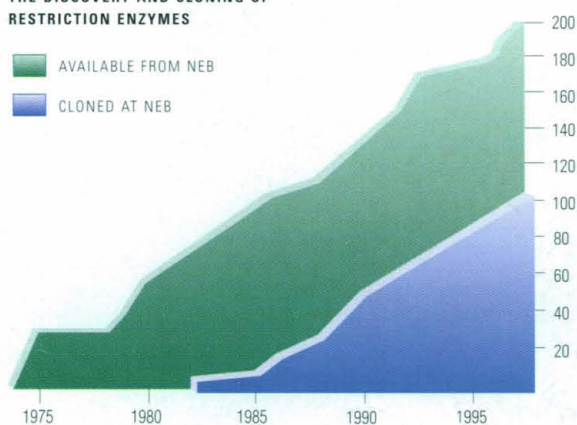
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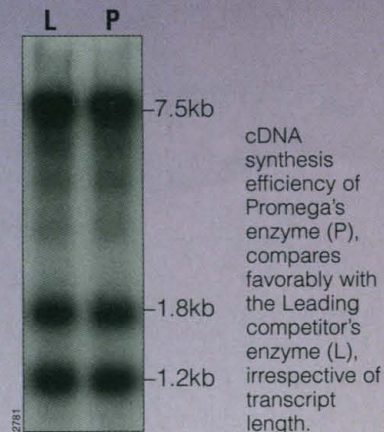
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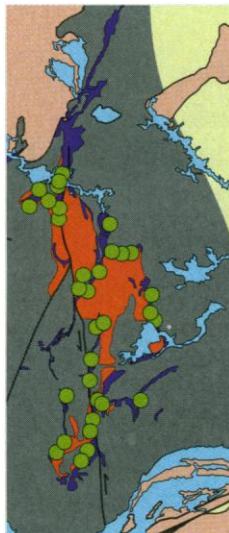
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COVER Artist's conception shows stem cells, the Breakthrough of the Year in 1999, under the microscope. The fate of many of the cells remains a mystery to researchers, as indicated by opaque cells. But under scrutiny, some stem cells reveal their ability to become different kinds of cells, including neurons, fat cells, muscle cells, and red blood cells. See the Breakthrough of the Year special section, beginning on p. 2238, and the Editorial on p. 2267. [Illustration: Steve Keller]



NEWS

NEWS OF THE WEEK

- 2244 **CLINICAL TRIALS: Gene Therapy Death Prompts Review of Adenovirus Vector**
- ▼2245 **MICROBIOLOGY: Promising Antibiotic Candidate Identified**
2361
- 2247 **SPACE: Europe Lofts X-ray Observatory**
- 2248 **NIMH: Mental Health Agency Shrugs Off Critics**
- 2248 **MARS EXPLORATION: Changes to Missions Could Delay Science**
- 2249 **SCIENTIFIC MISCONDUCT: Researcher Rebuked for 20-Year-Old Misdeed**
- 2250 **COMPUTER SCIENCE: Big Blue Aims to Crack Protein Riddle**
- 2251 **NASA: NRC Panel to Propose Station Institute**

- 2251 **PCR: Taq Polymerase Patent Ruled Invalid**

- 2253 **LAB SAFETY: Licenses Suspended at 3 Toronto Hospitals**

NEWS FOCUS

- 2254 **GEOPHYSICS: Ancient Continent Opens Window on the Early Earth**
- 2256 **BIOMEDICINE: Does Cancer Therapy Trigger Cell Suicide?**
- 2258 **SCIENTIFIC MISCONDUCT: Europe Stresses Prevention Rather Than Cure**
- 2260 **SPACE SCIENCE: Indian Agency Eyes Moon in Shift Toward Research**
- 2261 **BIOLOGICAL IMAGING: Scanners Get a Fix on Lab Animals**

DEPARTMENTS

NETWATCH
2227

**THIS WEEK IN
SCIENCE**
2229

**BREAKTHROUGH OF
THE YEAR**
2238

SCIENCESCOPE
2247

RANDOM SAMPLES
2265

CONTACT SCIENCE
2267

NEW PRODUCTS
2367

RESEARCH

RESEARCH ARTICLE

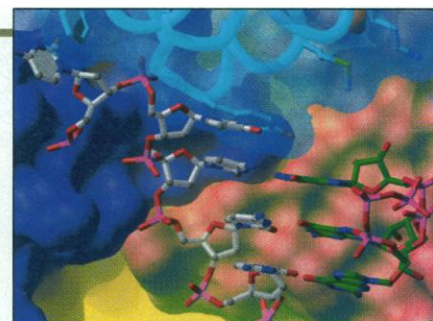
- 2305 **Structure of a Transcribing T7 RNA Polymerase Initiation Complex**
G. M. T. Cheetham and T. A. Steitz

REPORTS

- 2309 **Phase-Coherent Amplification of Matter Waves** M. Kozuma, Y. Suzuki, Y. Torii, T. Sugjura, T. Kuga, E. W. Hagley, L. Deng
- ▼2312 **Exciton Storage in Semiconductor Self-Assembled Quantum Dots** T. Lundstrom, W. Schoenfeld, H. Lee, P. M. Petroff
2286
- 2314 **Experimental Tunneling Ratchets** H. Linke, T. E. Humphrey, A. Löfgren, A. O. Sushkov, R. Newbury, R. P. Taylor, P. Omling
- ▼2317 **Three-Dimensional Atomic-Scale Imaging of Impurity Segregation to Line Defects** D. Blavette, E. Cadel, A. Fraczkiewicz, A. Menand
2285
- 2319 **Deflection of the Local Interstellar Dust Flow by Solar Radiation Pressure** M. Landgraf, K. Augustsson, E. Grün, B. A. S. Gustafson
- 2323 **Short-Lived Oxygen Diffusion During Hot, Deep-Seated Meteoric Alteration of Anorthosite** C. I. Mora, L. R. Riciputi, D. R. Cole

2305

A transcribing
T7 RNA
polymerase



- 2325 **Surfactant-Mediated Two-Dimensional Crystallization of Colloidal Crystals**
L. Ramos, T. C. Lubensky, N. Dan, P. Nelson, D. A. Weitz
- 2328 **Postnatal Sex Reversal of the Ovaries in Mice Lacking Estrogen Receptors α and β**
J. F. Couse, S. C. Hewitt, D. O. Bunch, M. Sar, V. R. Walker, B. J. Davis, K. S. Korach
- 2331 **Isolation of West Nile Virus from Mosquitoes, Crows, and a Cooper's Hawk in Connecticut** J. F. Anderson, T. G. Andreadis, C. R. Vossbrinck, S. Tirrell, E. M. Wakem, R. A. Frech, A. E. Garmendia, H. J. Van Kruiningen



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SCIENCE'S COMPASS

EDITORIAL

- ▼ 2267 **Breakthroughs 1999**
2238

LETTERS

- 2269 **A Loss to Science** R. J. Birgeneau. Dietary Supplements: What Is in the Public's Best Interest? J. N. Hathcock; S. M. Talbott. *Response* S. H. Zeisel. **Scrutinizing Creativity** D. Hollenberg. *Response* J. Goldenberg, D. Mazursky, S. Solomon. **A Comb-Wide Web** J. Tautz. **Corrections and Clarifications**

POLICY FORUM

- 2275 **FOOD SAFETY: Food Irradiation—The Neglected Solution to Food-Borne Illness** R. Lutter
2277 **GENETIC TECHNOLOGIES: Commercialization of Genetic Research and Public Policy** B. M. Knoppers, M. Hirtle, K. C. Glass

BOOKS ET AL.

