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SCIENCE

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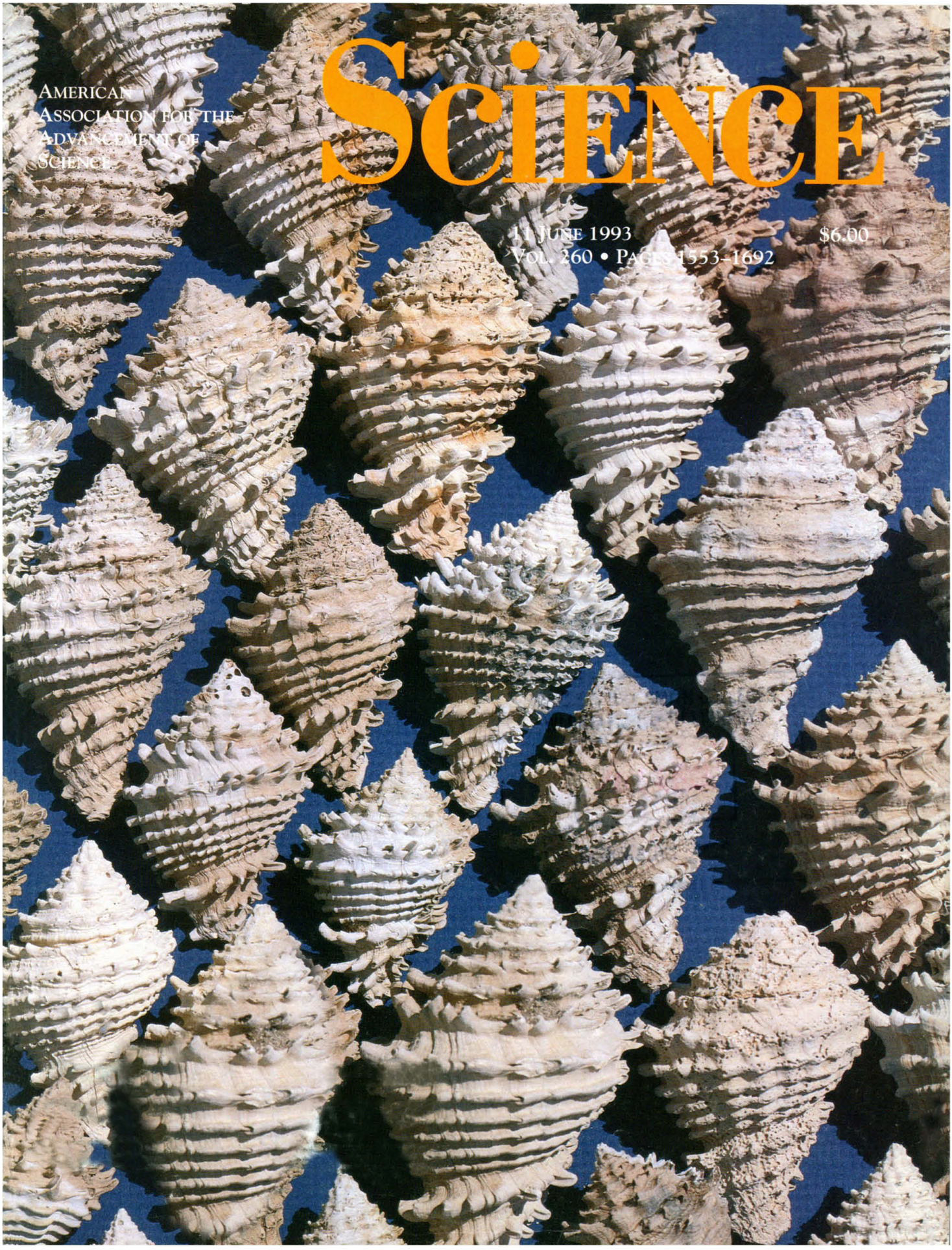

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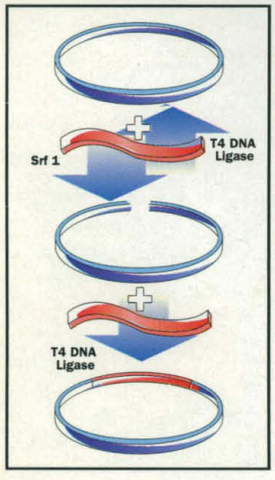

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1. Bauer, J., et al. (1992) *Stratagies* 5:2-64

*The polymerase chain reaction (PCR) process is covered by patents in the United States owned by Hoffmann-La Roche. Use of the PCR process requires a license.

