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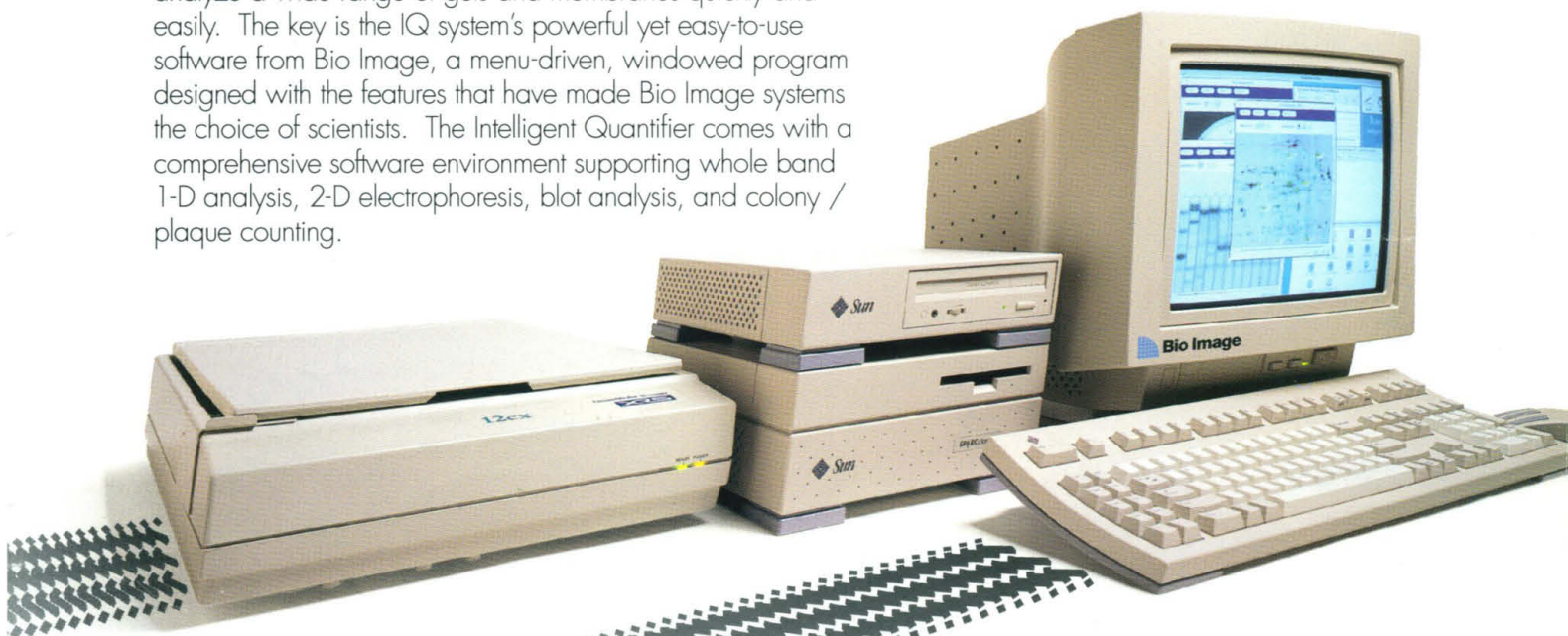


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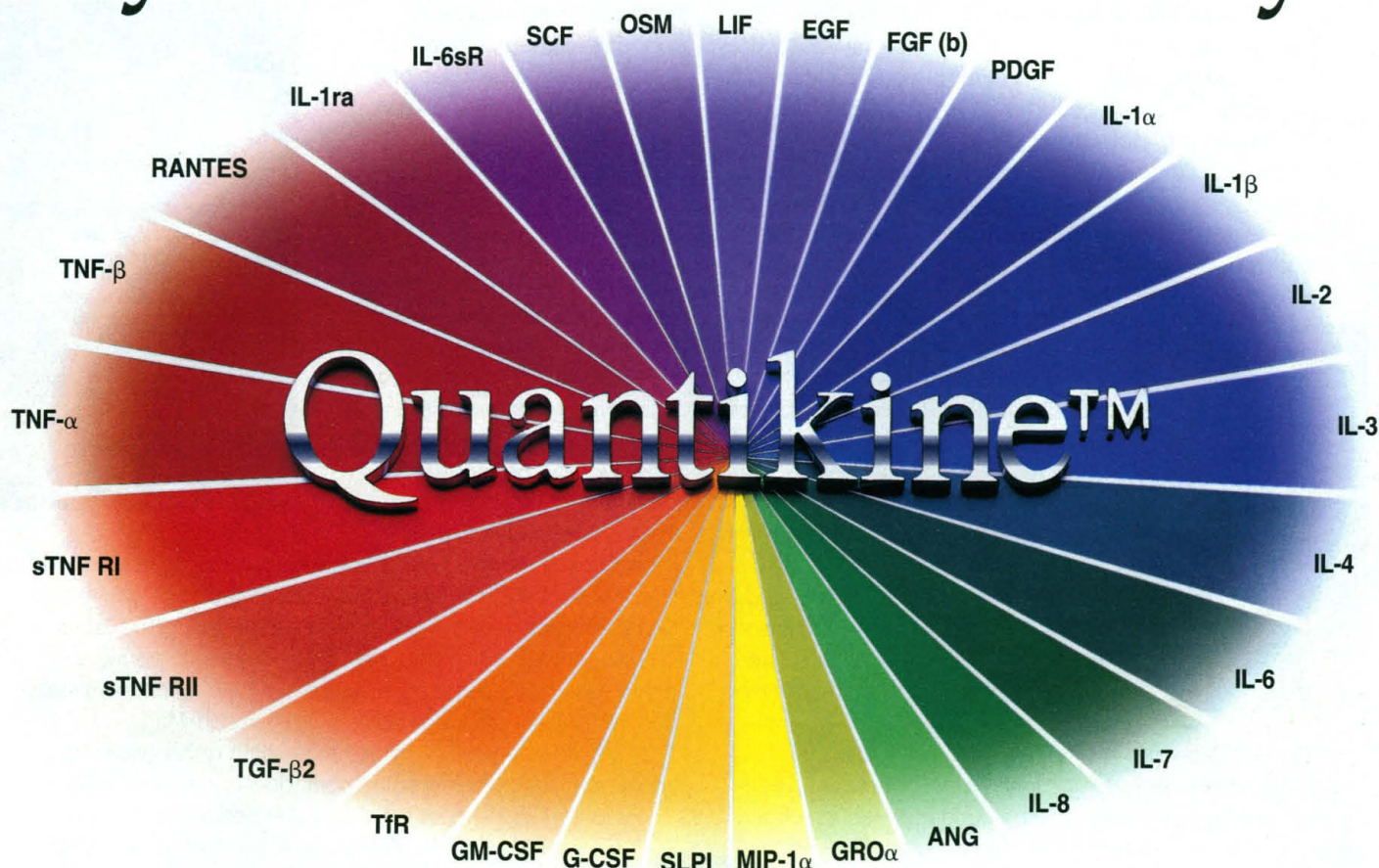
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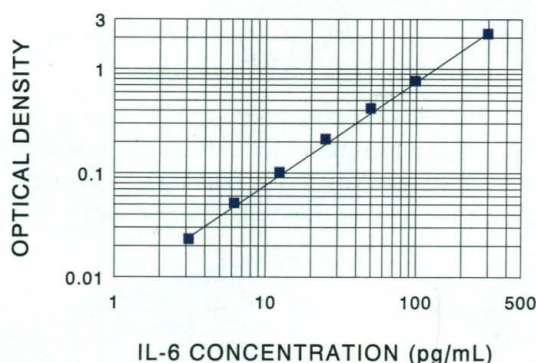
1. Daniel Cohen et al., *Cell*, 70:1059-1068.
2. Raul Cano, *Genetic Engineering News*, June 1, 1993
3. Peter Small, Stanford University, Private Communication