- 2279 **HISTORY OF SCIENCE: *The Sun in the Church Cathedrals as Solar Observatories*** J. L. Heilbron, reviewed by A. Van Helden
2280 **ENERGY TECHNOLOGY: *From Space to Earth The Story of Solar Electricity*** J. Perlin, reviewed by D. Faïman

PERSPECTIVES

- 2281 **COMPUTATIONAL ANALYSIS: Y_2K** C. J. Cramer and J. T. Roberts

2298

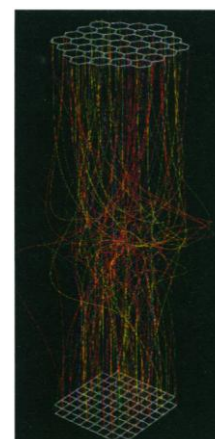
- ▼ 2283 **COGNITION: An Innate Basis For Language?** D. V. M. Bishop
2355
2284 **MOLECULAR BIOLOGY: Mutant Dyskerin Ends Relationship with Telomerase** J. W. Shay and W. E. Wright
▼ 2285 **MATERIALS SCIENCE: Imaging Elusive Solute Atoms** M. K. Miller
2317
▼ 2286 **DEVICE PHYSICS: Toward Efficient Smart Pixels** J. P. Kotthaus
2312
2287 **MOLECULAR BIOLOGY: DNA Methylation de Novo** A. Bird

TECH.SIGHT

- 2289 **ISOTOPE GEOCHEMISTRY: New Tools for Isotopic Analysis** T. Ireland
2291 **SOFTWARE: *Mathematica 4.0***, reviewed by J. A. Waas
2293 **TechSightings**

VISIONS OF THE FUTURE: ESSAY CONTEST

- 2296 **Technology Transfer** R. Kohen
2298 **Appointment as Expert Juror** M. A. Krug
2300 **NIH Grant Application** J. T. Vogelstein, J. V. Vogelstein, B. Vogelstein



2291

Renaissance software

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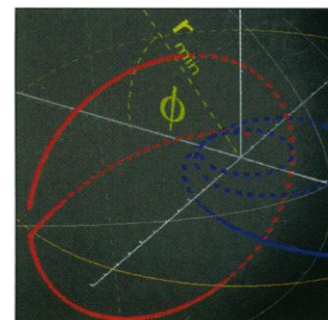
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- 2333 **Origin of the West Nile Virus Responsible for an Outbreak of Encephalitis in the Northeastern United States** R. S. Lanciotti *et al.*
2337 **Binding of Transcription Termination Protein Nun to Nascent RNA and Template DNA** R. S. Watnick and M. E. Gottesman
2339 **Requirement of Yeast *SGS1* and *SRS2* Genes for Replication and Transcription** S.-K. Lee, R. E. Johnson, S.-L. Yu, L. Prakash, S. Prakash
2342 **Posttranscriptional Gene Silencing in *Neurospora* by a RecQ DNA Helicase** C. Cogoni and G. Macino
2345 **Evolution of Shape Complementarity and Catalytic Efficiency from a Primordial Antibody Template** J. Xu, Q. Deng, J. Chen, K. N. Houk, J. Bartek, D. Hilvert, I. A. Wilson
2349 **Crystal Structure of *Thermotoga maritima* Ribosome Recycling Factor: A tRNA Mimic** M. Selmer, S. Al-Karadaghi, G. Hirokawa, A. Kaji, A. Liljas
2352 **Microglial Activation Resulting from CD40-CD40L Interaction After β -Amyloid Stimulation** J. Tan, T. Town, D. Paris, T. Mori, Z. Suo, F. Crawford, M. P. Mattson, R. A. Flavell, M. Mullan
▼ 2355 **Cognitive Modularity and Genetic Disorders** S. J. Paterson, J. H. Brown, M. K. Gsödl, M. H. Johnson, A. Karmiloff-Smith
2283
2358 **Mediation by a CREB Family Transcription Factor of NGF-Dependent Survival of Sympathetic Neurons** A. Riccio, S. Ahn, C. M. Davenport, J. A. Blendy, D. D. Ginty
▼ 2361 **Use of the Cell Wall Precursor Lipid II by a Pore-Forming Peptide Antibiotic** E. Breukink, I. Wiedemann, C. van Kraaij, O. P. Kuipers, H.-G. Sahl, B. de Kruijff
2245

TECHNICAL COMMENTS

- Filtering Reveals Form in Temporally Structured Displays** E. H. Adelson and H. Farid. *Response* S.-H. Lee and R. Blake

www.sciencemag.org/cgi/content/full/286/5448/2231a



2319

Solar sweep creates a dust gap

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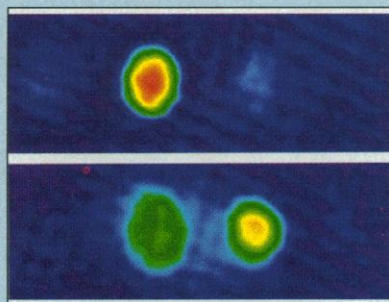
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QUANTUM RATCHETS

Particles can be made to move in one direction by applying a time-varying asymmetric potential. For proteins and small molecules, these "ratchets" act classically, but quantum-mechanical effects have been predicted for particles that can tunnel through their potential barriers. One manifestation is that the ratchet would reverse the net direction of particle flow as a function of temperature. Linke *et al.* (p. 2314) have now verified this effect experimentally for electron flow in a semiconductor heterostructure and present a simple model that explains why current reversals occur.

COHERENT INCREASES IN CONDENSATES

Recent work has shown that Bose-Einstein condensates exhibit superradiance—the interaction between coherent light and the condensate can set up a grating of atoms with well-defined momentum. Kozuma *et al.* (p. 2309) have controlled this emission process by using a small, well-defined seed condensate and by applying



well-timed laser pulses that add more atoms to the grating. They demonstrated amplification of the initial matter wave by a factor of 10. Moreover, they show that this amplification is coherent—it maintained the phase of the initial seed condensate. This matter wave amplifier is analogous to the optical wave amplifier that revolutionized the optical laser.

VIEWING IMPURITIES

Dislocations and other defects have long been known to affect the distribution of impurity atoms in the material, which are enriched in the vicinity of the defects. Such "Cottrell atmospheres" lead, for example, to strain-aging in steels. However, direct imaging of this effect, which could shed

light on enrichment rates, has been hampered by instrument limitations. Blavette *et al.* (p. 2317; see the Perspective by Miller) used a three-dimensional atom probe technique to image such enrichments on an atomic scale in iron-aluminum alloys. The increased solute concentrations are accompanied by an unexpected depletion in aluminum, which is likely to affect the plasticity of the material.

