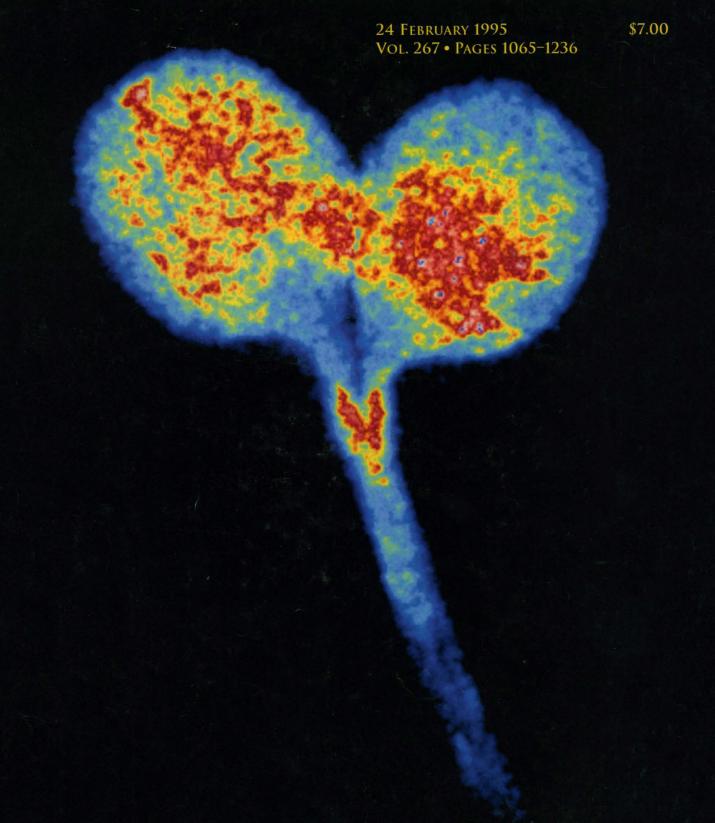
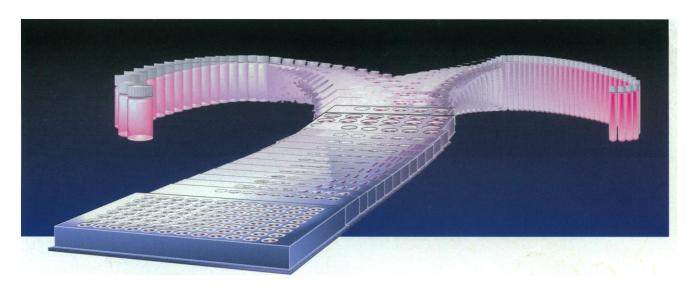


# SCIENCE





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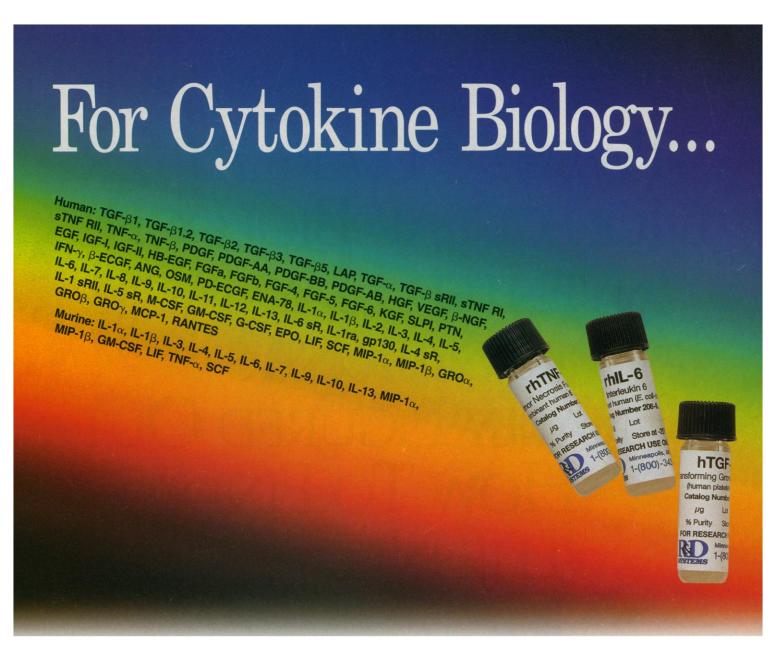