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RNA

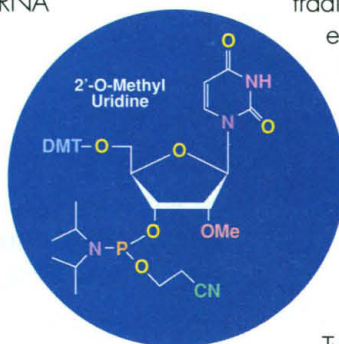
RNA oligomers have shown promise in therapeutic and diagnostic applications, including inhibition of viral replication, cancer etiology, and gene regulation and expression.

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.

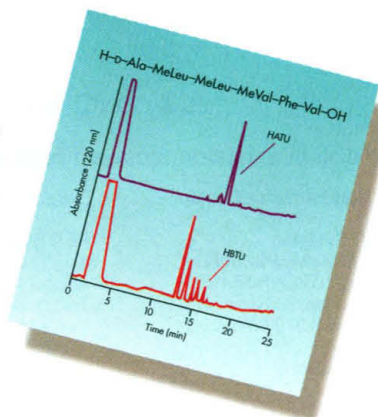
PNAs can be used in many of the same applications as traditional DNA. Their greatest contribution, however, may come from applications that can't be performed using traditional DNA oligonucleotides, such as restriction enzyme blocking, PCR clamping, and DNA mapping.

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

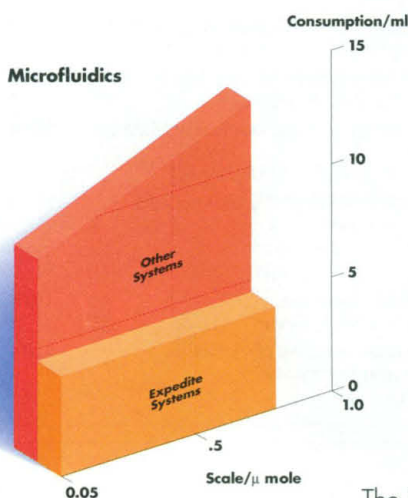
PEG-PS (polyethylene glycol-polystyrene) peptide synthesis supports from Biosearch help you achieve improved peptide purity with shorter cycle times.

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

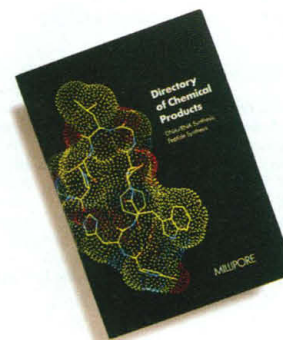
The synthesis of cyclic, branched chain, sulfonated, glycosylated, and phosphorylated peptides have traditionally been time consuming and problematic.

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(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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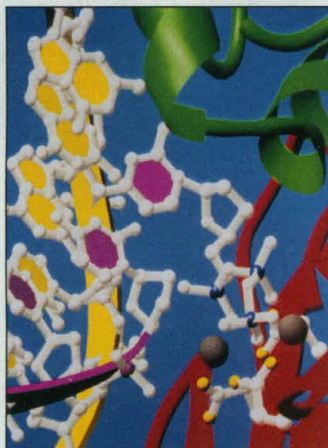
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1836

New look for
South Pole?



1891 & 1930

DNA polymerase β
structure and mechanism

NEWS & COMMENT

- NSF Eyes New South Pole Station 1836
A Design for Life in the Freezer
- AIDS Vaccine Research: U.S. Panel 1839
Votes to Delay Real-World Vaccine Trials
- French Science: In Midst of a Freeze, 1840
Science Minister Calls for Expansion
- Quantity No Longer Counts in Britain 1840
- Misconduct Panel Sets Ambitious Agenda 1841
- Crane Experiment Finally Perches 1842
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- The Inner Sanctum of the Proton 1843
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- A Dark Matter Recipe Is Tested—And 1845
Found Wanting
- A Challenge to p16 Gene as a Major 1846
Tumor Suppressor
- Cancer Research: A New Test Gives 1847
Early Warning of a Growing Killer
- Genome Initiatives Tackle 1848
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PARASITOLOGY

NEWS REPORTS

- Fighting Parasites on a Shoestring 1857
- Finding 'Sustainable' Ways to Prevent 1859
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Help Control Parasites

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- THIS WEEK IN SCIENCE 1825
- EDITORIAL 1827
Progress in Parasitology
- LETTERS 1829
Sedimentology of the K-T Boundary: H. E. Clifton
and R. H. Dott Jr. • Dioxin Effects: G. M. Reggiani
• Quantum Uncertainty Principle: No Loopholes:
J. Schwinger • History Lesson: C. A. Carr
- SCIENCESCOPE 1835

- RANDOM SAMPLES 1850
- BOOK REVIEWS 1952
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reviewed by C. Quigg • *e: The Story of a Number*,
P. Borwein • *Morphological Change in Quaternary
Mammals of North America*, E. L. Lundelius Jr. •
Reverse Transcriptase, R. A. Weiss • *Vignettes*, etc.
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- INSIDE AAAS 1962

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A false-colored scanning electron micrograph of *Schistosoma mansoni* (magnification $\times 2500$). This blood fluke penetrates the skin of humans after spending part of its life cycle in freshwater snails. Infection causes schistosomiasis, with the anemia and inflammation that result from the fluke settling in


intestinal blood vessels. The special section beginning on page 1857 focuses on the biology of parasites and the impact of parasitic diseases. The section pages are identified by an icon representing the head of the tapeworm *Taenia solium*. [Cover micrograph: CNRI/Science Photo Library/Photo Researchers, Inc.]



