AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

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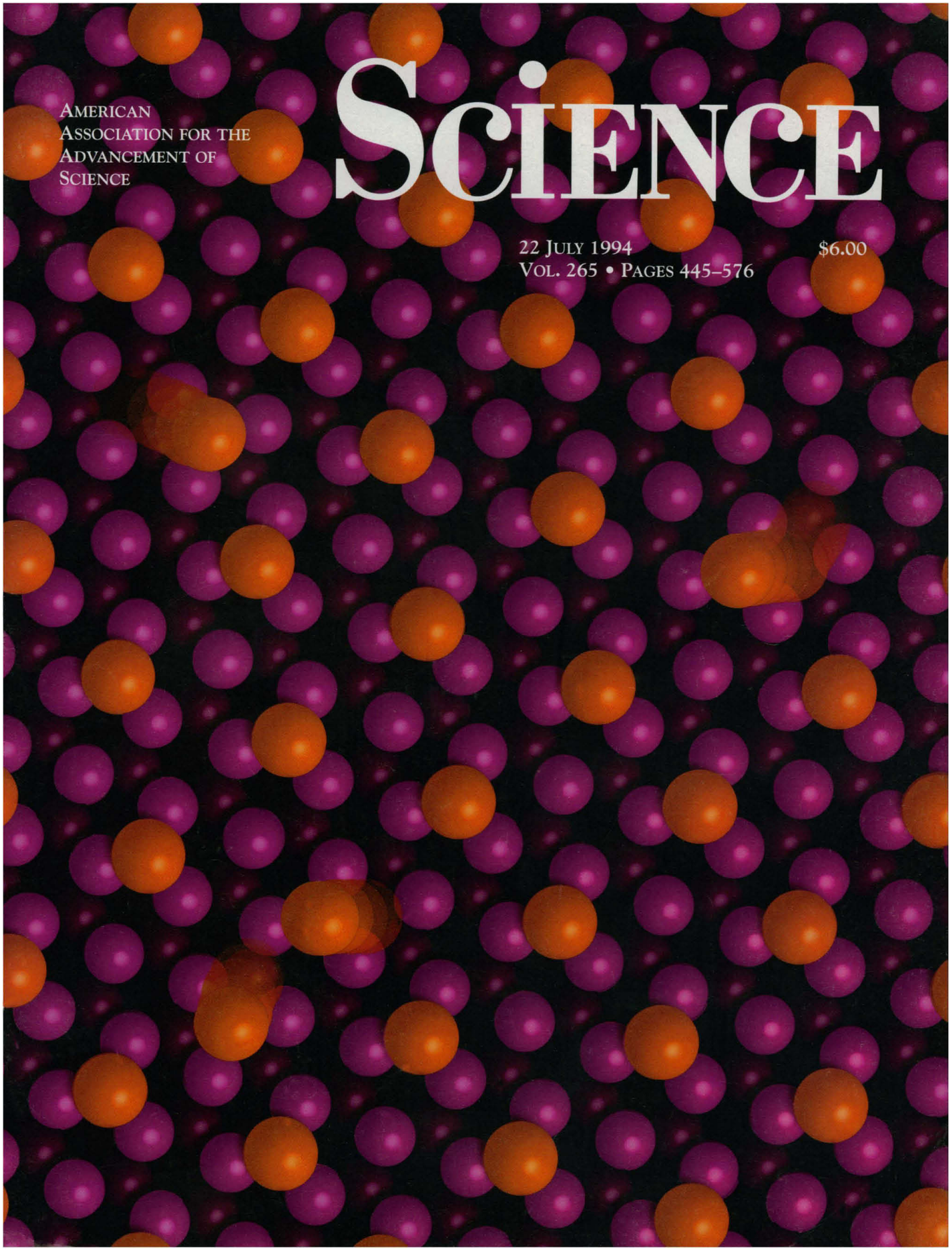
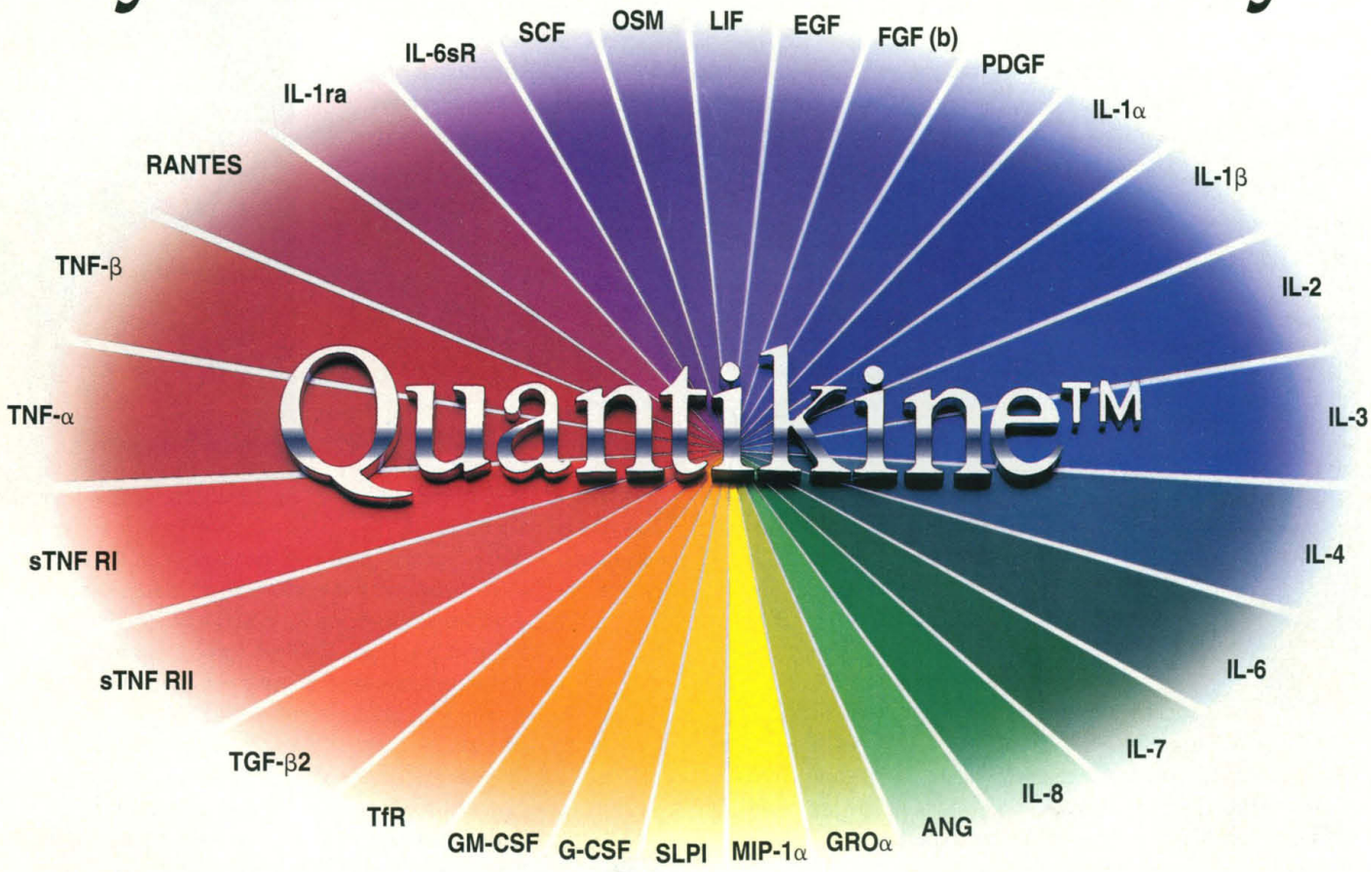