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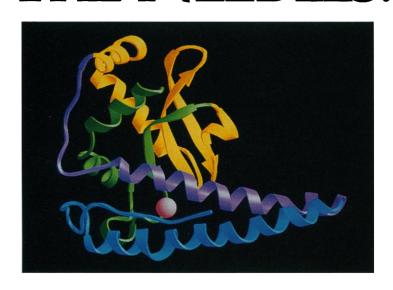
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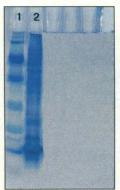
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# TWENTY YEARS AFTER MOLECULAR BIOLOGISTS INVENTED HAYSTACKS, SOMEONE'S FINALLY FIGURED OUT HOW TO FIND THE NEEDLES.





Crude cytokine prep. Lane 1: MW markers. Lane 2: Crude.

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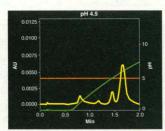
attempts with conventional chromatography columns and instruments and still don't have a clean molecule to work with.

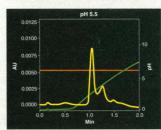
# Is it the pH? the gradient? the loading? the surface chemistry? the...

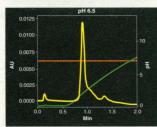
You're in uncharted territory. There's no way to know which variable holds the key, and you don't have the luxury to test them all. Time is running out.

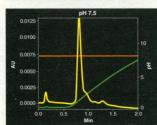
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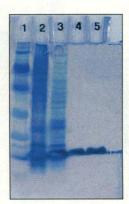
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Molecular image courtesy of J Tainer, G. Borgstahl and H. Parge: Metallioprotein Structure and Design Group, the Scripps Research Institute.

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The firefly luciferase gene can serve as an effective reporter for gene expression in vivo. In this *Arabidopsis* seedling, the luciferase gene was fused to the promoter region of the *CAB2* gene, whose expression is regulated by light and the circadian clock. Expression is

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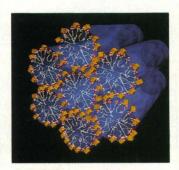
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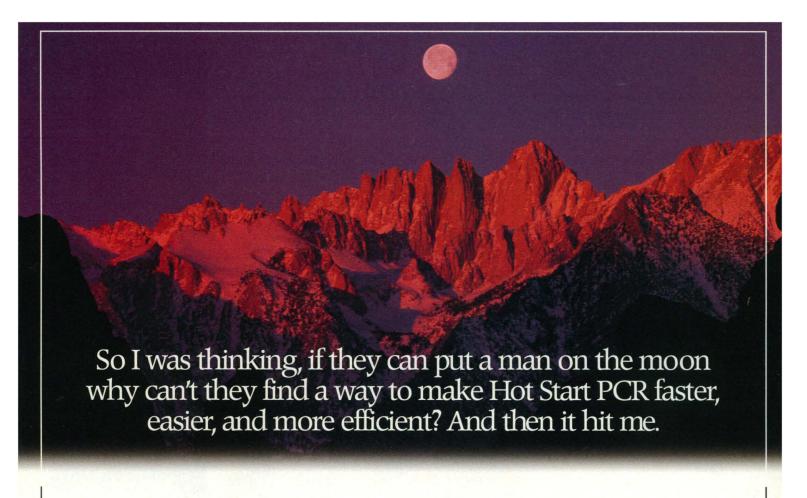
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# THIS WEEK IN SCIENCE

edited by DAVID LINDLEY

## **Mesophase shifts**

In the biomimetic approach for synthesizing materials with nanoscale structures, assemblies of organic molecules serve as templates for assembling an inorganic structure. Firouzi et al. (p. 1138) present an alternative approach for assembling nanocomposite materials, using inorganic ions (silicate anions) that interact strongly with surfactants to form a variety of mesoscale phases representing silicate analogs of liquid crystals. Variation of temperature and composition can be used to control the phase behavior, and the silicate units can then be irreversibly polymerized to form mesoscale materials.

