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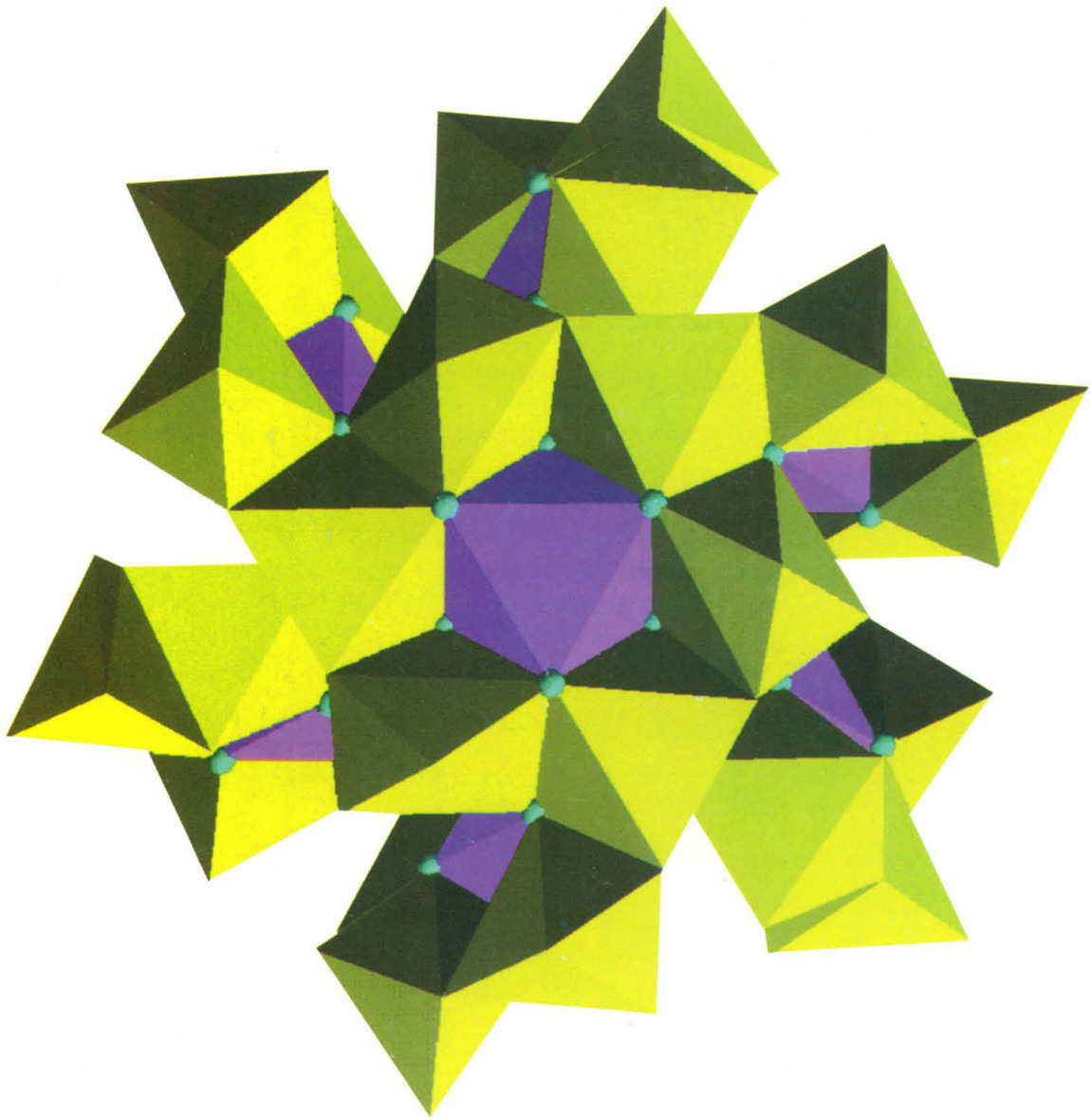

