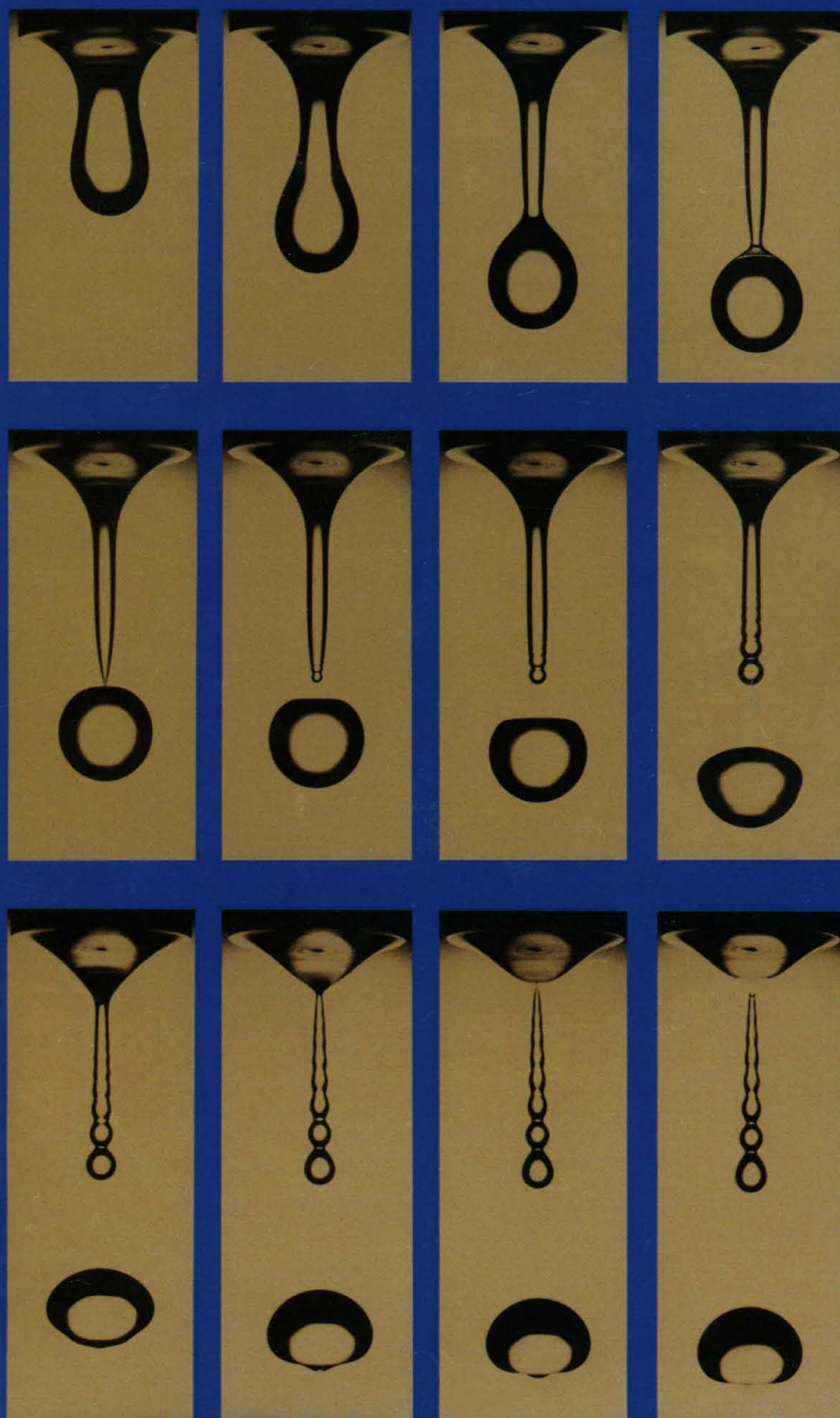


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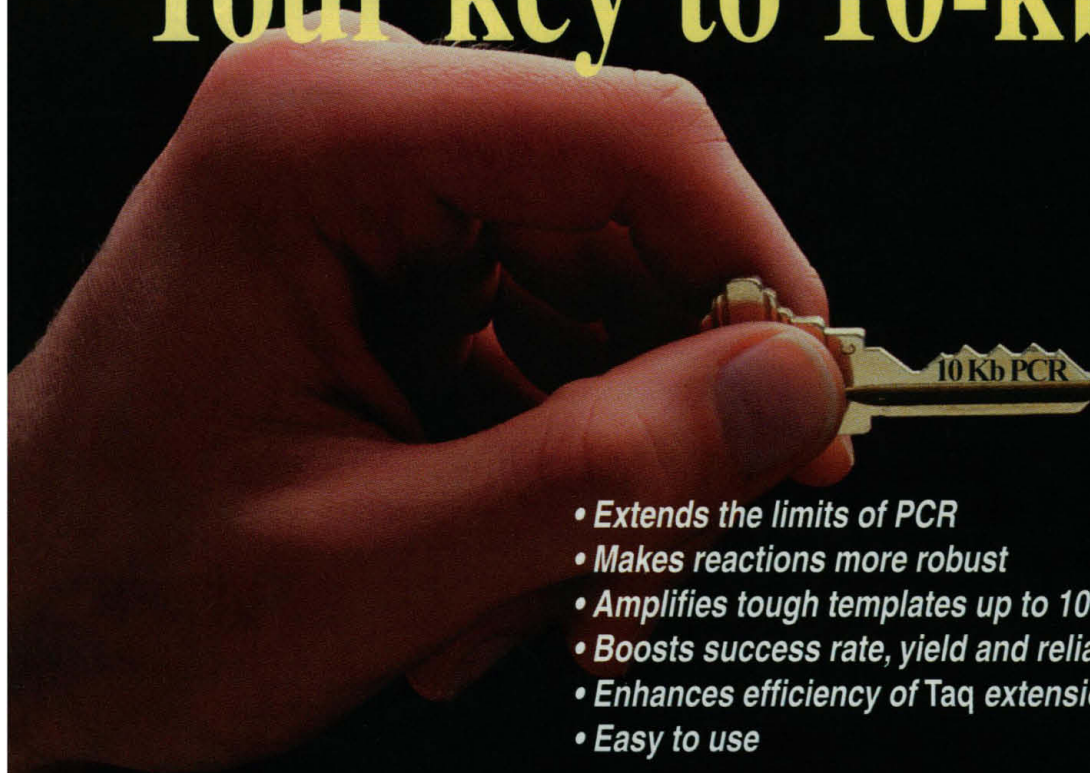
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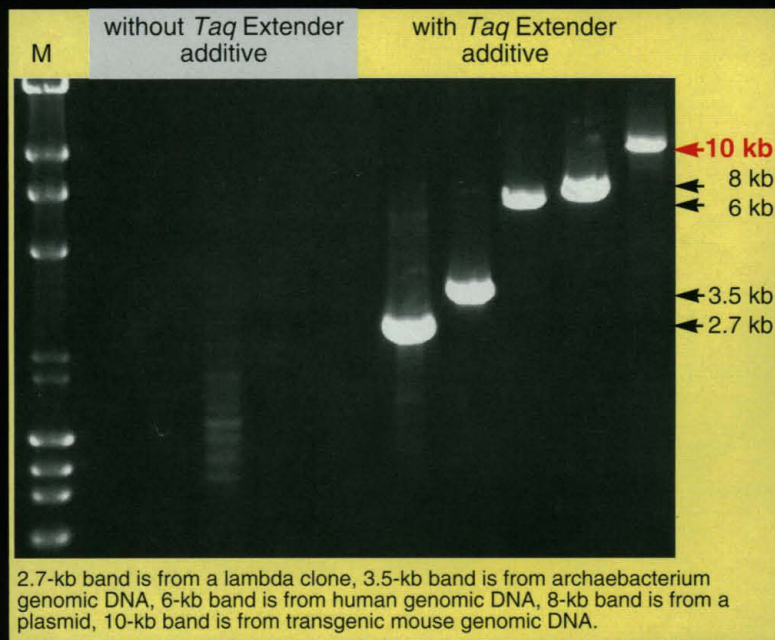