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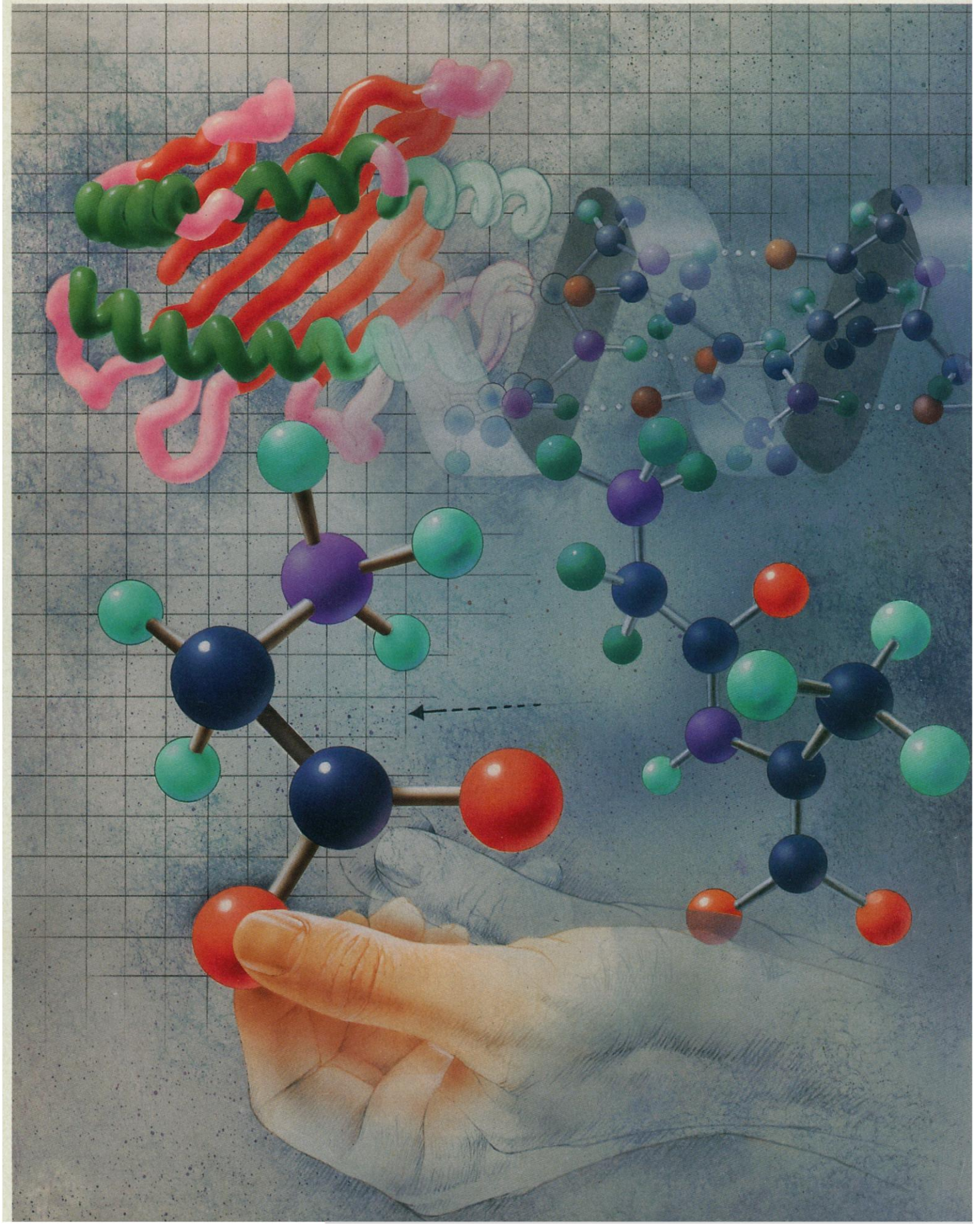

PROTEINS

How innovative technologies solve today's problems.

Today's protein research environment is more exciting and demanding than ever before. With each breakthrough, researchers discover new challenges as they strive to do more in less time with smaller amounts of material. In many cases, they are solving these problems with the application of alternate technologies.

PROTEIN QUARTERNARY STRUCTURE: WHERE DO TRADITIONAL TECHNIQUES FALL SHORT?

Quantification of stoichiometry and binding affinities is critical, both in quality control of recombinant proteins and in anti-viral drug development. Yet direct measurement of these thermodynamic properties has been hampered by empirical methods that rely on molecular weight standards and unjustified assumptions or methods that interfere with equilibrium between associated and non-associated protein moieties. To avoid such problems, Beckman Instruments now offers a modern analytical ultracentrifuge described by Dr. Preston Hensley of SmithKline Beecham:

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MAXIMIZING SEQUENCER PRODUCTIVITY: CAN NEW TECHNOLOGY CROSS-CHECK SAMPLE PURITY *BEFORE* SEQUENCING?

Separation scientists continually find that the isolation and purification of a sample prior to sequence are more difficult and time-consuming than the sequencing itself. Reverse-phase HPLC is well-established but does not provide an adequate verification of purity.

Beckman Instruments has successfully demonstrated how a combination of technologies — HPLC and capillary electrophoresis (CE) — can efficiently verify purity and solve the problem of wasted sequencer time. CE performs purity analysis in a fraction of the time spent with more traditional techniques.

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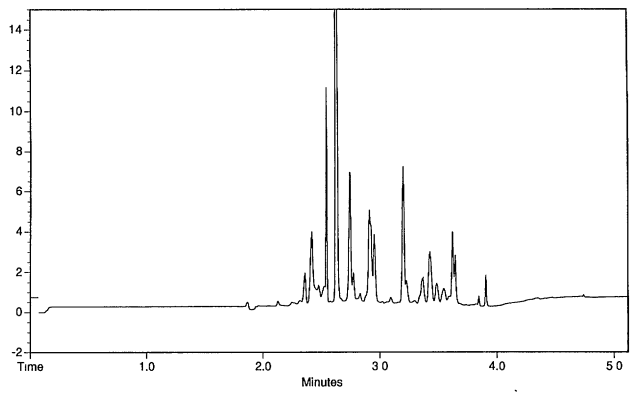
"The Beckman P/ACE™ capillary electrophoresis apparatus has exceeded our expectations of usefulness and this instrument heralds a very exciting future in the study of biological molecules. Its speed and sensitivity have made it the preferred choice to HPLC in the analysis of protein and peptide purity in many cases; preparative work continues to be done by HPLC."

Beckman has integrated HPLC and CE with its Gold software, producing the only LCCE system available today. With the Porton LF 3000 Protein Sequencer, Beckman provides a complete protein workstation for the determination of primary structures.

COMPOUND DETECTION: IS THERE A WAY TO GET HIGH RESOLUTION *AND* HIGH SENSITIVITY?

With its speed and resolution, CE is increasingly being used for the study of microsamples and peptide fragments. And now, to counter its inherent sensitivity limitation, Beckman offers a laser-induced fluorescence (LIF) detection option that expands detection limits to the femtomolar range.



Tryptic digest of ß-lactoglobulin analyzed with CE. (700 attomoles injected.)

For more information about applications of the techniques discussed in this article, the Beckman Plus, or for information and dates on Beckman's worldwide Protein Discovery Tour, write to Beckman Instruments, Inc., Bioanalytical Systems Group, 2500 Harbor Boulevard, Fullerton, California 92634-3100. Or call, toll-free in the U.S.A. 1-800-742-2345.

