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Stratagene's RoboCycler[®] temperature cyclers are now authorized for use in PCR.⁺ This means that you no longer have to pay additional licensing fees to Perkin-Elmer. In 1995, when you buy a RoboCycler system, Stratagene will give you the PCR authorization at no charge! Plus, use of the RoboCycler temperature cycler now gives you an fully licensed system for 1 2 3 4 5 m Est C PCR in your research.

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⁴ Practice of the patented polymerase chain reaction (PCR) process requires a license, Stratagene's thermal cycler is an Authorized Thermal Cycler. Its use with Authorized Reagents provides a limited PCR license in accordance with the label rights accompanying such reagents. It may also be used with PCR licenses available from The Perkin-Elmer Corporation. Patents pending

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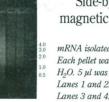
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Figure 1.

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mRNA isolated from 8 x 10⁷ HeLa cells. Each pellet was resuspended in 50 µl RNase-free H₂O. 5 µl was loaded onto a 1% agarose gel. Lanes 1 and 2: FastTrack[®] 2.0 Lanes 3 and 4: Magnetic Beads

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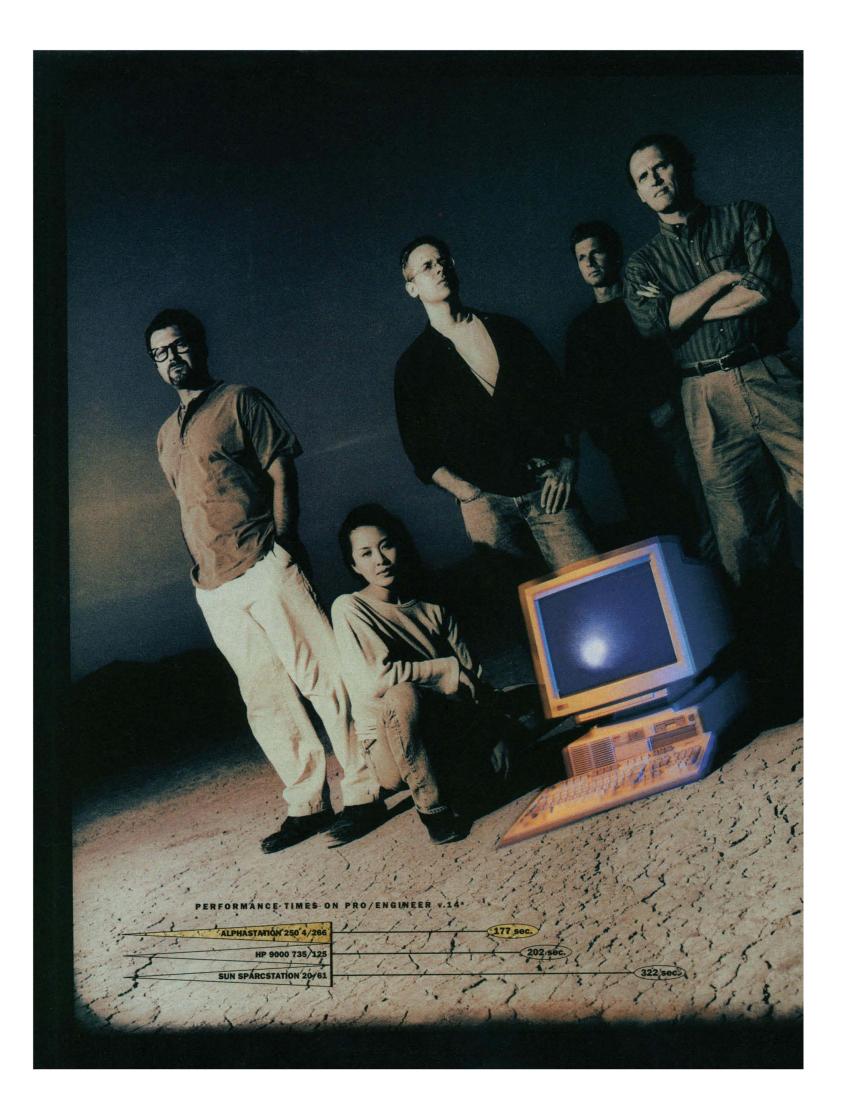
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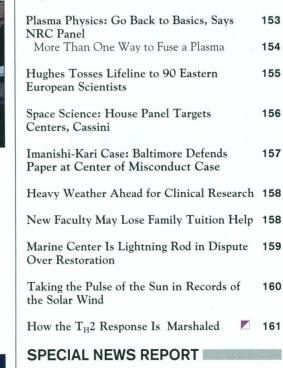
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Physicists Create New State of Matter