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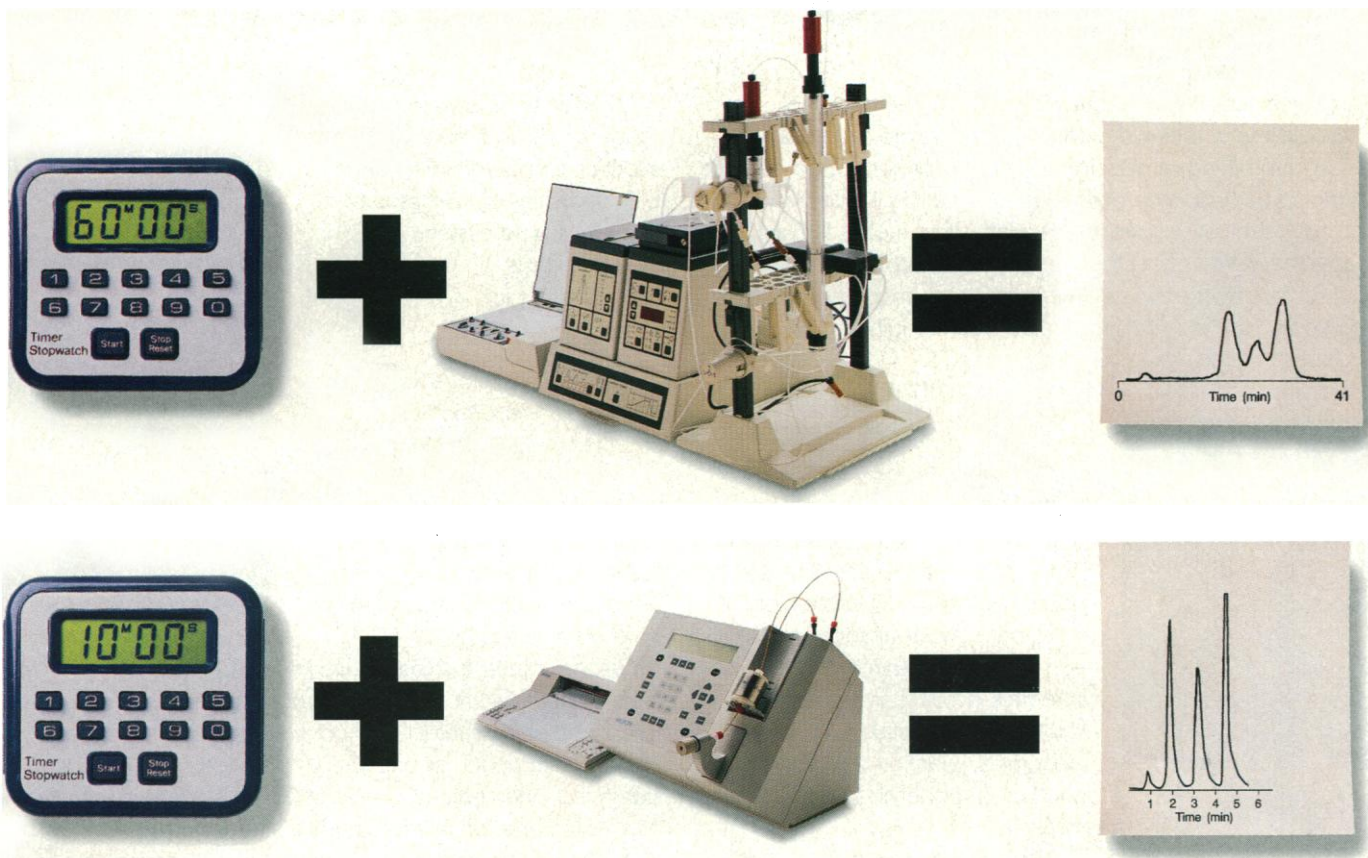
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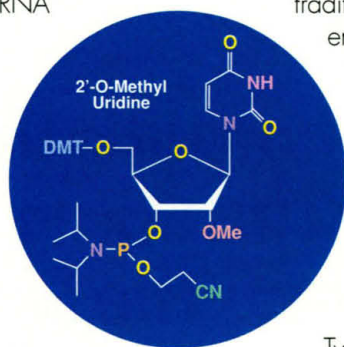
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RNA oligomers have shown promise in therapeutic and diagnostic applications, including inhibition of viral replication, cancer etiology, and gene regulation and expression.