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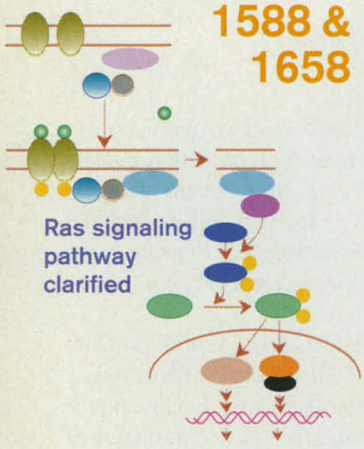


1588 & 1658

Ras signaling pathway clarified

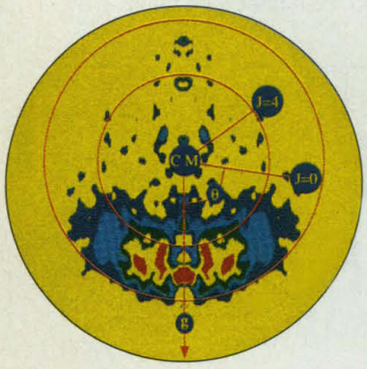
NEWS & COMMENT

RESEARCH NEWS

PERSPECTIVE

ARTICLES

RESEARCH ARTICLE



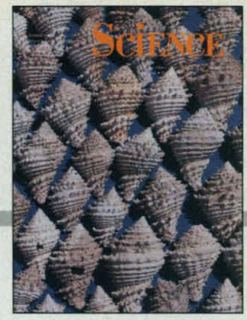
1605

A closer look at simple chemical reactions

DEPARTMENTS

COVER

Fossil shells of the gastropods *Hystrivasum locklini* and *Hystrivasum horridum* from the upper Pliocene Pinecrest Beds (2.0 to 3.5 million years old), Sarasota, Florida. These species are among many that became extinct during the late Pliocene only to be replaced by new species, yielding a biota whose diversity has not changed in 3.5 million years. See page 1626. Other evolutionary events related to the closing of the Isthmus of Panama are discussed on pages 1603, 1624, and 1629. [Photo: Joe Traver; specimens are from the Paleontological Research Institution, Ithaca, NY]



REPORTS

TECHNICAL COMMENTS

MARIE READ

1643

Courtship display of the golden-collared manakin

Indicates accompanying feature

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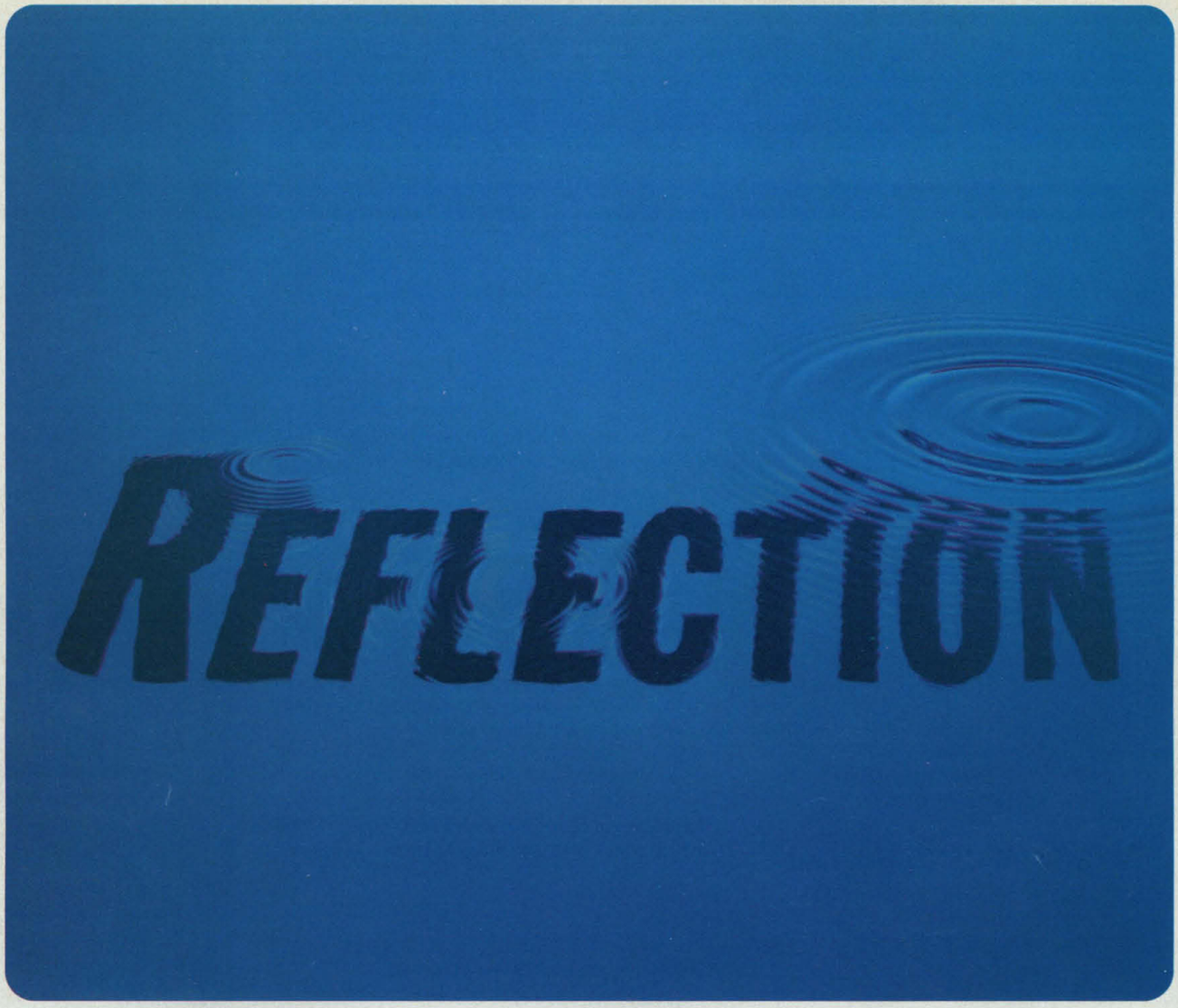

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More than just aftershocks

One of the unexpected results of the recent Landers earthquake in southern California was that seismicity suddenly increased in many other sites in the western United States at distances of more than 1000 kilometers from the epicenter. Hill *et al.* (p. 1617) overview this activity and discuss possible explanations for such remote triggering, which challenges models of stress changes in response to earthquakes. Most of the sites are north and east of the epicenter and are areas of active strike-slip or normal faulting. Sites such as Long Valley or Yellowstone are areas of recent magmatism. Complex interactions between seismic waves and crustal fluids or magma bodies may be responsible.