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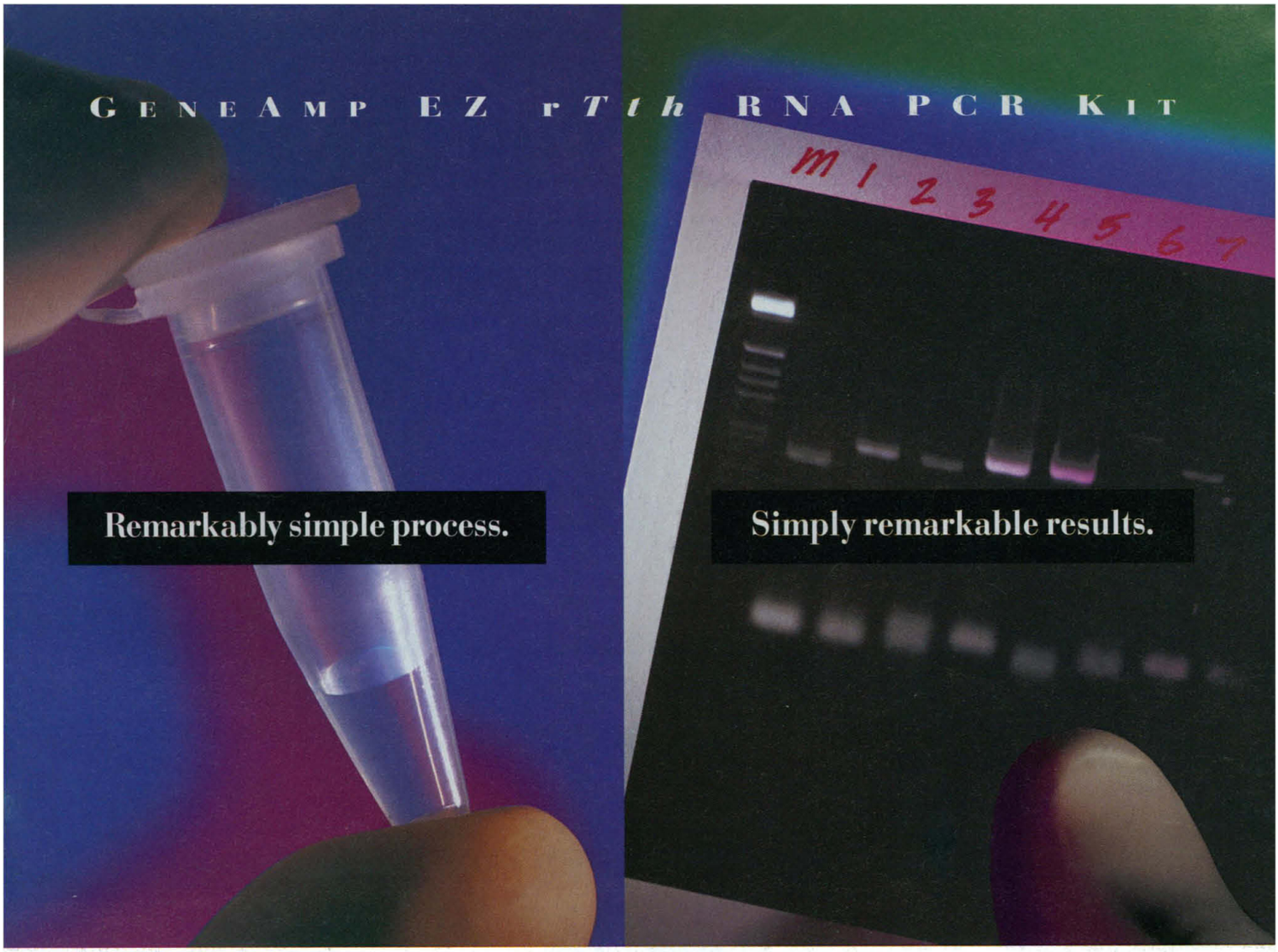

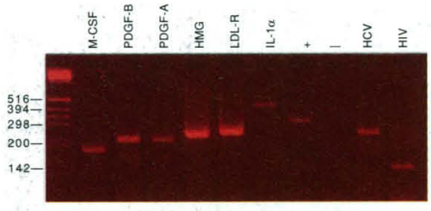

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Imagine Having The Tools To

Remember the milestones in your life. The ones that revealed your talent to create, solve, explore, and discover.

Maybe it was a special science fair project. Or a certain insight you had in a college lab. Or maybe it was a tool, like an EM, that let you really delve into what makes things tick. Somehow it all came together into a career in the sciences.

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

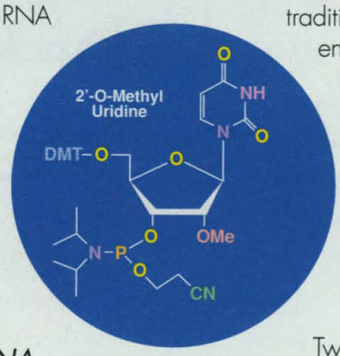
RNA

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.)



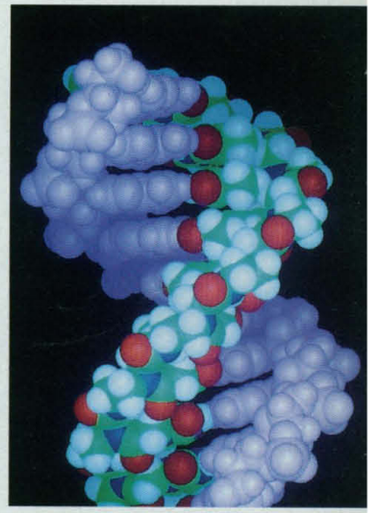
Therapeutic and diagnostic grade DNA

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.

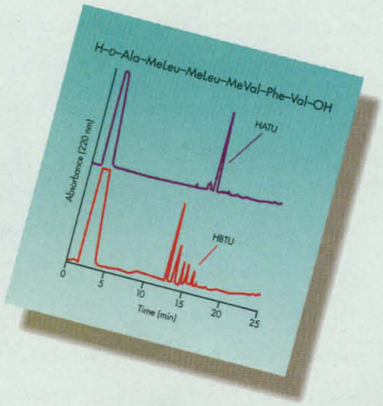
PNAs can be used in many of the same applications as traditional DNA. Their greatest contribution, however, may come from applications that can't be performed using traditional DNA oligonucleotides, such as restriction enzyme blocking, PCR clamping, and DNA mapping.