Cytokine Immunoassays



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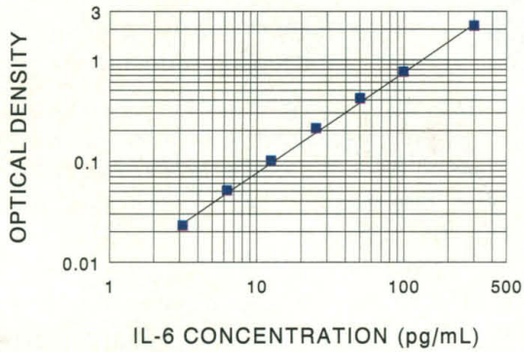
Standard curve for IL-6 in serum diluent using the 2 hour shaker option.



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Biosearch specializes in creating tools that fuel your inner drive to discover. Tools that allow your imagination to take on today's frontiers.

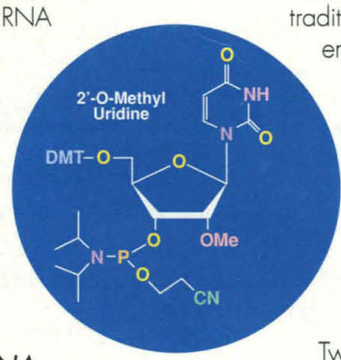
RNA

RNA oligomers have shown promise in therapeutic and diagnostic applications, including inhibition of viral replication, cancer etiology, and gene regulation and expression.

To bring these applications within easy reach, Biosearch was the first to introduce a complete, automated RNA synthesis system with nucleotide monomers, reaction columns, pre-packaged reagents, and optimized synthesis protocols.

Our new Expedite™ RNA chemistry makes your work-up procedures faster, easier, and more efficient. The milder cleavage and deprotection conditions reduce chain degradation and increase yield. The Expedite RNA reagents employ our patented betacyanoethyl phosphoramidite chemistry that's become the method of choice in DNA and RNA synthesis.

Our researchers are currently developing protocols for large-scale synthesis of RNA oligomers. (Photo of RNA crystal, courtesy of Dr. Alex Rich, MIT, was synthesized at a scale of 70 μ mole on Biosearch's 8800 Synthesis System.)