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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.

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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.

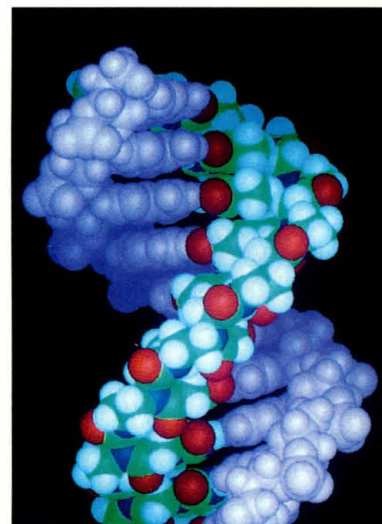
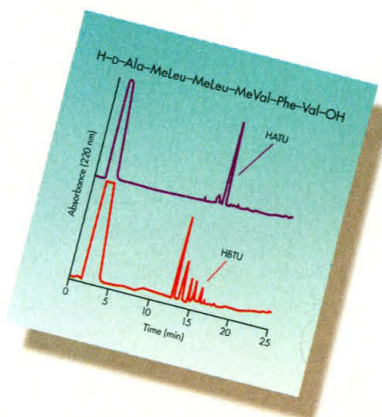
PNAs can be used in many of the same applications as traditional DNA. Their greatest contribution, however, may come from applications that can't be performed using traditional DNA oligonucleotides, such as restriction enzyme blocking, PCR clamping, and DNA mapping.

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.



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PEG-PS™ peptide synthesis supports

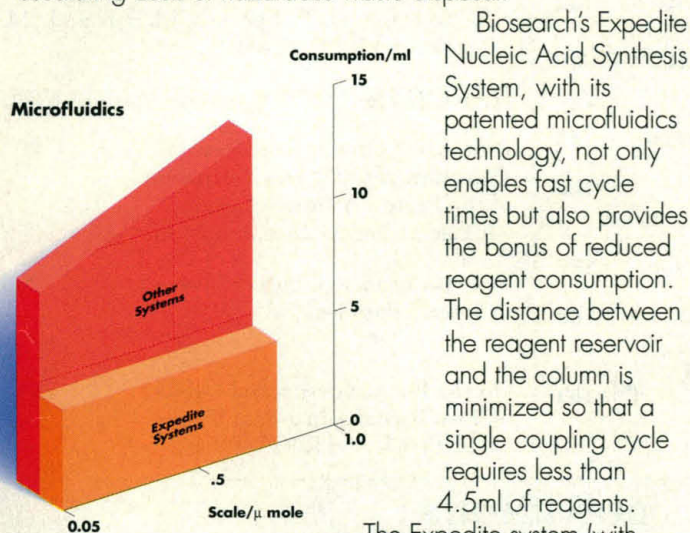
PEG-PS (polyethylene glycol-polystyrene) peptide synthesis supports from Biosearch help you achieve improved peptide purity with shorter cycle times.

