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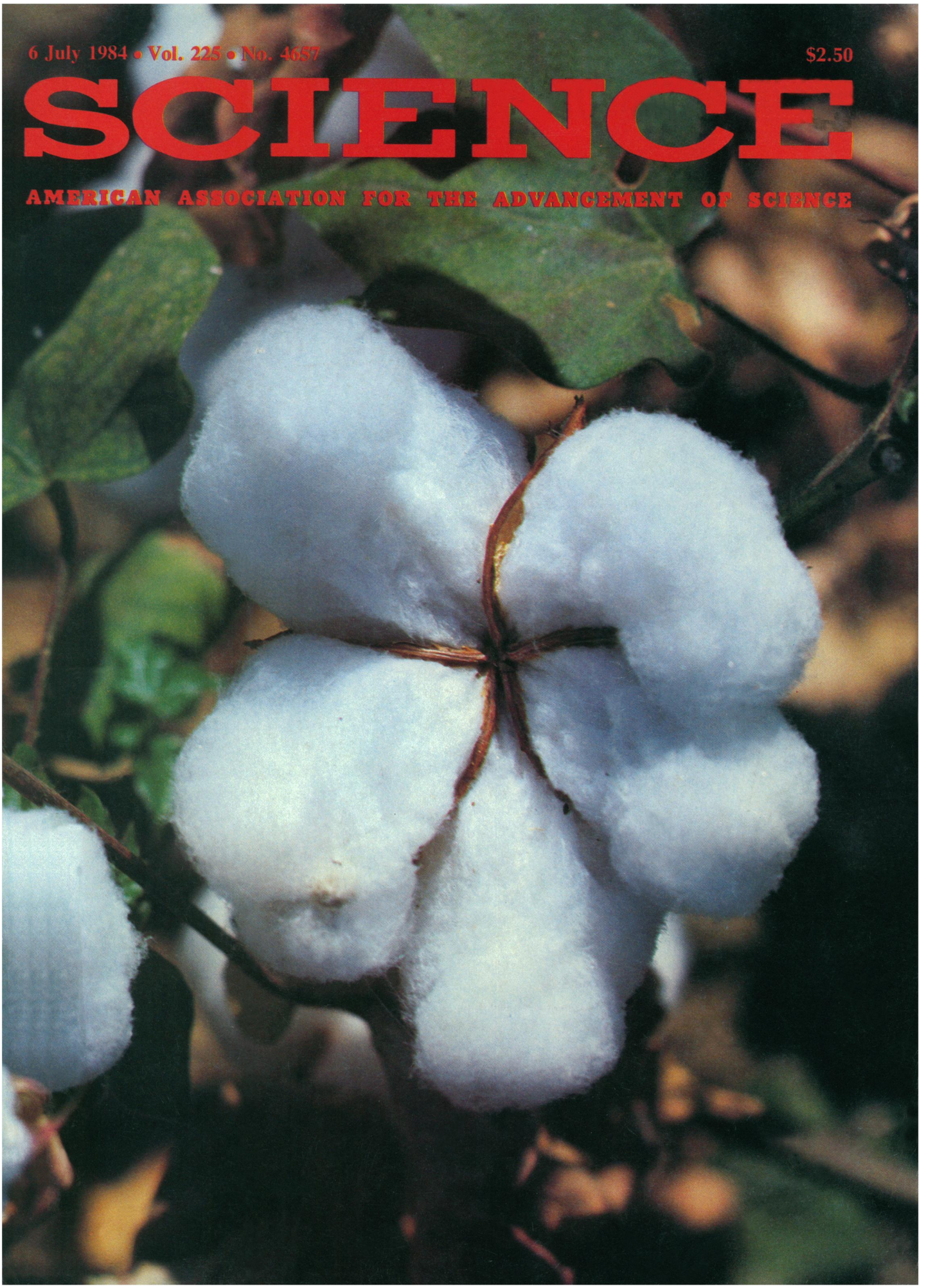


