

Science

An abstract 3D molecular model is the central focus of the cover. It features several interconnected components: a large, light grey, textured mass on the left; a smaller, similar mass at the bottom left; a large, vibrant blue mass on the right; and a central cluster of red and green elements. The entire model is set against a solid black background, which makes the colors of the molecular structure stand out.

24 September 1999

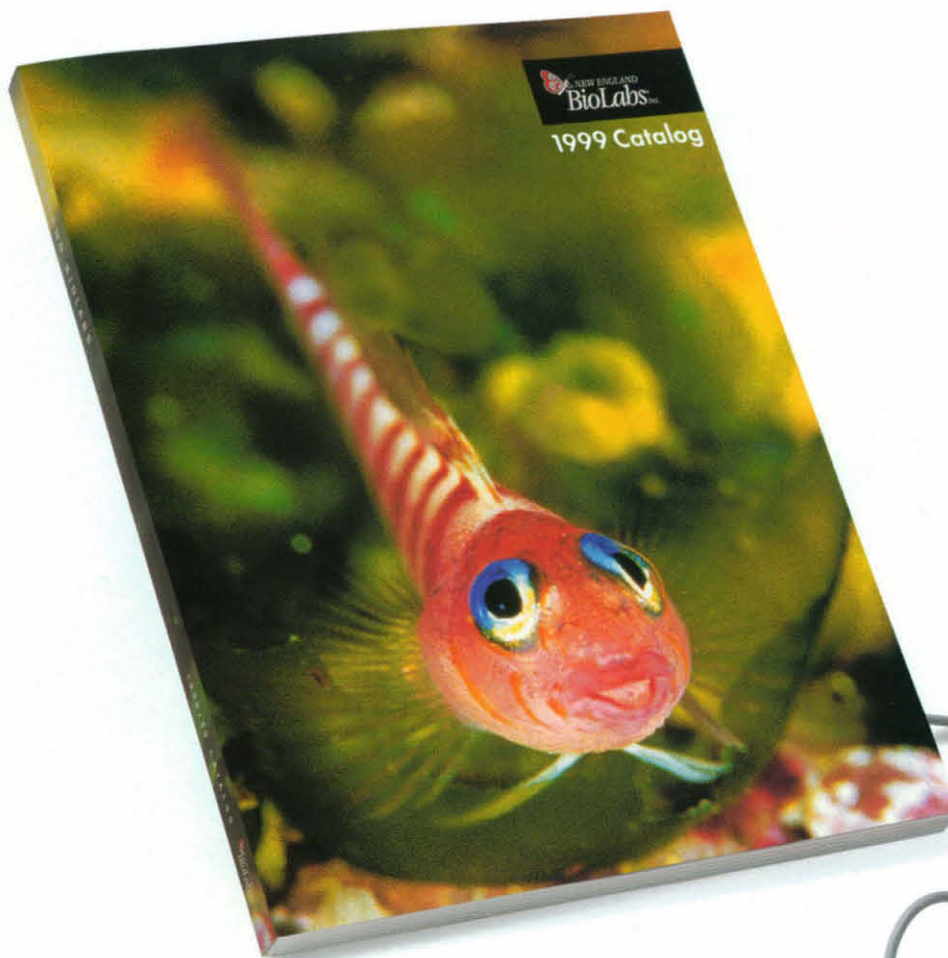
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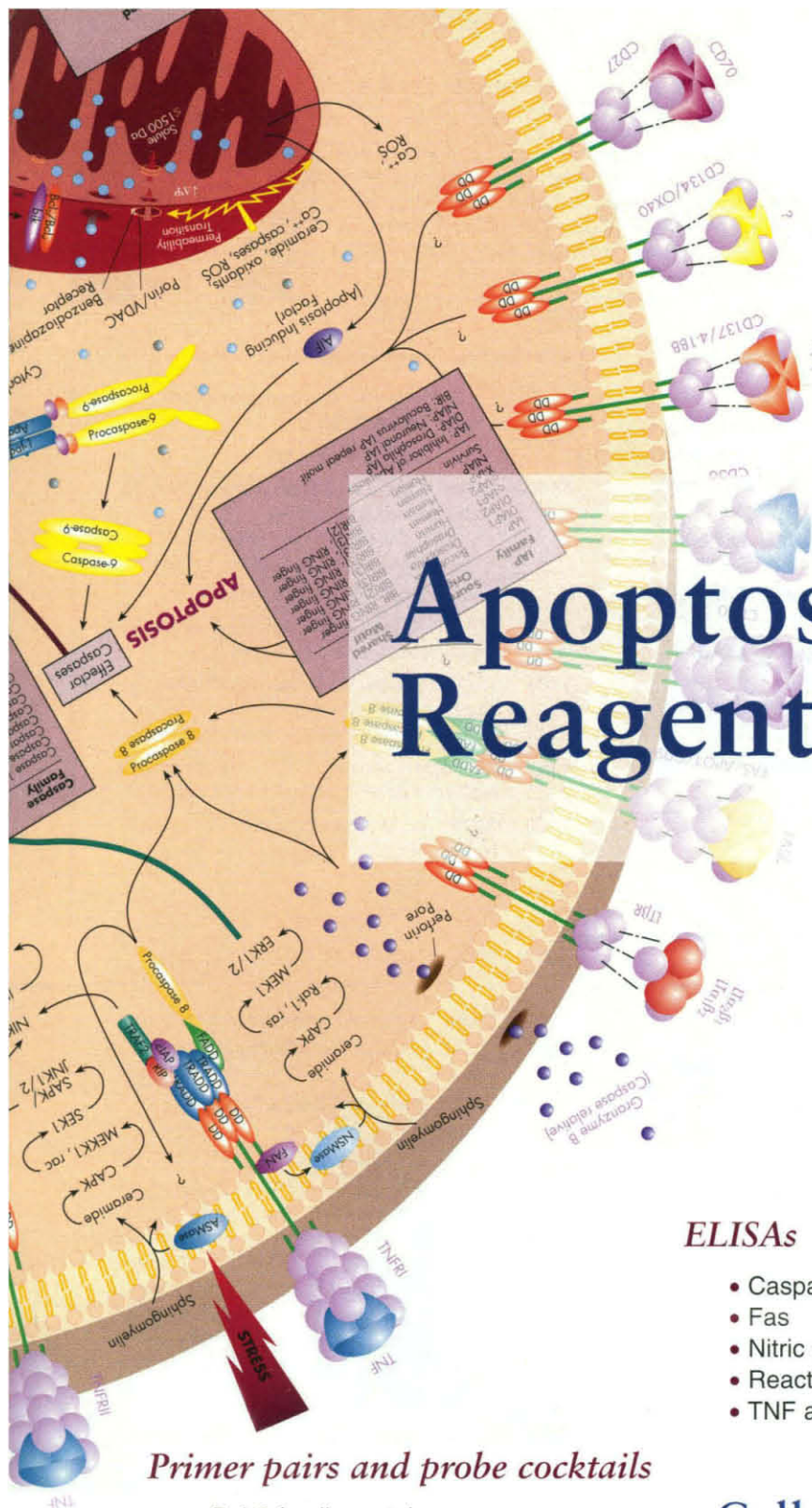
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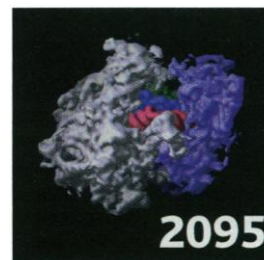
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COVER (Upper left) X-ray crystal structure of the *Thermus thermophilus* 70S ribosome at 7.8 Å resolution. Transfer RNAs (green, blue, and red) bound to the aminoacyl, peptidyl, and exit sites, respectively, occupy the cavity between the 30S (light blue) and 50S (gray) ribosomal subunits. (Lower right) The two ribosomal subunits are moved apart to show the relative orientations of the three transfer RNAs. [Image: J. H. Cate, M. M. Yusupov, G. Zh. Yusupova, T. N. Earnest, H. F. Noller]



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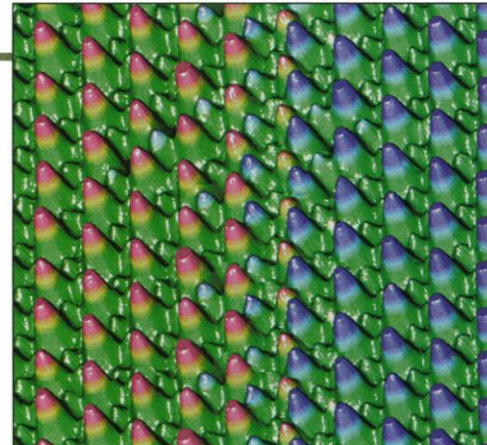
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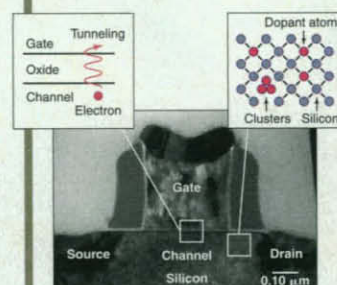
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Control of cell size