ARTICLE

- Low-Barrier Hydrogen Bonds and Enzymic Catalysis** 1887 
W. W. Cleland and M. M. Kreevoy

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- Structures of Ternary Complexes of Rat DNA Polymerase β , a DNA Template-Primer, and ddCTP** 1891 
H. Pelletier, M. R. Sawaya, A. Kumar, S. H. Wilson, J. Kraut

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J. D. Clark, J. de Heinzelin, K. D. Schick, W. K. Hart, T. D. White, G. WoldeGabriel, R. C. Walter, G. Suwa, B. Asfaw *et al.*

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M. E. Leonowicz, J. A. Lawton, S. L. Lawton, M. K. Rubin


- Time-Resolved Imaging of Translucent Droplets in Highly Scattering Turbid Media** 1913
R. R. Alfano, X. Liang, L. Wang, P. P. Ho


- The X-ray Surface Forces Apparatus: Structure of a Thin Smectic Liquid Crystal Film Under Confinement** 1915
S. H. J. Idziak, C. R. Safinya, R. S. Hill, K. E. Kraiser, M. Ruths, H. E. Warriner, S. Steinberg, K. S. Liang, J. N. Israelachvili

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T. Kimura, K. Nakayama, J. Penninger, M. Kitagawa, H. Harada, T. Matsuyama, N. Tanaka, R. Kamijo, J. Vilček *et al.*

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P. A. Frey, S. A. Whitt, J. B. Tobin

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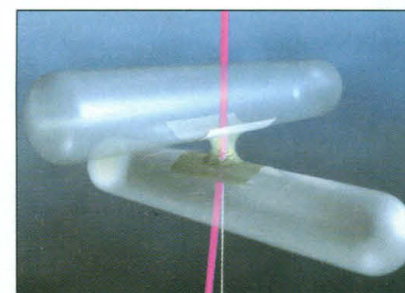
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J. J. Letterio, A. G. Geiser, A. B. Kulkarni, N. S. Roche, M. B. Sporn, A. B. Roberts

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S. Mayor, K. G. Rothberg, F. R. Maxfield



1915

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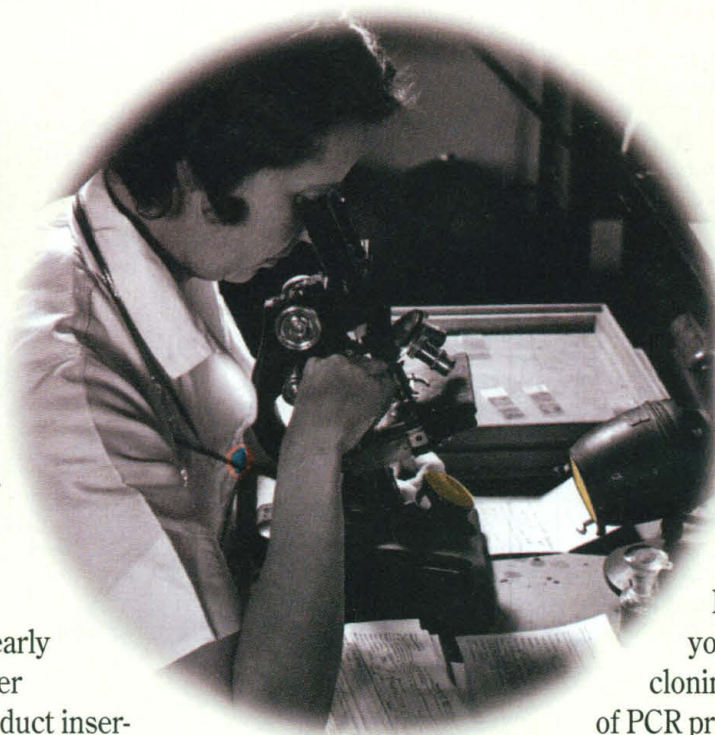
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Easier up than down

Recent modeling of mantle convection has focused on the effect of the phase transition between the upper and lower mantle on the pattern of convection. Liu (p. 1904) notes that the Clapeyron slope of the reaction changes from negative at temperatures below 1700°C to 2000°C to neutral to slightly positive at higher temperatures, which might be appropriate for regions of upwelling in the mantle. In convection models containing this effect, hot plumes ascend easily through the region of the phase transition, whereas cold downwellings are impeded at it.

■

Tool transition

A key locality for understanding the transition from *Homo erectus* to *Homo sapiens* and for determining the timing and evolution of tool use is the Middle Awash Valley, Ethiopia. Stratigraphic correlations have been hampered by faults and poor age control. Argon-argon dates on interbedded tuff and a revised stratigraphic correlation by Clark *et al.* (p. 1907) imply that the fossil transition occurred at least by 600,000 years ago here. A change from Oldowan to Acheulean artifacts appears to be associated with a change in sedimentary facies, not hominid fauna, and thus suggests that hominids used different tools in different settings.

■

Clearing the picture

Conventional optical imaging methods are difficult to use when the object of study is embedded in a material that strongly scatters light. Ultrafast lasers and optical gates make it possible to ignore the highly scattered pho-

DNA polymerase: Structures and mechanism

Although a number of DNA polymerase structures have been reported, the mechanistic steps involved in elongating the DNA strand can be hard to infer in part because these enzymes are large and have domains that perform other catalytic functions. However, DNA polymerase β (pol β) is relatively small (335 residues), highly conserved, and has no other known functions. In a research article, Pelletier *et al.* (p. 1891) present crystal structures of two ternary complexes of the 31-kilodalton catalytic domain of rat pol β with a DNA strand (an 11-nucleotide template and a 6-nucleotide primer) and a chain terminator, 2',3'-dideoxycytidine triphosphate. Three aspartate residues (Asp¹⁹⁰, Asp¹⁹², and Asp²⁵⁶) coordinate two magnesium ions and the 3'-OH group that effects the lengthening of the DNA chain. In an accompanying report, Sawaya *et al.* (p. 1930) present the structure of whole pol β enzyme and compare it with other known polymerase structures. They argue that the presence of two invariant Asp residues suggests a common nucleotidyl transfer mechanism.

tons and capture those of interest. Alfano *et al.* (p. 1913) report imaging results in which a Kerr-Fourier gating configuration was used to image translucent drops in scattering solution. In contrast to studies with solid test object, the droplets have no sharp boundaries and differ only in concentration from the background material.

■

Seeing the squeeze

When confined or put under stress, complex fluids such as liquid crystals undergo structural rearrangements. Idziak *et al.* (p. 1915) report the development of an apparatus to study such complex liquids by means of x-ray diffraction. A surface forces apparatus, which permits control of the separation of two mica surfaces to ± 1 angstrom, was modified for use in an intense synchrotron x-ray beam. Under conditions of confinement and shear, the smectic liquid crystal 4-cyano-4'-octylbiphenyl adopted distinct planar configurations, including one that is not normally seen under flow conditions.

Maternal rescue

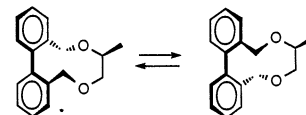
The embryonic expression pattern of transforming growth factor- $\beta 1$ (TGF- $\beta 1$) suggests that this multifunctional protein plays a vital role in mammalian development. Surprisingly, though, mice carrying two inactivated alleles of the TGF- $\beta 1$ gene appear to develop normally for the first 7 days of life. Letterio *et al.* (p. 1936) provide evidence that the survival of these "knock-out" mice can be attributed in part to maternal TGF- $\beta 1$, supplied to the pups transplacentally and in breast milk. These results illustrate that a gene knockout is not necessarily the same as a protein knockout, and thus sound a general cautionary note about the interpretation of such experiments.

■

Catalysts from RNA

Although RNA consists of only four distinct ribonucleotides, it can interact specifically with a surprisingly wide variety of small biological molecules. Prudent *et al.* (p. 1924) combined automated synthesis of one to two

hundred nucleotide-long segments of RNA and amplification of rare sequences by the polymerase chain reaction to generate a library of RNAs with randomized sequences. They then sifted through this library to find RNAs that catalyze the isomerization of a



simple, substituted biphenyl molecule. Acceleration of the reaction seems to occur through stabilization of the transition state and energy realized from binding of the substrate. That RNAs might perform such functions, in accordance with general principles of catalysis, suggests that prebiotic RNAs may have had similar abilities.