DUST IN THE SOLAR WIND

Interstellar dust grains in the outer solar system have been sampled during the last 10 years by the Ulysses and Galileo spacecraft. Landgraf *et al.* (p. 2319) examined the dust detector data and noticed a deficit of grains within a specific mass range at distances between 2 to 4 astronomical units (the Earth-sun distance) from the sun. In a model study, they show that this deficit could arise through solar radiation pressure overwhelming solar gravitation for these specific grains, thus removing them from this narrow region. The authors' model is consistent with grains composed of astronomical silicates, magnetite, or graphite.

FLAT COLLOIDAL CRYSTALS

The assembly of colloidal particles of one charge and surfactants of the opposite charge normally creates three-dimensional fractal aggregates. Ramos *et al.* (p. 2325) examined the interaction of negatively charged latex particles with vesicles made from neutral and cationic surfactants. In certain composition ranges, the latex particles assembled into two-dimensional (2D) crystals of several hundred particles that were robust against dilution or shearing. In the authors' model for crystal formation, the latex particles adsorb onto a vesicle until charge is neutralized and then attract to form a "raft." The bilayers present on the particles eventually fuse and form the final crystal.

POCKETING THE TEMPLATE

RNA polymerase from T7 bacteriophage (T7RNAP) is a single subunit enzyme that binds to specific promoter DNA sequences and initiates transcription. During the initiation phase, short RNA products are repeatedly synthesized and released until a transition occurs to give a stable elongation complex that can transcribe the complete T7 phage DNA. Cheetham and Steitz (p. 2305) present a 2.4 angstrom structure of a transcribing T7 RNA initiation complex that provides in-

sight into how the enzyme selects for synthesizing RNA and how RNA products up to about 8 nucleotides long can be formed without breaking promoter contacts. The authors provide evidence for a "scrunching" model in which the DNA template accumulates in the active site pocket of T7RNAP during the early stages of transcription: Once the pocket is filled, either the RNA product will be abortively released or T7RNAP will dissociate from the promoter to allow entry into the processive elongation phase.

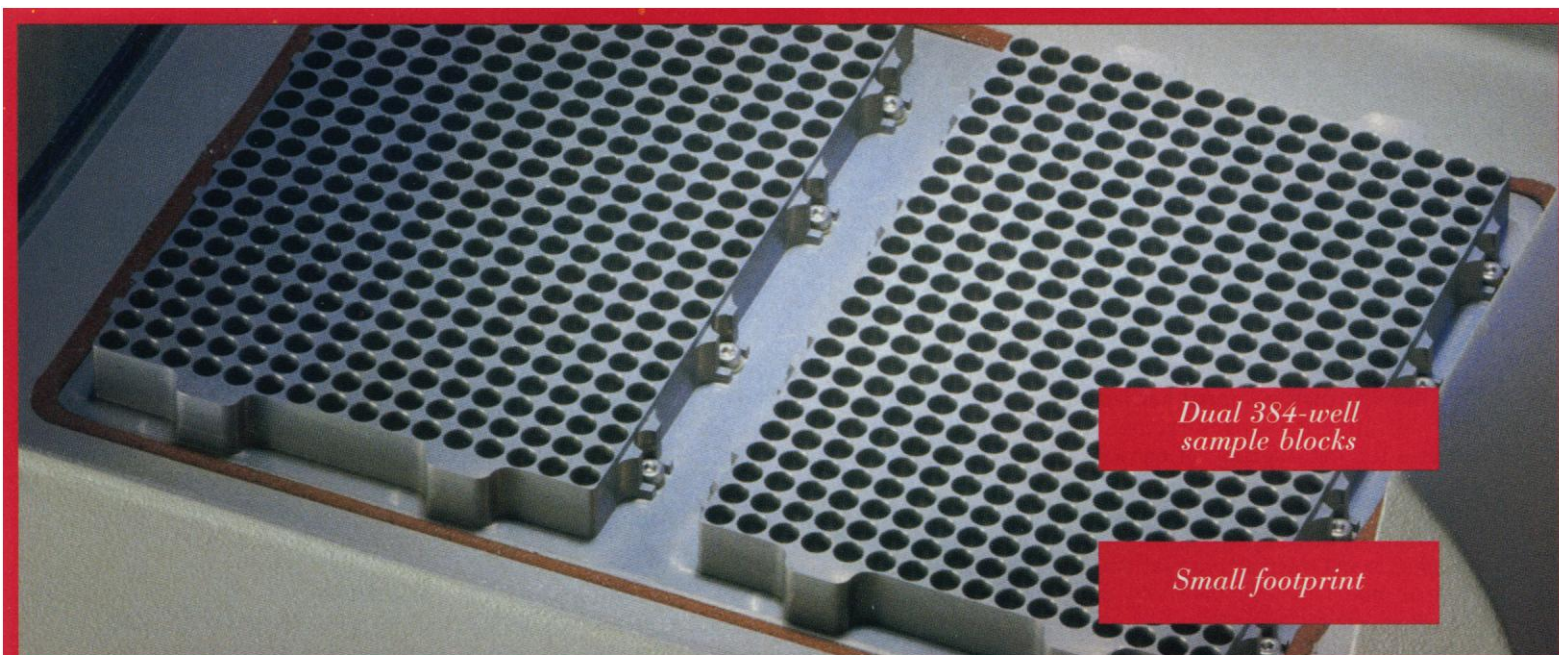
TWO FOR NUN

In transcribing DNA template into RNA, either sequence elements or protein factors can signal the end to transcription. The phage factor Nun stops transcription of phage template by binding to the nascent transcript and blocking the progress of bacterial RNA polymerase (RNAP). What are the molecular interactions between Nun and the transcription machinery that enable the phage factor to stop the large bacterial RNAP? In the presence of zinc, the Nun COOH-terminus inhibits its own RNA binding by blocking the amino-terminal binding domain. However, another phage protein, NusA, can stimulate the binding of Nun to RNA. Watnick and Gottesman (p. 2337) studied these interactions further with photochemical cross-linking analyses and found that Nun directly contacts the nascent RNA, RNAP, and double-stranded DNA. Contact with DNA occurs at the DNA binding site of RNAP. Nun may arrest transcription by acting to anchor the RNAP to DNA. Thus, Nun, along with RNAP, contacts both the nascent RNA and template DNA.

DNA HELICASE DEFECTS

Bloom's syndrome and Werner's syndrome are two human disorders that are characterized by growth retardation and a high incidence of cancers. The genes reported to be mutated in these disorders, the Bloom's syndrome gene *BML* and Werner's syndrome gene *WRN*, encode DNA helicases. Two reports focus on action of homologs of *BML* and *WRN*, the yeast gene *SGS1* and *Neurospora* gene *qde-3*, respectively. Cogoni and Macino (p. 2342) cloned the *qde-3* gene and show that it participates in post-transcriptional gene silencing, which suppresses the expression of a foreign gene when introduced into a cell. Lee *et al.* (p. 2339) showed that mutation of *SGS1* and

CONTINUED ON PAGE 2231



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another helicase homolog *SGS2* resulted in defects both in transcription by the RNA polymerase I molecule and in DNA replication. The combination of gene silencing, transcription, or replication effects exhibited by homologs of the Bloom's and Werner's syndrome genes may contribute to the various genetic defects observed in the human disorders.