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

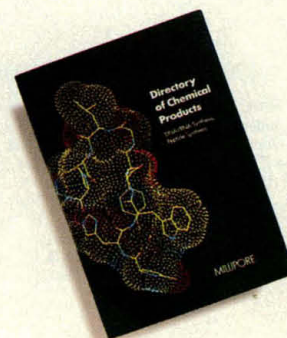
The synthesis of cyclic, branched chain, sulfonated, glycosylated, and phosphorylated peptides have traditionally been time consuming and problematic.

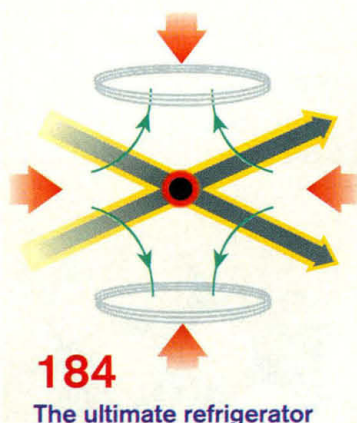
To synthesize these complex peptides quickly and efficiently, Biosearch scientists have perfected convenient techniques using allyl-based protecting groups. Allyl amino acids can be selectively deprotected in a manner which is compatible with other classical protecting groups (such as Fmoc, Boc, *t*Bu), sensitive amino acids (Met, Trp), and side chain modifications (Tyr(SO₃H)). 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.

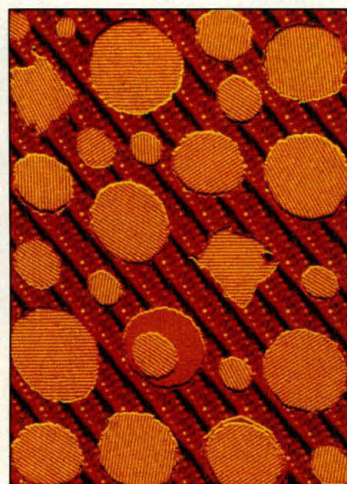
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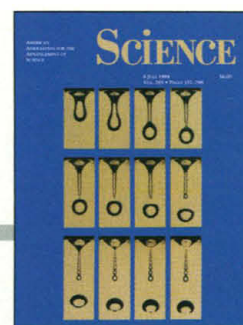
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COVER

A series of photographs showing the different stages of fission that occur when a pendant water drop falls from a circular plate 1.25 centimeters in diameter. Two examples of the drop breaking up are visible (in the 5th and 11th frames). The drop was illuminated from

behind by a strobe light with a 5-microsecond duration, and the total time lapse for the whole sequence is about 0.1 second. See page 219. [Photos: Xiangdong D. Shi, Michael P. Brenner, and Sidney R. Nagel]



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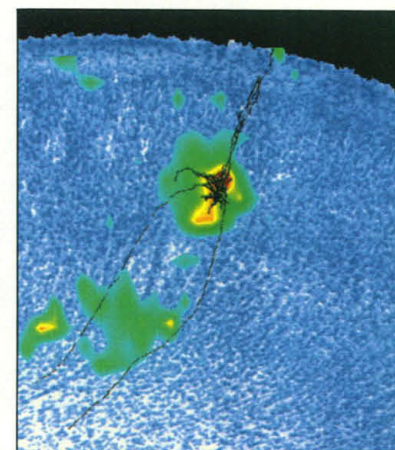
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Ozone and acids

Protonated ozone (O_3H^+) has been invoked as an intermediate in certain chemical reactions, but it has been difficult to prepare this compound. Cacace and Speranza (p. 208) used a Fourier transform ion cyclotron mass spectrometer to follow the reaction of ozone with very strong acids to form O_3H^+ . Their estimate of the proton affinity of ozone agrees well with theory.

Heavy in the heavens

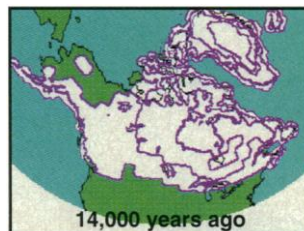
Heavy elements generated in stars must be cycled through the interstellar medium in order to end up in planets, but detecting them is not easy: Abundances are low, and the most prominent spectroscopic lines are in the ultraviolet. Cardelli (p. 209) used the Hubble Space Telescope to identify elements from gallium and germanium up to lead in interstellar gas. Comparison of their abundances with solar system values suggests that condensation of these elements onto dust grains is a more complex process than has been assumed, a point amplified in a Perspective by York (p. 191).