# **Icy clarity**

The AMANDA project is a proposed astrophysical muon and neutrino detector of cubic-kilometer proportions that will use photomultiplier tubes (PMTs) embedded in antarctic ice to detect Cherenkov radiation from energetic particles. In a pilot test, Askebjer et al. (p. 1147) deployed PMTs at depths of up to 1 kilometer in south polar ice, and found that although the ice is extremely transparent, trapped air bubbles scatter light rays with a mean free path of 25 centimeters. The ice is predicted to be bubblefree at about 1150 meters, at which depth a feasible detector might be located.

## Roughly flat

Because most objects perceived by humans or captured in images are seen in reflected rather than emitted light, the way a surface scatters incident light is fundamental to its appearance. Nayar and Oren (p. 1153) present a reflectance model for textured surfaces that generalizes the classical Lambert law and takes careful account of surface characteristics, masking effects, and shadowing. The model describes the ways in which surface roughness and detector resolution interact to yield a perceived appearance. For very rough surfaces the model predicts silhouette images devoid of depth—an effect that may be responsible for the flat-disk appearance of the full moon.

#### **Function follows form**

Genome sequencing generates the primary structure of a protein-the sequence of covalently linked amino acids-allowing comparison with other proteins of known sequence and function. But the function of a protein also depends strongly on its three-dimensional conformation, and tertiary structures are not nearly so readily obtained or compared. Babbitt et al. (p. 1159) present the analysis of a family of structurally similar enzymes, all catalyzing reactions that begin with the proton abstraction from weak carbon acids. The function of one gene product, a previously unassigned open reading frame, was inferred by combining a chemical understanding of the type of reaction catalyzed with information from the gene structure of the particular *Escherichia coli* operon.

# Hot rhythms

The per<sup>L</sup> mutation in the period (per) gene of fruit flies not only lengthens the circadian rhythm but renders it temperature-sensitive. The mutation site lies in a dimerization domain of the PER protein, and Huang et al. (p. 1169) show that single amino acid substitutions at the site render the dimerization interaction strength temperature-dependent. The dimerization domain also interacts with another region of PER, and the authors argue that the perL mutation upsets a balance between the temperature sensitivities of the inter- and intra-molecular PER interactions, thereby disrupting the normal mechanism of temperature compensation in the flies' circadian rhythm.

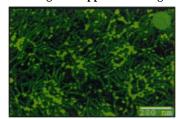
#### Sticky cells

Adhesion between cells is what gives organisms their bodily integrity. Dammer *et al.* (p. 1173) used atomic force microscopy to measure directly the binding strength between the adhesion

# ... and only man is vile

By excavation of bird bones from archaeological sites, Steadman (p. 1123) has documented the decline and disappearance of numerous species of birds on Pacific islands throughout Melanesia, Polynesia, and Micronesia. The beginning of the most dramatic losses coincides with the arrival of prehistoric humans on the islands, at times ranging from 30,000 to 1500 years ago, and comparison with the fossil record suggests that the extinction rate over the past several thousand years is considerably higher than it was before human occupation. These observations indicate that loss of biodiversity is not exclusively a problem of the modern industrial world, but has occurred in the past whenever humans have moved into new territories.

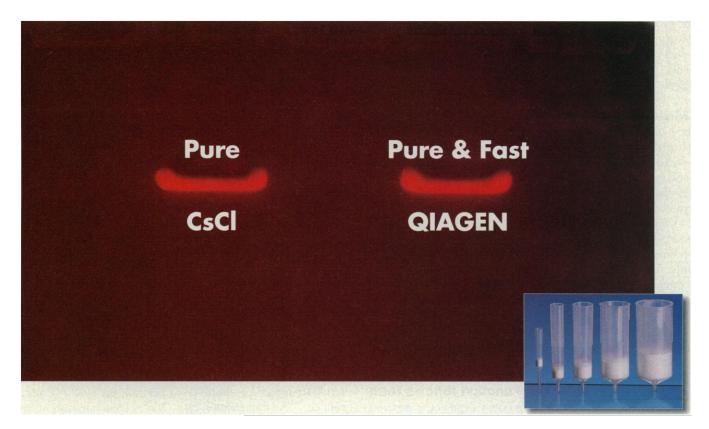
proteoglycans (APs) that hold a marine sponge together; the force required to pull the molecules apart jumps in increments of about 40 piconewtons, corresponding to the separation of a pair of AP arms. The total binding strength between two APs is enough to support the weight



of 1600 cells. With 1000 APs per cell, the available adhesive forces seem adequate to maintain the sponge's form.