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

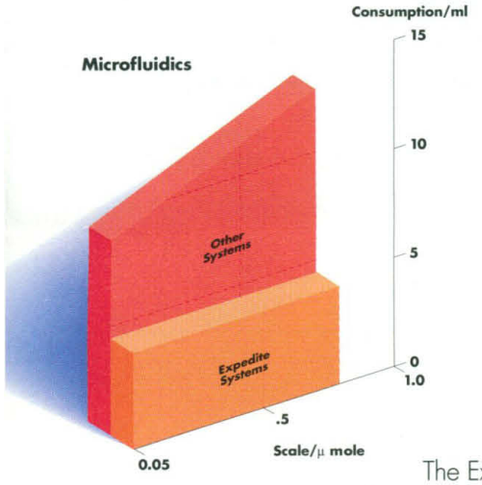
PEG-PS (polyethylene glycol-polystyrene) peptide synthesis supports from Biosearch help you achieve improved peptide purity with shorter cycle times.

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.

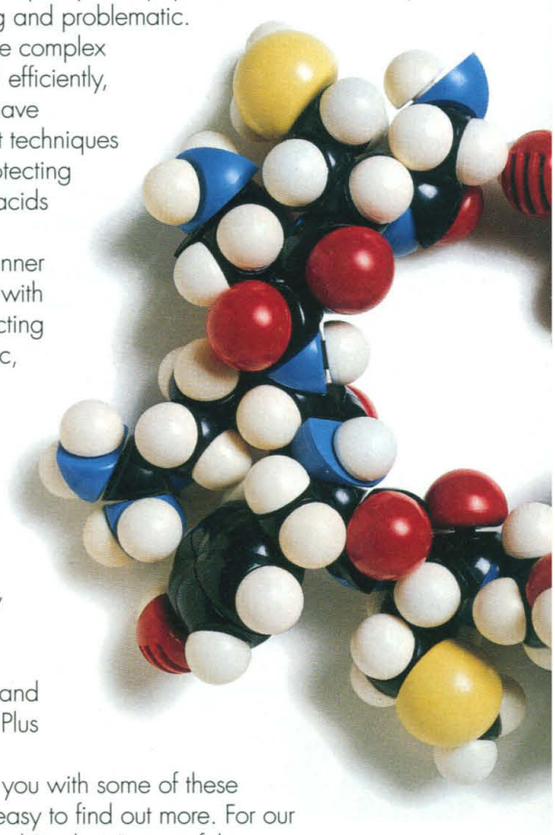
Biosearch membrane supports use a proven PTFE membrane system that directly replaces traditional controlled pore glass (CPG) supports. Membrane devices have standard luer fittings, so they can be plugged into any brand of synthesizer.

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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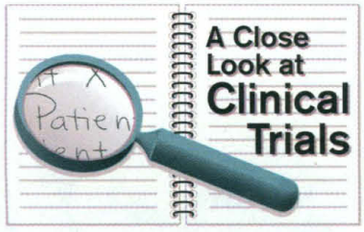


1534

1549 & 1590
The evolution of flowering plants

NEWS

SPECIAL NEWS REPORT

PERSPECTIVES

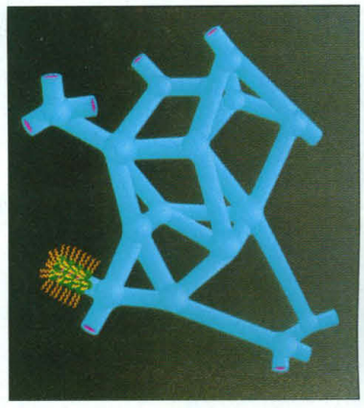
ARTICLE

DEPARTMENTS

COVER

View along the [111] direction of a thallium(III) oxide crystal. Blue-green spheres represent oxygen atoms and colored polyhedra represent different thallium sites. Nanometer-scale layered structures composed of this material are electrodeposited by pulsing an applied potential. Varying the potential can favor the formation of oxygen vacancies or cation interstitials. These materials have structural similarities to the high transition temperature superconductors. See page 1573. [Model: Robert Van Leeuwen and Jay A. Switzer]