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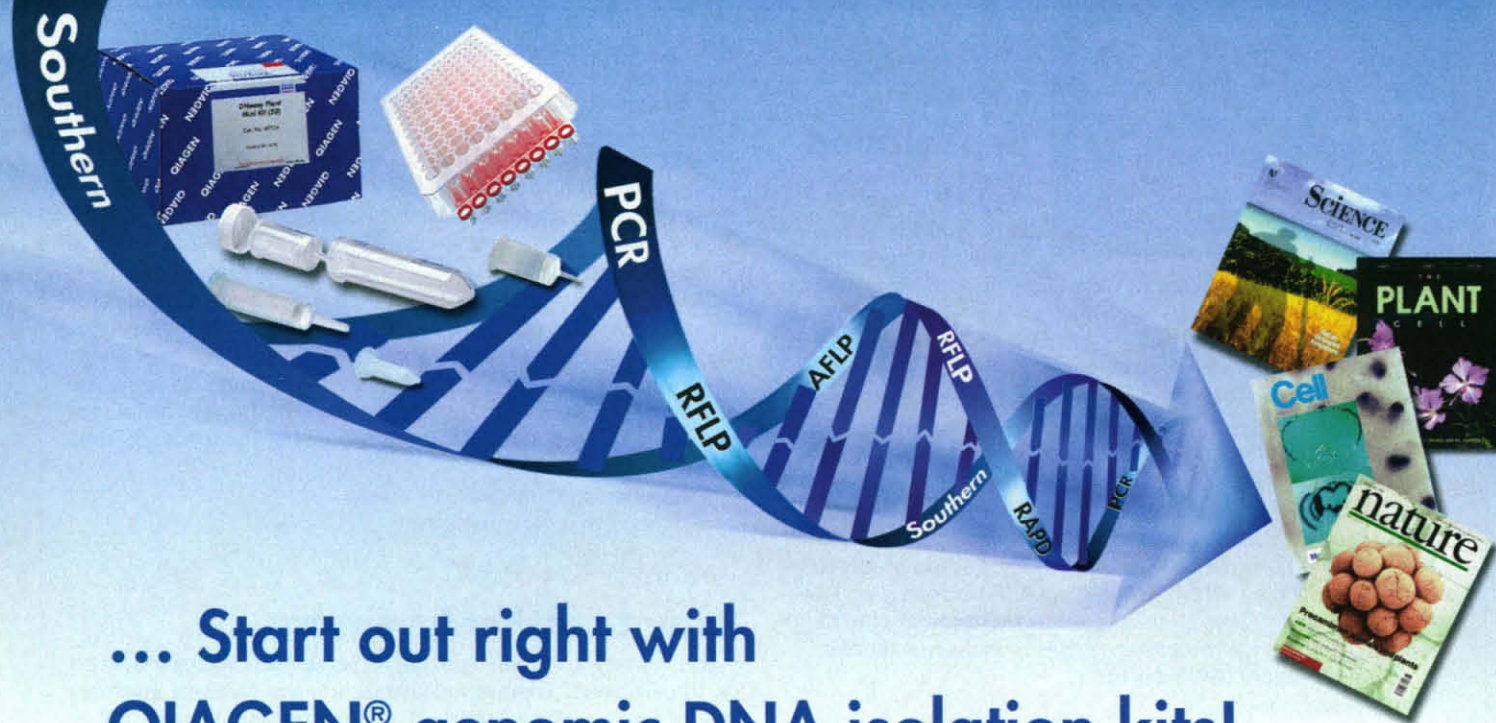
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A (NOT QUITE) PERFECTLY STILL LANDSCAPE

Mars Pathfinder landed and surveyed the boulder-strewn area of Ares Vallis. On the basis of the morphology of the rocks and surface, it was suggested that the current landscape was created about 2 billion years ago through catastrophic flooding and dust storms and that little further processing has occurred. Horz *et al.* (p. 2105) now identify an impact-produced crater of about 25 centimeters in diameter on one particular rock (Stimpy) and suggest that other fractures and angular shapes observed on other rocks are related to small-scale impacts. The authors then calculated a realistic range of sizes and velocities for iron and chondritic projectiles that could enter the martian atmosphere and create the small craters and fractures. Thus, it seems that dynamic processes may still be altering the cartoon-character shaped rocks of Ares Vallis, and these small-scale features can provide additional understanding about the present and past martian environment.

CHARGE DENSITY WAVES AND DEFECTS

Many metallic systems exhibit charge-density waves (CDW), which are modulations of the valence charge density that lower both the energy and the symmetry of the system. Weitering *et al.* (p. 2107) have studied the effects of defects on the two-dimensional CDW formed by an overlayer of tin on the (111) face of germanium, which forms domains of threefold symmetry. Point defects (substitutions of germanium for tin in the overlayer) were found to "pin" a particular orientation of the CDW. Moreover, the distribution of defects was nonstatistical, which suggests that defects moved to accommodate the CDW at its onset temperature. Such hopping occurred at temperatures well below those for the atoms to be mobile, which indicates that the formation of CDW lowers the barrier for such motion.

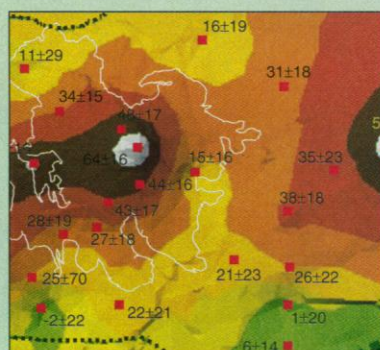
MICROMANAGING POLYETHYLENE SYNTHESIS

Catalysts made from early transition metals such as zirconium and titanium have long been used to polymerize ethylene and other small alkenes. Kageyama *et al.* (p. 2113; see the Perspective by Lehmus and Rieger) show that when a titanium compound (titanocene) is incorporated within the nanometer-scale channels of mesoporous silica fibers, polyethylene of

very high molecular weight (>6 million) is formed when a methylalumoxane co-catalyst is present. The polyethylene, which is extruded from the channels as filaments with diameters of 30 to 50 nanometers, forms highly ordered, extended-chain crystals.

THE GRAVITY OF THE SITUATION

Long Valley Caldera in California is a large, nearly circular collapsed roof of a magma reservoir that formed during a catastrophic eruption about 73,000 years ago. The magma reservoir continues to be replenished today, and



the area has been monitored for changing patterns in surface and subsurface deformation related to magmatic and hydrothermal activity (the heating of the local water system by the hot magma reservoir). Battaglia *et al.* (p. 2119) used extensive gravity measurements of Long Valley Caldera conducted in 1982 and 1998 along with surface deformation measurements to distinguish the progress of magmatic activity from hydrothermal activity. They found a positive residual gravity signal that is related to the intrusion of magma about 10 kilometers beneath the resurgent dome. These results can be used to assess the growth of the magma reservoir and to estimate the potential for an eruption.

THE MANTLE'S NOBLE GASES

Noble gases such as neon and xenon can be used to trace the evolution and interaction between Earth's mantle and atmosphere because nuclear processes can produce characteristic anomalies in their isotopic distributions. Caffee *et al.* (p. 2115) measured the isotopic composition of xenon in carbon dioxide-rich gases from

wells in Colorado, New Mexico, and southern Australia. They found excesses of xenon isotopes compared to Earth's atmosphere that were consistent with excesses that have been measured in meteorites. They suggest that the noble gases are derived from a lower mantle source that has not been substantially degassed from its primordial, solar-like composition and that this source has remained isolated from mixing by convective processes. Their results have important implications for the age of Earth, the timing of the atmosphere's formation, and the subsequent evolution of our planet.

RNAS INSIDE THE MACHINE

Ribosomes are the cellular entities that translate information, encoded as nucleotide sequences, into protein-based machines that carry out the catalytic, structural, and signaling functions necessary for life. In bacteria, these entities are themselves composed of 50 to 60 distinct protein molecules and three distinct RNA molecules that are arranged into a complex, with a mass of approximately 2.5 million daltons (see the Perspective by Liljas and the news story by Pennisi). Information is provided in the form of messenger RNA (mRNA, which is essentially a copy of the nucleotide sequence of a gene). The keys to decoding are supplied by transfer RNA (tRNA) molecules that bind specifically to the mRNA at one end and carry amino acids at the other end; these amino acids are then assembled into peptide sequences. An overall view at 7.8 angstroms of the ribosome and the binding interactions with tRNA are presented by Cate *et al.* (p. 2095; see the cover), and a close-up analysis of the arrangement of the largest RNA molecule is described by Culver *et al.* (p. 2133).