BIOSYSTEMS UPDATE

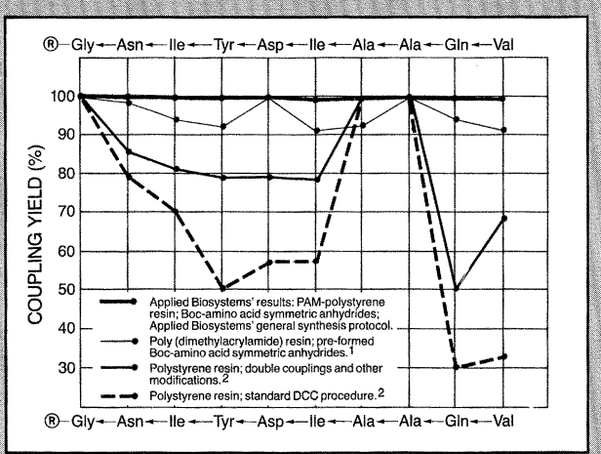
A New Approach to Automated Peptide Synthesis

Applied Biosystems is pleased to announce the first instrument designed for high efficiency peptide synthesis. The key to the high coupling yield of the Model 430A Peptide Synthesizer is an activation unit which converts the amino acid to a very efficient acylating species immediately prior to the coupling step. The defined protocol has been optimized for general peptide synthesis, but the fully programmable system allows straightforward adaptation to other chemistries.

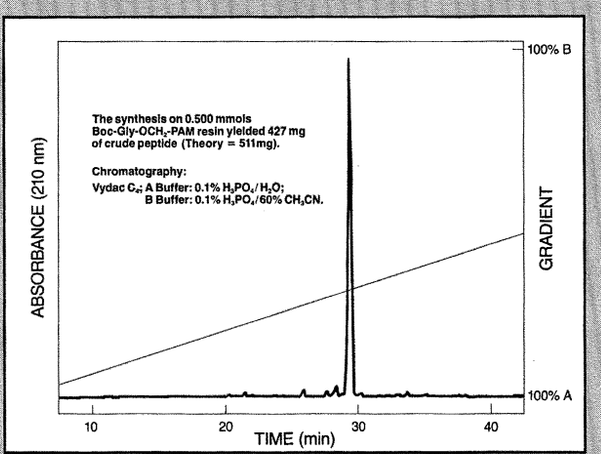
Cycle times with the general synthesis protocol are approximately one hour. A single loading of protected amino acids, reagents, and solvents will give up to 50 synthesis cycles. To insure high coupling yields, Applied Biosystems manufactures and supplies all synthesis reagents.

The data below summarize the results of the synthesis of the decapeptide Acyl Carrier Protein (65-74). These results illustrate the combined capabilities of the novel automated synthesis procedure and the high quality peptide synthesis reagents and loaded resins.

The new Model 430A Peptide Synthesizer was introduced at FASEB and Analytica, and will be exhibited at the ASBC Meeting. Write or phone if you'd like more information.



Amino acid incorporation during assembly of Acyl Carrier Protein residues 65-74.



HPLC chromatogram of crude, HF cleaved Acyl Carrier Protein (65-74).

ANALYTICAL METHOD	STEP YIELD (%)									
Quantitative Ninhydrin Monitoring[3].	—	99.9	99.6	99.5	99.4	99.1	99.2	99.2	99.1	98.9
Preview Quantitation by Solid Phase Sequencing of Protected, Resin Bound Peptide[4].	—	—	99.4	—	99.3	99.1	99.2	—	98.9	98.7
	RELATIVE AMINO ACID EQUIVALENTS									
Amino Acid Analysis of HF Cleaved, Deprotected Peptide	1.00	0.97	0.90	0.94	0.97	0.90	0.96	0.96	0.94	0.98
Amino Acid Residue	Gly←	Asn←	Ile←	Tyr←	Asp←	Ile←	Ala←	Ala←	Gln←	Val

Step yield quantitation and amino acid analysis results for Acyl Carrier Protein (65-74) chain assembly using Applied Biosystems' general synthesis protocol. Only single couplings were used throughout the synthesis (except for Gln).

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Applied Biosystems

APPLIED BIOSYSTEMS, INC., 850 Lincoln Centre Drive, Foster City, CA 94404 • (800) 874-9868 • In California (800) 831-3582
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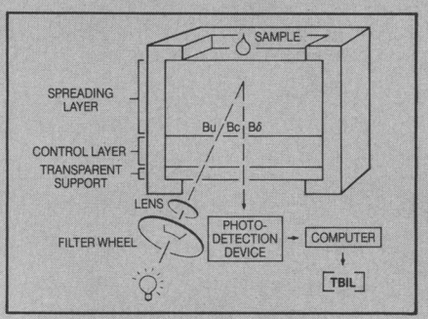
Making headway against jaundice a fraction at a time.