REPORTS



1576
Water conduits in a microemulsion

Indicates accompanying feature

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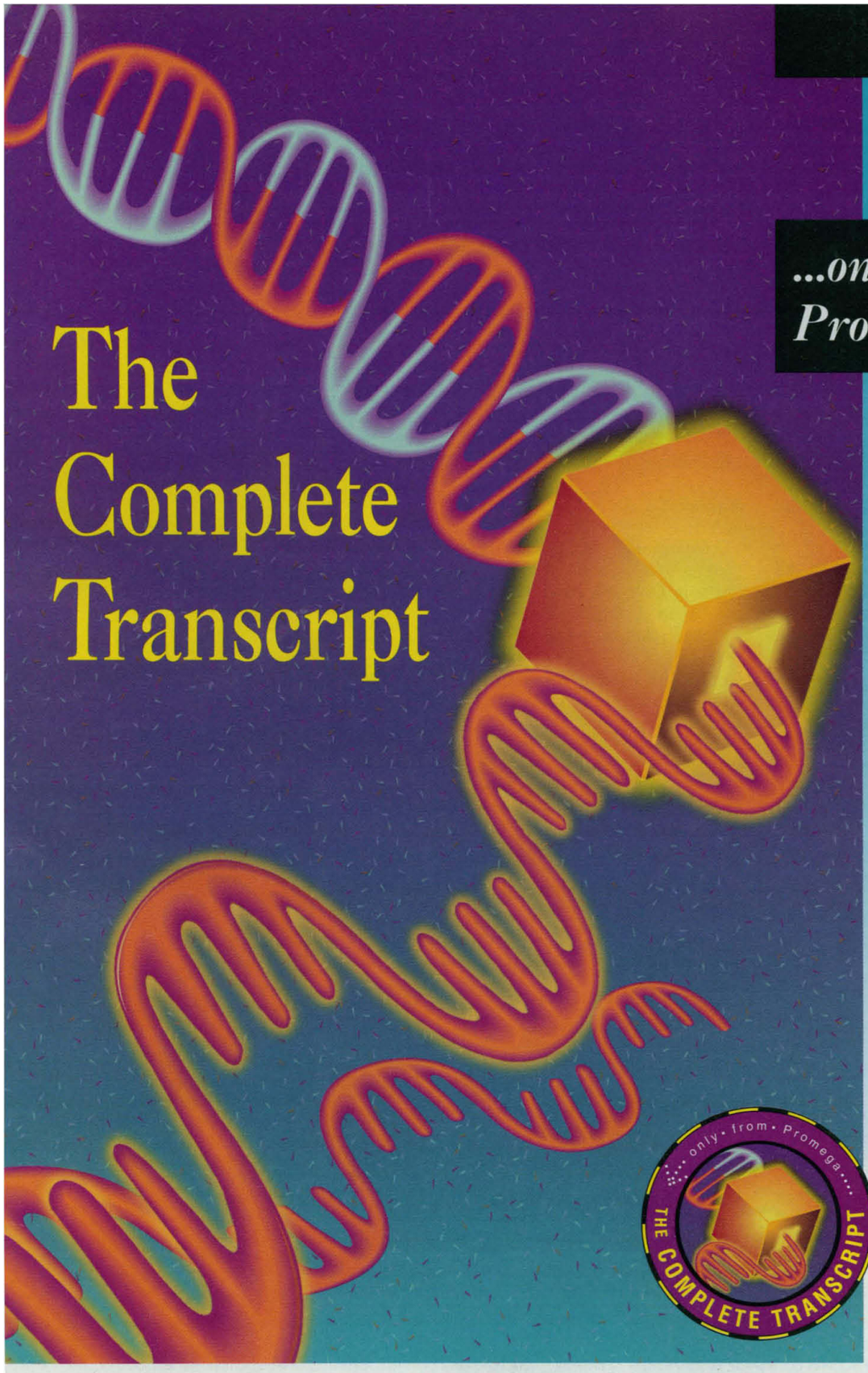

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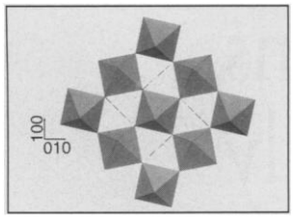
THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Trapped below

Hydrous minerals are likely to be unstable at the high pressures of Earth's interior, and the dominant mineral in Earth's lower mantle is thought to be $(Fe,Mg)SiO_3$ in the perovskite structure. Meade *et al.* (p. 1558)



used a synchrotron infrared light source to show that samples of perovskite synthesized at high pressures can contain large amounts of structurally bound hydrogen. If mantle perovskites contain comparable amounts, the lower mantle could contain about 12 percent of the hydrogen in the hydrosphere.

■

Construction zone

The design and building of new materials with well-characterized structures and carefully controlled properties continues apace. Weinbach *et al.* (p. 1566) used grazing incidence synchrotron diffraction to show how up to three layers of amphiphilic molecules may be assembled on an air-liquid interface to give crystalline polymorphs. Such polymorphs may well serve as models for nucleation and growth processes. Going into three dimensions, Walsh *et al.* (p. 1576) constructed a continuous reticulate framework of calcium phosphate from a bicontinuous reverse microemulsion. They used the organized structure of the microemulsions as a template to form a solid framework. The calcium phosphate was prepared in the aqueous phase. When the oil fraction was removed, the solid remained as a "fossil" of the aqueous phase.