A PROTEIN VERSION OF TRNA

The translation process that synthesizes peptides is ended by release factors that liberate the completed peptide and a ribosome recycling factor (RRF) that participates in the release of the messenger RNA and the fission of the two ribosomal subunits. Selmer *et al.* (p. 2349) now provide the crystal structure of RRF and find that it looks remarkably like a molecule of transfer RNA (tRNA). The two molecules each contain two arms of the same dimensions that are set at the same angle. The only major difference is that RRF does not extend to the 3'-CCA terminus of the tRNA, the spot where the amino acid is attached. The shape similarity suggests that RRF binds to the tRNA entry site on the stationary ribosome during disassembly.

INFLAMMATION IN ALZHEIMER'S DISEASE

Activation of microglial cells in the brain may be responsible for the inflammatory component of Alzheimer's disease. Tan *et al.* (p. 2352) now show that cultured microglial cells exposed to the pathogenic amyloid- β peptide ($A\beta$) exhibit an increase in surface expression of CD40, a receptor that is important in the inflammatory response. Exposure of $A\beta$ -treated cells to the ligand for CD40 resulted in activation of microglial cells and an increase in their production of the inflammatory

cytokine tumor necrosis factor α . These findings suggest that $A\beta$ can promote the interaction of microglial cells with CD40 ligand that leads to inflammation.

DEVELOPMENT'S ROLE IN COGNITIVE DEFICITS

Normal adults who suffer brain damage can exhibit a cognitive performance pattern in which some abilities are spared while others are significantly diminished. These phenotypes often are used as models for cognitive deficits observed in various genetic disorders, one of which is Williams syndrome (WS). Adult WS individuals perform relatively poorly on visual-spatial and numerical tasks while displaying approximately normal verbal skills. Paterson *et al.* (p. 2355; see the Perspective by Bishop) study a group of WS infants and find that they do well on number but less well on language. This dissociation suggests that cognitive development may not occur in strictly modular fashion and that cognitive profiles in genetic disorders may change during development.

ANTIBIOTIC ACTION

Expanded usage of antibiotics has led an alarming increase in resistance of bacteria to the currently available store of antibiotics and spurred the search for new classes of antibiotics. Breukink *et al.* (p. 2361) have examined the mechanism of action for a promising peptide antibiotic called nisin Z. Nisin is derived from *Lactococcus lactis* and is a common food preservative. Like vancomycin, nisin Z targets the Lipid II bacterial membrane component. However, unlike vancomycin, nisin Z performs its bactericidal effect by poking holes in the bacteria. Insights into the actions of nisin may assist in developing a new class of highly efficient antibiotics.

TECHNICAL COMMENT SUMMARIES

Visual Mechanisms

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/286/5448/2231a

Lee and Blake (Reports, 14 May, p. 1165), designed an experiment to test whether the visual system could resolve larger geometric objects using only unpredictable but synchronized changes among local features. Their results led to the suggestion that there may be a new visual mechanism sensitive to temporal structure.

Adelson and Farid comment that these results "can be explained with well-known mechanisms" because in their experiments, which involved changes in the temporal structure of an object and background, "there will be moments by chance when one region's contrast is high while the other's is low..."

Lee and Blake respond that "to assert that these infrequent, hypothetical events explain the perception of form seems conjectural" but "agree that there is no need to posit the existence of new visual mechanisms."

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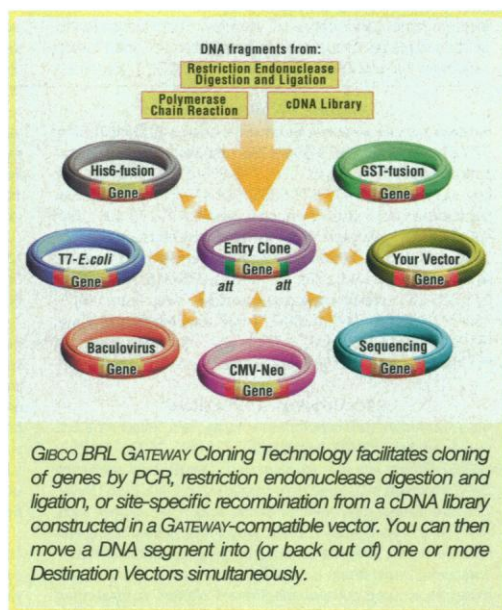
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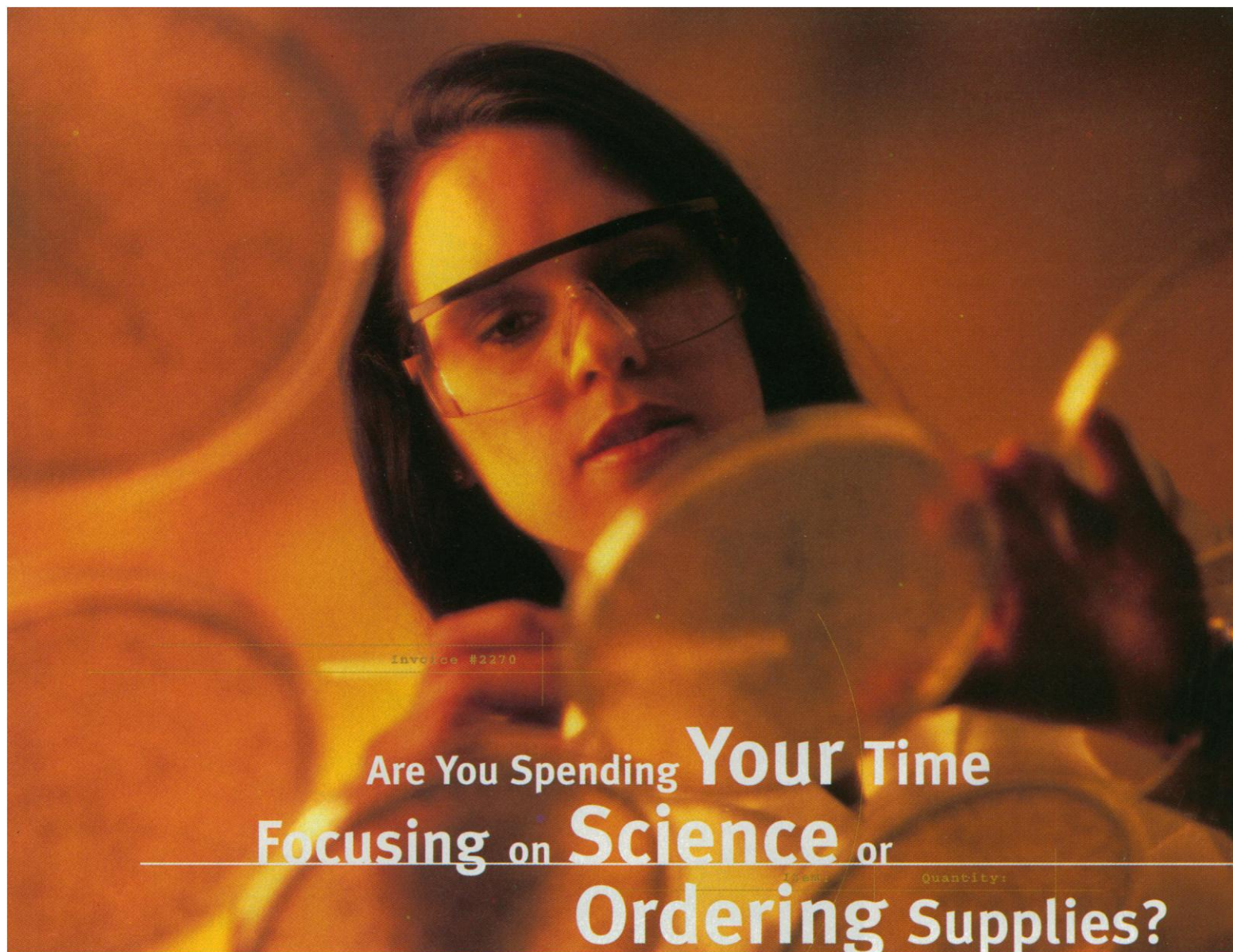
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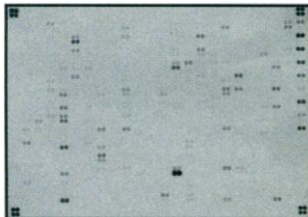