THE BIGGER THE CELL, THE BIGGER THE FLY

Cells of a specific type maintain a characteristic cell size, and in multicellular organisms, this effect has an influence on the size of organs or the complete animal. Even as more knowledge about control of the cell division cycle is accumulated, the mechanisms by which cells control cell size remain poorly understood. Montagne *et al.* (p. 2126) provide evidence that implicates a role for a signaling pathway that controls translation in the control of cell size. *Drosophila* that lack DS6K, the homolog of the mammalian p70 ribosomal protein S6 kinase, develop slowly and are only about

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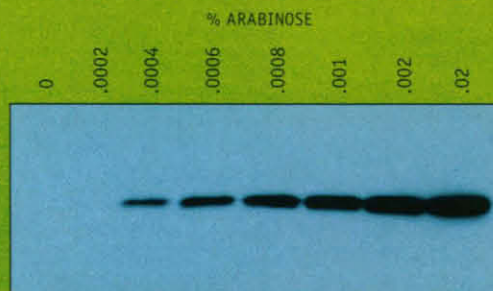
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THIS WEEK IN SCIENCE

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half the size of their normal counterparts. The change in size of the fly is a cell-autonomous event that reflects changes in cell size while cell number remains constant. In a Perspective, Leever discusses how these results, together with recent findings that cell size is influenced through signaling from the insulin receptor (which also controls the activity of DS6K), begin to define a critical pathway that regulates the size of individual cells.

SUPPRESSING CANCER AND AUTOIMMUNITY?

Mutations of the *Pten* tumor suppressor gene, which encodes a phosphatase, occur in both sporadic and inherited human cancers. Di Cristofano *et al.* (p. 2122) show that mice carrying heterozygous mutations in *Pten* develop lymphomas and suffer from autoimmune disease in a manner similar to that seen in mice with inactivating mutations in Fas or Fas ligand. T and B cells from the *Pten* heterozygous mice were impaired in Fas-mediated apoptosis. These results implicate *Pten* in the Fas response and suggest that it may play a role as a suppressor of autoimmunity as well as cancer.

INHIBITING PATHWAYS INSTEAD OF MOLECULES

One of the medically important roles that the phosphatase calcineurin plays in regulating T cell responses is the dephosphorylation of the transcription factor NFAT, which then can move into the nucleus and initiate transcription and cell activation. Current immunosuppressive drugs inhibit calcineurin, and therefore inhibit all of its

functions, which may contribute to the known toxicity of the drugs. Aramburu *et al.* (p. 2129; see the news story by Hagmann) have made a more specific inhibitor of the NFAT activation pathway by identification of a peptide that binds with high affinity to the site on calcineurin to which NFAT binds, thereby inhibiting the association of the two proteins and specifically blocking only the NFAT pathway in the cell. This result demonstrates that interaction sites may make good targets for specifically inhibiting a particular signaling pathway and provide alternatives for the development of therapeutics.

IT'S THE MUSCLES AND THE MOTION

The primary motor cortex subserves movements yet it is unclear what properties are encoded by these neurons—does firing of these neurons correlate with a pattern of muscle activation or with the direction of the desired movement in space? Kakei *et al.* (p. 2136) have designed a task to dissociate these parameters for a series of wrist motions. By recording from neurons in the motor cortex of a monkey during this task, they identify two main populations, one in which the neuronal activity does appear to be connected to muscle activation independent of the relation to extrinsic spatial coordinates and another in which the neuronal firing appears to be tied closely to the direction of movement in space. Thus, they suggest that both muscle and spatial representations are encoded, although further work will be needed to establish how they are combined to guide actual movements.

TECHNICAL COMMENT SUMMARIES

MOLECULAR AND FOSSIL GAPS

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/285/5436/2031a

M. Foote *et al.* (Reports, 26 Feb., p. 1310) analyzed the rates of extinction and preservation in fossil lineages to address discrepancies between fossil and molecular dates for the origins of key lineages. Their analysis was inconsistent with the proposed early origination of eutherian mammals deduced from molecular data [S. B. Hedges and S. Kumar, *Nature* **392**, 917 (1998)].

Hedges and Kumar comment that "several critical aspects of [Foote *et al.*'s] model are flawed" and then re-assess and attempt to reconcile the molecular and fossil data. J. D. Archibald questions Foote *et al.*'s treatment and placement of a key group of possible early placental mammals, the zhelestids. Finally, T. H. Rich *et al.* comment that one reconciliation of the molecular and fossil age estimates—that crown group taxa were evolving in a geographically isolated and poorly sampled region—may be supported by a new fossil find in Australia.

In response, Foote *et al.* defend their analysis and treatment of the zhelestids and argue that the new fossil finds, even if accepted, are insufficient to explain the gap in many lineages. They state that even "accepting Hedges and Kumar's calibration ... the gap [between the fossil and molecular records] is implausible."

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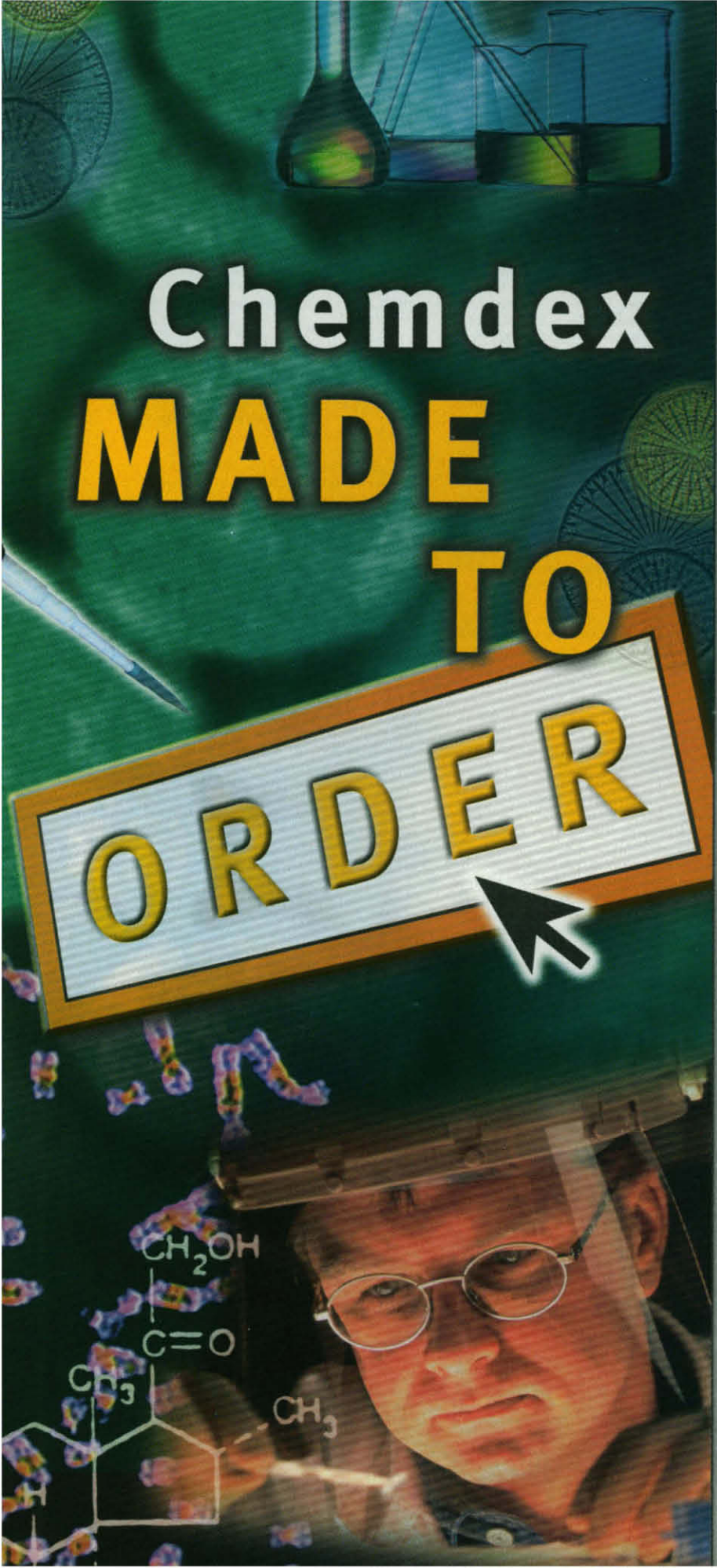
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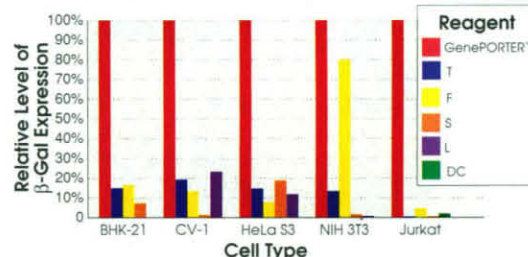
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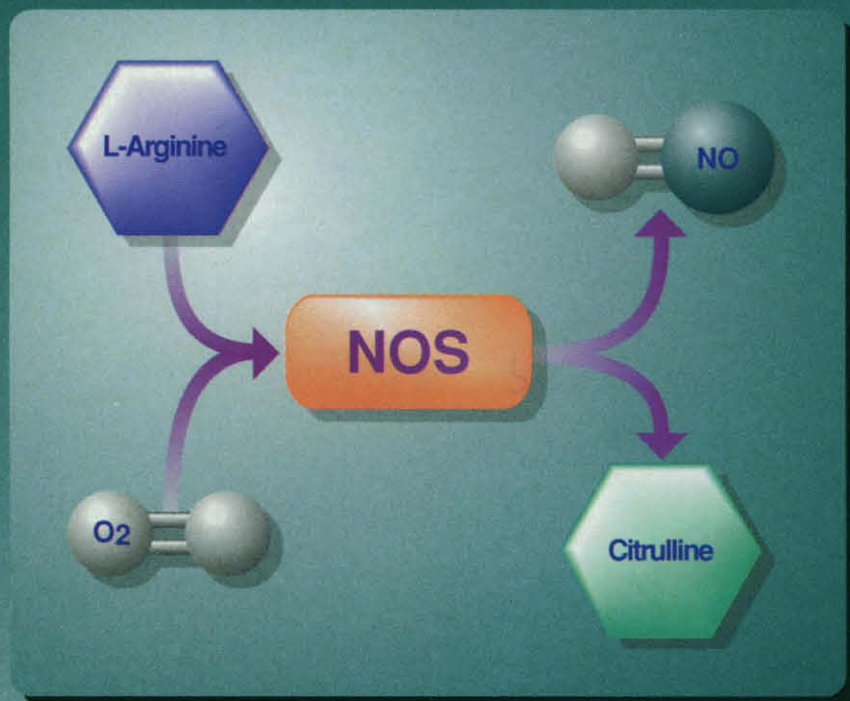