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COVER

False-color image of the velocity distribution in a cloud of rubidium atoms that have formed a Bose-Einstein condensate. Color indicates the density of atoms having the velocity specified by the two horizontal axes. The high-density blue and white spire is an image of lowenergy atoms that have condensed into a single quantum state. The average speed of the atoms in the spire is about 0.5 millimeter per second. See page 198 and the related News story on page 152 and the Perspective on page 182. [Image: M. R. Matthews]

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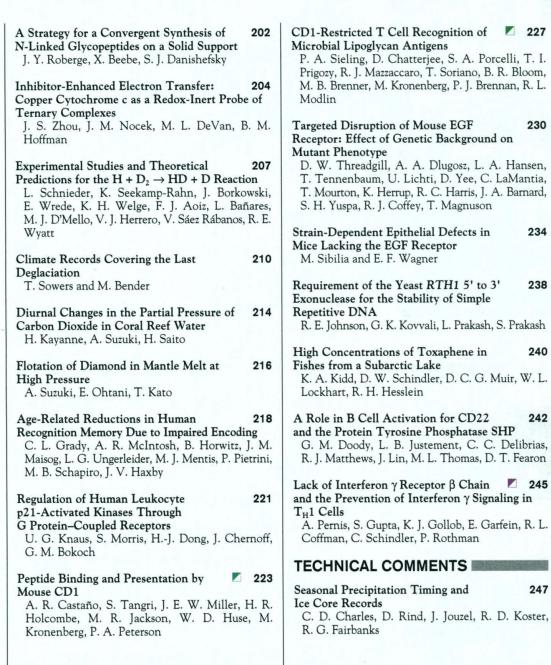
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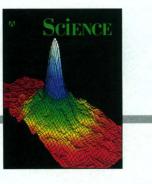
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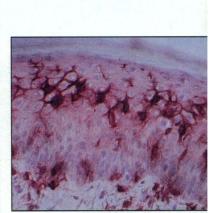
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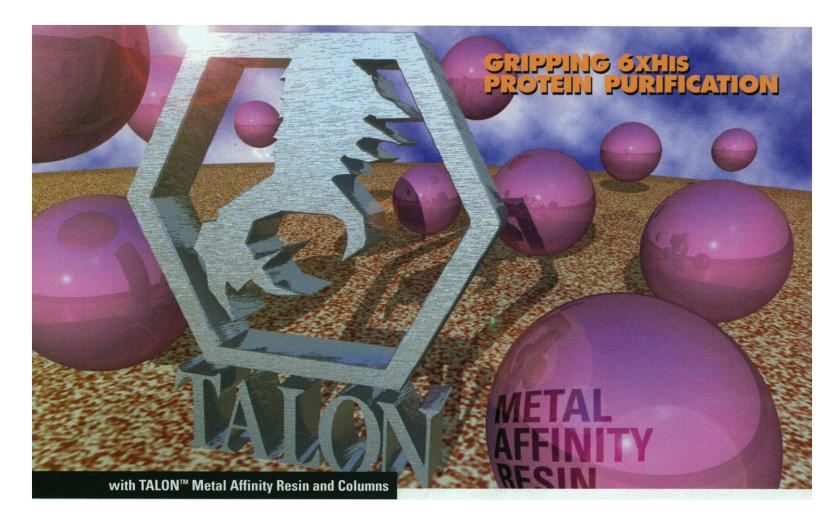
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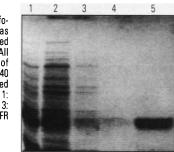
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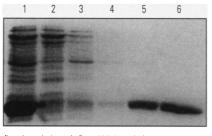
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Native. N-terminal, 6xHis mouse dihydrofolate reductase (DHFR, 19.5 kDa) was expressed in *E. coli.* 800 µl of the clarified lysate was applied to 100 µl of TALON. All bound protein was eluted with 300 µl of 100 mM EDTA, pH 8.0. 20 µl of lysate and 40 µl of each subsequent fraction was loaded onto a 12% polyacrylamide/ SDS gel. Lane 1: clarified lysate. Lane 2: flowthrough. Lane 3: first wash. Lane 4: third wash. Lane 5: DHFR final elution.