■

Tyrosine kinases and SCID

A tyrosine kinase associated with the T cell receptor, ZAP70, has been identified as the genetic basis of some forms of severe combined immunodeficiency (SCID). Elder *et al.* (p. 1596) describe a homozygous mutation in the kinase domain of ZAP70 from a 1-year-old SCID patient. Almost none of this patient's T cells were $CD8^+$, and the $CD4^+$ cells present could not be activated by T cell receptor pathways. Chan *et al.* (p. 1599) describe an autosomal recessive form of SCID in which mutations in the ZAP70 gene led to an absence of detectable protein. These results suggest that ZAP70 plays a critical role in T cell development and activation.

■

Magnetic imaging

A force microscope has been constructed by Rugar *et al.* (p. 1560; see news story by Service, p. 1532) that responds to modulations of forces generated from nuclear magnetic resonance of protons within a solid sample. An ammonium nitrate sample was mounted on a microfabricated cantilever arm and placed within an inhomogeneous high magnetic field. Modulation of an applied radio-frequency field then caused the magnetic moment of the proton spins to generate an oscillating force that caused the can tilever arm to vibrate at a resonance frequency. A spatial resolution in one dimension of 2.6 micrometers could be achieved.

■

Recycling reactions

Methane in natural gas could form an abundant feedstock for fuels and polymers provided that efficient routes are found to couple the molecules by forming carbon-carbon bonds. Jiang *et al.* (p. 1563) report on an oxidative route that forms ethylene over silver-based catalysts with overall yields as high as 85 percent. They overcame one of the difficulties in such an approach, oxidation of the ethylene, by trapping it in a molecular sieve and recycling the unreacted methane.

■

Ties that bind

Binding of biomolecules by proteins can show a wide range of specificity. Tame *et al.* (p. 1578) determined the crystal structure of the OppA protein, which binds a wide variety of short peptide ligands in the periplasm of bacteria. Modeling studies reveal that the peptide is buried in the protein's interior, a mode that normally confers specificity. However, OppA binds the ligands through their similar main chains and provides large hydrated cavities to accommodate the various side chains. In the family of lentiviruses, of which HIV is a member, a trans-activator (Tat) protein binds to RNA and regulates transcription of the viral DNA in a complex fashion. Willbold *et al.* (p. 1584) determined the solution structure of Tat from equine infectious anemia virus, also a lentivirus. Basic amino acids from three different domains of the protein are positioned on a hydrophobic core to form an RNA binding site. This structure explains previous results in which amino acids not directly interacting with the nucleic acid were still found to be important for proper recognition.

■

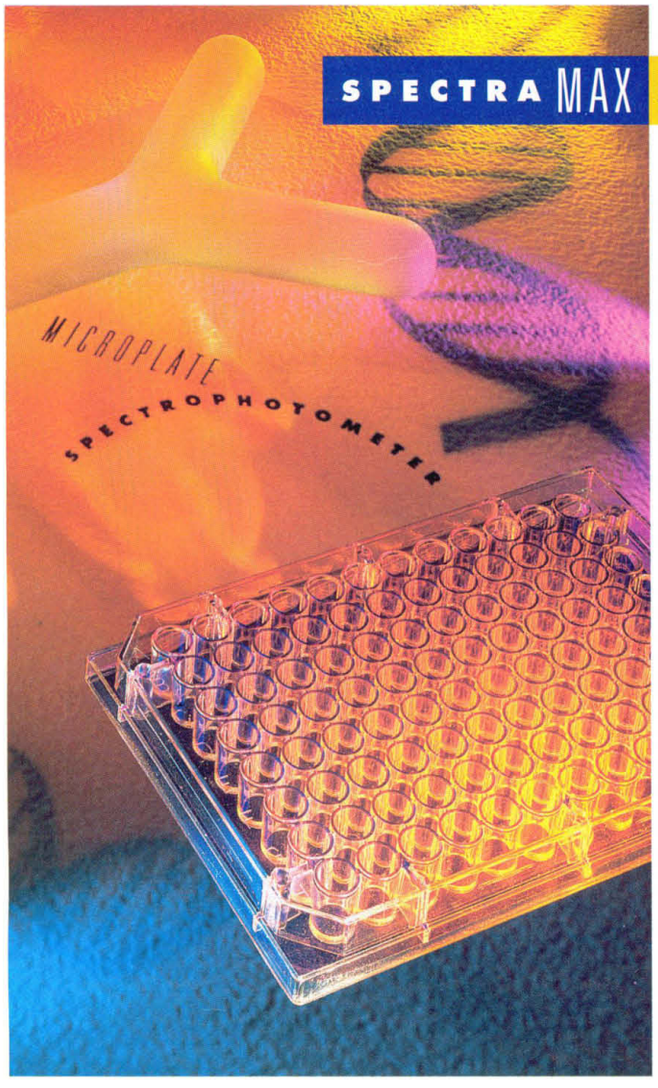
More than a G protein

Many hormone receptors activate intracellular enzymes through heterotrimeric guanine nucleotide binding proteins (G proteins). The α_1-adrenergic receptor activates the G protein G_q. Nakaoka *et al.* (p. 1593) purified and cloned a guanosine triphosphate–binding protein they call G_h. Like the activated form of G_q, activated G_h can stimulate α phospholipase C. However, the α subunit of G_h is unusually large and is similar in sequence to mammalian transglutaminase type II. This activity of G_h can be inhibited by activation of the α_1-adrenergic receptor, suggesting that receptor activation may switch the function of G_h from transglutaminase to signal transducer.