# Tying the ends together

Cell survival depends on an ability to repair double-strand breaks (dsb) in DNA, such as those caused by x-rays. Cell lines lacking the Ku protein component of DNA-activated protein kinase (DNA-PK) are known to be defective both in dsb repair and in V(D)J recombination, the process by which antigen receptor gene segments are assembled. Two reports this week examine the consequences for these processes of the loss of another component of DNA-PK, the p350 subunit. Lees-Miller et al. (p. 1183) have found that a radiation-sensitive human cell line defective in dsb repair is missing the p350 subunit, yet contains the Ku protein. Kirchgessner et al. (p. 1178) use colocalization experiments to propose that p350 is the gene responsible for the severe combined immunodeficient (SCID) phenotype in mice, and to bolster the evidence that the human homolog to murine SCID is on chromosome 8q11.



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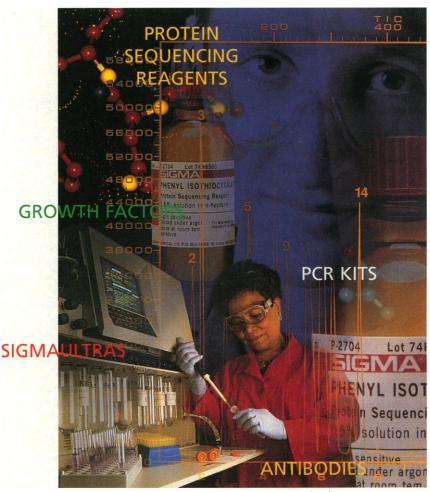
Data kindly provided by F. Ehlert, Institute for Molecular Biology and Tumor Research, Marburg, Germany.

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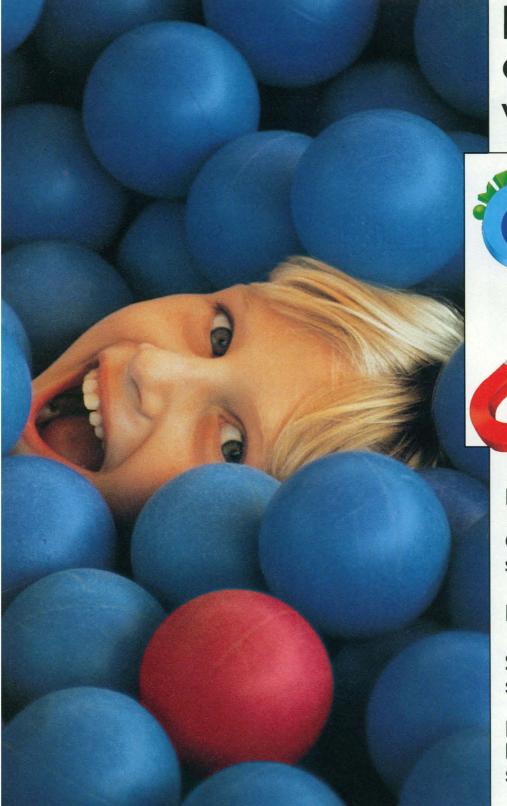
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# Research Notes from **Nikon**

# Multiprobe Fluorescence Technique Finds Increasing Application in Research

Fluorescence in situ Hybridization (FISH), first introduced in the late 1970's, has played an important role in identifying chromosomes, detecting chromosomal abnormalities, and determining the number, size and location of specific DNA sequences in mammalian cells. Today, thanks to advances in probe technology and fluorescence microscopes, FISH is becoming increasingly important as a research tool and may eventually become a standard clinical diagnostic technique in areas such as cytogenetics, prenatal diagnosis and tumor biology.