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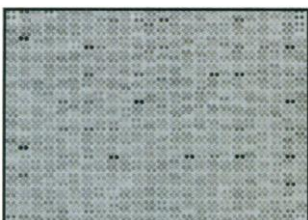
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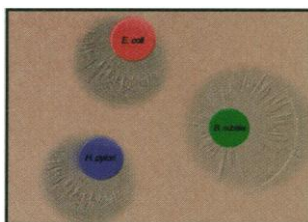
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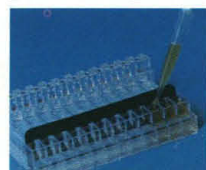
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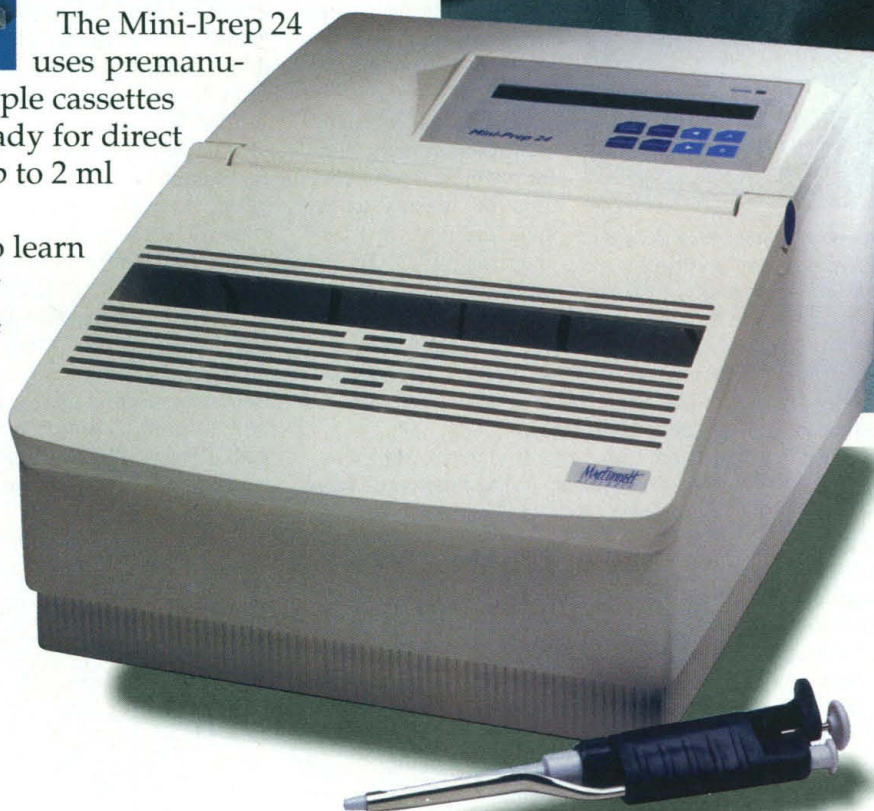
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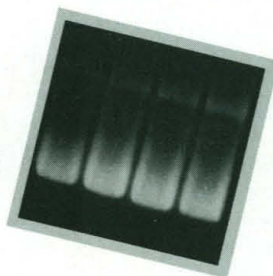
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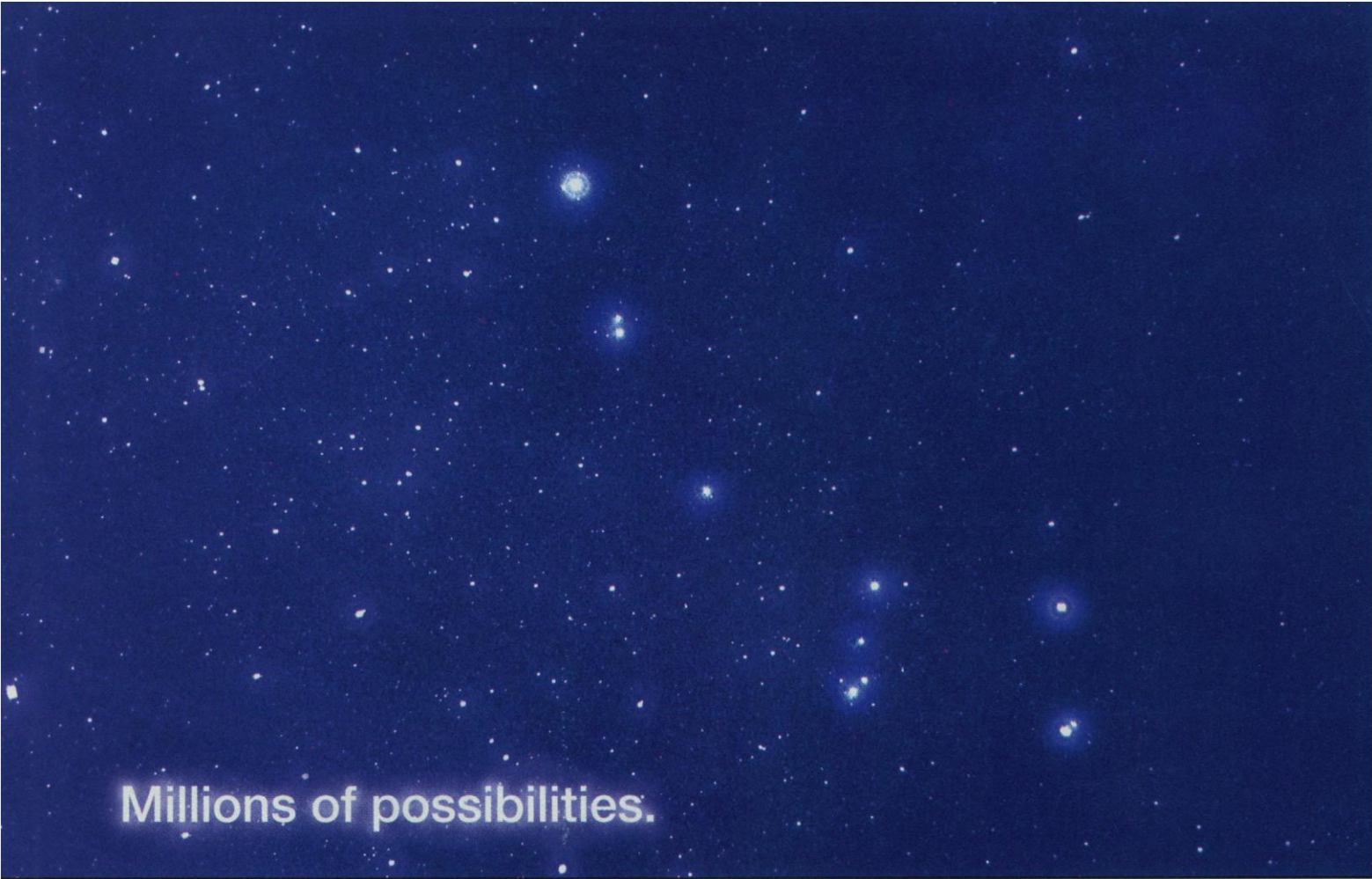