■

Signal crossing

During development, connections between sympathetic neurons and their target tissues are mediated by neurotransmitters. Cell culture studies by Habecker and Landis (p. 1602) reveal that synapses between sympathetic nerves and sweat glands in the rat form through a series of signaling and differentiation steps. The neurons making the connection initially use norepinephrine as their neurotransmitter, and their release of catecholamines stimulates the release of a sweat gland factor from the glands. This factor acts as a cholinergic differentiation factor for the neuron, which then switches to acetylcholine as its neurotransmitter. Release of acetylcholine then stimulates maturation of the sweat gland.



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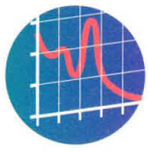
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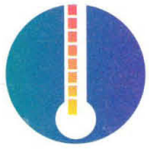
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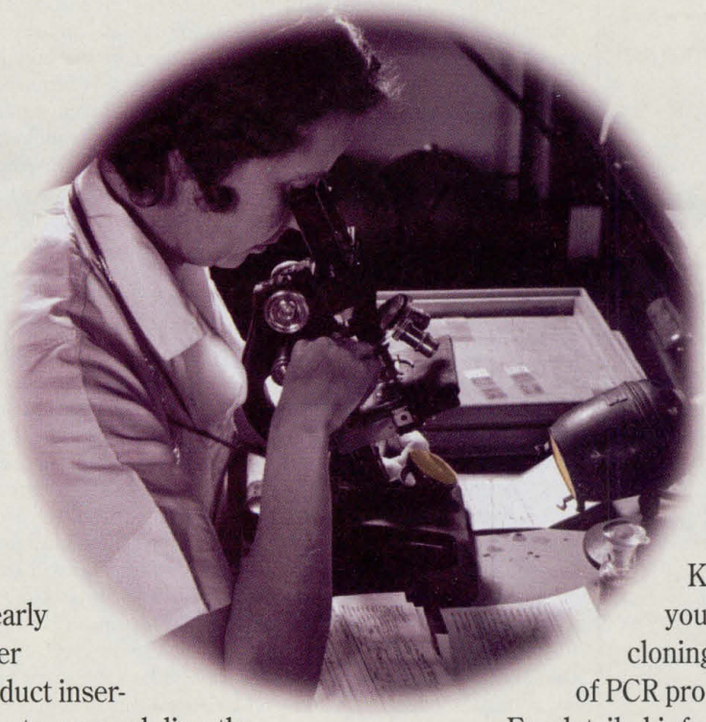

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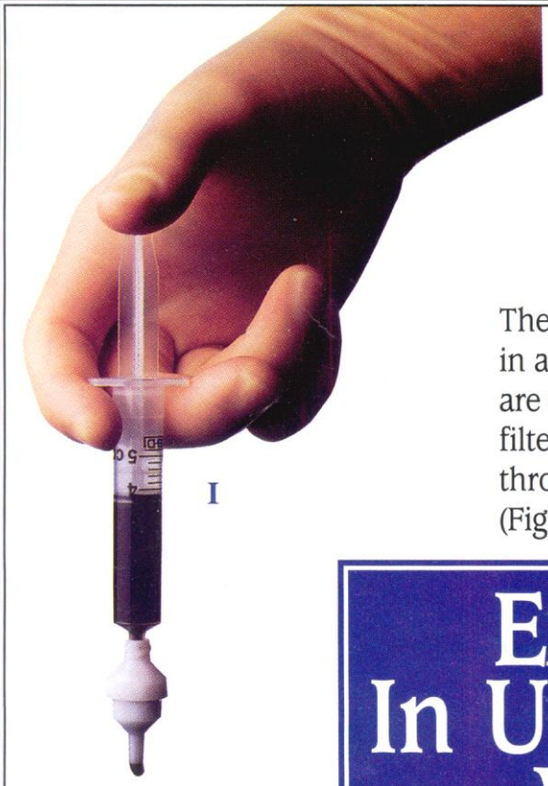

I

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II

The blood sample is placed in a syringe. The white cells are adsorbed by the Leukosorb filter as the blood passes through the fibrous matrix (Figure I).

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The process is now completed. The resulting DNA lysates can be used directly for hybridization or for PCR amplification (Figure III). Total time from start to finish is less than one hour. For a free sample pack, contact Pall at one of the locations listed below.