Denaturing. N-terminal, 6xHis mouse DHFR (19.5 KDa) was expressed in *E. coli.* 600 µl of clarified lysate was applied to a TALONspin Column containing 0.5 ml of TALON-NX Metal Affinity Resin and centrifuged for 2 min at 2,000 x g. 20 µl of lysate (Lane 1) and 40 µl of each subsequent fraction was loaded onto a 12% polyacrylamide/SDS





gel. Lane 1: clarified lysate. Lane 2: flowthrough. Lane 3: first pH 7.0 wash. Lane 4: second pH 7.0 wash. Lane 5: DHFR, first pH 6.0 elution. Lane 6: DHFR, second pH 6.0 elution.

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edited by PHIL SZUROMI

Climate leads and lags

Many detailed climate records have been obtained of the most recent deglaciation, including from ice cores in Greenland and Antarctica. These provide a basis for understanding the sequence of climate changes globally, provided that at least a common and accurate time scale for the records can be constructed. Sowers and Bender (p. 210) used the record of oxygen isotopes trapped in ice as a time-stratigraphic marker to calibrate the Greenland and Antarctic ice cores. Comparison shows that warming in Antarctica and increase in atmospheric methane and CO, began 3000 years or so before warming in Greenland.

Clearing the air

Emissions of methyl chloroform (trichloroethane, CH_3CCl_3), a synthetic greenhouse gas, have been restricted under the Montreal Protocol. Global measurements by Prinn *et al.* (p. 187; see the Perspective by Ravishankara and Albritton, p. 183) indicate that concentrations of CH_3CCl_3 have in fact declined since mid-1990. The relation of this decline to hydroxyl radical concentrations, an important "scavenger" molecule, is also discussed.

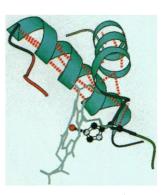
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Following folding

The metastable forms that occur before a protein reaches a fully unfolded state have been probed in hydrogen exchange experiments with native cytochrome c. Bai *et al.* (p. 192) found that the step from one form to another proceeds by the unfolding of one or more cooperative units of the struc-

Stopping the Signal

Membrane immunoglobulin (mIg) serves as an antigen-specific receptor on the surface of B lymphocytes. If a signal is delivered via mIg in the absence of a second, costimulatory, signal, the B lymphocyte becomes unresponsive and may die. What prevents the delivery of the mIg signal, and therefore inactivation of the immune response, when B cells meet antigen circulating in the body? Doody *et al.* (p. 242) suggest a role for CD22, a molecule associated with mIg. CD22 binds to, and activates, SHP, a phosphatase that negatively regulates signaling through mIg. Dissociation of CD22 from mIg may be mediated by receptors on helper T cells, which also deliver the costimulatory signal.



ture. These units are loops or mutually stabilizing pairs of whole helices and loops.

Many particles, one box

The particles known as bosons behave quite differently than their cousins, the fermions. Fermions (such as electrons) in the same quantum state avoid each other, whereas bosons prefer to stay together, as for example in superfluid helium. Under the right circumstances, bosons should theoretically condense into a single quantum state, the Bose-Einstein condensate. Experimental evidence for this elusive state of matter has been sought for 15 years, and now Anderson et al. (p. 198) report the existence of Bose-Einstein condensation in a vapor of rubidium atoms confined by magnetic and optical fields. As discussed in the Perspective by Burnett (p. 182), the creation of such a state opens a range of possible fundamental studies in physics. Background and comment on the discovery are provided in the news story by Taubes (p. 152).