Superheated argument

Water vapor is the most important greenhouse gas, and over the oceans a super greenhouse effect can be imagined where higher temperatures increase evaporation, which acts to further trap energy. The degree to which temperatures are in turn ultimately regulated by formation of clouds or some other processes is controversial. Lubin (p. 224) presents recent experimental measurements of the super greenhouse effect in the western Pacific, where sea surface temperatures are the high-

Ice sheets and paleoclimates

Two key but poorly constrained variables for understanding Pleistocene climates are the volume and topography of the great ice sheets. For example, the elevation of the ice sheets likely had large effects on weather patterns. Peltier (p. 195; see news story by Kerr, p. 189) shows how globally distributed records of post-glacial sea level rise, adjusted to account for changes in the shape of the Earth resulting from melting of the ice sheets, can be used to reconstruct ice sheet topography, thickness, and volume. Northern Hemisphere ice sheets were probably thinner and stood lower with respect to sea level than previously thought.



est in the world. The results quantify the direct role that a super greenhouse effect and strong convection play in surface heating there.

Disrupting nucleation

One way to order macroscopic objects is to confine them; for example, coins tend to stack inside a glass jar. Patrick *et al.* (p. 231) show that confining organic molecules that normally form ordered surface layers in fact slows down ordering so that nucleation rates can be measured. They etched monolayer-deep surface pits or "corrals" in graphite that varied in diameter from 50 to 5000 angstroms. This surface was coated with an organic liquid crystal and the degree of ordering was followed by scanning tunneling microscopy, which monitors the first adsorbed layer. The presence of corral step edge appears to inhibit the ordering process.

Proliferation pathways

A new member of the Ras family of guanine nucleotide binding proteins that serve as molecular switches controlling nu-

merous biological processes has been cloned by Maguire *et al.* (p. 241). The Gem protein is most similar to Rad, a Ras family member that is overexpressed in muscle from patients with Type II diabetes; Gem and Rad appear to define a subfamily of Ras-related proteins. Transcription of the gene encoding Gem is transiently activated in human T cells treated with mitogens, and Gem may also be regulated by phosphorylation on tyrosine. Overexpression of Gem inhibits proliferation of both normal and transformed cells.

Painful to touch

Touching a surface made up of cool and warm bars (Thunberg's thermal grill) feels painfully hot, but the origin of this sensation has been unclear. Craig and Bushnell (p. 252) asked human subjects to rate the intensity of heat, cold, and pain sensations from warm, cool, and thermal grill stimuli. They also made recordings from three major thermosensory neurons in a cat exposed to the same stimuli. Cells responsive to cooling responses (COLD cells) and cells receptive to heat, cold, and pinch (HPC cells) were both very re-

sponsive to a cool stimulus (20°C). Addition of a warm stimulus (40°C) had little effect on output of the HPC cells but diminished the response of the COLD cells. The illusion of pain due to severe cold produced by the thermal grill is likely caused by the differential activity in the COLD and HPC neurons.