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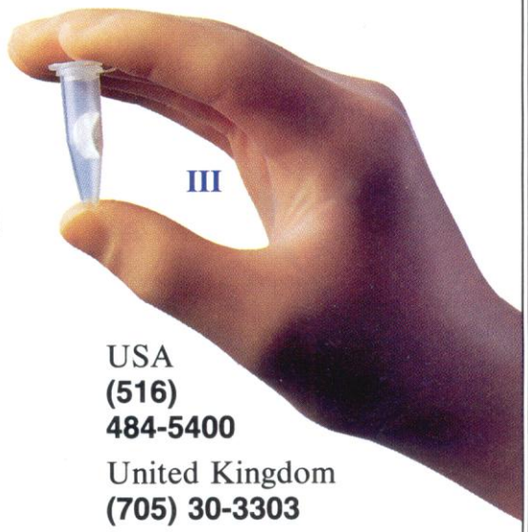

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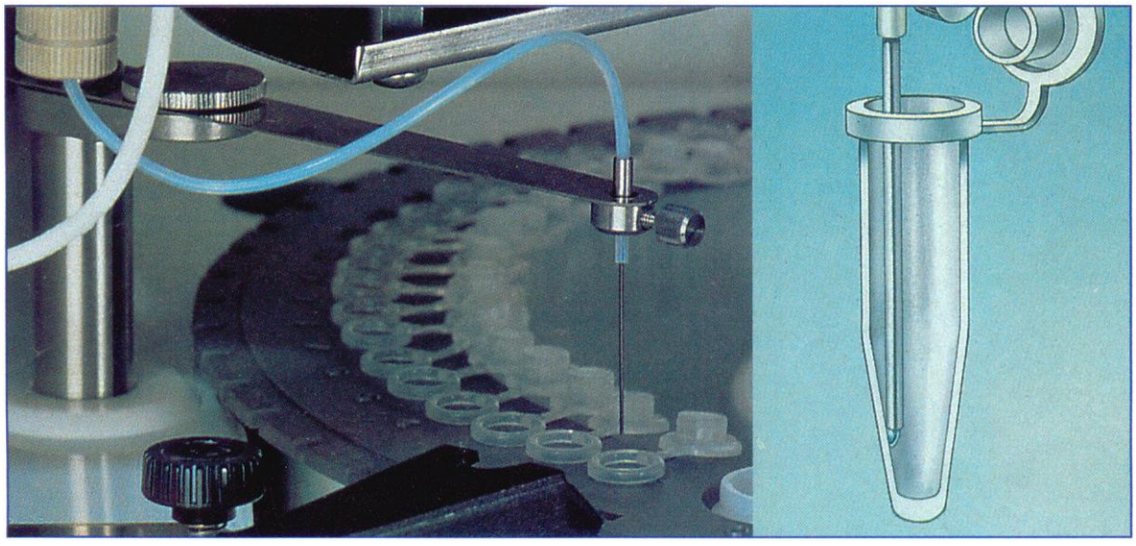

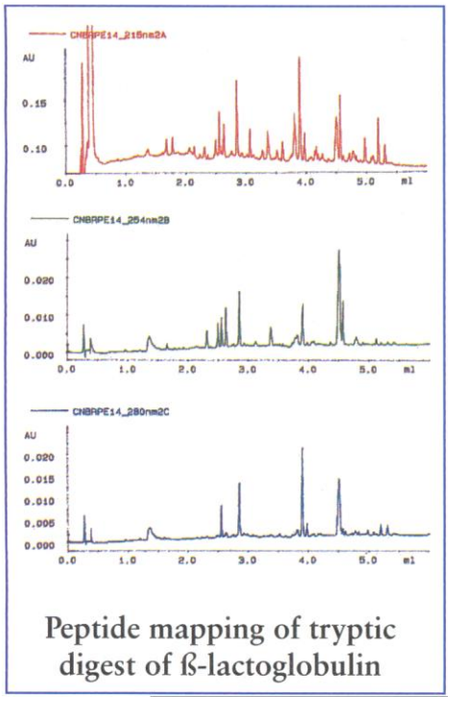

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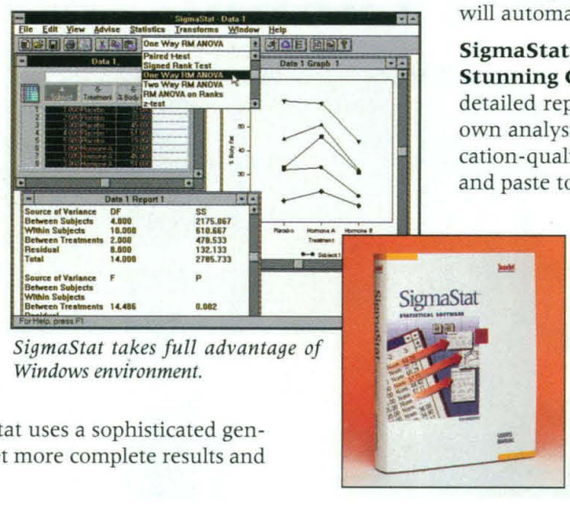