As biomedical researchers continue to discover more and more human diseases with their causes rooted in genetic abnormalities, Fluorescence in situ Hybridization (FISH) has become an increasingly important tool for the analysis of genetic cellular characteristics. This highly sensitive technique is fast, easy to interpret, and yields statistically relevant data. It can be used to identify both normal and abnormal chromosomes and to determine the presence and location of specific genomic sequences with unprecedented detail and clarity.

In FISH, the hybridization reaction biochemically targets gene sequences so their location and size can be determined using fluorescence microscopy. DNA from a chromosome-specific probe is labeled by chemically modifying it to insert a reporter molecule that can be

observed via fluorescence. The labeled DNA is then hybridized to metaphase chromosomes or interphase nuclei for which chromosome-specific staining is desired. The technique is sufficiently sensitive to detect and characterize both numerical and structural aberrations, making it valuable for detection of a number of genetic disorders.

# Multicolor probes permit simultaneous analyses

The FISH technique depends on the availability of probes that bind specifically to regions of genetic or cytogenetic interest. It is a powerful research tool because multicolor probe labeling permits simultaneous use of several different probes inside a single cell, allowing the researcher to analyze multiple genetic sequences and check for several genetic disorders at the same time

In clinical studies, multicolor FISH analyses have shown striking differences in chromosome frequency in interphase cells from solid tumors, both from the same tumor and from tumors of different patients. Several of these studies are focused on relating tumor aggressiveness to specific chromosomal sequences to improve tumor prognosis beyond what is possible today.

# New technology for new techniques

As FISH and other direct probe techniques have emerged, the need for more sophisticated fluorescence microscope systems has increased dramatically. Since individual sites on a chromosome are so minute, high numerical aperture, high transmission objectives are needed

to image them. And simultaneous use of 2, 3 or 4 fluorescent probes necessitates multiple filters to image multiple sites.

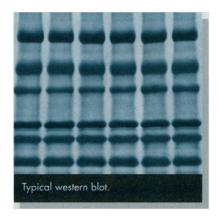
In response to these needs, Nikon has introduced the new Quadfluor Epi-Fluorescence Illumination System, along with a series of higher numerical aperture objectives with higher transmission characteristics.

The new CF Plan Fluor objectives feature new optical cements and high transmission coatings to permit broader wavelength ranges (UV — Deep Red) and brighter images that are color aberration free with extremely high contrast and low background autofluorescence. The Quadfluor Illuminator offers expanded filter cube capacity and enhanced filter designs with even better signal to noise ratio performance. It accepts up to four filter cubes at once to separate different signals, or a multiband filter cube to image several fluorochromes simultaneously. The filters can be rapidly switched via an extremely smooth yet very precise linear slider, allowing excellent image registration and making the Quadfluor Illuminator ideal for today's multi-probe techniques.

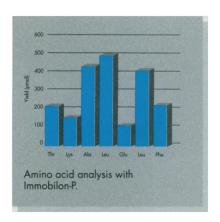
For more information on Nikon's new Quadfluor Epi-Fluorescence Illumination System, call Nikon at (516) 547-8567, fax us at (516) 547-0306 or contact us on the Internet at nikonbio@aol.com.

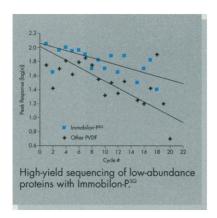
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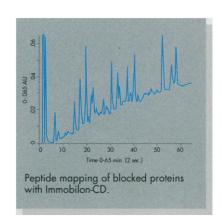