■

Foiling the clot

Proteins secreted from the salivary glands of leeches interfere with blood clotting, thus permitting the leech to suck blood from its host. These proteins inhibit binding and proteolytic reactions that would normally serve to localize and activate host processes such as platelet aggregation and generation of the fibrin clot. Krezel *et al.* (p. 1944) solved the solution structure of decorsin, one member of this group of leech proteins, that contains the sequence of amino acids arginine-glycine-aspartate that is recognized by host cell adhesion proteins known as integrins. Further, in comparison with other leech salivary proteins, a common three-dimensional structural motif is apparent even though these proteins share little amino acid sequence similarity and inhibit by different mechanisms.

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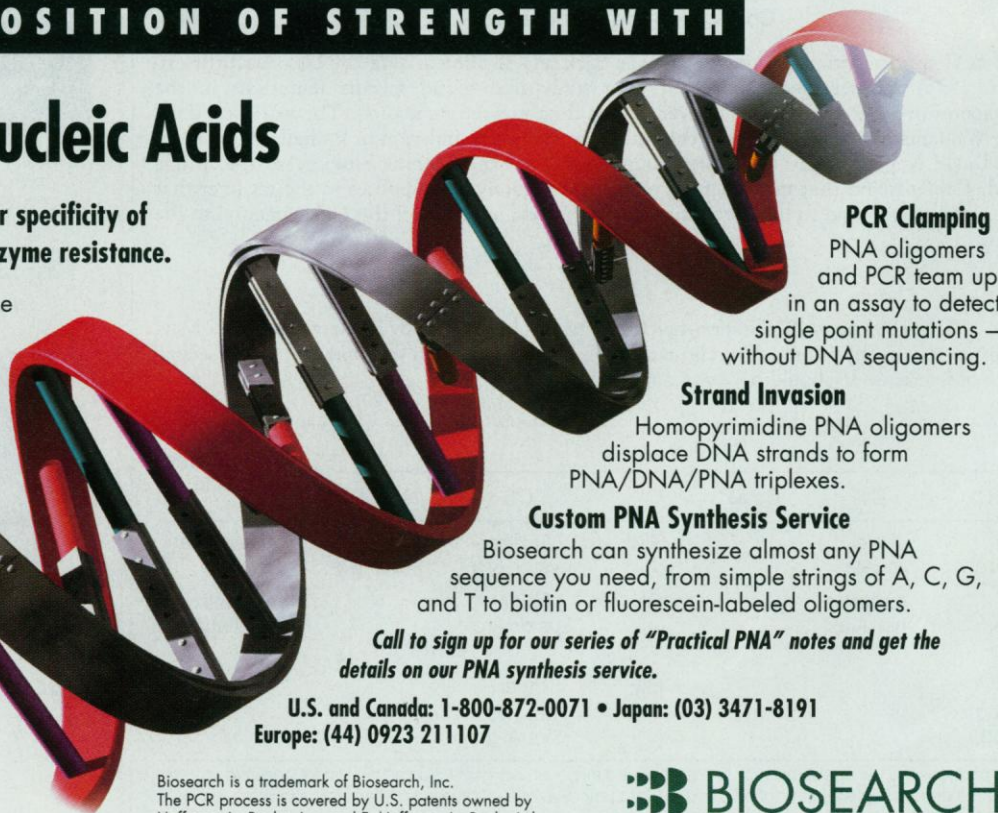
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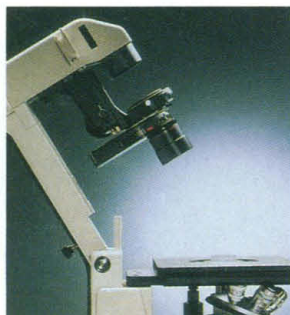
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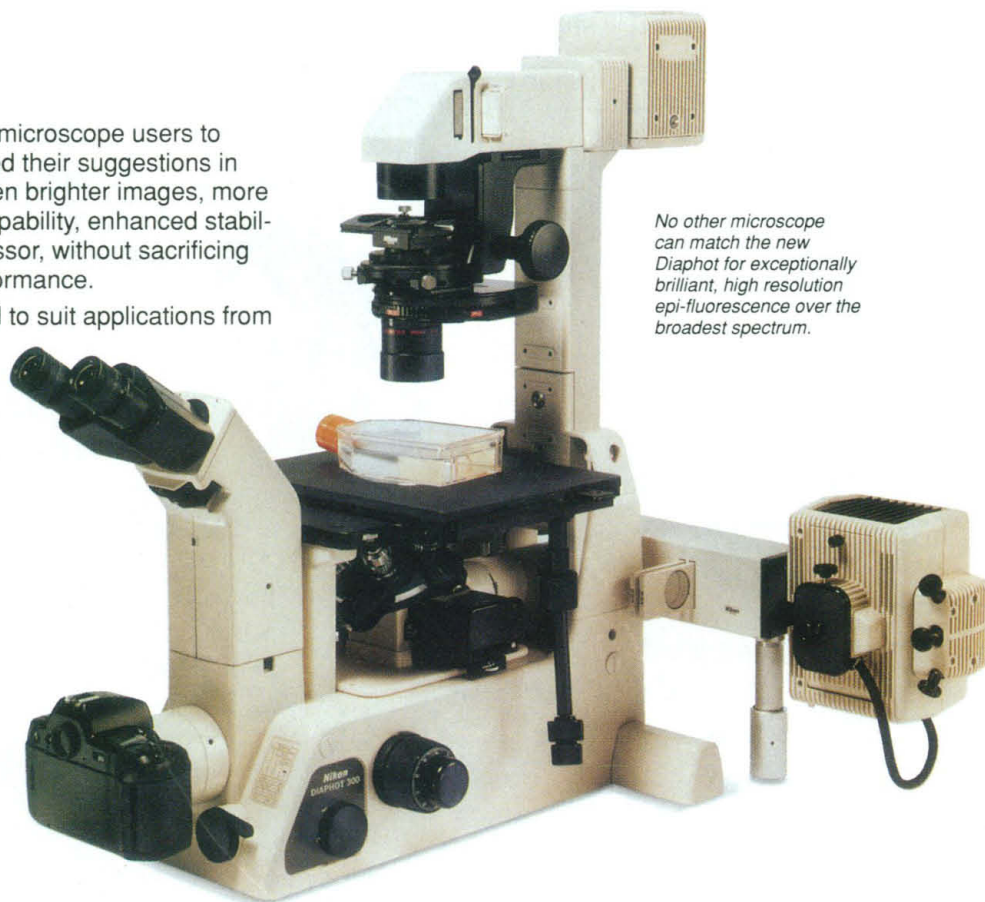
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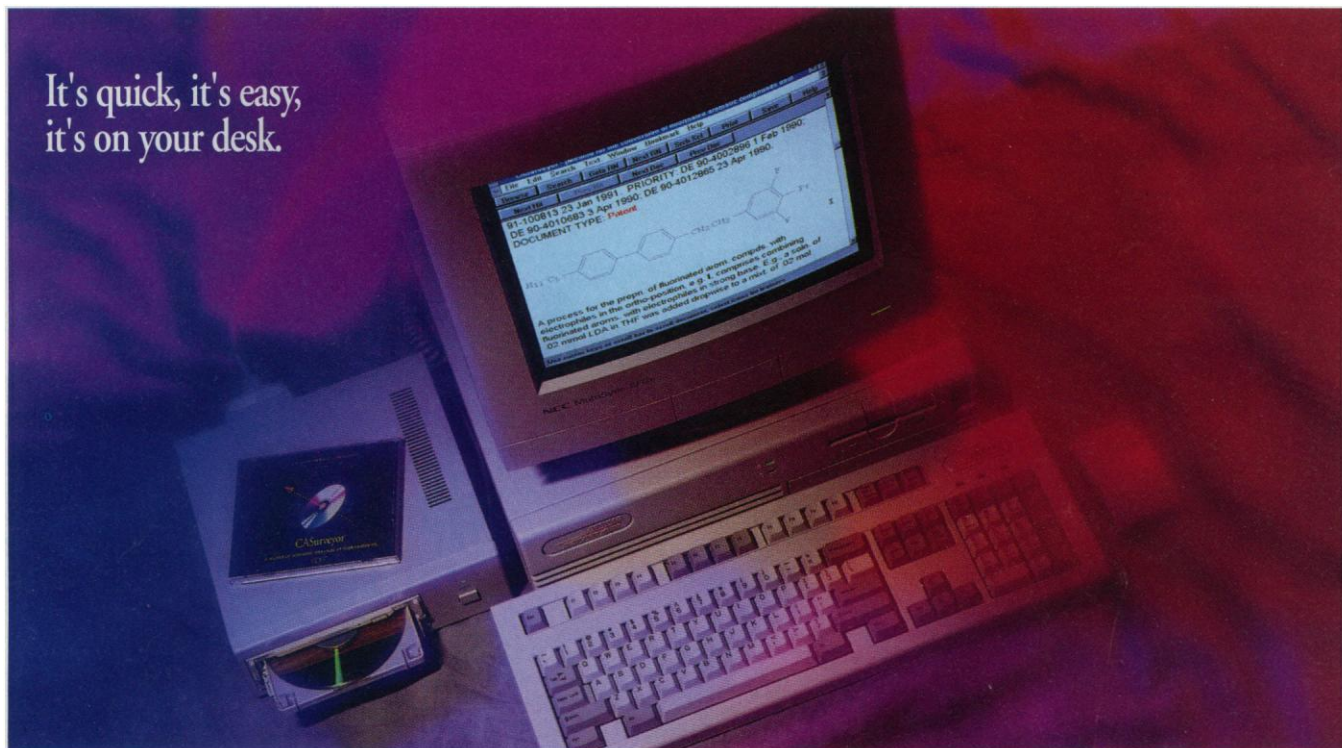
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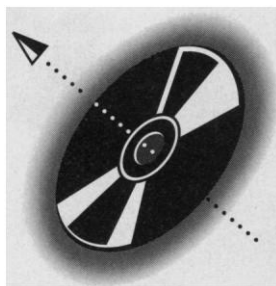
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The Space Station. It's about life on Earth.