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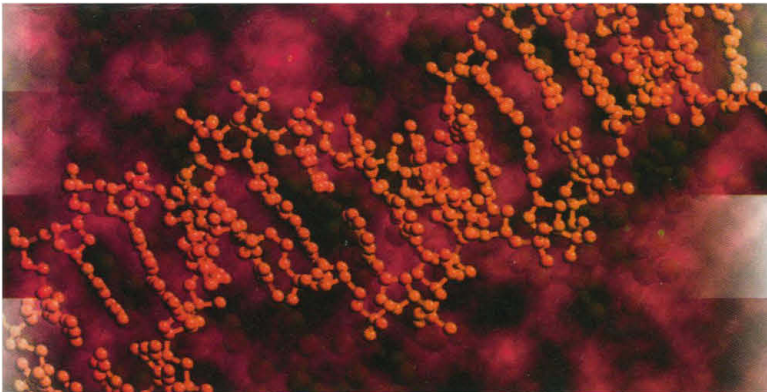
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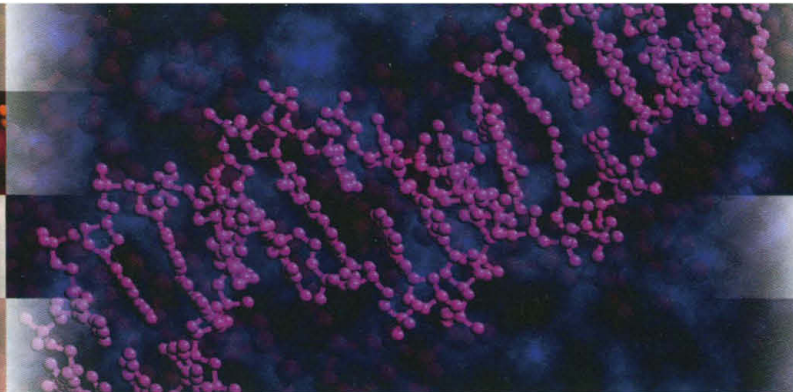
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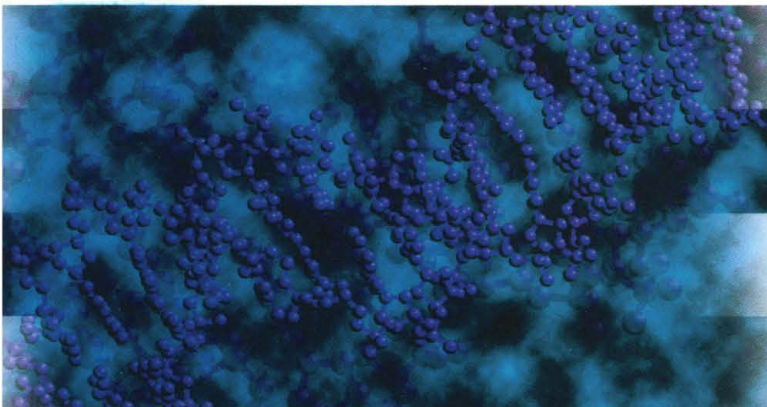
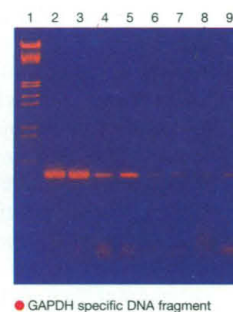
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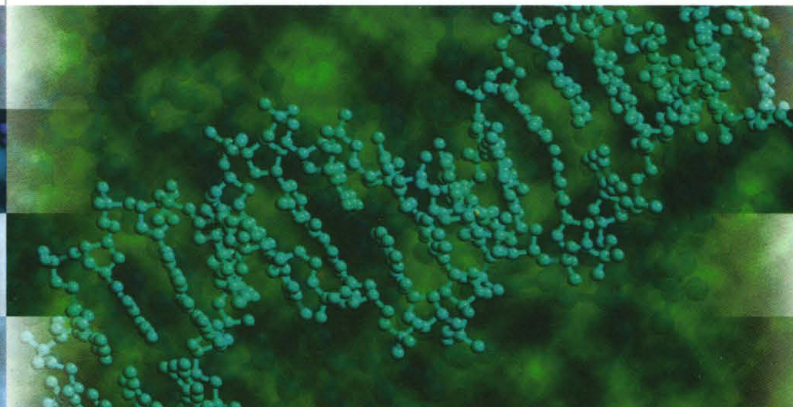
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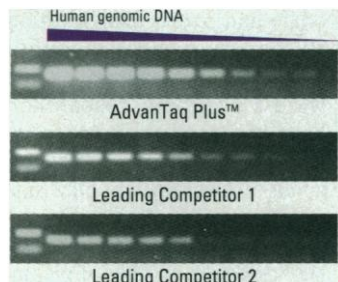