Kodak scientists have isolated what may be the first true human "biliprotein." The existence of this bilirubin fraction may lead to an advance in the diagnosis and treatment of jaundice-related disorders.

This important verification came to light during product-improvement testing procedures for Kodak Ektachem clinical chemistry slides. In the process of separating and identifying different bile pigments in serum, a fourth bilirubin fraction, delta (B_δ), was rediscovered. It is distinct from unconjugated bilirubin and is strongly linked (possibly covalently) to albumin.

Not only have we isolated and characterized this virtually unknown fourth fraction, we have developed a new assay procedure which enables labs to measure the delta fraction simply, rapidly, and accurately.

Last year we introduced an Ektachem chemistry slide to measure neonatal bilirubin. By means of dry film layers, this slide measures both unconjugated bilirubin (Bu) and mono- and diconjugated bilirubin (Bc) together. But the delta bilirubin fraction, which is tightly bound to a serum protein believed to be albumin, is not detected by the BuBc slide.



This year we are introducing a Kodak Ektachem fractionated bilirubin panel composed of BuBc and TBIL (Total Bilirubin), from which estimates of B_δ can be calculated. The new TBIL slide quantitates all three bilirubin fractions (Bu + Bc + B_δ) while the BuBc slide now measures Bu and Bc as individual fractions. The difference in bilirubin quantitated by the two slides is B_δ.

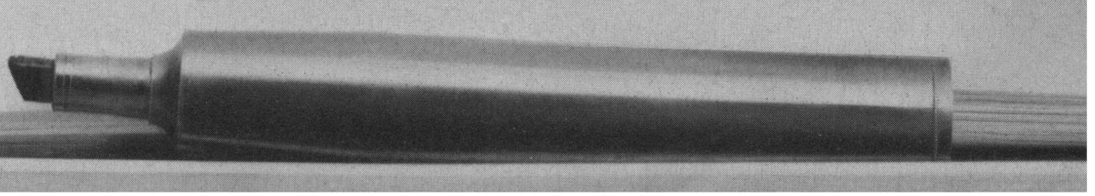
We think the fractionated bilirubin panel may lead to a better understanding of the molecular basis of jaun dice. This, in turn, can make it easier for health care professionals to diagnose biliary atresia and cytomegalovirus in newborn infants. And to screen for hepatobiliary disease, make differential diagnoses, indicate therapeutic strategies, and support prognoses.

For more information, write for "Bilirubin—Its Components in Serum and the Kodak Assay" to: Eastman Kodak Company, Dept LCSM-1, 343 State Street, Rochester, NY 14650.

Kodak

Kodak. Where technology anticipates need.

$$[B_\delta]=[TBIL]-[Bu]-[Bc]$$



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AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

COVER

Open cotton boll at the Westside Field Station in California's San Joaquin Valley. Resistance against mites was induced in cotton seedlings by exposure to mites during early development. See page 53. [Jack Kelly Clark, Cooperative Extension, University of California, Davis 95616]

LETTERS

Regulation of Biotechnology

Irving S. Johnson's editorial (20 Apr., p. 243) correctly praises the historical performance of the National Institutes of Health (NIH) Recombinant DNA Advisory Committee (RAC). Observers of the DNA discussions over the past decade cannot disagree with his conclusions about the expertise, competence, and service provided by the RAC.

The focus of the current debate, however, is not the RAC's past performance. The question of how to ensure a sufficient, timely, and publicly acceptable review of environmental, safety, and health questions consistent with existing federal statutes is what now needs thoughtful consideration as the products of biotechnology begin to be commercialized.

All of us share Johnson's opinion that the commercialization of biotechnology should not be unduly impeded. Utilizing the RAC as "a single and unified oversight system," as Johnson suggests, will not serve those goals. The implied extension of the RAC's mandate from laboratory research through market approval is neither appropriate, considering existing statutory mandates, nor widely supported.