■

Odd fullerenes

Gas-phase synthesis of fullerenes normally generates species with an even number of carbon atoms. McElvany *et al.* (p. 1632) have detected the large, odd-numbered fullerenes C_{119}, C_{129}, and C_{139} in toluene extracts of fullerene soot. These molecules are apparently dimerization products that lose one carbon atom through oxidative processes. Pursuing this idea, they found that reaction of C_{60} with ozone generated the C_{119} product and that reaction of C_{70} and C_{60}/C_{70} mixtures with ozone led to the respective C_{139} and C_{129} products. Ozone-catalyzed reactions may open up new routes in fullerene chemistry.

■

Ready in minutes

Solid-state synthesis of inorganic compounds often requires heating the reactants to high temperatures for long periods of time. Landry and Barron (p. 1653) report that the chalcopyrites $CuInS_2$, $CuInSe_2$, and CuInSSe can be synthesized from elemental powders in as little as 3 minutes in a conventional microwave oven. Although metal blocks usually produce discharges in microwave ovens, metal powders can disperse the charge that builds up. Eddy currents within the particles can heat them to temperatures exceeding 1000°C. The morphology of the polycrystalline products suggests that the particles were quenched from a molten state.

■

Thriving after a long separation

The Isthmus of Panama began closing several million years ago, and Pacific and Atlantic faunas were finally isolated about 3 million years ago. It has been widely believed that mass extinctions occurred in the Atlantic marine species because of this event. Extensive resampling of Carribean mollusk species by Jackson *et al.* (p. 1624) and of mollusks and gastropods in Florida by Allmon *et al.* (p. 1626; cover) suggests otherwise. Extinction events occurred after the seaway closed (about 2.4 million years ago), and speciation has compensated for much of the losses so that diversity has remained roughly constant. Knowlton *et al.* (p. 1629) examined rates of genomic evolution in snapping shrimps and show that the isolation "event" was actually staggered in stages over millions of years. In a Perspective, Vermeij (p. 1603) discusses how these findings and other new data are revising our understanding of extinctions, species formation, and diversity in tropical America during the last several million years.

Plumage progress

The flow of traits under positive selection across a species hybrid zone has been expected, but examples are unusual. Parsons *et al.* (p. 1643) have studied an avian hybrid zone in Panama between the white-collared manakin and the golden-collared manakin. In the hybrid zone, birds with golden plumage turn out to be genetically and physically otherwise like the white-collared manakin. The authors believe that the gold-colored plumage traits have spread because of the breeding habits of the manakins. Manakins breed in leks, in which males compete for mates with elaborate courtship displays. Males with brighter plumage may be more successful and mate with the most females.

■

Bent into shape

Bending of DNA by transcription complexes has been imaged by scanning force microscopy. Rees *et al.* (p. 1646) examined the structure of a transcription complex formed at the λP_L promoter when *Escherichia*

coli RNA polymerase is bound. The initial open complex formed by the polymerase forms a bend in the DNA, and the DNA is more severely bent by polymerase during RNA elongation. The structure of DNA is considerably affected by polymerase and changes when an open promoter complex matures into an elongation complex.