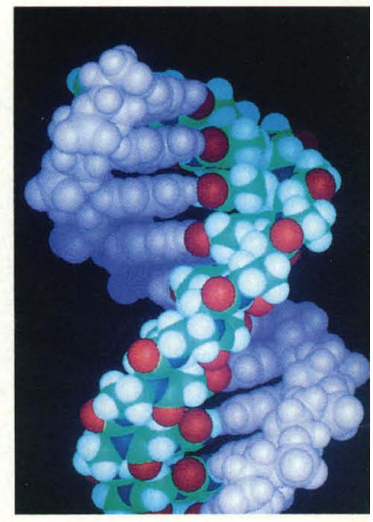
Therapeutic and diagnostic grade DNA

Researchers in the clinical and diagnostic use of DNA are on the verge of creating a new class of pharmaceuticals. Biosearch is proud to pioneer new tools for their work.

Biosearch is the world's leading supplier of systems, chemicals, and reagents for the synthesis, purification, and analysis of therapeutic and diagnostic DNA. We've tightened the specifications on our products to ensure that they can be used for the most demanding applications. A Certificate of Analysis is automatically supplied with all of our DNA synthesis reagents.

We've also substantially expanded our manufacturing capacity to meet the needs for large single-batch production of material, minimizing your need for internal quality control.

In addition to standard reagents, Biosearch can also supply phosphoramidites and bulk quantities of synthesized oligomers on a custom-synthesis basis.



PNA

Peptide Nucleic Acids–PNA oligomers. These molecules are so novel that they're rewriting the very nature of nature. Biosearch is the world leader in the development and synthesis of these exciting new molecules.

Similar to DNA and RNA, PNA carries information in sequences of the four bases: adenine, guanine, cytosine, and thymine. In PNA, however, these code carriers are connected to a completely different backbone–a polyamide backbone similar to that found in peptides. PNA oligomers are more stable than their natural counterparts yet bind more specifically and with higher affinity to natural DNA and RNA.

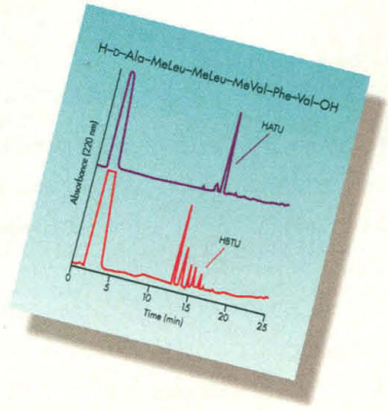
PNAs can be used in many of the same applications as traditional DNA. Their greatest contribution, however, may come from applications that can't be performed using traditional DNA oligonucleotides, such as restriction enzyme blocking, PCR clamping, and DNA mapping.

Biosearch can provide you with custom PNA oligomers, or the monomers, supports, and reagents to synthesize your own oligomers.

HOAt and HATU peptide coupling reagents

Two new coupling reagents, HOAt and HATU, simplify your peptide synthesis. These new reagents enhance coupling yields and reduce racemization and coupling times. They are particularly effective with difficult couplings and in the synthesis of peptides containing hindered amino acids.

HOAt and HATU have structures similar to the commonly used reagents HOBt and HBTU, and are compatible with all standard activation strategies.



Keep Up With Your Imagination.

PEG-PS™ peptide synthesis supports

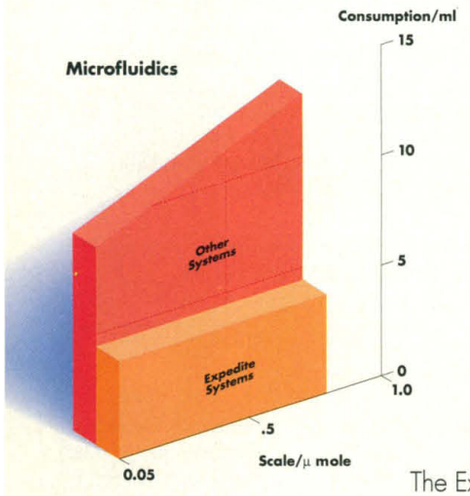
PEG-PS (polyethylene glycol-polystyrene) peptide synthesis supports from Biosearch help you achieve improved peptide purity with shorter cycle times.

Unlike traditional supports, PEG-PS beads more closely resemble the nature of the growing peptide chains. Solvation of the peptide resin is higher, resulting in a higher peptide purity. Synthesis is fast and effective due to high coupling efficiency and minimal side reactions.

PEG-PS supports are easy to handle, compatible with a wide range of solvents, and are especially well suited for the synthesis of long or difficult peptides.

Microfluidics

In the real world, achieving "end product" is not the only concern. There are dozens of production costs as well as the escalating costs of hazardous waste disposal.