Existing federal statutes and programs define in many circumstances which agency has the responsibility for review of laboratory research, for review of field or clinical research, and for approval for commercial use. The case of insulin produced by genetically engineered *Escherichia coli* is illustrative. The RAC was involved at the research level, and the Food and Drug Administration (FDA) became involved when commercialization was the primary issue. The product was examined and approved for use by the FDA, like any other drug, on criteria set forth in the Food, Drug and Cosmetic Act, such as clinical trials, product purity, and possible side effects. Similar cases are presented by the Environmental Protection Agency's (EPA's) review for commercial use of pesticides and probably chemicals, and for review by the U.S. Department of Agriculture (USDA) of products within its statutory responsibilities.

In a hearing before my Investigations and Oversight Subcommittee, the question of release into the environment of genetically engineered organisms was examined in great detail. At that hearing, EPA asserted (with the approval of the Office of Management and Budget) jurisdiction under the Toxic Substances Control Act (TSCA) over the release into the environment for *commercial purposes* of genetically engineered organisms, and jurisdiction over genetically engineered pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The RAC did not suggest that it had jurisdiction in this area. While not without question, EPA's interpretation of its TSCA authority has received support in Congress and in the genetic engineering industry.

The question of how to review releases into the environment on a limited scale for research purposes is less clear. For example, FIFRA gives EPA authority to control field-scale tests of pesticides by issuing experimental use permits. However, EPA's regulations generally exempt from permit requirements all experiments under 10 acres. Under TSCA, EPA can regulate chemicals used for research purposes, but it cannot require researchers to notify EPA before use in the laboratory. The parameters of USDA's jurisdiction are even cloudier.

For these reasons the recently released staff report of the Investigations and Oversight Subcommittee recommended that an interagency committee be established to sort out jurisdictional lines and to develop a reasonable road map for industry and the public. In such a process, it may well be that limited field studies could be exempt under appropriate EPA standards or that a RAC review could be used by EPA or others in reaching their decisions. The just-formed Cabinet Council under the direction of the President's Office of Science and Technology Policy could provide the mechanism to sort out the jurisdictional questions, but it will need to act quickly and decisively if it is to be successful in promoting the twin goals of rapid commercialization and appropriate review of public health and environmental considerations. Judge John J. Sirica's recent order (*1*) temporarily enjoining NIH's approval of release into the environment experiments funded by NIH reinforces the need for prompt development of an acceptable regulatory process.

There are several additional reasons why the RAC, as currently organized and constituted, cannot play the role suggested by Johnson. They include the lack of statutory authority to require submissions to the RAC and the lack of authority to make and enforce decisions outside its jurisdiction; by its charter, the RAC is limited to NIH-funded research (although, as Johnson correctly notes, the RAC has been reviewing some indus-

try laboratory research proposals for some time). The RAC also lacks the necessary procedures and the institutional capability to make timely reviews of large numbers of applications. The absence of statutory authority and regulatory procedures may have made the RAC an ideal process for review of laboratory research, as Johnson states. The rationale for an informal approach is less persuasive, however, when other agencies have statutory authority and when the statutes require a delicate balancing of science and public policy, such as the case of a clinical trial, field-scale test, or approval for commercial use.

An additional difficulty in extending RAC's jurisdiction is its focus. The RAC's orientation has been toward laboratory safety, and it has focused on containment procedures. While the RAC's expertise can be expanded to include an ecological perspective, the scope of the RAC's charter and expertise is limited to recombinant DNA, and it has specifically excluded many significant technologies, now or soon to be widely used, such as protoplast fusion and cell fusion.

To implement Johnson's proposal would require (in the light of the existing statutory authority of FDA, EPA, and potentially USDA) legislation to create a new organization that would of necessity need to greatly expand and codify the RAC. Indeed, the resulting agency would not be likely to have the attributes that make the RAC so attractive and well regarded. For all of these reasons, I prefer the approach my subcommittee has recommended.

ALBERT GORE, JR.
Subcommittee on Investigations and Oversight, Committee on Science and Technology, U.S. House of Representatives, Washington, D.C. 20515

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The main thrust of my editorial was that there was a unique benefit to be derived from a single and unified *scientific* oversight system. Because of the universality of recombinant DNA technology, information gained in one research area may be useful in another. The implication that the RAC's mandate should extend "from laboratory research through market approval" was not made nor intended. We agree that such a procedure would be inappropriate. We also agree that public safety is a primary concern. The safety of this research to date has been well documented. Mechanisms to evaluate the products of this research before they become available to the public are also well established under the regulatory authority of the appropriate government agencies. As Gore suggests, the RAC's oversight of genetically engineered human insulin and its approval and regulation by the FDA is a good case study and example of how the existing system has worked effectively from the outset.