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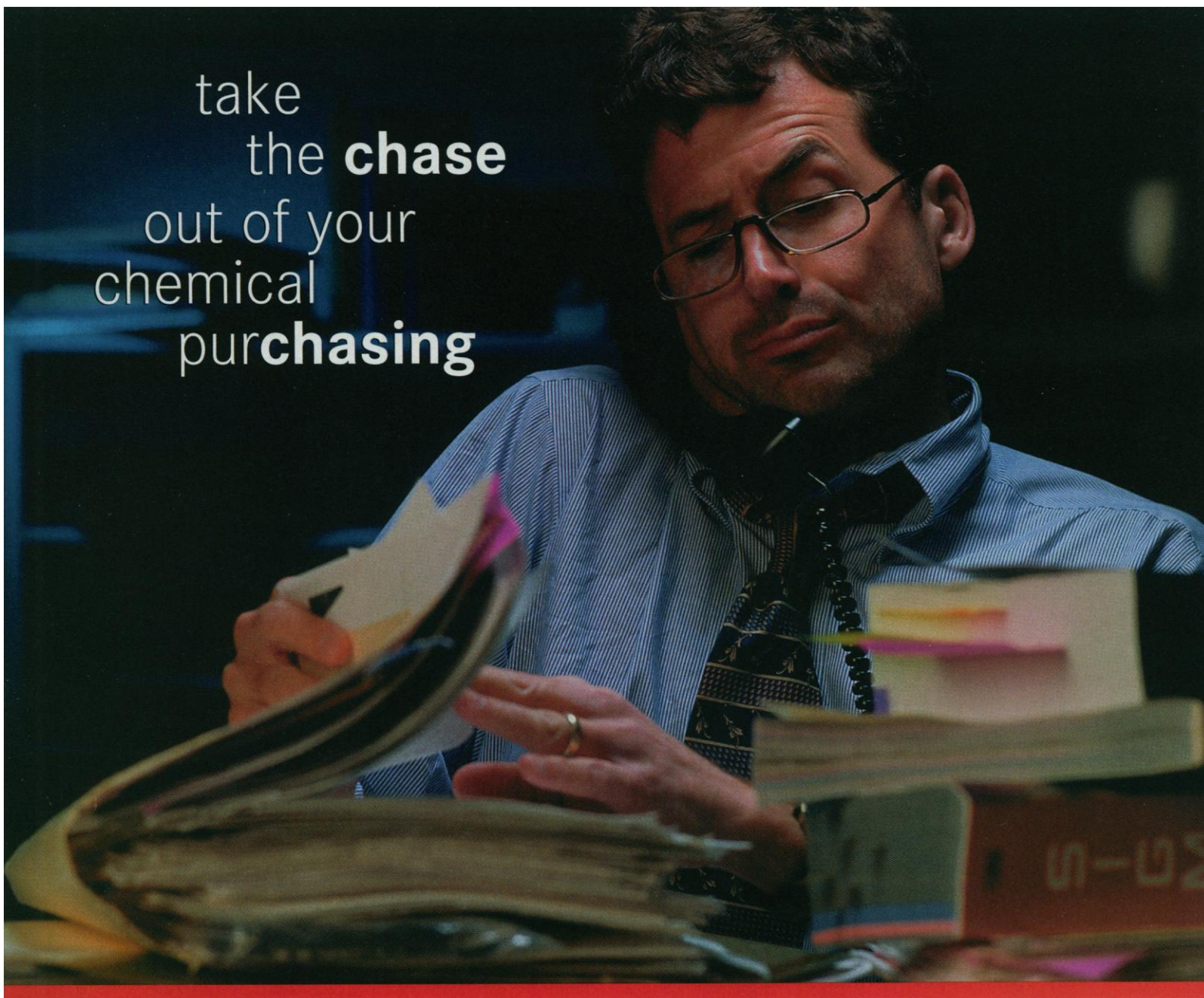
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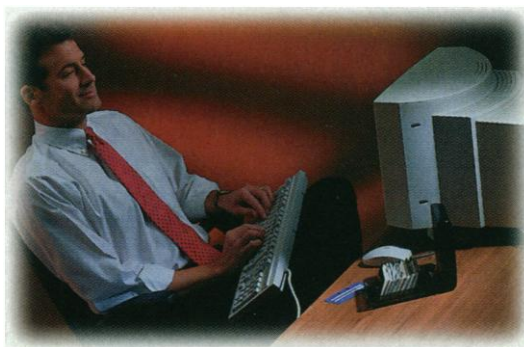
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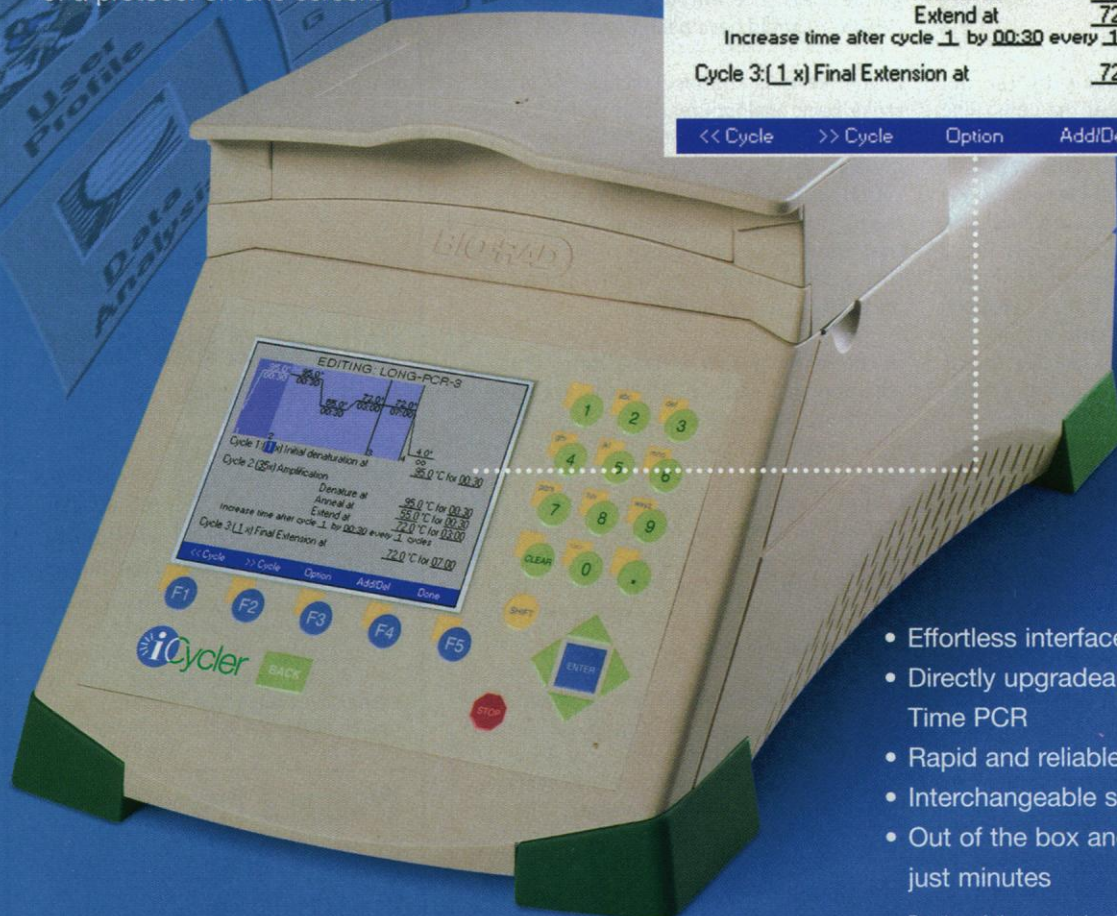
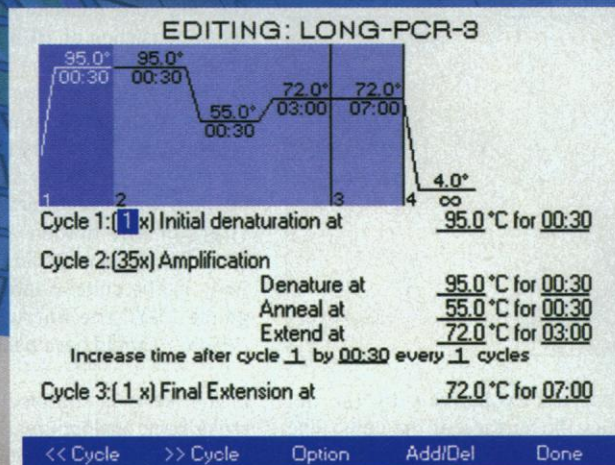
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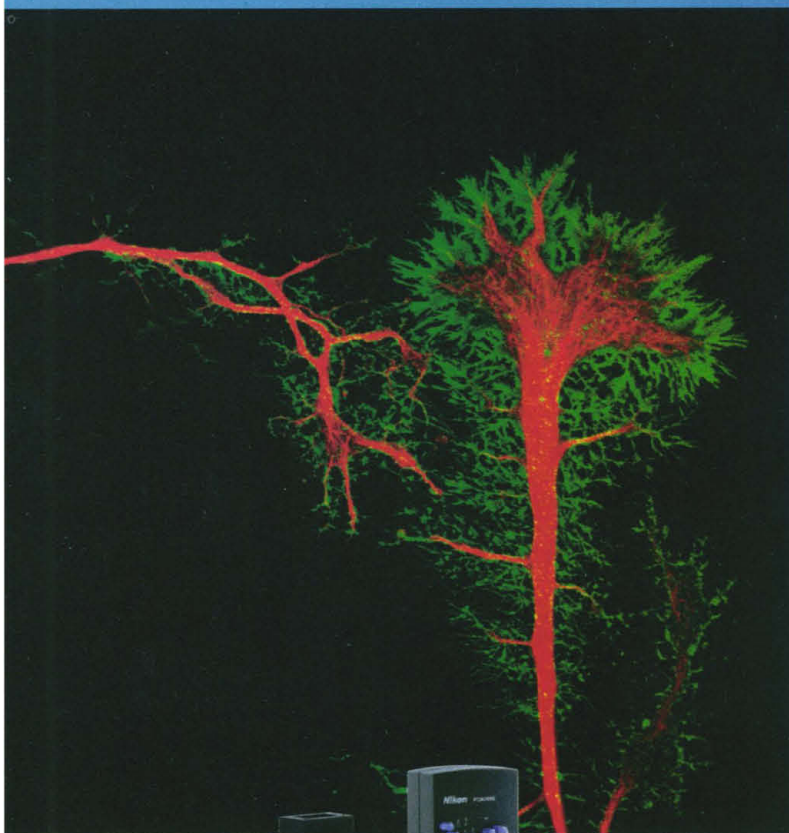
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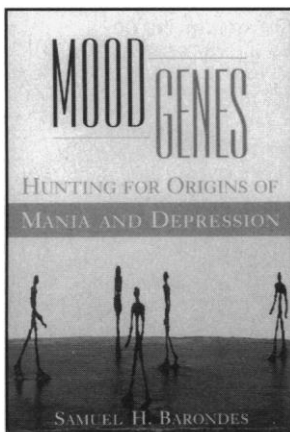
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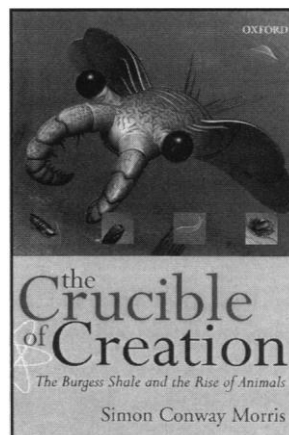