Biosearch's Expedite Nucleic Acid Synthesis System, with its patented microfluidics technology, not only enables fast cycle times but also provides the bonus of reduced reagent consumption. The distance between the reagent reservoir and the column is minimized so that a single coupling cycle requires less than 4.5ml of reagents. The Expedite system (with optional trityl monitor) can also separate the chlorinated waste–simplifying disposal tasks and reducing associated costs.

Membrane synthesis

Perform nucleic acid synthesis on a membrane? It's now possible–and practical–thanks to Biosearch Nucleic Acid Membrane Supports, a breakthrough synthesis technology developed by Biosearch.

Biosearch membrane supports use a proven PTFE membrane system that directly replaces traditional controlled pore glass (CPG) supports. Membrane devices have standard luer fittings, so they can be plugged into any brand of synthesizer.

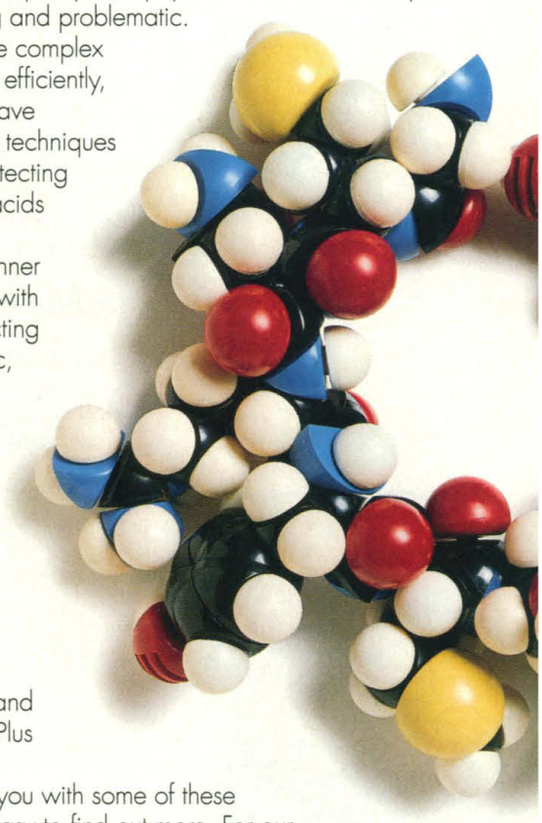
Biosearch membrane supports allow you to synthesize both long and short oligomers on the same type of membrane; no longer do you need to select the size of the CPG according to the length of the oligomer.

With Biosearch membrane supports, not only do you eliminate beads, but there's no centrifuging and no washing. Just remove the membrane from its holder, cleave, and deprotect.

Allyl-based protection for complex peptides

The synthesis of cyclic, branched chain, sulfonated, glycosylated, and phosphorylated peptides have traditionally been time consuming and problematic.

To synthesize these complex peptides quickly and efficiently, Biosearch scientists have perfected convenient techniques using allyl-based protecting groups. Allyl amino acids can be selectively deprotected in a manner which is compatible with other classical protecting groups (such as Fmoc, Boc, *t*Bu), sensitive amino acids (Met, Trp), and side chain modifications (Tyr(SO_3H)). Biosearch has also developed protocols for the fully automated synthesis of cyclic peptides, branched peptides, and MAPs on our 9050 Plus PepSynthesizer.™



If we've intrigued you with some of these innovative tools, it's easy to find out more. For our "Directory of Chemical Products"–one of the most comprehensive synthesis tool kits in the world–call the Biosearch Group in the US and Canada at 1-800-872-0071, in Germany at (49) 040-853267-36, in Japan at (03) 3471-8191, in France at (33) 1 30127002, and in the UK and the rest of Europe at (44) 0923 211107.

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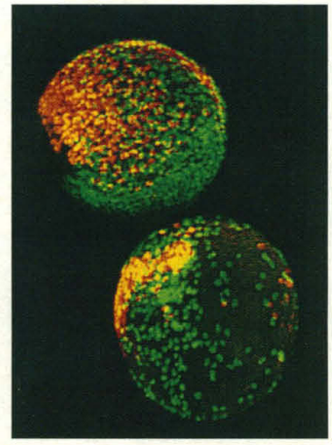
COVER

Motions of atoms on a germanium surface showing the fundamental excitations from crystalline order that bring about transformations of solids. The interstitial-like (lower left) and vacancy-like (middle right) excitations correspond to those responsible for mass transport, many phase transitions, and catalysis. This atomic-scale view of such dynamic phenomena is made possible by the tunneling microscope. See page 490. [Illustration: Jeff Knight]