However, jurisdiction over the release of genetically engineered organisms to the environment is made by claiming the novel DNA fragment as a chemical. This jurisdiction appears to be aimed at the research and development studies that precede the product. The imposition of unnecessary regulation at the research level would inhibit progress and limit our ability to maintain a competitive international position in biotechnology. It thus would not be in the public interest.

The subcommittee staff report has recommended creation of a special interagency committee to resolve jurisdictional problems. Although this is a sound objective, the Cabinet Council on Natural Resources and Environment has already created a Working Group on Biotechnology at the assistant secretary level. This Council has a charter broad enough to encompass almost all areas of potential regulatory concern or confusion.

I agree that the focus of the current debate is not the RAC's past performance. That has clearly been successful. The issue is more closely bound to environmental release of genetically engineered organisms and plants and statutory authority. Additional study may indeed be required on environmental release of genetically engineered microorganisms and plants; this should occur before any additional regulatory or legislative restrictions are placed on research. I believe these applications are assessable through liaison between the various working groups of the RAC, EPA, and USDA.

Let us maintain the RAC's oversight of the science and not invoke statutory regulation of research. Let us strengthen the liaison between the advisory role of the RAC and the appropriate regulatory agency for the product. I believe this is in the public interest and the best interest of science, biotechnology, and international competition. These various interests are not mutually exclusive.

IRVING S. JOHNSON
Lilly Research Laboratories, Indianapolis, Indiana 46285

6 July 1984, Volume 225, Number 4657 **SCIENCE**

Is Taking Sides a Good Idea for Universities?

Universities are being exhorted by a wide variety of interest groups to take official positions on issues such as military research, the U.S. corporate presence in South Africa, and restrictions on information flow. Often the groups making such demands are perplexed by the resistance they meet, since they believe their particular perspective to be in the long-term interest of the human community and, therefore, of the university community as well.

It is essential to understand, however, that over the past century American colleges and universities have been transformed from quiet centers of traditional moral, political, and social values into educational and research centers at which inquiry is more important than dogma. It is only in recent times that the faculties and students of colleges and universities have acquired both the freedom and the obligation to consider subjects and pursue lines of investigation that may contradict prevailing beliefs in science or threaten the vested interests of powerful social and political groups. It is only in this century that the notion of academic freedom as a defining characteristic of universities has become pervasive.

This is a fundamental change. But the distinction between universities as institutions and faculty and students as individuals is often not recognized by the various publics who support universities and who look to the university as an institution for an affirmation or reaffirmation of particular points of view.

The work of the academic community is undeniably related to and supported by a particular set of values. These include the value of knowledge, the benefit of fair and open inquiry, respect for other points of view, and the possibility of human progress. In addition, most universities are now on record as taking a stand on some moral issues such as affirmative action and research on human subjects. We must, however, be very cautious about adding to this list. Without developing a means of distinguishing ideas from ideologies we risk the possibility of undermining the environment that supports our principal commitments and responsibilities. Returning to an earlier model of moral, political, and scientific orthodoxy would, however, undercut academic freedom and open discourse, transforming the character of contemporary higher education and undermining the university's capacity to make positive contributions to society.

Although academic freedom is not the only value that should inform our actions, we should consider no erosion of academic freedom without carefully scrutinizing the reasons for it. Perhaps we could ask ourselves questions such as the following as we prepare for the discussions.

1) What is the source of the university's right to free inquiry and what is its relation to the society that grants that right? In particular, what obligations accrue from this right?

2) If the university as an institution takes a moral or political stand, what implication does this have for members of the community with other points of view?

3) How do we identify those moral and political issues on which a university should adopt a particular point of view? For example, is the range of admissible inquiry a matter for administrative decision? If so, under what circumstances do we allow restrictions on teaching and research programs that offend an individual's moral or political values?

Experience indicates that transforming moral sentiments into policy statements requires carefully articulated ideas of the mission of a university and the impact of teaching and research on that mission. In this context, I believe that a university remains a creative part of society only as long as it remains an intellectually open community and not the ally of a particular point of view.—HAROLD T. SHAPIRO, *President, University of Michigan, Ann Arbor 48109*

SPACELAB 1

Special Issue of *Science*, 13 July 1984

First Results of Research Conducted Using Spacelab 1