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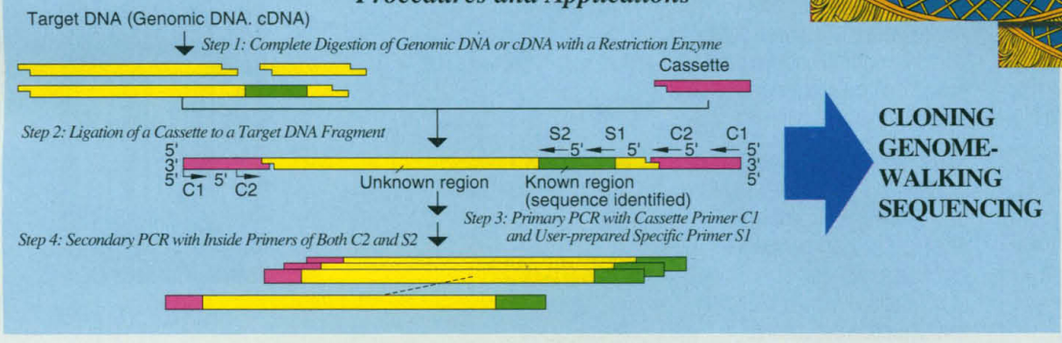

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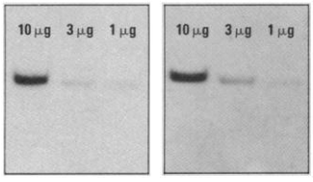

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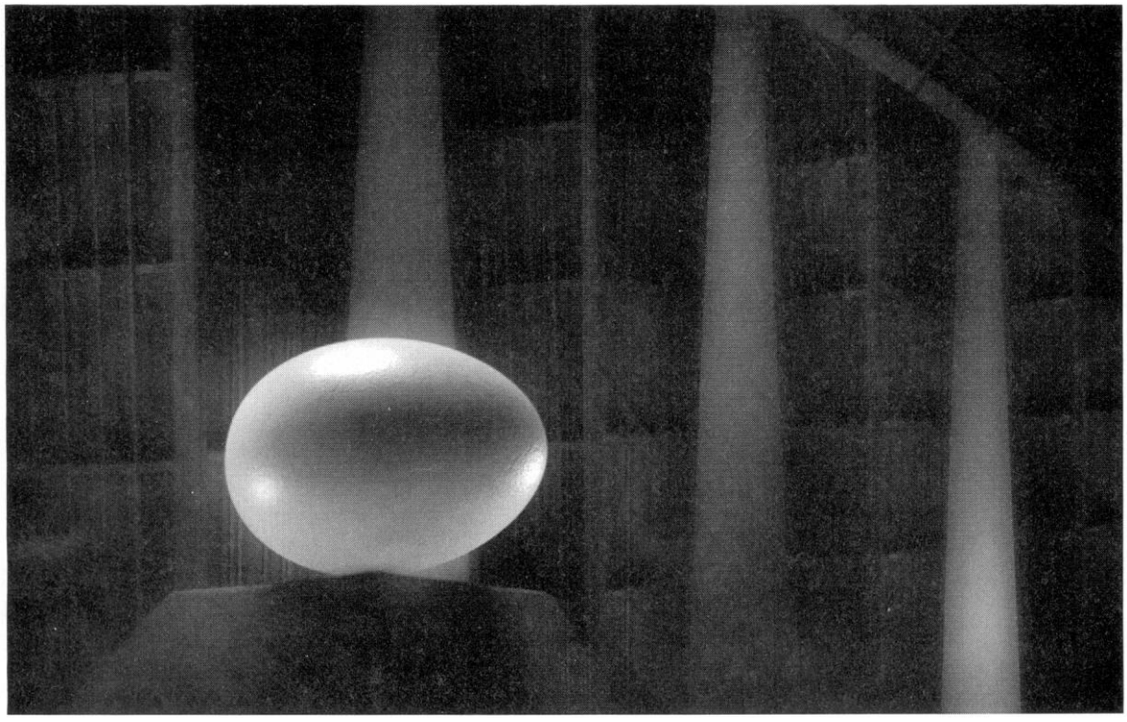

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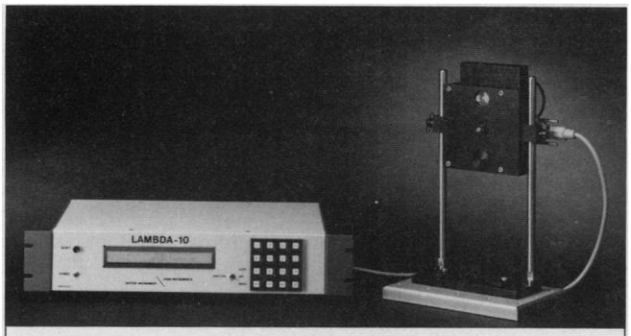

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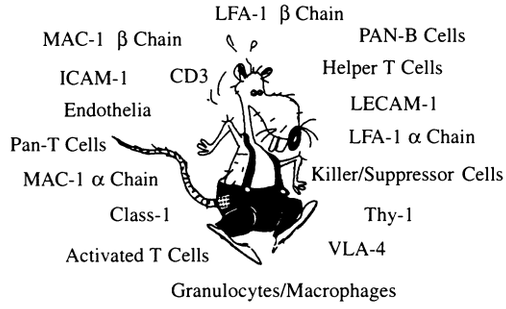

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