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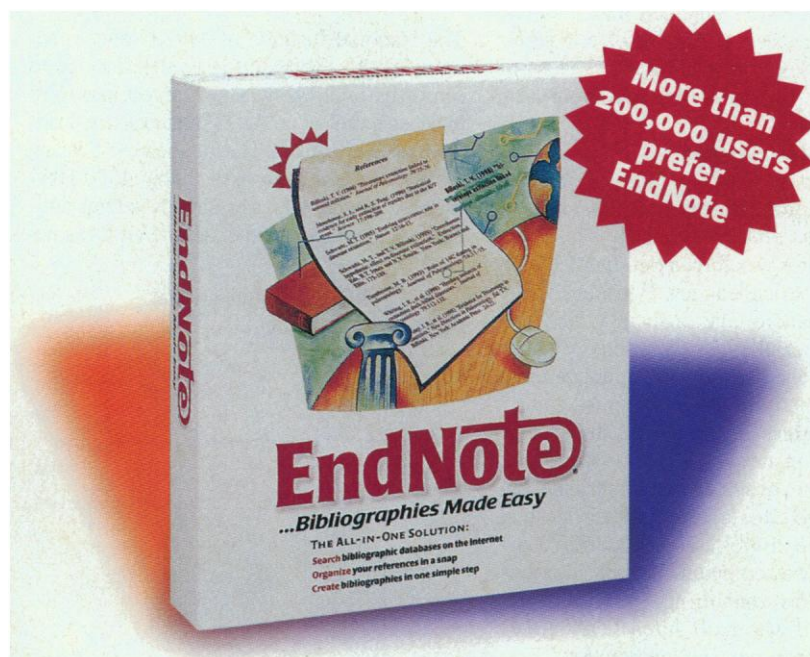
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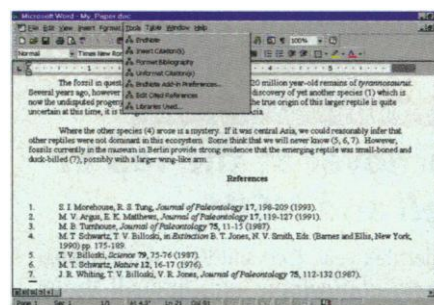


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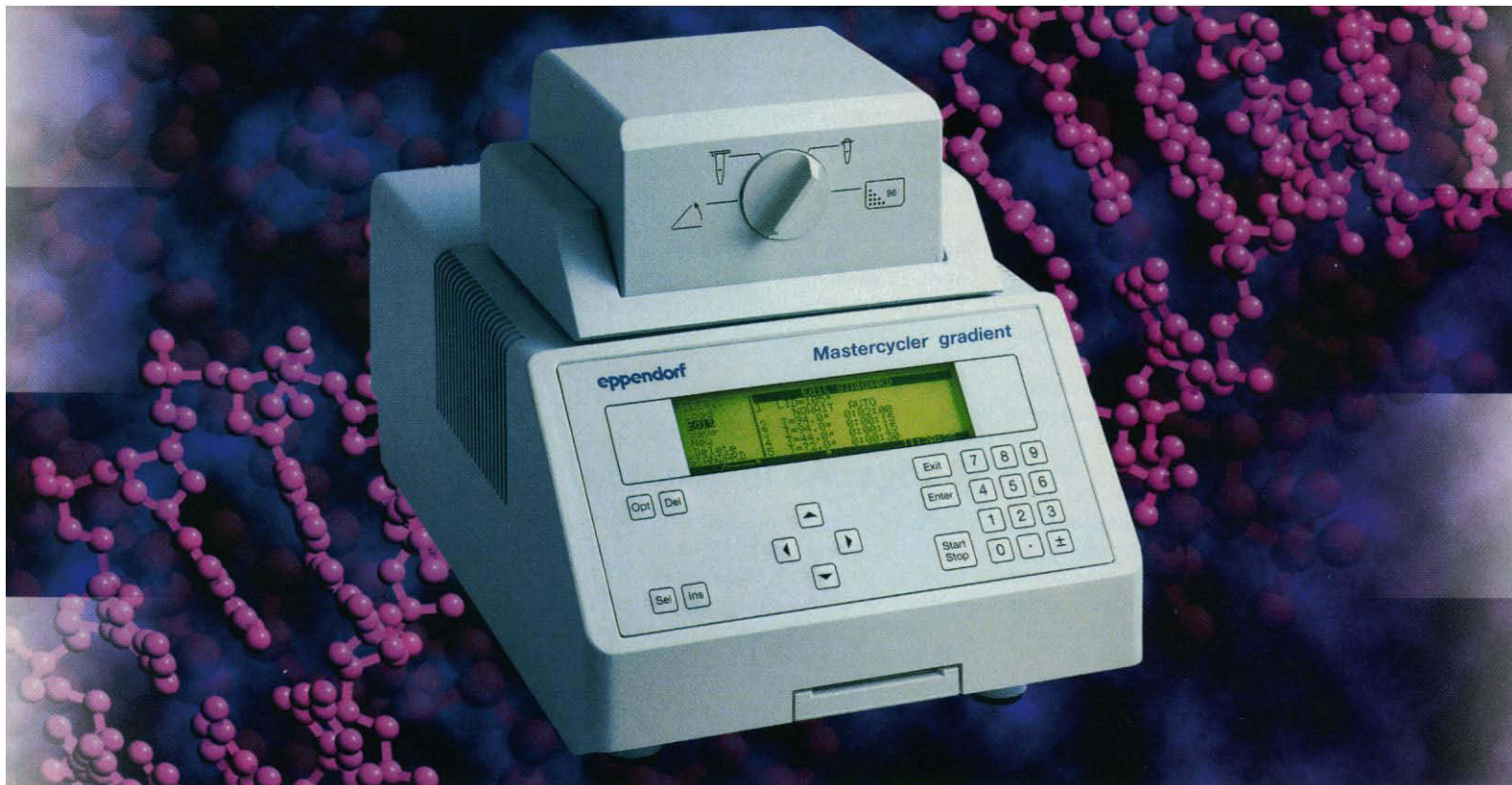
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Examples of how **THE GUIDE*** recommendations apply to the One Cage™ System

Number of animals recommended per cage based on 80 sq. inches of usable floor area, 7-3/4" interior cage height:

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HAMSTERS (>100g.) 

RATS (200-400g.) 

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*Based on the Animal Welfare Act of 1966 as amended 1985 and the Guide for the Care and Use of Laboratory Animals, Institute of Laboratory Animal Resources, Commission of Life Sciences, National Research Council, National Academy Press, 1996.