Deep diamond ore

At depths in the mantle, it has been suggested that the density of melts may exceed that of the solid mantle, because of structural and compositional changes in the melts with increasing pressure. Suzuki *et al.* (p. 216) show in experiments that diamond crystals float in primitive mantle melts at pressures of about 20 gigapascals. One implication is that diamond may accumulate at depths of 500 km or so in the Earth.

What CD1 sees

Various CD1 molecules are expressed on the surfaces of many cell types, and although they show some similarities to the major histocompatibility complex (MHC) proteins, their possible functions in antigen presentation have been unclear. Castaño *et al.* (p. 223) show that mouse CD1 molecules bind peptides with a particular motif of aromatic or bulky hydrophobic residues. Unlike

MHC class I molecules, strong binding requires rather long peptides (about 20 residues). Sieling *et al.* (p. 227) show that human CD1b molecules recognize microbial lipoglycan molecules, which are nonpeptide antigens that must be internalized in order to be presented to the T cells (see also the Perspective by Bendelac, p. 185).

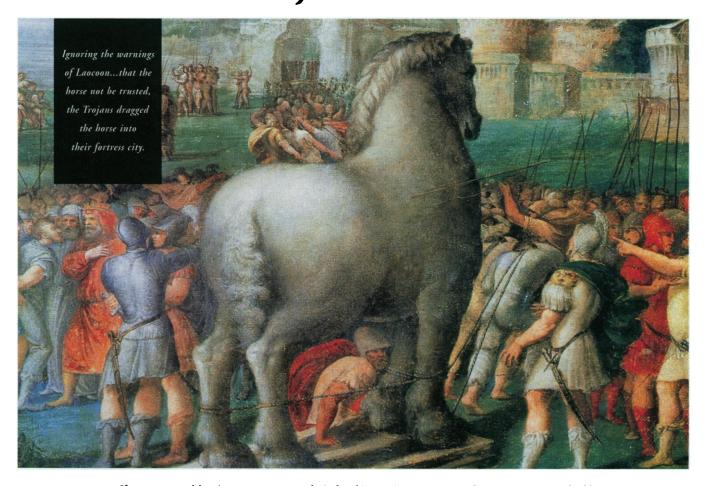
Strain Effects in K/O Mice

Epidermal growth factor (EGF) and related ligands are involved in many aspects of animal development. Threadgill et al. (p. 230) and Sibilia and Wagner (p. 234) have uncovered some unexpected complexity in EGF signaling in the mouse by knocking out the EGF receptor. The specific result of absence of the EGF receptor depended upon the genetic background of the mouse. Lethality in one mouse strain occurred at mid-gestation and was probably due to defects in the placenta; in another strain, mice lacking the EGF receptor survived as long as 3 weeks after birth but suffered abnormalities in several systems.

Forgetting with age

As we get older, our memory becomes less reliable. To investigate why this occurs, Grady et al. (p. 218) measured cerebral blood flow (an index of neuronal activity) in young and old people while they observed and then recognized human faces. Only some of the areas of the brain activated in young people were activated when the older people observed the faces. Agerelated memory losses seem due in large part to impaired encoding of stimuli, as well as to problems with recognition itself.