TECHNICAL COMMENTS



517

Cellular fate in zebrafish

◩ Indicates accompanying feature

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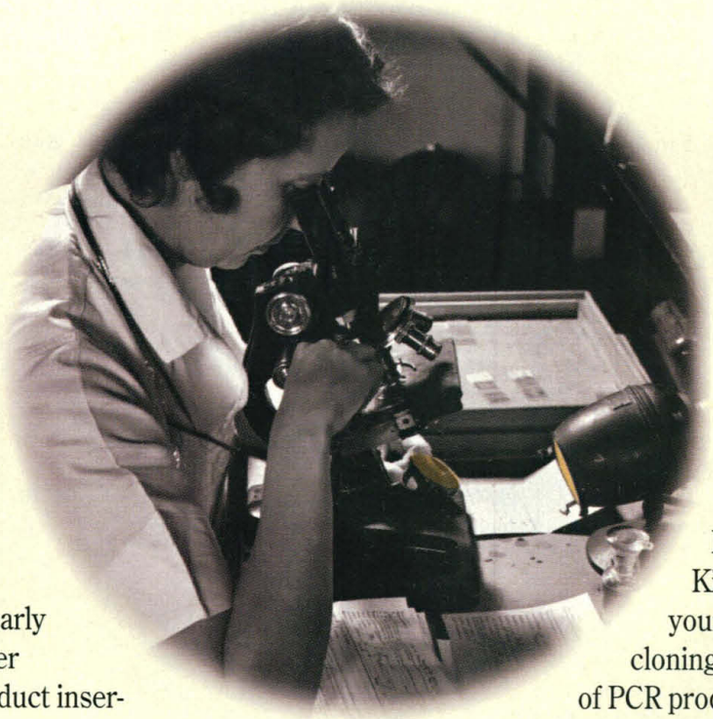

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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

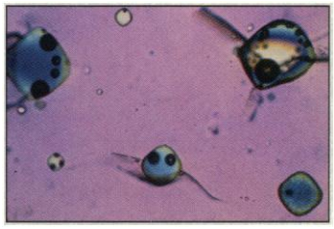
Faster with lead

Atomic diffusion in solids proceeds mainly through the movement of vacancies or of atoms in interstitial sites, but such processes are difficult to observe directly. Hwang *et al.* (p. 490; see cover) found that they could follow such motions on a germanium (111) surface upon which they had adsorbed a small fraction of a monolayer of lead. These lead atoms catalyzed the movement of atoms so that diffusion processes occurred at relatively low temperatures (below 80°C) rather than at several hundred degrees Celsius. The authors have used scanning tunneling microscopy images to explain the role of dangling bonds in these motions and to model the phase transition that occurs between the c(2×8) and (1×1) surface structures.

■

Sulfur sources

Some large volcanic eruptions, such as Mount Pinatubo eruption of 1991, release large amounts of sulfur dioxide (SO_2) to the atmosphere and thus



significantly affect global climate; however, analyses of glass formed from such eruptions have typically indicated that the magma contained insufficient dissolved sulfur to account for the amount released. Wallace and Gerlach (p. 497) provide analyses of water and carbon dioxide contents in glass inclusions in crystals erupted from Mount Pinatubo. In conjunction with sulfur analyses, these data indicate that before eruption the magma likely coexisted with a separate SO_2-rich vapor phase.

■

Working instruments

Scanning microscopes, which were originally developed to image surfaces, are also being used to modify surfaces for device applications. Rüetschi *et al.* (p. 512) used a scanning force microscope (SFM) to create waveguides, which are structures that guide light propagation through total internal reflection, in liquid crystal displays. The nylon polymer layer that contacts the liquid crystal was scratched with the SFM, which modified the material's refractive index to produce waveguides 6 micrometers in width. Salling and Lagally (p. 502) used a scanning tunneling microscope to pattern a silicon (001) surface at room temperature. Trenches one atomic layer deep and with atomically straight edges were formed.

■

Uncertain fate

The assignment of a specific fate to the cells produced during embryonic cell divisions is one of the main challenges of early development. In some organisms, the fate of even the earliest blastomeres can be predicted because the cell cleavages are organized by an already established body axis. The zebrafish embryo, however, does not seem to establish the body axis until after early cleavage. Helde *et al.* (p. 517) show that descendants of early cleavage cells in zebrafish will demonstrate a subset of possible fates, but because clones of cells scatter to different degrees, the specific fate of any single early cleavage cell cannot be predicted.

■

NO origins

In neurons undergoing long-term potentiation (LTP), a model for synaptic changes underlying learning and memory, signals from the postsynaptic cell are thought to act on the presynaptic cell to increase its transmitter release and the strength of the synaptic connection. One candidate for this messenger is nitric oxide (NO), a diffusible molecule generated by NO synthase (NOS). This enzyme has several isoforms, including a soluble form associated with neurons (nNOS) and a membrane-localized form associated with epithelial cells (eNOS). O'Dell *et al.* (p. 542) found that LTP in the CA1 region of the hippocampus of mice in which the gene encoding nNOS was disrupted was similar to that of wild-type mice, but LTP induction could still be blocked by NOS inhibitors. They suggest that eNOS rather than nNOS generates the most of the NO involved in LTP induction.