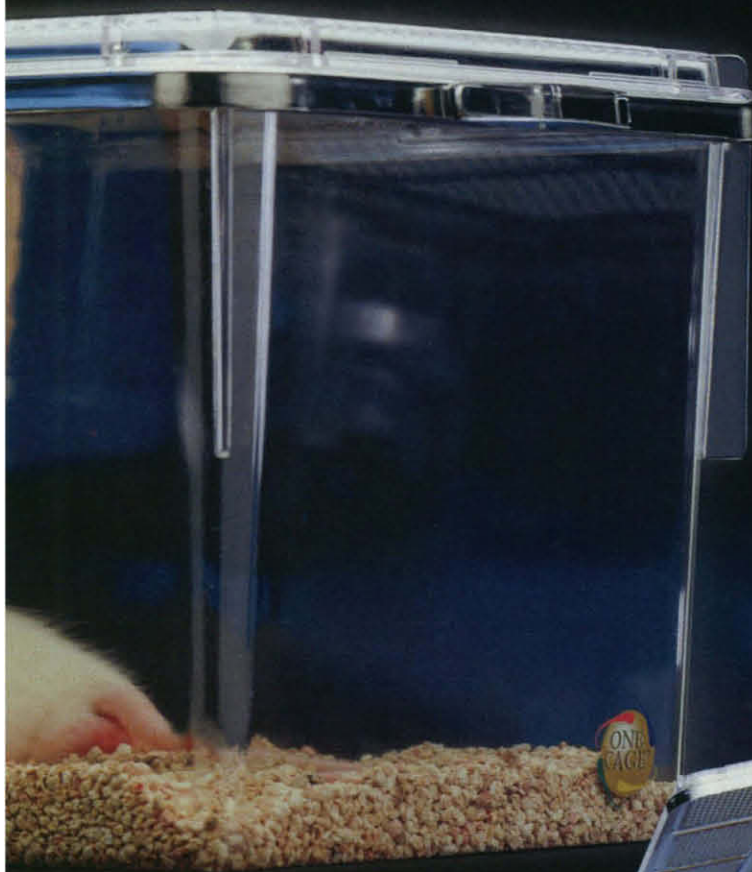


With One Cage, 560 mice, 448 hamsters, 224 rats, or 112 guinea pigs can be housed in a single rack. This represents up to a 273% increase in animal populations. (A facility housing 2,200 rats would require 37 racks housing 30 cages with 60 rats per rack (based on old-style racks). Compare this to 10 One Cage racks housing 224 rats per rack.)

You can house more rodents in less space while meeting interior cage height and floor space requirements.

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tops, water bottles, and racks is extremely labor intensive and time consuming. With One Cage, you will no longer require multiple cage sizes and there are fewer components to deal with.