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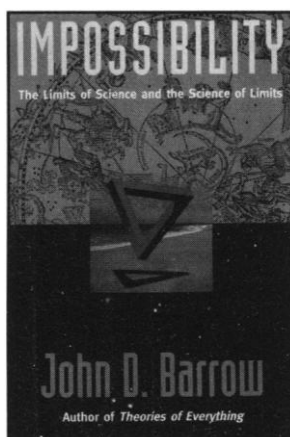
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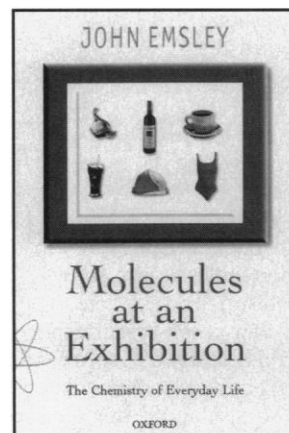
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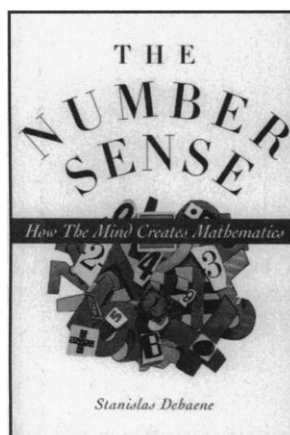
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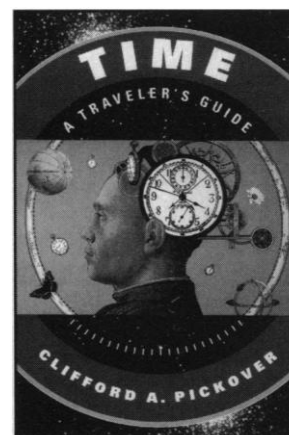
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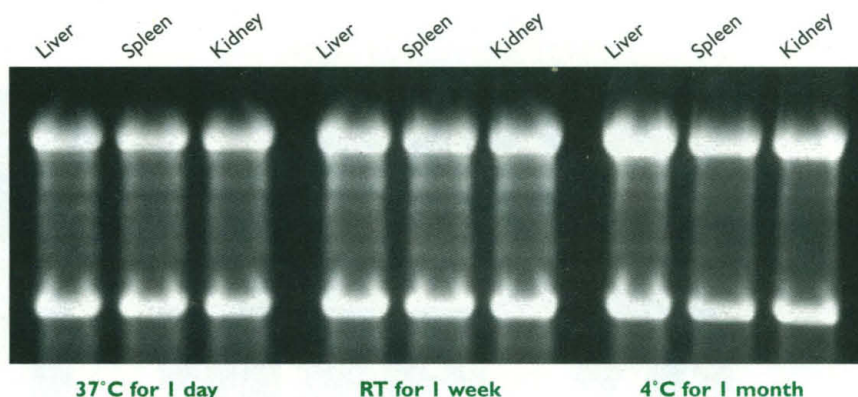


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