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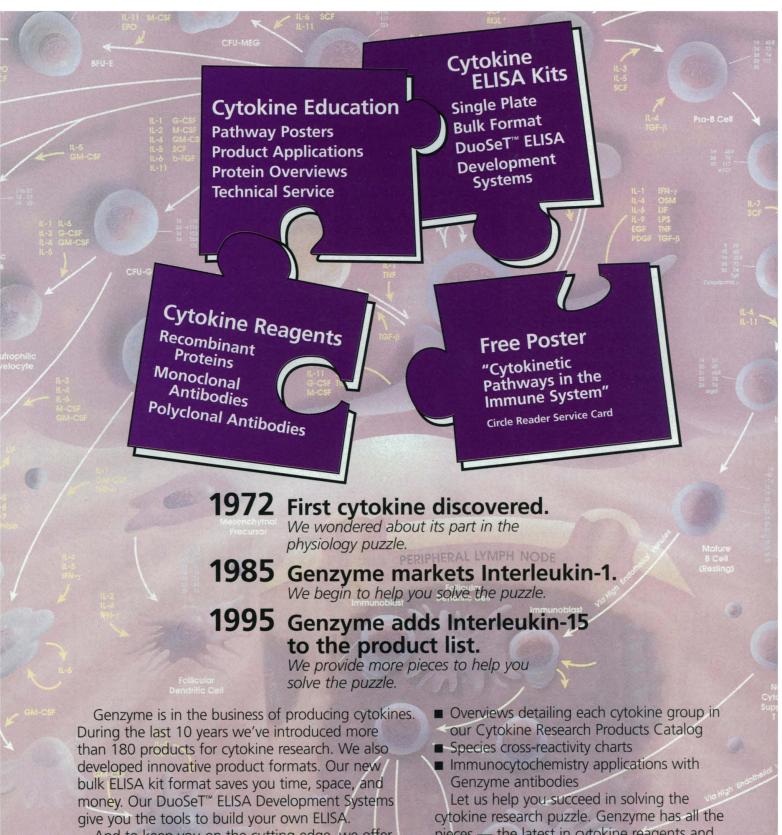
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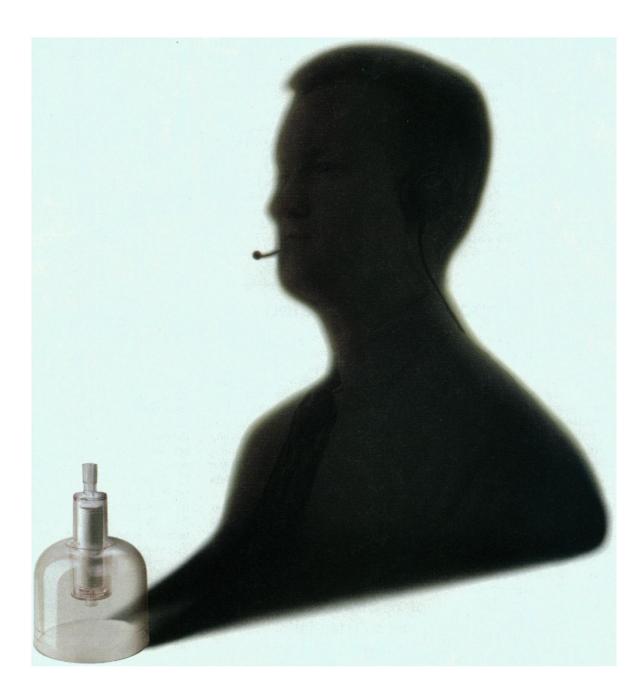
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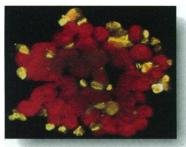
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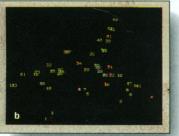
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¹ Gold, R. et al. (1994) Differentiation between Cellular Apoptosis and Necrosis by the Combined Use of In Situ Tailing and Nick