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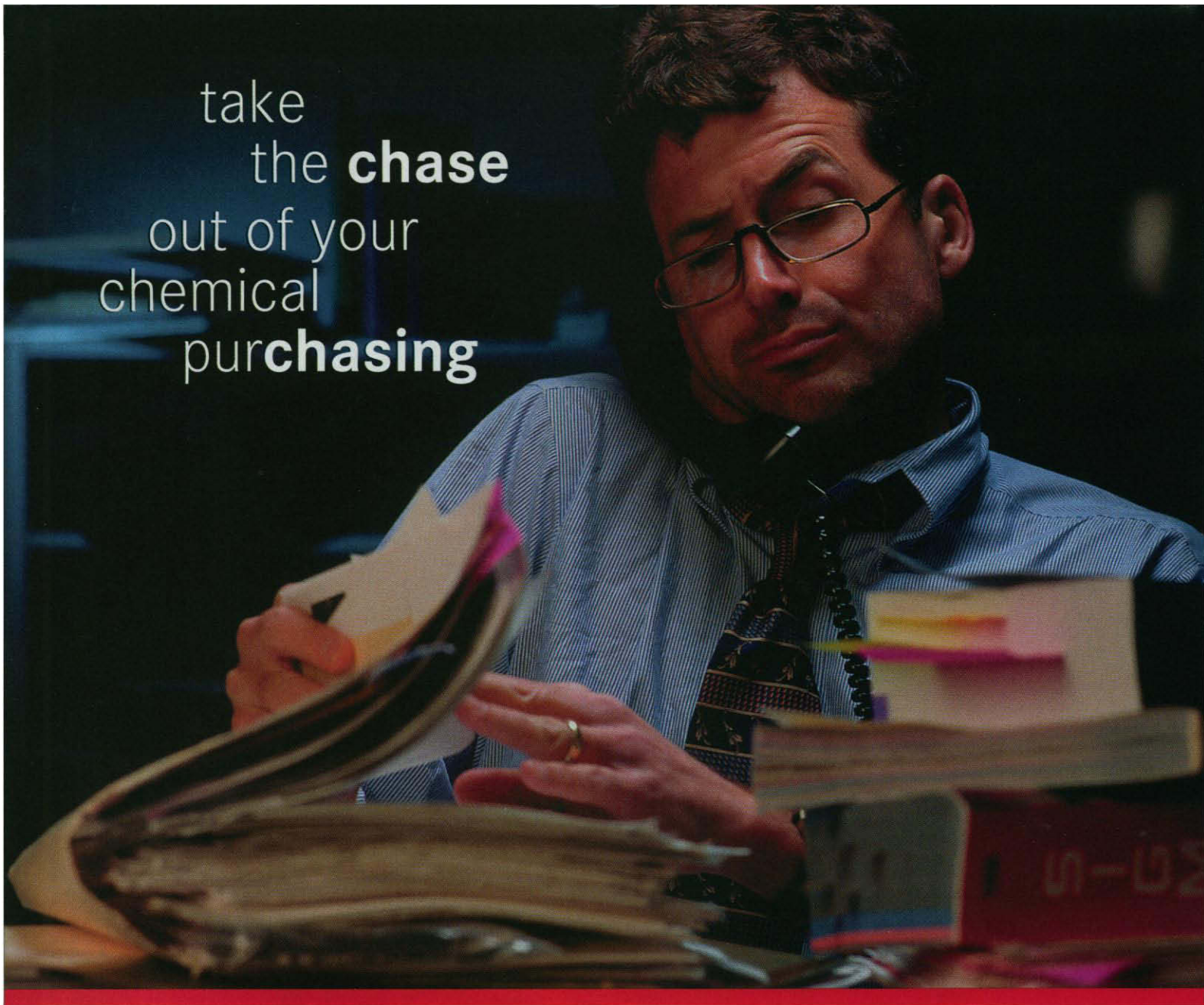
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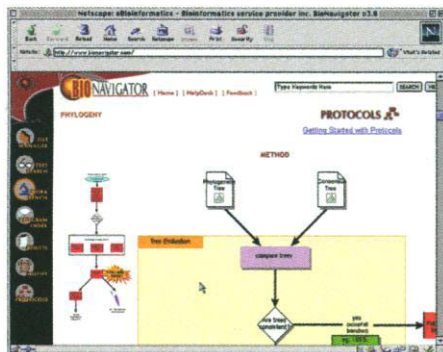
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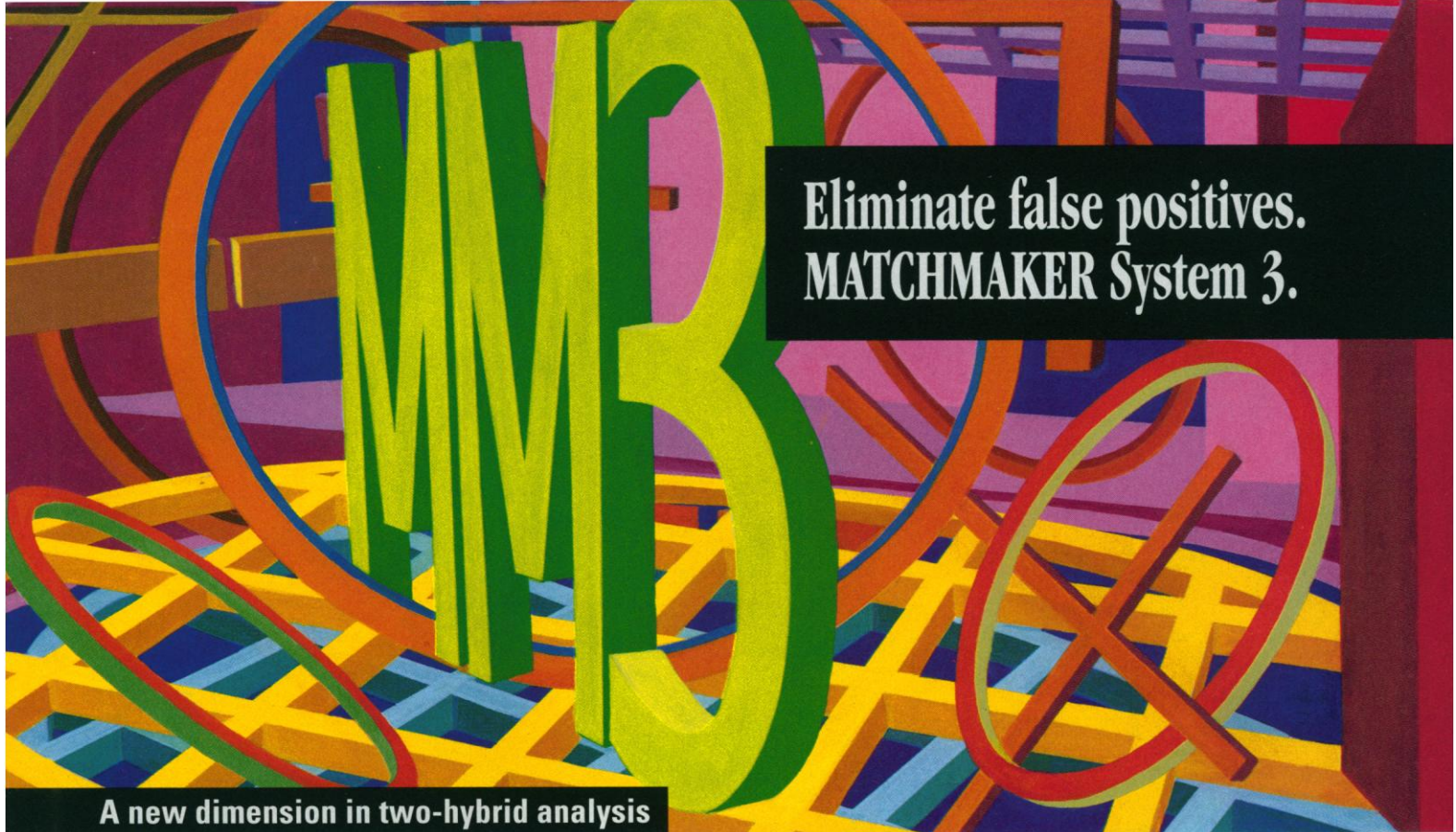
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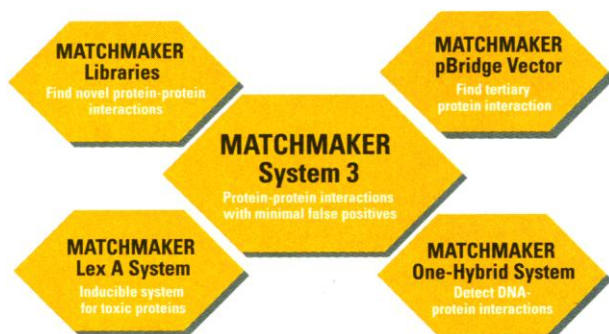
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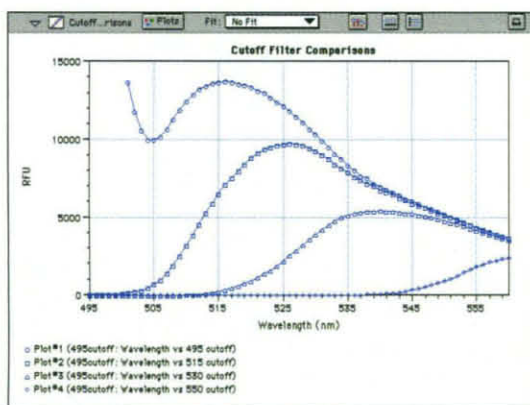
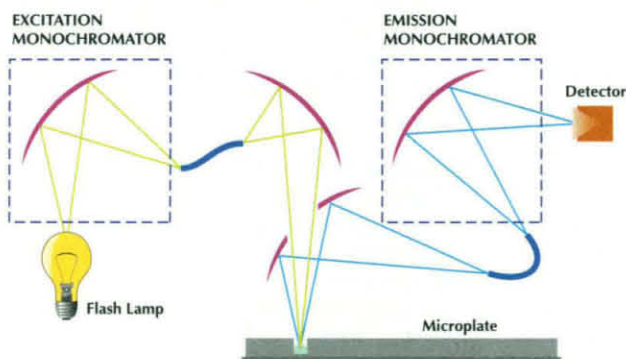
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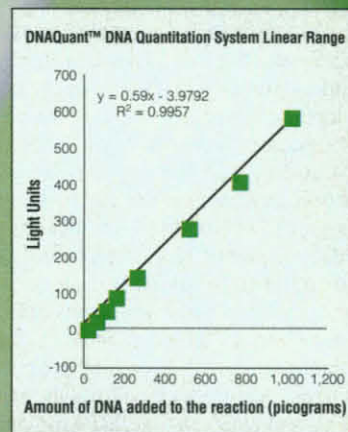
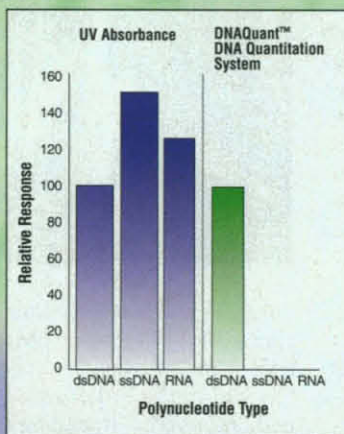
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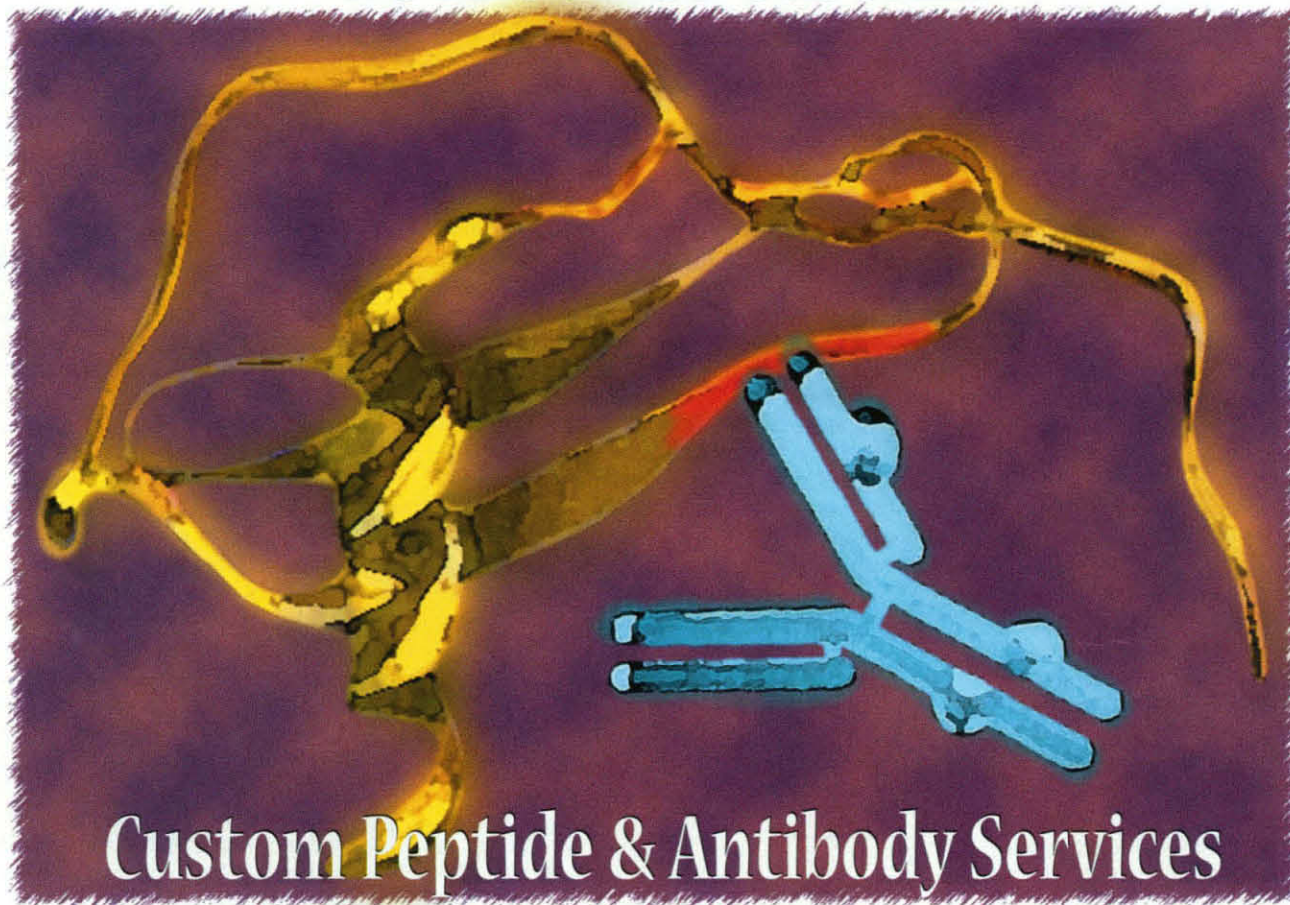
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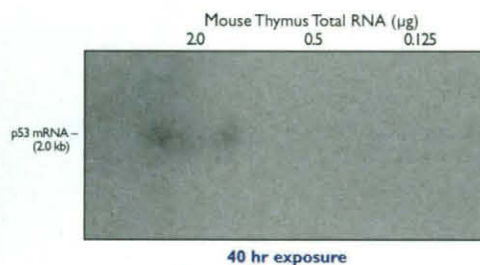
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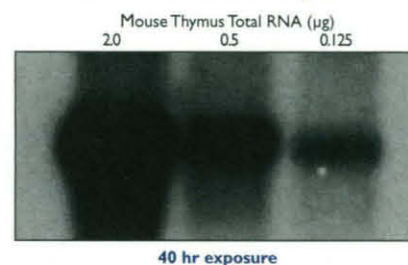
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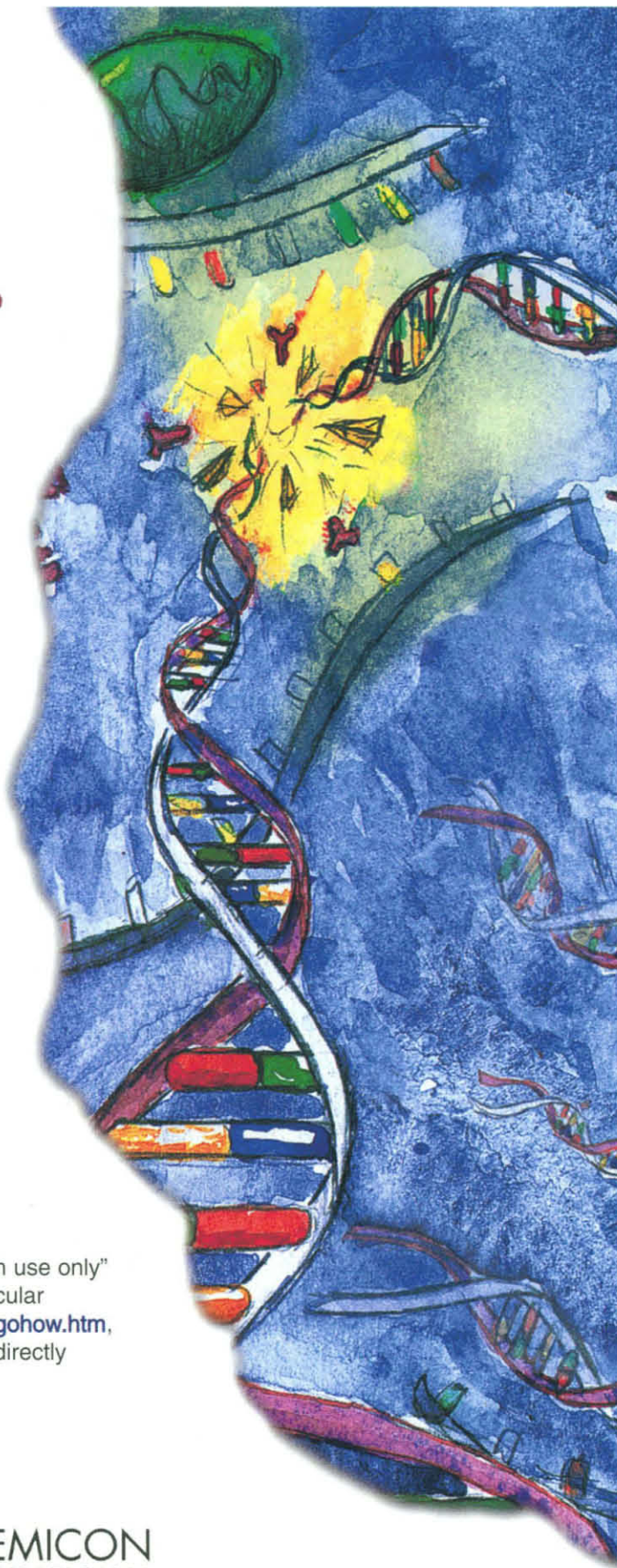
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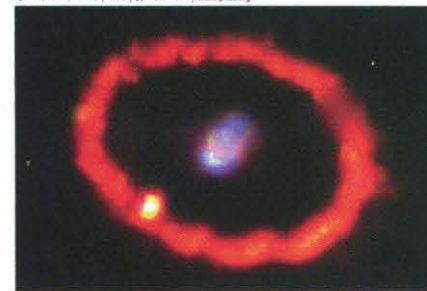
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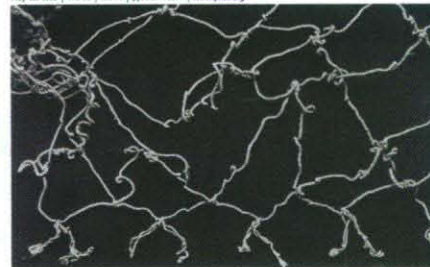