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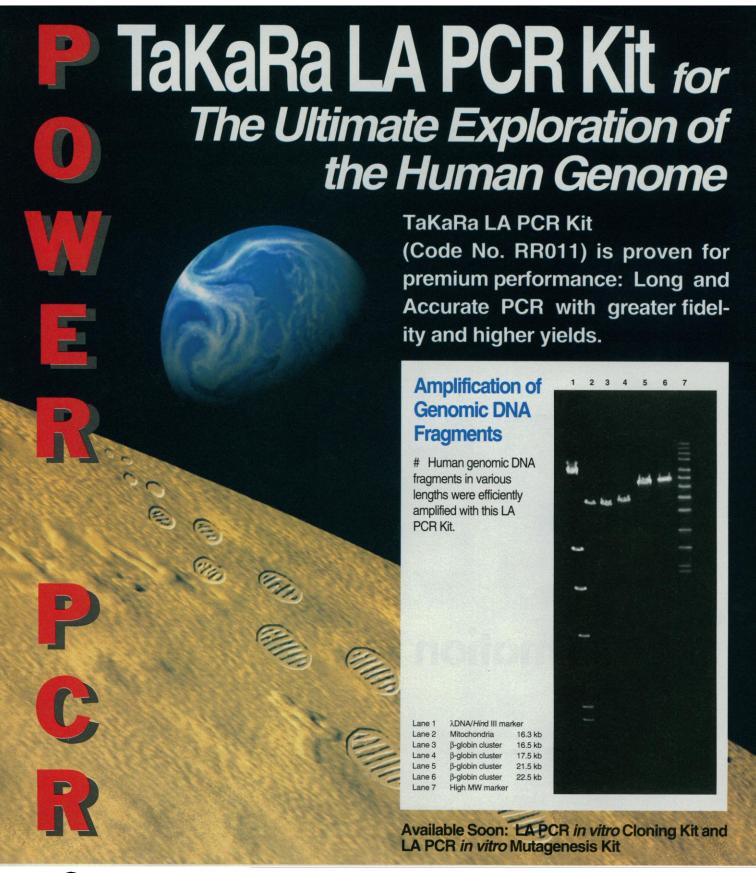
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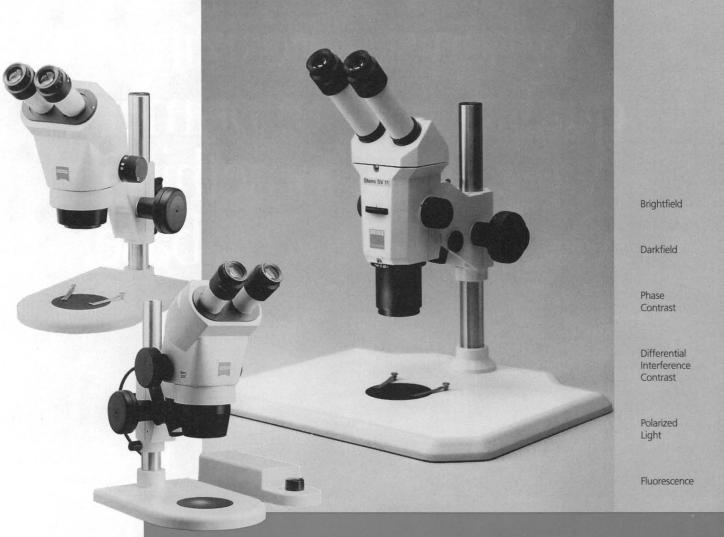
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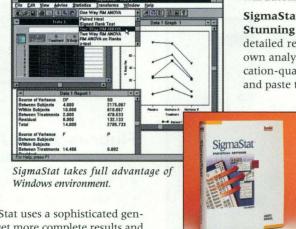
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20th Annual AAAS Colloquium on Science and Technology Policy April 12-14, 1995 The Capital Hilton Hotel

The AAAS Science & Technology Policy Colloquium provides a forum in which federal and industrial policymakers and members of the scientific, engineering, and academic communities can participate in an open discussion of issues relating to science and technology policy.

The Colloquium occurs after the release of the President's budget but before final congressional action, thus allowing for

the timely exchange of information about the budget and the consequences of various policy issues involving science and technology.

Who should attend: Scientists, administrators, industrial R&D managers, policymakers, academicians, association officials, federal grant recipients, students, and others with an interest in science and technology policy.

# PROGRAM OVERVIEW

# Wednesday, April 12

(registration opens at 12 noon; program starts at 2 p.m.)

Keynote: John H. Gibbons, Assistant to the President for Science and Technology, and Director, OSTP.