PROGRESS REPORT

JUNE 1994

EXPRESS RACK CONCEPT PUTS SPACE WITHIN REACH OF MORE SCIENTISTS.

From Shuttle liftoff to orbit is 30 minutes or so.

But launching an experiment has been painfully slow by comparison—typically from 36 to 48 months.

One reason for the long lead time has been the physical limits of the spacecraft—the available room, power, plumbing and other features.

And part of the lengthy process has been the detailed paperwork that necessarily surrounds complex undertakings.

SPACE STATION DESIGN SAVES YEARS.

On Space Station, however, a new idea called Express Rack is targeting both types of problems and could reduce lead time for researchers to about 11 months.

The Express Rack concept removes both physical

and bureaucratic roadblocks.

In terms of paperwork, the new approach does in several pages what once took several

Middeck Locker Class Payloads

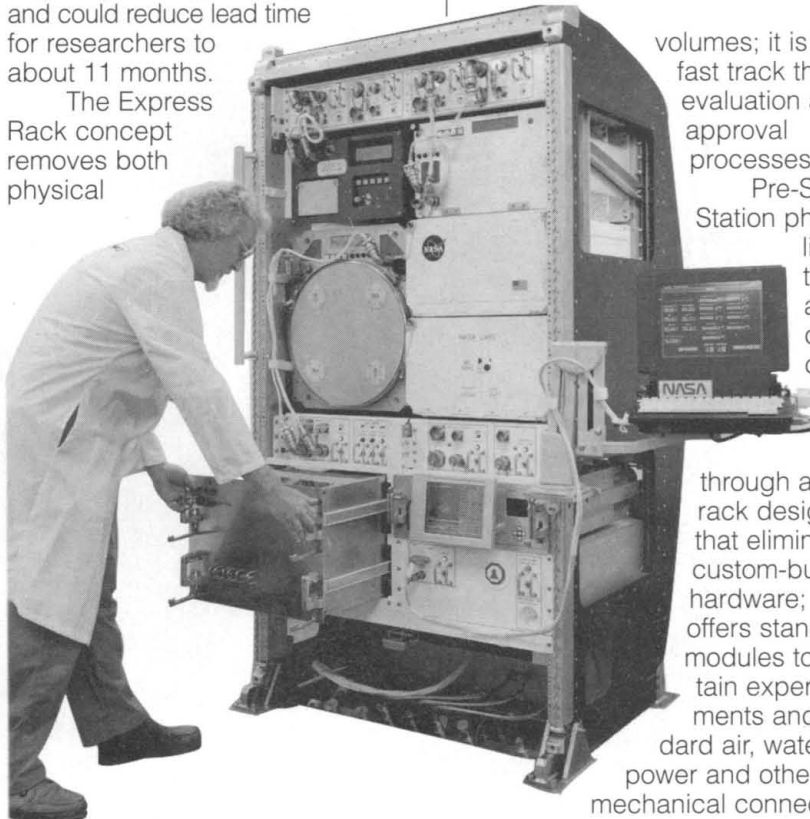
Drawer-Class Payloads

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International Standard Payload Rack

Space Station Hardware
Express Payload Integration Equipment
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Rack Essentials Package



volumes; it is a fast track through evaluation and approval processes.

Pre-Space Station physical limitations are overcome

through a new rack design that eliminates custom-built hardware; it offers standard modules to contain experiments and standard air, water, power and other mechanical connections.

LIKE AN ADJUSTABLE BOOKSHELF. WITH PLUMBING.

Space Station Express Racks will accept modules of different sizes—like a bookshelf frame designed for adjustable shelves and storage units—plus all the expected laboratory interfaces.

This flexibility allows a wide variety of experiments without requiring customization of the laboratory itself.

Experiments can be designed, installed, reconfigured or substituted in minutes instead of days.

The bottom line for science: More researchers will be able to conduct more experiments in less time—a goal that gets right to the heart of the Space Station mission.

For more information about Space Station Express Racks or the program, including details on how to use the system for a planned experiment, write to the Space Station address shown at the end of this report.

BOEING

SPACE STATION PARTNERS NOTE GAINS, CALL FOR MORE.