■

Reflections on a nearby moon

The Apollo 11 astronauts left behind on the moon's surface a reflector capable of returning a detectable signal from a terrestrial laser back to the Earth. The Earth-moon distance can be measured to within a few centimeters, and 25 years of accumulated orbital data have been used to test tidal theory, general relativity, and models of the moon's internal structure. Dickey *et al.* (p. 482) describe what has been achieved by lunar laser ranging since Apollo 11 and what continued monitoring has to offer.

■

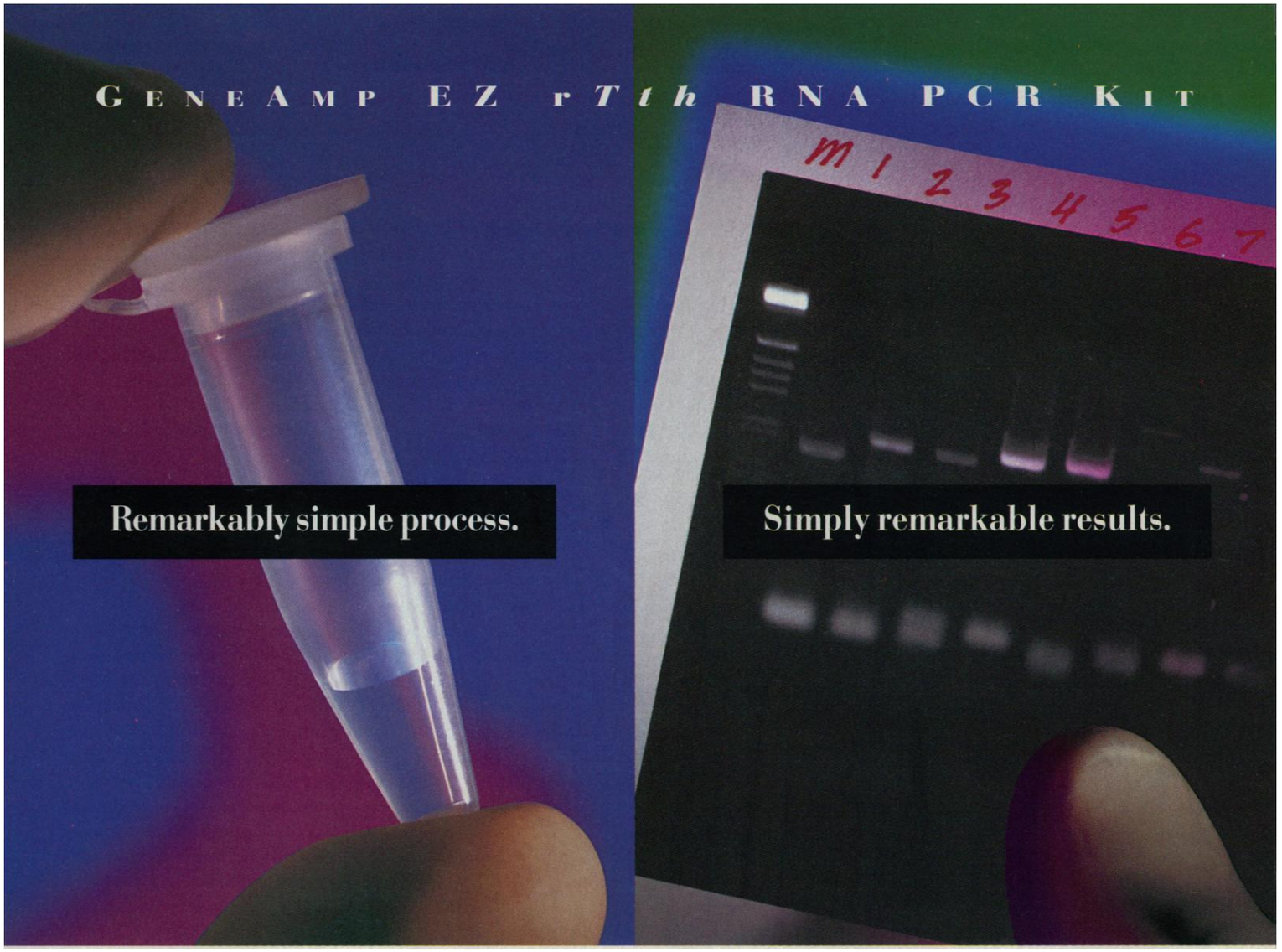
A number of functions

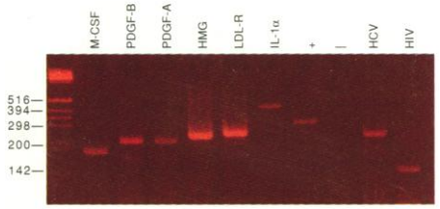
The 14-3-3 proteins, first identified in brain extracts over 25 years ago, are a highly conserved family of eukaryotic proteins whose wide range of expression is matched by an equally wide range of ascribed functions. Two reports shed light on the role of these multifunctional proteins in cellular signal transduction. Ford *et al.* (p. 533) show that 14-3-3 proteins in fission yeast are required for the DNA damage checkpoint, a critical feature of cell cycle control. Pallas *et al.* (p. 535) document a physical association between mammalian 14-3-3 proteins and a polyomavirus transforming protein previously found to associate with proteins involved in cell proliferation.