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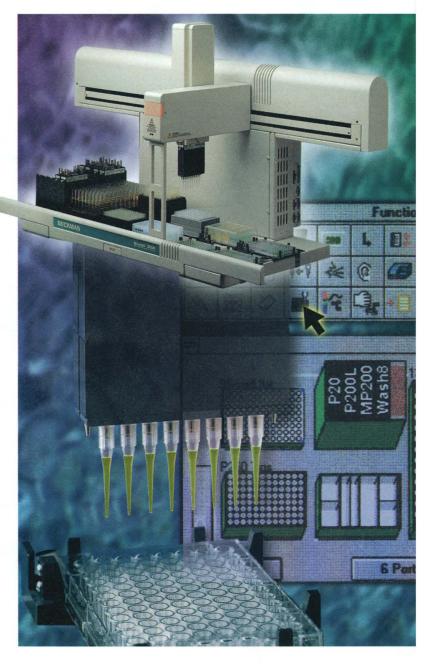
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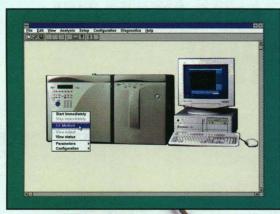
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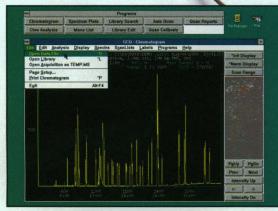
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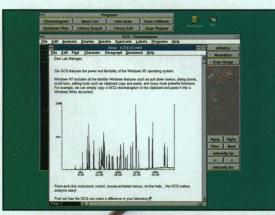
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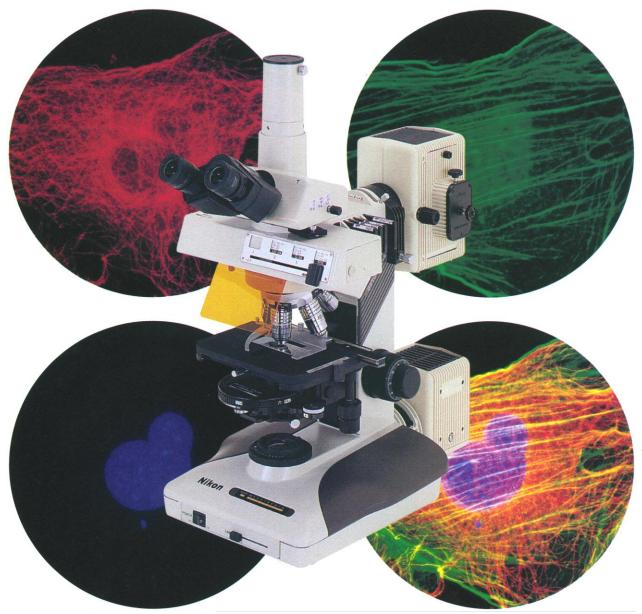




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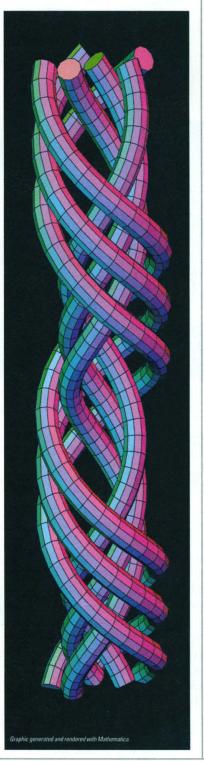