Space agency officials for the international partners building the Space Station recently commended NASA for improving program efficiency and clarifying the potential for including more countries in the program.

The agencies and nations include the Canadian Space Agency (CSA), the European Space Agency (ESA), the National Space Development Agency of Japan (NASDA), and Russia's Space Agency (RSA).

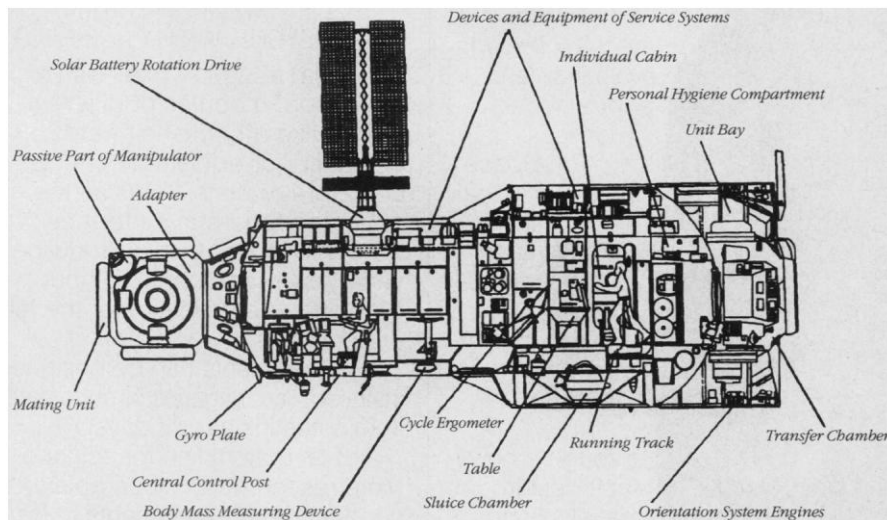
One of the key discussion points at a recent Washington, D.C., meeting was the successful Space Station System Design Review.

Progress in bringing Russia into the program as a new partner was called "remarkable."

The heads of agencies agreed the new Station configuration has several important benefits—including increased robustness, more capabilities, earlier availability to users.

They noted the importance of defining in more detail the utilization strategy for the Space Station, particularly in terms of the Russian contribution.

And all agency heads expressed determination that the international Space Station program be accomplished without further delay.



SHUTTLE FLIGHTS TO MIR PLANNED.

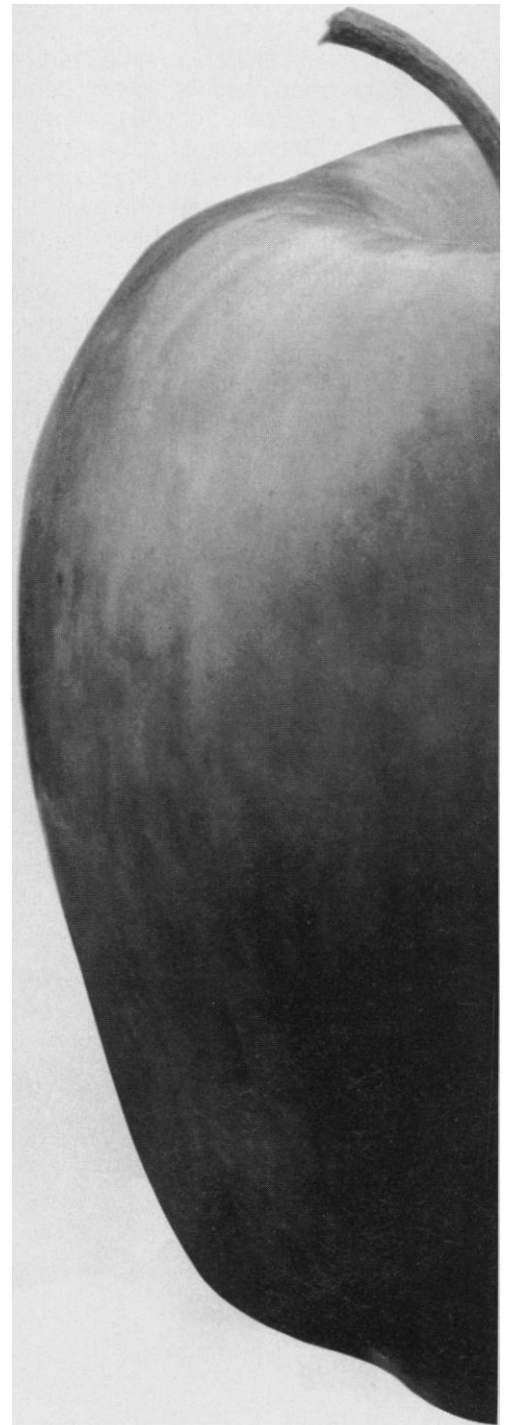
An updated Mixed Fleet Manifest from NASA details plans for ten Space Shuttle flights to Russia's Mir space station.

The flights are precursors to the assembly of the international Space Station.

The manifest calls for Shuttle

flights to Mir in May and October 1995; April, August, September and December 1996; March, July, September and November 1997.

A month later, in December 1997, plans call for the first element launch of the international Space Station.



It's about life on Earth.

*If the earth
were the size of an
apple, the life-
supporting layer
would be thinner
than its skin.*

THE SPACE STATION WILL OFFER ITS SCIENTIFIC CREW A CLEAR, UNBLINKING LOOK AT THE HOME PLANET.

We use of very little of the earth—just that thin band between the crust and the atmosphere's upper limits.

If the earth were the size of an apple, that life-supporting layer would be thinner than its skin.

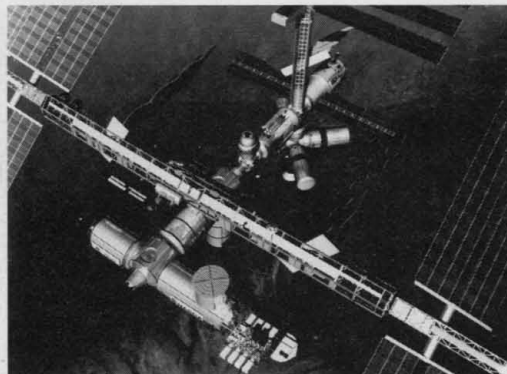
There is much to be learned by having humans observe it from a platform in space.

In natural resources research the possibilities include investigation of river basins, urban/wilderness interactions, crops and natural vegetation and surface mapping.

Ocean monitoring is possible, including mapping of surface temperatures, tracing currents, recording ice coverage.

The atmosphere can be studied in new ways, from charting the vertical distribution of gases and aerosols to observing weather patterns and storms.

And the Space Station is an ideal platform for near-Earth environmental studies, including the measurement of global radiation exposure to such events as



gamma-ray bursts.

In a different area entirely, the Space Station itself is a live-in environmental lab—a man-made ecosystem that contains the requirements of human life.

For example, its systems maintain the temperature and humidity humans require; air and water are used, then purified and recycled; all the living creatures on board are monitored—including bacteria.

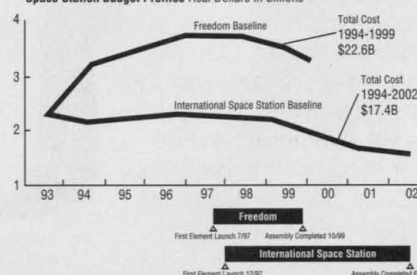
Like the home planet, the Space Station is a closed system, a small and fragile oasis in space. In learning how to live in space, we may learn a great deal more about living on Earth.