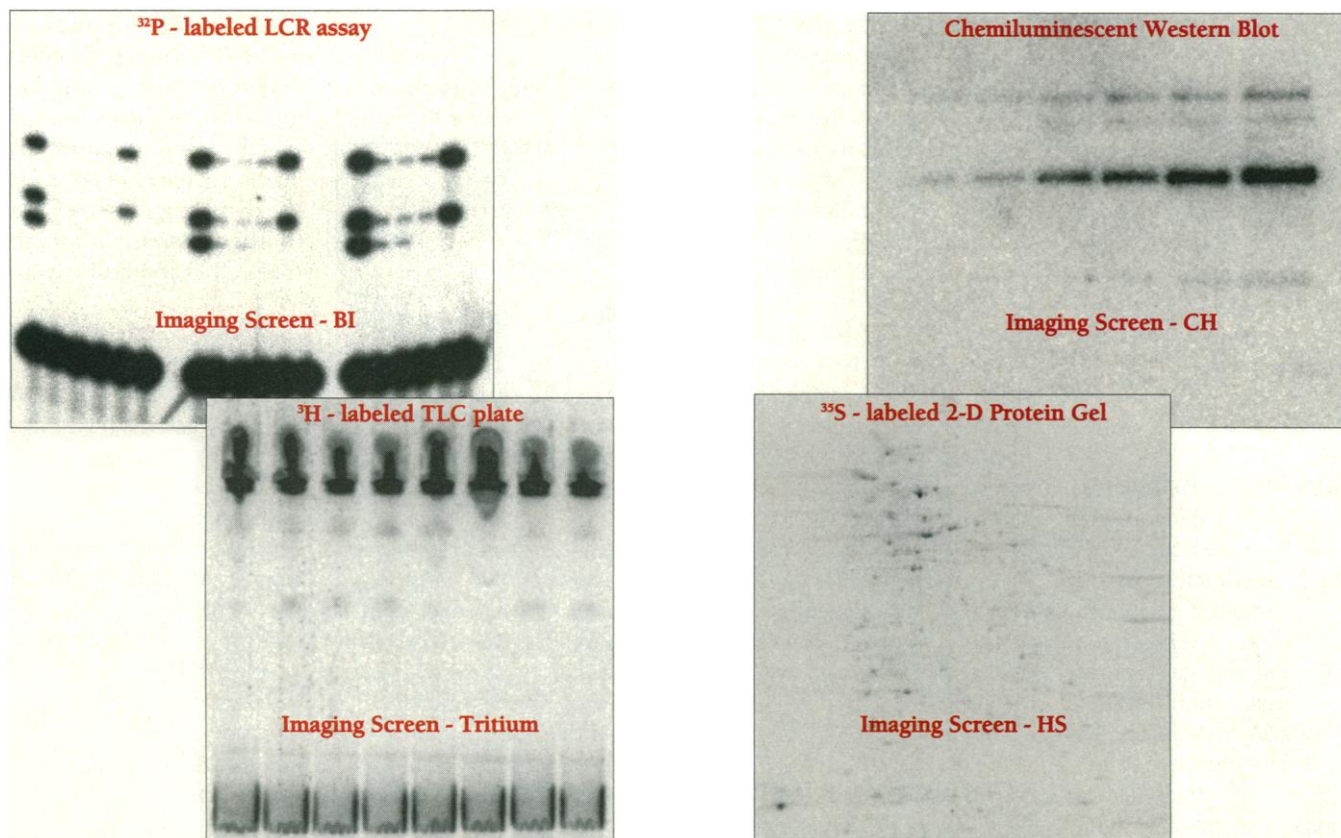
Cortical connections

Neuronal activity influences the formation, maintenance, and dissolution of synapses. The establishment of the patchy or columnar organization of neuronal connections in the visual cortex depends on receiving visual input, but the dynamics of connecting and disconnecting individual neurons has been a less tractable problem. Dalva and Katz (p. 255) used a photoactive compound and pinpointed illumination with a laser to locate functional connections between neurons in visual cortex slices taken from developing ferrets. Local or intracolumnar connections were most numerous at the time of eye opening and then appeared to undergo synapse elimination. However, the number of long-distance connections peaked later and only later became organized into a columnar array.

Doing without

Functional proteins of the class I major histocompatibility complex (MHC) are usually associated with β_2 -microglobulin. Balk *et al.* (p. 259) show that CD1d, an MHC class Ib ligand for CD8^+ T cells expressed by epithelial cells in the human intestine, lacks β_2 -microglobulin and N-linked sugars and is probably processed along a specialized pathway.

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