■

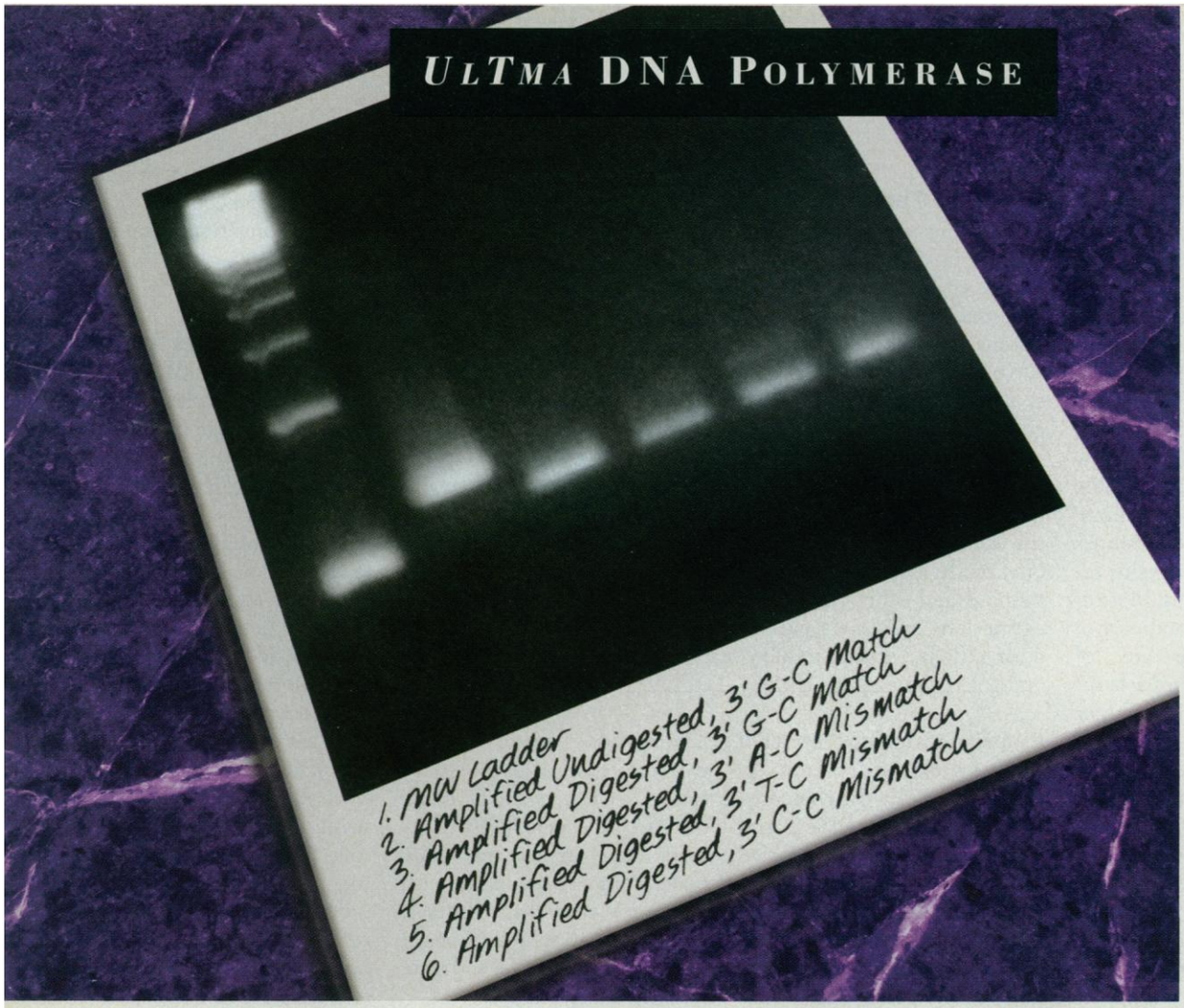
Requirements for the late stage of LTP

Long-term potentiation (LTP) is a form of enhanced communication between nerve cells such that the response of the post-synaptic neuron increases. This phenomenon has been studied extensively in the hippocampal region of the brain and has been proposed as a mechanism for the formation of memories. Experimental investigations have focused mostly on the earlier periods of LTP, which last 1 to 3 hours, and have implicated protein kinases. Frey *et al.* (p. 1661) show that the later phase of LTP, lasting up to 10 hours, requires protein synthesis and may depend on cyclic adenosine monophosphate–dependent protein kinase (PKA). Because the protein synthesis inhibitors did not block the early phase of LTP, they suggest that the later phase requires recruitment of other molecules in addition to those participating in the establishment of early LTP.

■

We should live so long

Studies by Carey *et al.* and Curtsinger *et al.* reported that mortality in fruit flies need not automatically increase with age. For other species studied, including humans, the mortality rate appears to follow the long-standing Gompertz model and increases exponentially. These recent results and their interpretation have stimulated much discussion, of which some is presented in a series of Letters (pp. 1565 to 1569) and Technical Comments (pp. 1664 to 1667).



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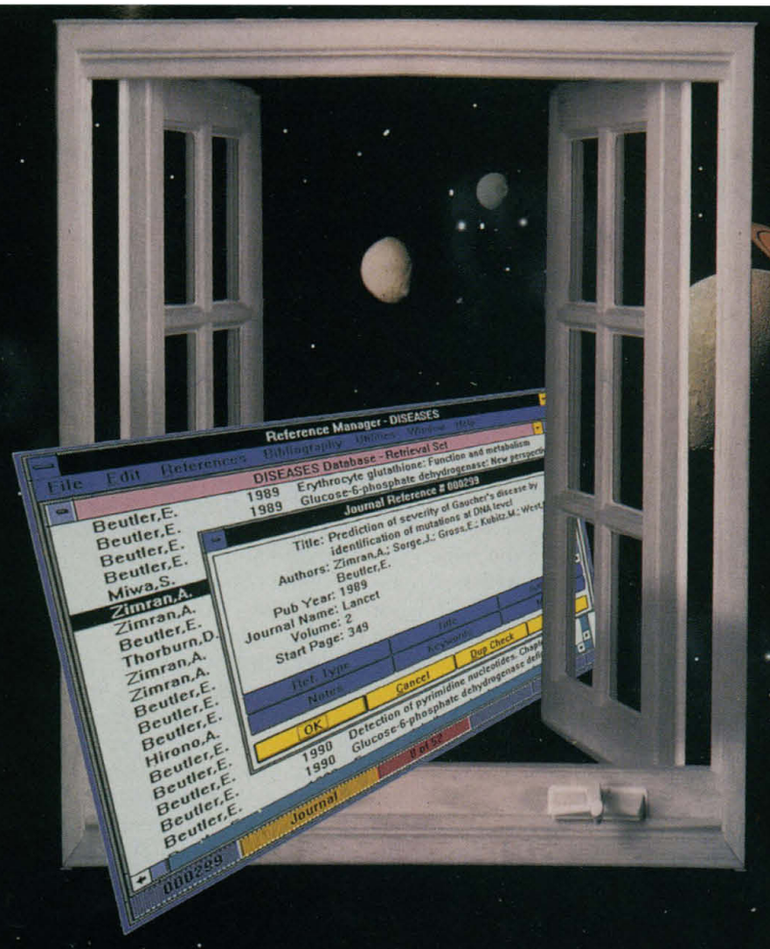

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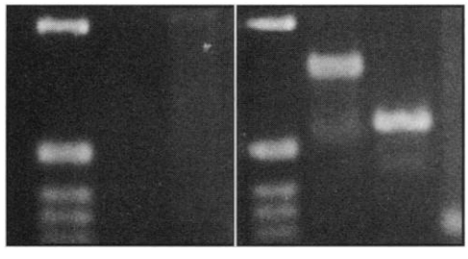