■

Drawing ahead

The motor cortex has been hypothesized to direct movement by means of a distributed population code in which the firing rates of several neurons represent a given motion. Schwartz (p. 540) made single-cell recordings from hundreds of neurons in the proximal arm area of the motor cortex of rhesus monkeys that had been trained to draw smooth spirals. The activity in the cells only preceded the movement when the curvature of the spiral was tight—less than 6 centimeters. In the straighter portions, the cells were active during or following the movement. Thus, only when the curvature of the movement exceeds a threshold value is the motor cortex likely to be causal in generating the spiral hand motions.





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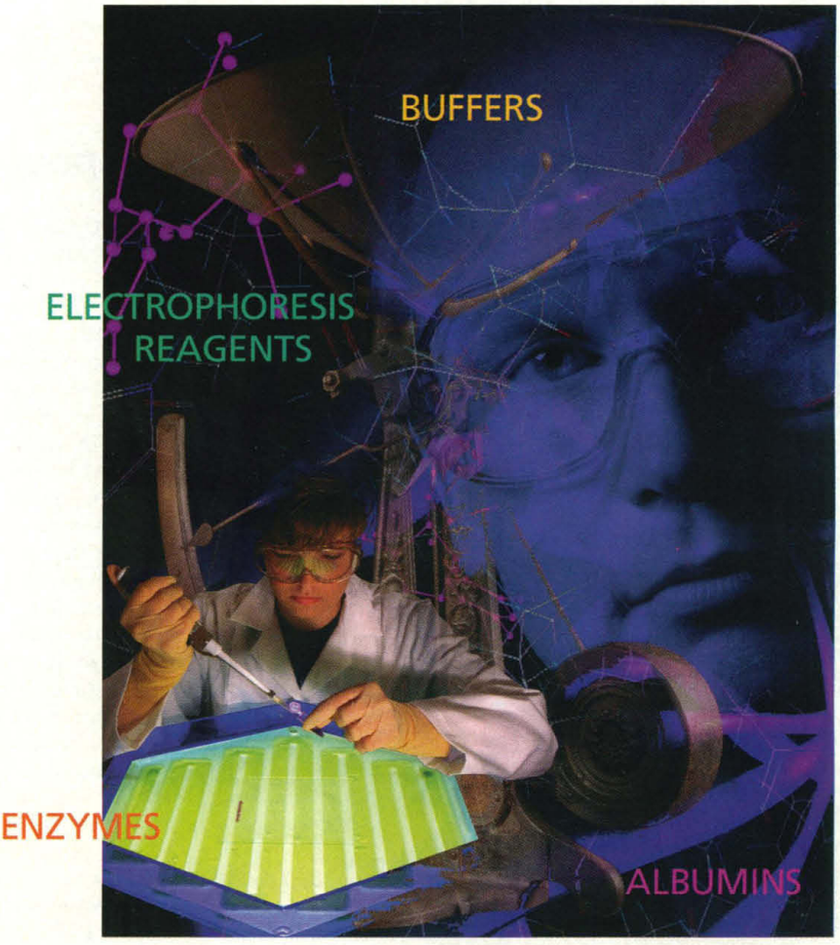

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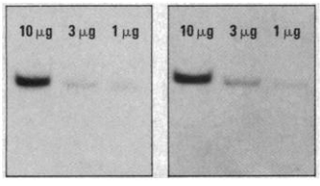

Parallel human genomic Southern blots demonstrate the high sensitivity and low background provided by the Genius System (right, 12-min. exposure) compared to probes prepared with ^{32}P (left, 3-day exposure).

Like traditional radioactive methods, the Genius System provides specific and reliable detection of target sequences.

But unlike other nonradioactive methods, the Genius System uses a unique antibody-based protocol that minimizes background interference, maximizes the signal-to-noise ratio, and produces your results faster.