CONGRESS FREES SPACE STATION FUNDS.

Congressional appropriators have freed \$450 million of the almost \$1 billion in fiscal 1994 Space Station funding. The funding had been "fenced" last fall—held in reserve—because of uncertainty over design of the international space laboratory.

A spokesperson for Sen.

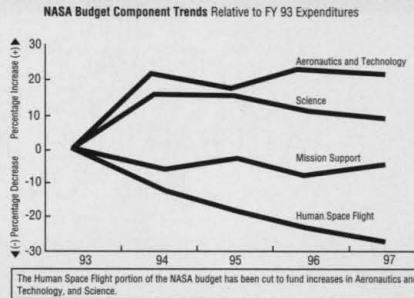
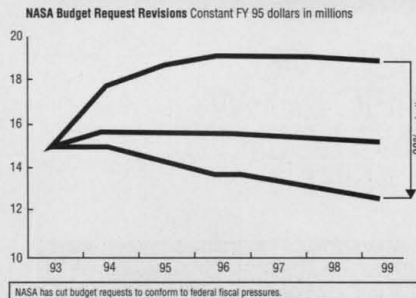
Space Station Budget Profiles Real Dollars in Billions



The International Space Station will take a smaller bite out of the NASA annual budget, cost almost \$5 billion less overall, and have increased capability.

BOEING

The Space Station. It's about life on Earth.



Barbara Mikulski, D-Md., chairperson of VA, HUD and Independent Agencies subcommittee of the Senate Appropriations committee, said the funds should be sufficient to carry the program through July 1.

At that point, the Senate and House subcommittees, with NASA appropriations oversight, will again examine the program's status.

SPACE STATION HARDWARE PRODUCTION MOVES INTO HIGH GEAR.

It's show time for workers responsible for manufacturing Space Station hardware.

The rate of production, already rapid, will increase over the rest of this year, reaching a peak in 1995.

"We're getting tons of material here now," said Jim Waterman, manager of Boeing's Space Station manufacturing facilities in Huntsville, Alabama.

And, he added, "thanks to the efforts of integrated product teams to avoid unnecessary changes in configuration, tons of hardware fabricated for Space Station Freedom can be incorporated in the new design."

Waterman estimated that 80% of all the engineering and hardware from Space Station Freedom is still usable.

In locking down the Space Station program, integrated product teams not only made the most of work done earlier, but also found more efficient ways to move forward.

An example: Several major steps in the integration of Space Station nodes were

combined, shaving as much as a year of flow time.

A quick overview of current hardware progress:

Node—Aluminum panels have been formed, welded and trimmed for the connecting node structural test article.

Common Module—The design has been changed to increase skin panel thickness from 1/8 to

3/16 inch. Waffle skin panels are being machined now; the module will be formed and welded by year end. Habitation and laboratory modules are 95% common; a single shell will be used to test and verify structural qualification for both.

Composite Racks—

A qualification rack is ready; flight racks are being manufactured at a rate of two per month.

Hatch Assembly—

Six will be assembled by year end; qualification tests begin in August.

Radial Ports—Two of four are complete.

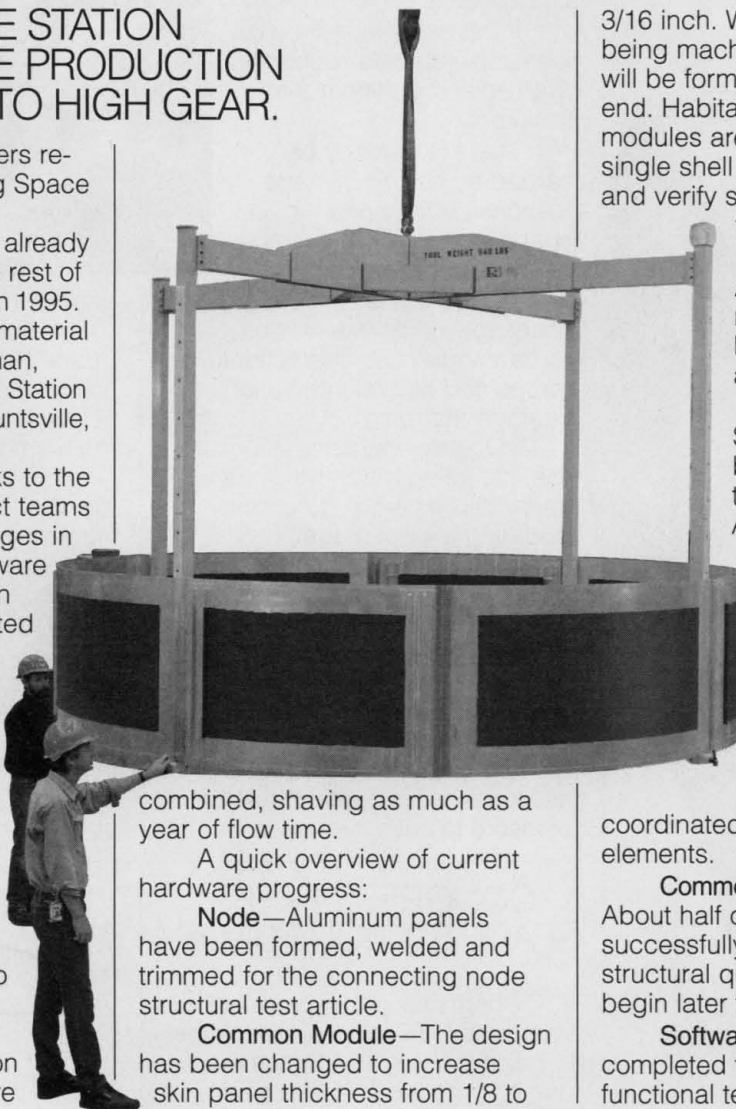
ECLSS—Environmental Control and Life Support System components are in qualification tests; ECLSS

functions are being coordinated with Russian Mir 2 elements.

Common Berthing Mechanism—

About half of the testing has been successfully completed; major structural qualification tests will begin later this year.

Software—Coding should be completed this year, followed by functional testing and integration.



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The NATO Science Committee has introduced a new mechanism for support, the **Networking Infrastructure Grant**, designed to improve the access to Computer Networking facilities of scientists in the countries of Central and Eastern Europe and Central Asia, NATO's Cooperation Partners (CPs). To qualify for such a grant the researchers must be involved in a common collaborative project between one or more institutes in CP countries and one or more institutes in NATO countries. The grant will enable the CP researchers to purchase equipment or services related to networking. Networking Infrastructure Grants are awarded primarily in the Priority Areas outlined below, but are not restricted to these areas.