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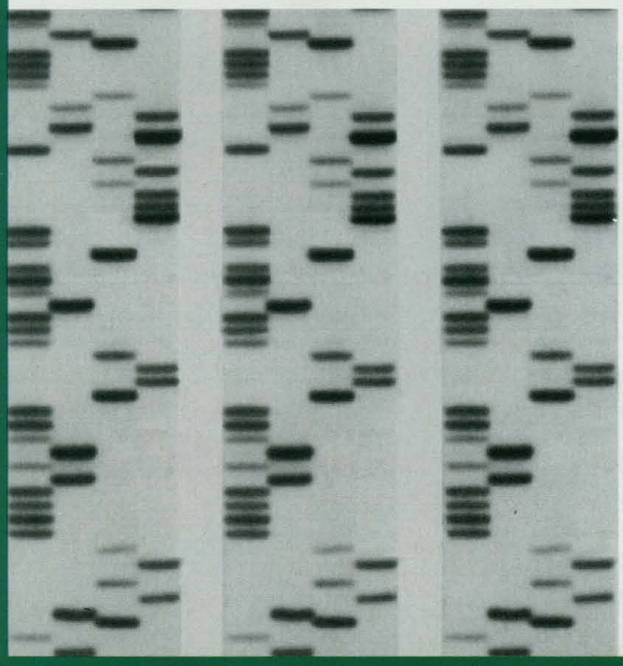

◀ Autoradiogram of chemiluminescent sequencing reaction using the CIRCUMVENT™ Phototope™ Kit. Sequencing reaction of a double-stranded DNA template using Vent$_R$™ (exo$^-$) DNA polymerase and thermal cycle sequencing procedure, followed by chemiluminescent detection. Lane order A, C, G, T.

Sears, et. al. (1992) Biotechniques 13, 626-633.

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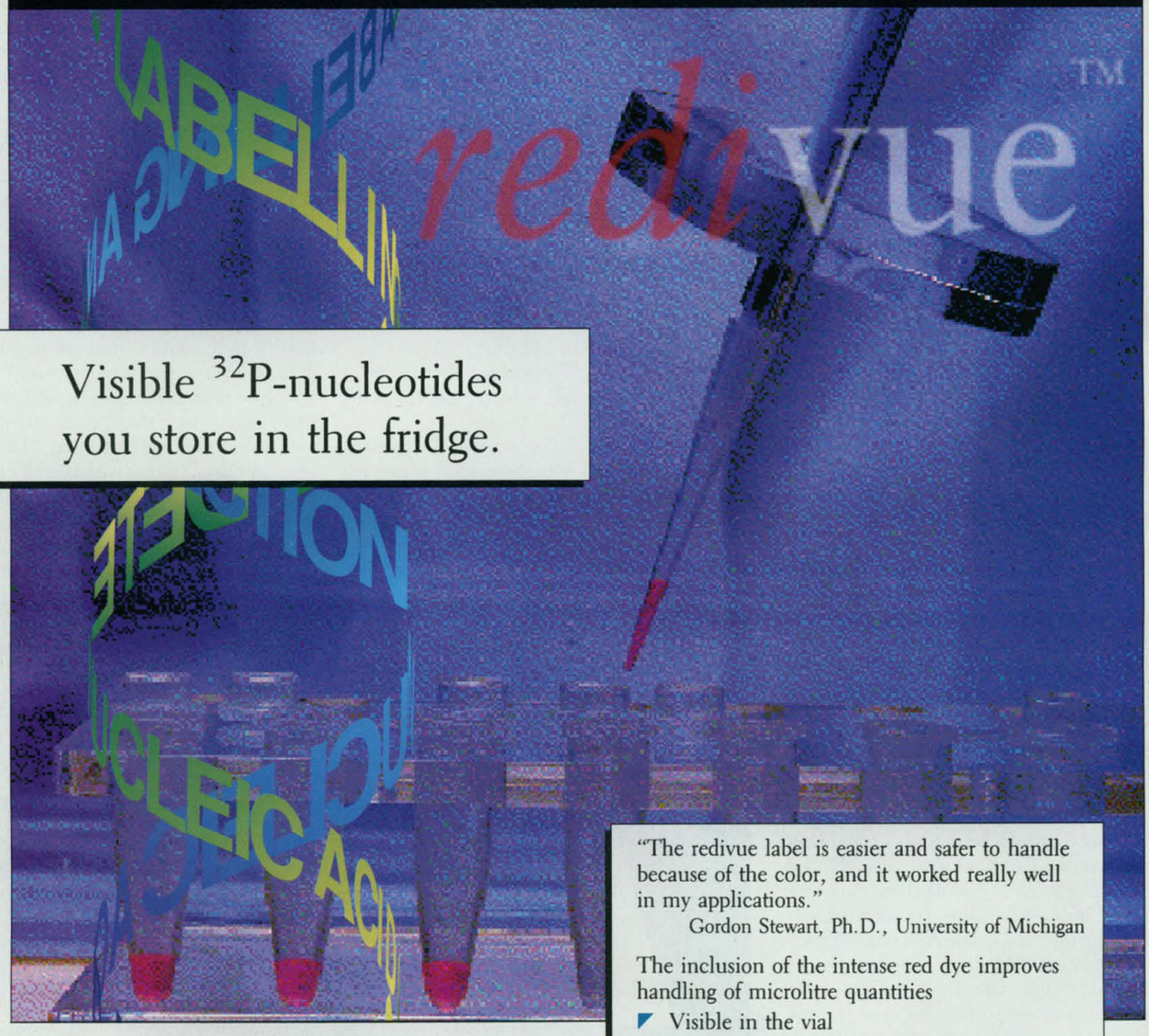