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i	$log[x_ ^n] := n log[x]$
8	$log'[x_] = 1/x$ (* derivative *)
ł	<pre>log/: InverseFunction[log] = exp</pre>
ł	log/: Series[log[x_], {x_, 1, n_}] :=
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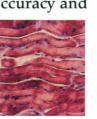
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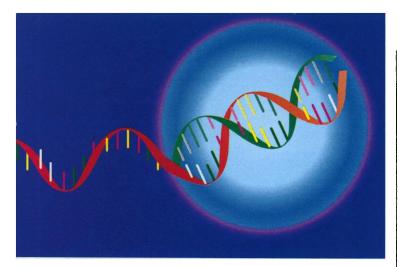
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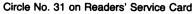
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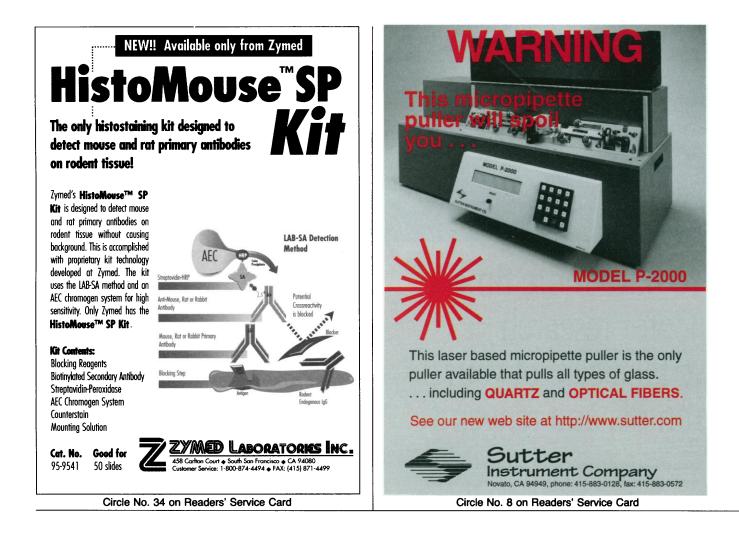
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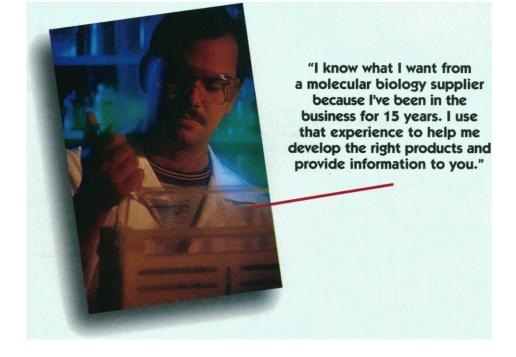
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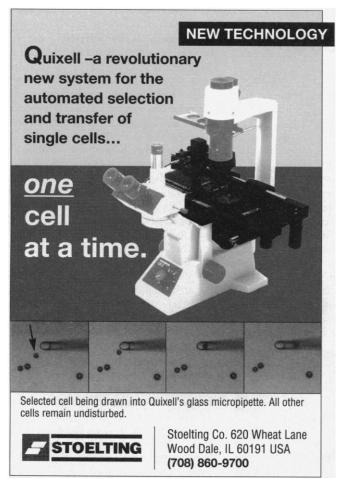


Ron Lirette, Ph.D.

- Presently directing research activities and product development for Sigma BioSciences.
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- Prior to Sigma, worked five years in a molecular biology group in the pharmaceutical industry.
- Also worked in academia at the Wistar Institute of Anatomy and Biology and at the University of Medicine and Dentistry of New Jersey.
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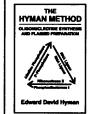
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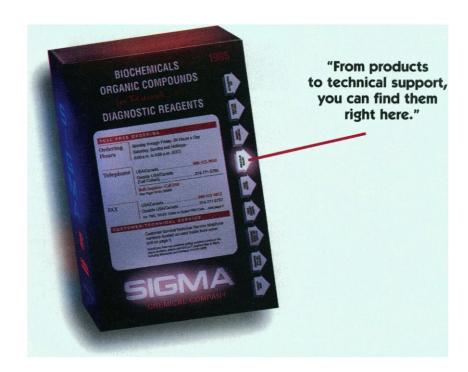
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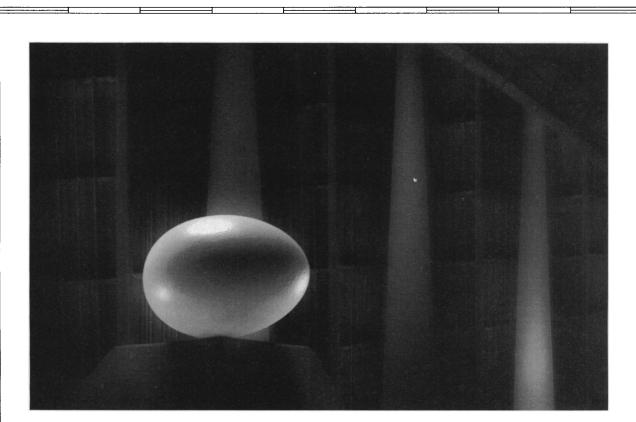
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