The Priority Areas for support under the NATO Science Programme for collaborative projects between NATO scientists and CP scientists are as follows:

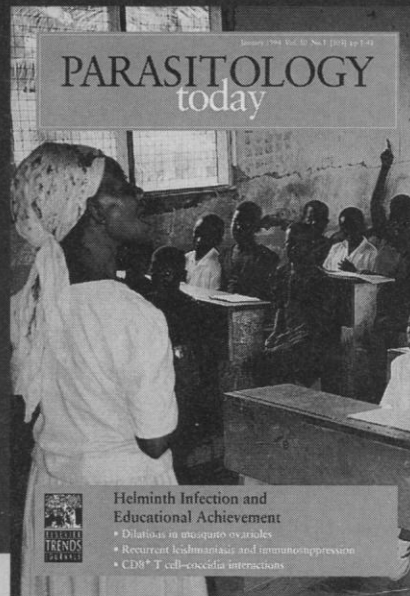
Disarmament Technologies
Environment
High Technology
Human Resources/Science and Technology Policy.

In these Priority Areas the following activities can also be supported, in addition to the Networking Infrastructure Grants: Collaborative Research Grants, Linkage Grants, Advanced Study Institutes, Advanced Research Workshops and Expert Visits.

Further information and application forms for the above grants are available on request from:
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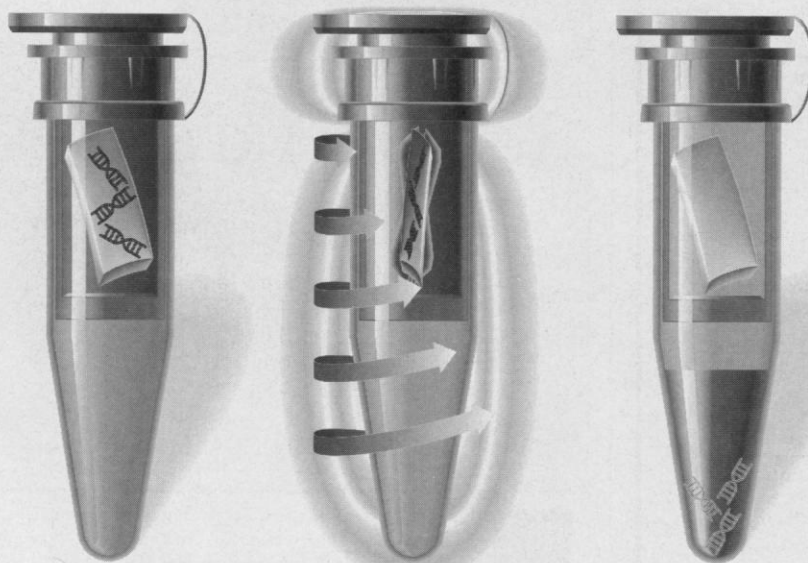
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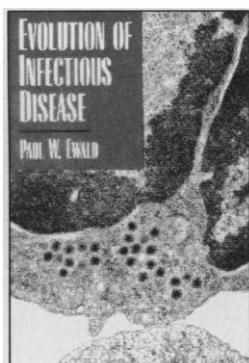
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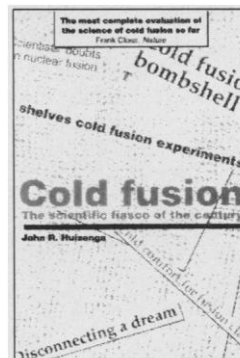
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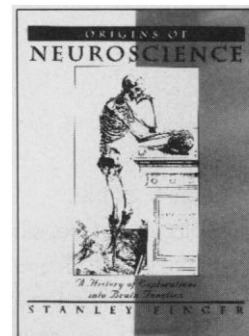
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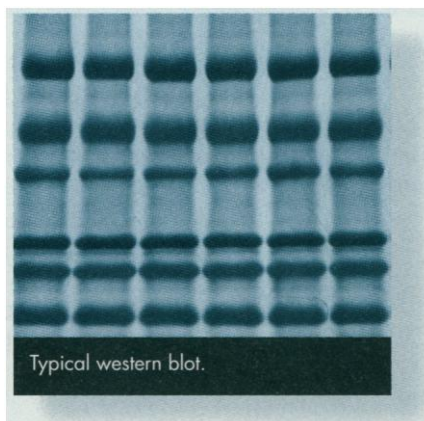
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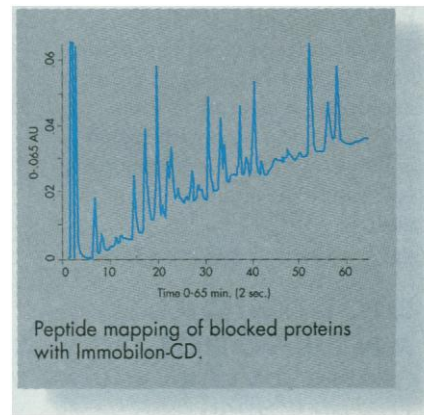
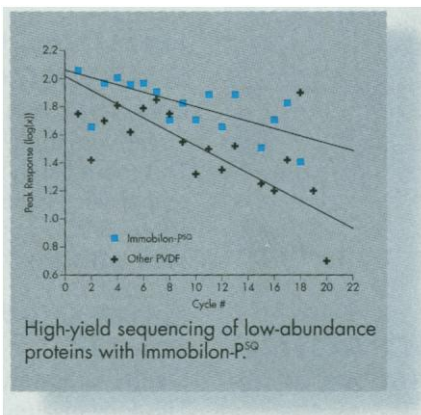
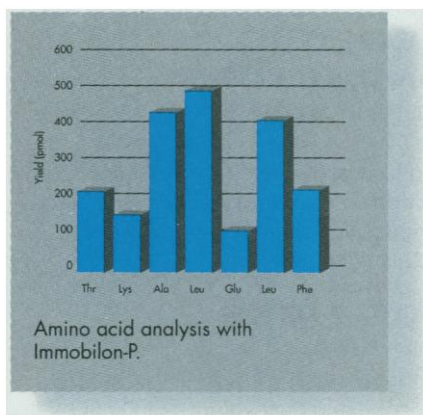
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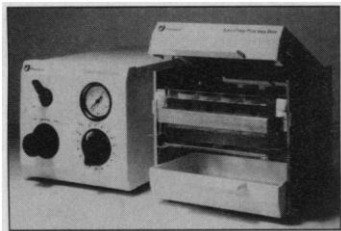
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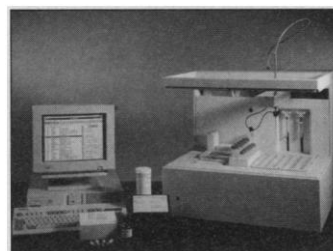
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Literature

Capcell Pak is a brochure on a novel high-performance liquid chromatography column that combines the characteristics of silica and polymer. The columns are available in six bonded phases of C18, C8, C1, phenyl, cyano, and amino. It includes more than 40 application chromatograms illustrating the separation of various compounds. **DyChrom. Circle 148.**

Pierce 94-95 Catalog and Handbook includes a 350-page technical section with information about techniques such as antibody production, antibody fragmentation, cross-linking and protein modification, clinical and research assays, electrophoresis, enzymatic labeling, gas chromatography, high-performance liquid chromatography, immunoassays, iodination, protein assays, and protein immobilization. **Pierce. Circle 149.**

Applications of the HP 3D Capillary Electrophoresis System describes 71 applications of this system. The 84-page booklet is intended mainly for analysts in the bioscience, pharmaceutical, environmental, and food industries, and the applications are grouped under these headings. **Hewlett-Packard. Circle 150.**

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