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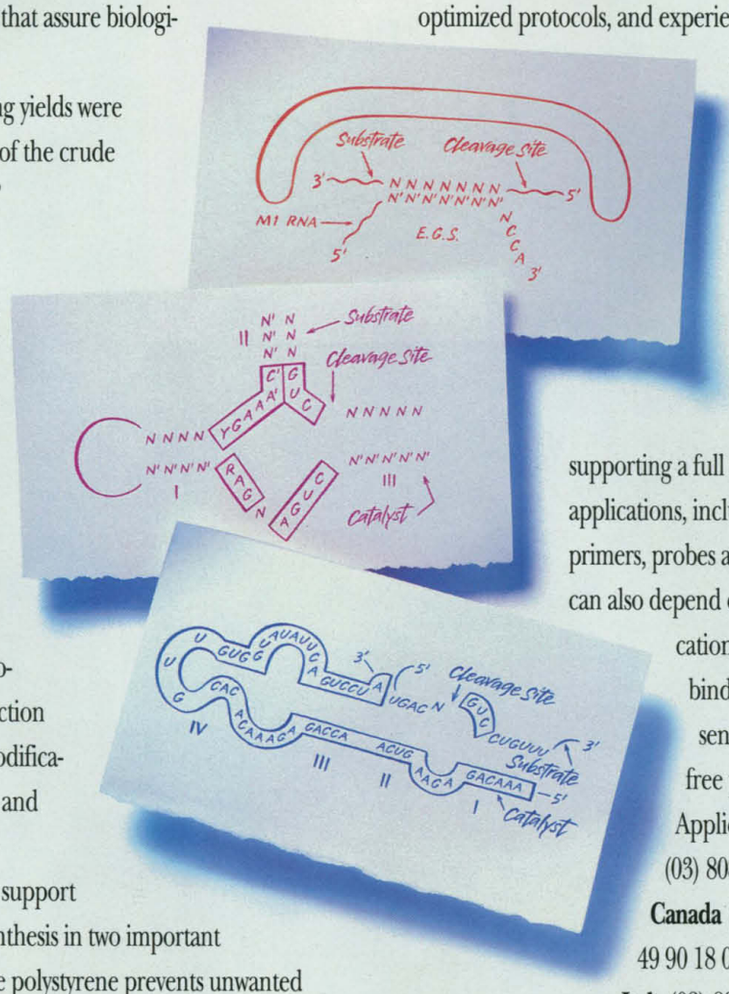

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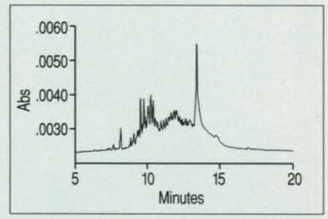

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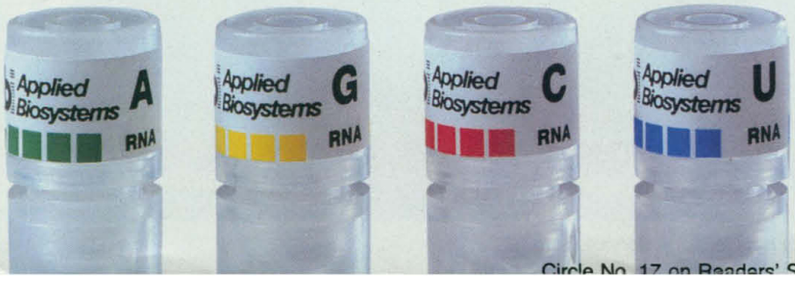

[1] Brian Sproat, European Molecular Biology Laboratory, Heidelberg, Germany

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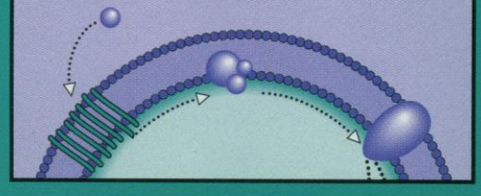

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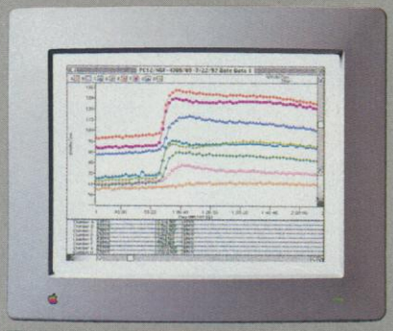
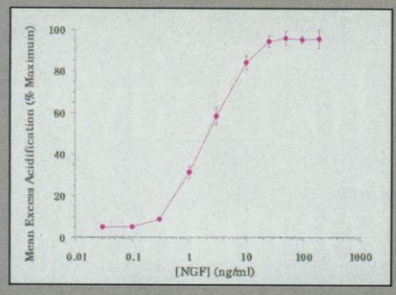
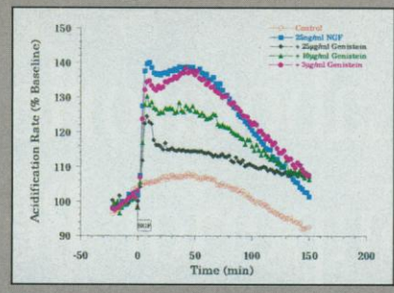
NGF



1 Real-time acidification rate data showing the response of PC12 cells to a 12 min. exposure to nerve growth factor (NGF:0.1-200ng/ml).

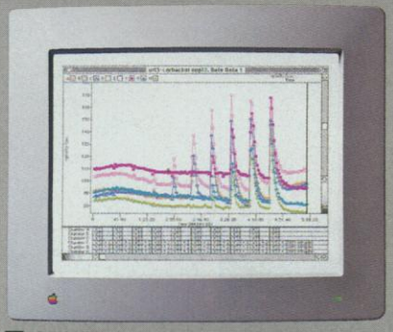


2 Dose response of PC12 cells to NGF. Each point represents data from 7 separate experiments. Calculated EC_{50} value for NGF was 1.9 ± 0.7ng/ml (~152 ± 50pM) ($\bar{x}$ ± S.E.M.).