# The New World of R&D Funding (Plenary Symposium)

- R&D and the New Congressional Leadership (Rep. Robert S. Walker\*, Chairman, House Science Committee)
- ► The Administration's New Budgeting Process (Alice M. Rivlin\*, Director, Office of Management and Budget)
- Overview of Federal Budget Proposals for R&D in FY 1996 (Stephen D. Nelson and Kathleen Gramp, AAAS)

# The William D. Carey Lecture (public invited)

Speaker to be announced

# Thursday, April 13

Beyond Competitiveness: A New Look at Science, Technology, and Economic Performance

#### (Plenary Symposium)

- Aggregate Economic Data and Individual Insecurity: If Business Is Doing So Well, Why Are Workers So Nervous?
- ► Technology, Jobs, and Wages in the New World Economy
- What's the Real Effect of Technology on Jobs and Earnings?
- Science, Technology, and Trade Performance
- Mobilizing Science and Technology for National Wealth Creation

**Luncheon Address:** Vint Cerf\*, Senior Vice President, MCI

#### **Concurrent Symposia**

- The Galvin Report and the Future of the DOE National Laboratories (J. David Roessner, organizer)
- Science The Endless Frontier Plus Five:
   Decisive Impacts of the Early Cold
   War Years on the Formulation of U.S.
   Science Policy (William Blanpied,
   organizer)
- Human Resources and Career Opportunities in Science and

Technology: Will There Be Enough Jobs? (Alan E. Fechter, organizer)

Major R&D Agency Budgets for FY 1995 (Concurrent small group sessions) DOD • DOE • NIH • NASA • NSF • DOC (NIST, NOAA)

# Friday, April 14

Breakfast Address: Mark O. Hatfield\*, Chairman, Senate Appropriations Committee

## **Concurrent Symposia**

- Megascience and International Collaboration (Alan Schriesheim, moderator)
- Reinventing the Federal Science Agencies: Goals and Structures (J. Paul Gilman, organizer)
- What DOD Needs in R&D (moderator to be announced)

#### Luncheon Address

Speaker to be announced

\*Invited speaker

Budget discussions will be supplemented by AAAS Report XX: Research and Development, FY 1996, a comprehensive analysis of the proposals for FY 1996 budget, prepared by AAAS and a group of its affiliated scientific, engineering, and higher education associations. Registrants will receive this report at the Colloquium; the 1995 AAAS Science and Technology Policy Yearbook (containing most of the colloquium addresses, plus other significant items) in early Fall; and Congressional Action on R&D in the FY 1996 Budget later in the Fall.

Resistation by completing and returning the enclosed form. For further information, contact: Directorate for Science and Policy Programs, AAAS, 1333 H Street, NW, Washington, DC 20005. Fax: (202) 289-4950. E-mail: snelson@aaas.org. Phone: (202) 326-6600 (for information). To register phone (202) 326-7075.

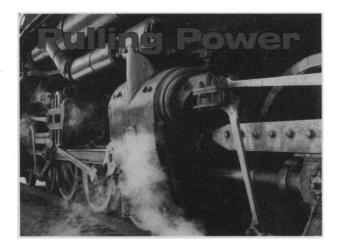
# AAAS Colloquium on Science & Technology Policy

April 12-14, 1995 The Capital Hilton Hotel, Washington, DC

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[1] After March 29, register in person at the Capital Hilton beginning at 12:00 pm, April rates apply only to employees of government, academic, and nonprofit organizations. S [3] Refund requests for registration fees and meal tickets must be submitted in writing Colloquium; no refunds will be made for cancellations received after 5 April. Publicatic AAAS Science and Technology Policy Yearbook, after the meeting; and Congressional Action	tudents rates apply only to f (to the address or FAX num ons: All registrants receive A	full-time undergraduate a ber above) by April 5, 19 AAS Report XX: Research	and graduate students and retirees. 95, and will be processed after the
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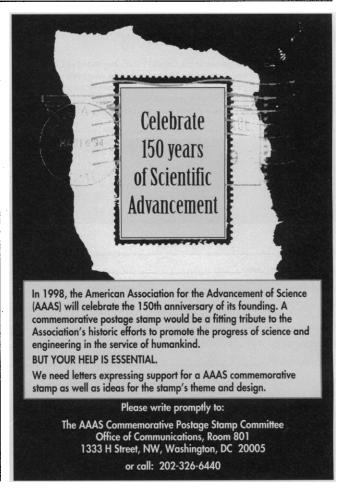
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