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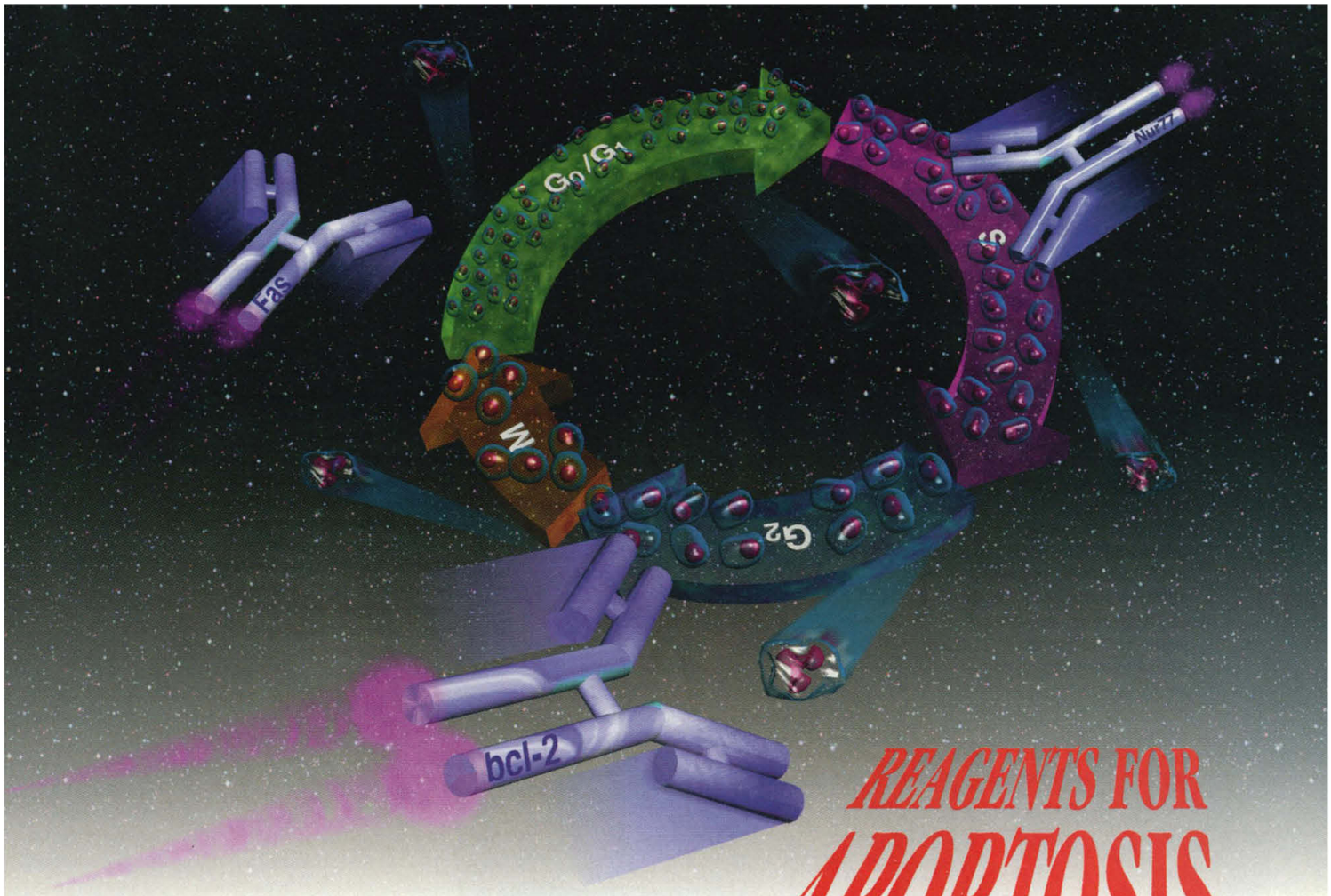

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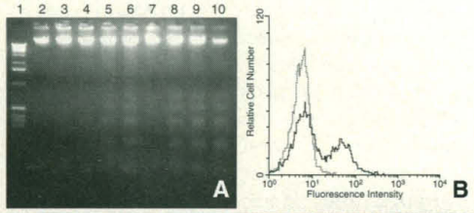

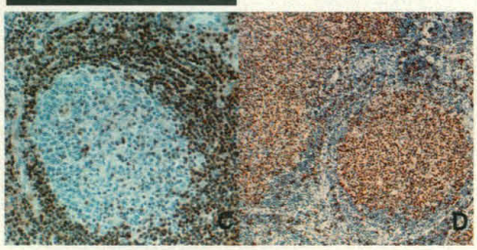

Figure A: DNA fragmentation induced by anti-mouse Fas. A28 cells were incubated at 37°C with 5ng (4,8), 25ng (5,9), and 50ng/ml (6,10) of anti-Fas for 1hr (2-6) and 2 hrs (7-10), and 50ng/ml hamster IgG (3,7). DNA ladder (1) and incubation without antibody (2). **Figure B:** Profile of peripheral blood lymphocytes stained with PE-conjugated anti-human CD95 (Fas/Apo-1) and analyzed on a FACScan™ (BDIS, San Jose, CA). **Figures C & D:** Polyclonal rabbit anti-human bcl-2. Formalin-fixed, paraffin-embedded, antigen unmasked normal lymphoid **(C)** and follicular lymphoma **(D)** tissues sections stained for bcl-2 expression using the ABC Immunoperoxidase (DAB) method. In normal tissue the mantle zone and intrafollicular region are stained, only occasional bcl-2 positive cells are seen in the germinal center. A reverse pattern of staining is observed in follicular lymphoma: tumor follicles are bcl-2 positive and few bcl-2 positive lymphocytes are observed between tumor follicles. (Hemotoxylin counterstain).

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