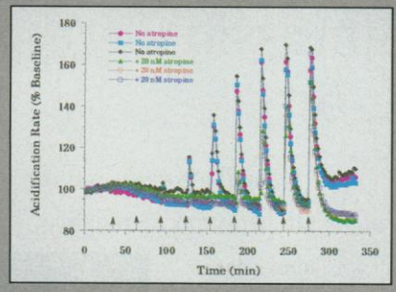


3 Dose dependent inhibition of NGF (25ng/ml) response by tyrosine kinase inhibitor, genistein (3-25μg/ml).

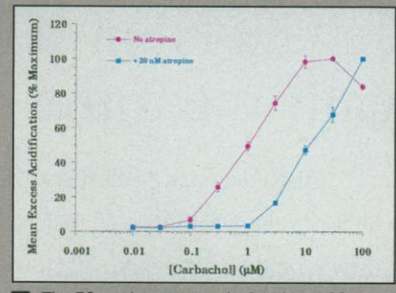
CARBACHOL



1 Real-time acidification rate data demonstrating stimulation of CHO cells transfected with muscarinic M_1 receptor. Increasing doses of carbachol (10nM-100μM) given in presence and absence of 20nM atropine.



2 Data from previous figure expressed as percentages of the basal acidification rates before initial addition of carbachol.



3 The EC_{50} values were calculated as 1.00 ± 0.08μM for carbachol alone and 11.50 ± 0.09μM for carbachol in the presence of 20nM atropine ($\bar{x}$ ± S.E.M.;n = 3).

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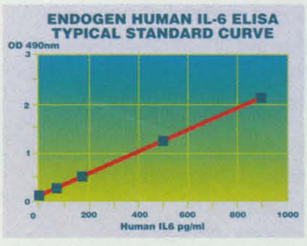

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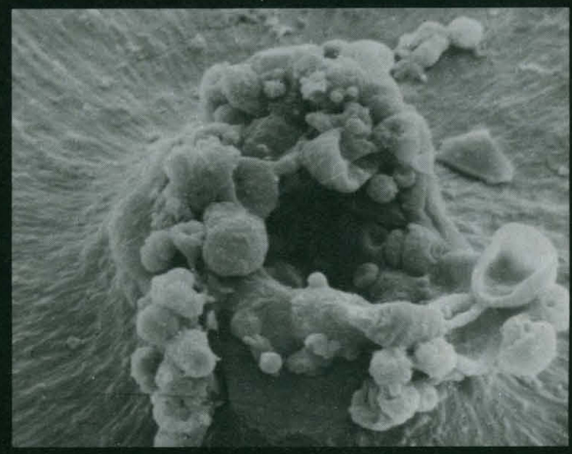

Scanning electron micrographs of primary rat mammary epithelial cells at 24 hours (inset) and 36 hours (background) on MATRIGEL® Basement Membrane Matrix. Photo courtesy of Dr. Margaret Neville.

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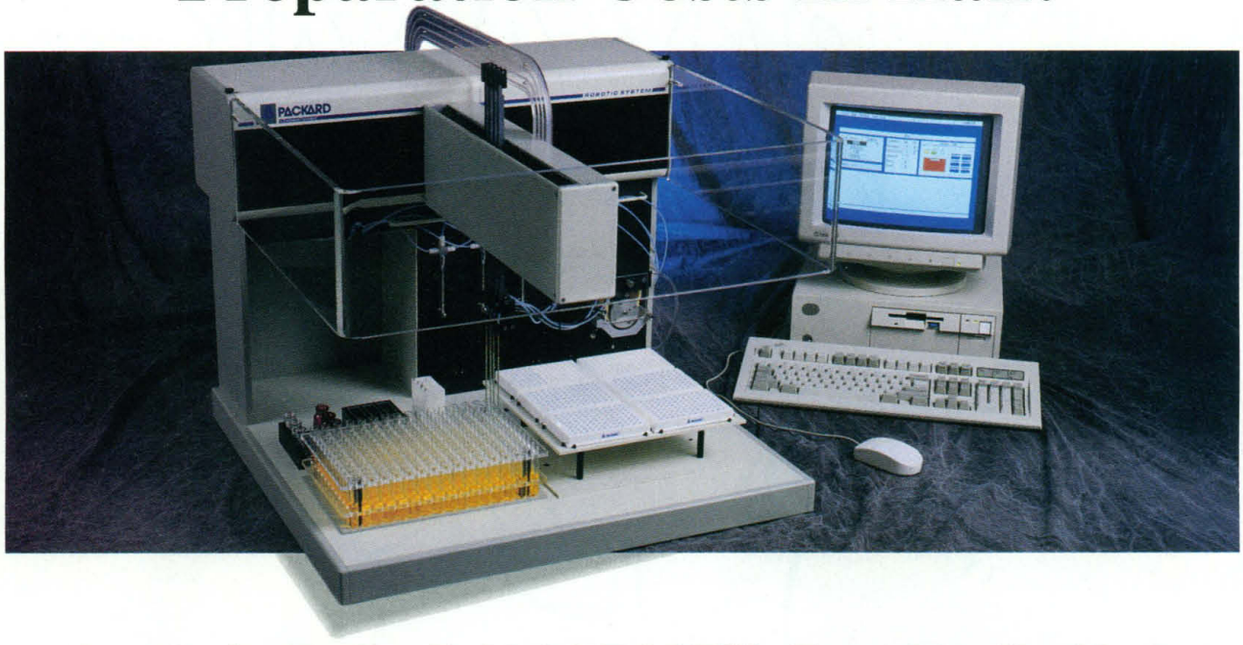

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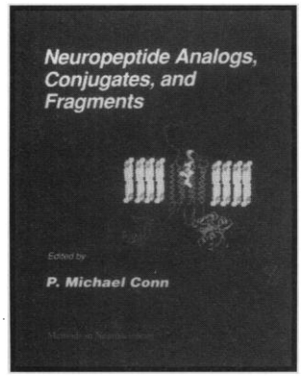

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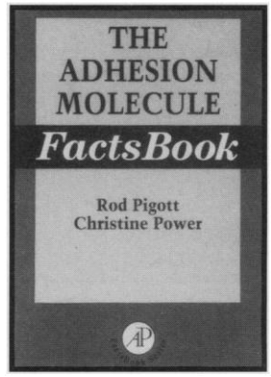

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