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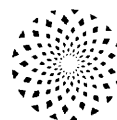
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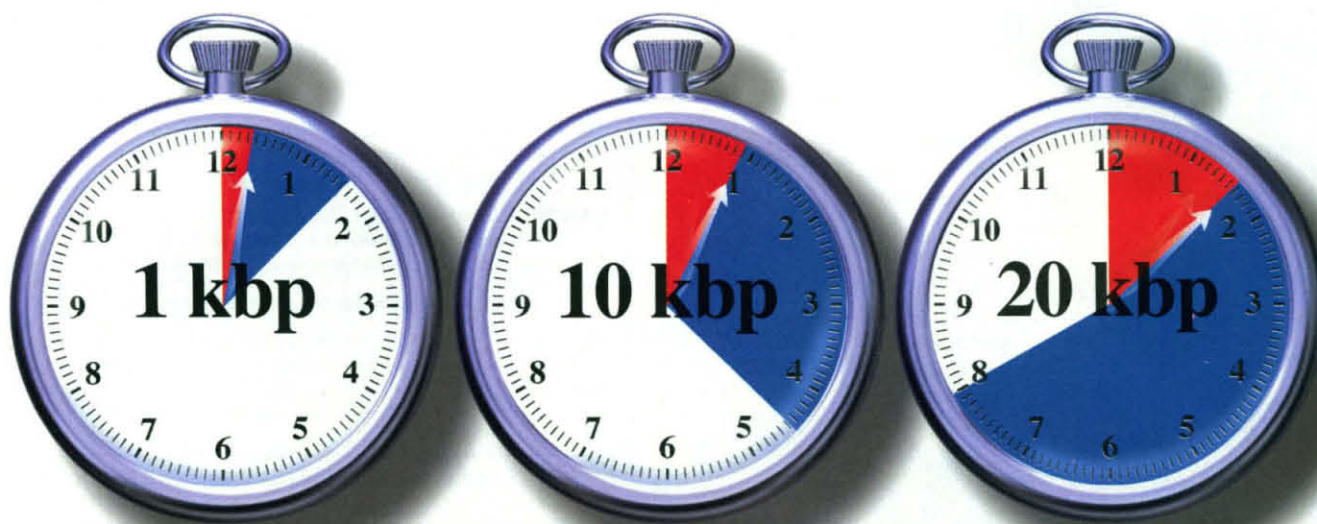
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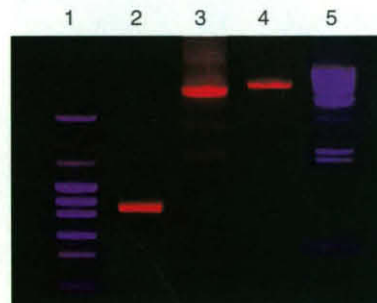
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4. 20 kbp
5. λ-Hind III marker

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NASA

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The National Aeronautics and Space Administration (NASA) announces two solicitations titled, "Research Opportunities in Space Life Sciences: Gravitational Biology and Ecology Program" (NRA 99-HEDS-02) and "Research Opportunities in Space Life Sciences: Biomedical Research and Countermeasures Program" (NRA 99-HEDS-03).

Research Emphases include:

99-HEDS-02

- Molecular Structures and Physical Interactions
- Developmental Biology
- Cellular and Molecular Biology
- Organismal and Comparative Biology
- Gravitational Ecology

99-HEDS-03

- Physiology
- Behavior and Performance
- Environmental Health Research
- Operational and Clinical Research
- Radiation Health Research

Proposals may be for ground-based research investigations or for space-flight experiments designed for the Shuttle middeck or for the early phase of utilization of the International Space Station. Letters of Intent to propose are due October 8, 1999 for NRA 99-HEDS-02 and October 15, 1999 for NRA 99-HEDS-03.

NRA 99-HEDS-02 will be open for the period of September 7 through December 1, 1999 and is available via the Internet at:

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NRA 99-HEDS-03 will be open for the period of September 16 through December 1, 1999 and is available via the Internet at:

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SYMPOSIUM - Beurs van Berlage, Amsterdam

KILLING CANCER CELLS

Chemotherapy: Concepts, Targets and Delivery

THURSDAY, November 18, 1999

Richard Klausner, NCI, Bethesda

Key note address

Joseph Schlessinger, NYU, New York

Cellular Signaling by Tyrosine Phosphorylation

Alfred Wittinghofer, Max-Planck-Institut, Dortmund

The GTPase Reaction of Ras as an Anticancer Target

Frank McCormick, UCSF, San Francisco

Cancer Therapy Based on the p53 Pathway

Gerard Evan, UCSF, San Francisco

Oncogenic Induced Apoptosis in Cancer

Michael Gottesman, NIH, Bethesda

How Does P-Glycoprotein Transport Drugs ?

FRIDAY, November 19, 1999

Piet Borst, NCI, Amsterdam

Mechanism of Multidrug Resistance in Cancer Cells

Branimir Sikic, Stanford University

Reversal of Multidrug Resistance in Cancer Cells

John Mendelsohn, M.D. Anderson, Houston

Receptor Blockade as Anticancer Therapy

Bob Pinedo, VU, Amsterdam

The Combined Use of Chemotherapy and Biologicals

Paul Nurse, ICRF, London

Controlling the Cell Cycle

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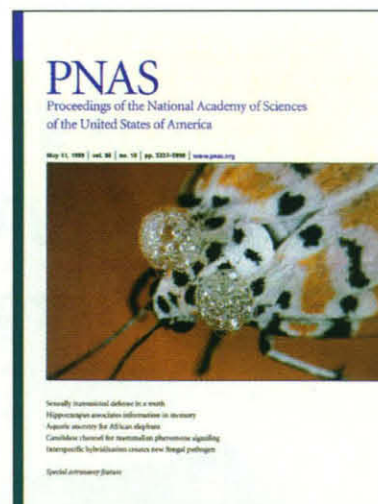
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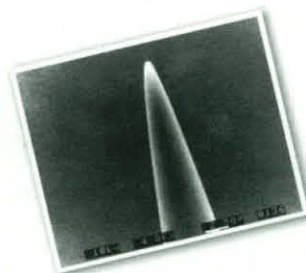
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The Amin Cycle

Let us consider a system in which a cylinder filled with an ideal gas is rotated. The radius of rotation of the cylinder is constant. The rotational speed of the cylinder can be varied by changing the value of ω (angular speed). The cylinder is equipped with a frictionless, moving piston located on the side closer to the center of the rotation. The piston can compress and expand the volume of the cylinder. The cycle comprises of the

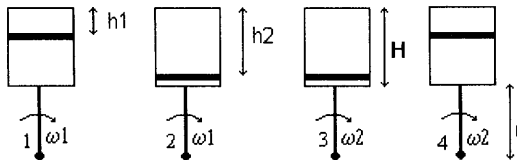


Figure 1

following processes (Figure 1):

(1-2) The gas expands isothermally at a temperature T in the cylinder at a constant low speed ω_1 .

(2-3) The rotational speed is increased from ω_1 to ω_2 at constant volume and temperature.

(3-4) The gas is compressed isothermally at a temperature T in the cylinder at a constant high speed ω_2 .

(4-1) The rotational speed is decreased from ω_2 to ω_1 at constant volume and temperature.

In a rotating cylinder, the molecules of the ideal gas have a distribution according to Boltzmann's distribution Law. The centrifugal acceleration is represented by $a = v^2/r$. However, $v = \omega r$, then $a = \omega^2 r$. Therefor according to Boltzmann's distribution Law, the pressure on the piston surface can be derived using equation 1.

$$\frac{dP}{P} = \int_{r+H-h}^{r+H} -\frac{m\omega^2 r}{kT} dr \Rightarrow P = P_o e^{-\frac{m\omega^2 r^2}{2kT}} \Big|_{r+H-h}^{r+H}$$

Equation 1

From the first law of thermodynamics, $dQ = dU + dW + dKE$. For an isothermal process, $dU = nC_v dT = 0$.

The work $dW = PdV$.

Let us analyze the energies at each step:

$KE = [\frac{1}{2}m\omega^2(r+H)^2 - \frac{1}{2}m\omega^2(r+H-h)^2]$. For all steps, $\frac{1}{2}m\omega^2(r+H)^2$ is constant and cancels out. Thus we shall not rewrite it again.

$$(1-2) dQ_{1-2} = nC_v dT + P_e dV + \frac{1}{2}m(\omega_1)^2 [(r+H-h_1)^2 - (r+H-h_2)^2]$$

$$= P_e dV + \frac{1}{2}m(\omega_1)^2 [(r+H-h_1)^2 - (r+H-h_2)^2]$$

$$(2-3) dQ_{2-3} = nC_v dT + PdV + \frac{1}{2}m[(\omega_1)^2 - (\omega_2)^2](r+H-h_2)^2$$

$$= \frac{1}{2}m[(\omega_1)^2 - (\omega_2)^2](r+H-h_2)^2$$

$$(3-4) dQ_{3-4} = nC_v dT + P_e dV + \frac{1}{2}m(\omega_2)^2 [(r+H-h_2)^2 - (r+H-h_1)^2]$$

$$= P_e dV + \frac{1}{2}m(\omega_2)^2 [(r+H-h_2)^2 - (r+H-h_1)^2]$$

$$(4-1) dQ_{4-1} = nC_v dT + PdV + \frac{1}{2}m[(\omega_2)^2 - (\omega_1)^2](r+H-h_1)^2$$

$$= \frac{1}{2}m[(\omega_2)^2 - (\omega_1)^2](r+H-h_1)^2$$

(According to the definition of a thermodynamic cycle
Net Heat = Net Work)

$$dQ_{Net} = dQ_{1-2} + dQ_{2-3} + dQ_{3-4} + dQ_{4-1} = P_e dV + P_e dV$$

$$dW_{Net} = P_e dV + P_e dV$$

$$\text{Efficiency } \eta = W_{Net} / Q_{1-2} = 1 + P_e dV / P_e dV$$

$$P_c = P_o e^{-\frac{m\omega_2^2}{2kT}(h_2^2 - h_1^2 - 2(r+H)(h_2 - h_1))} \dots (2)$$

$$P_e = P_o e^{-\frac{m\omega_1^2}{2kT}(h_1^2 - h_2^2 - 2(r+H)(h_1 - h_2))} \dots (3)$$

$$P_c dV_{comp} + P_e dV_{exp} =$$

$$P_o (h_2 - h_1) \left(e^{-\frac{m\omega_2^2}{2kT}(h_2^2 - h_1^2 - 2(r+H)(h_2 - h_1))} - e^{-\frac{m\omega_1^2}{2kT}(h_1^2 - h_2^2 - 2(r+H)(h_1 - h_2))} \right)$$

$$\Rightarrow P_c dV + P_e dV \neq 0$$

$$dV_{comp} = h_2 - h_1 \text{ and } dV_{exp} = h_1 - h_2$$

In the Amin Cycle, the heat conversion efficiency depends on the magnitude of the acceleration difference only. The cycle gives similar results for different types of accelerations and various combinations of Isothermal, Adiabatic and Polytropic processes.

References:

1. Feynman, R., Leighton, R., Sands, M., "The Feynman Lectures on Physics: Addison-Wesley Publishing Co., 1989.
2. Saad, M, "Thermodynamics - Principles and Practice, Prentice-Hall, Inc., 1997

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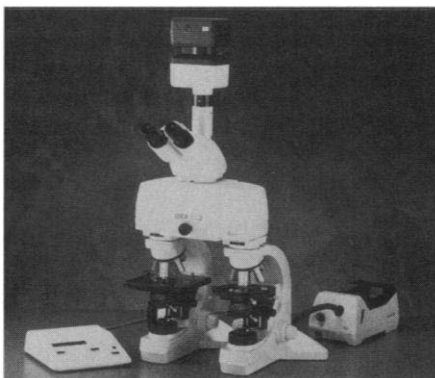
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CONTINUED ON PAGE 2150

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LITERATURE

Introduction to Sample Handling is a booklet designed to help infrared (IR) users of all skill levels obtain the best quality spectra from their samples. Certain sample collection techniques are more effective than others for specific sample types, so it is important to know which one to use. The methods reviewed in the booklet include transmission, attenuated total reflection, diffuse reflectance, and true specular reflectance/reflection-absorption. The booklet includes a description of how each sampling method works, what types of samples can be analyzed, and the advantages of each method.

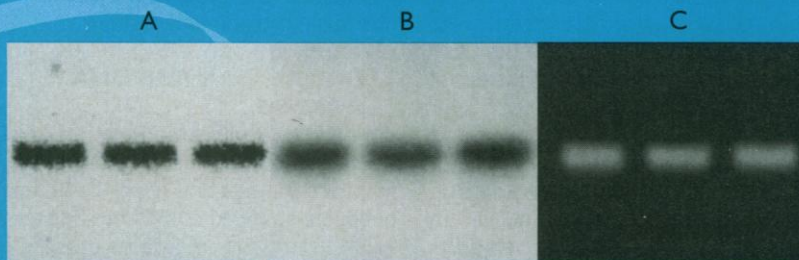
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