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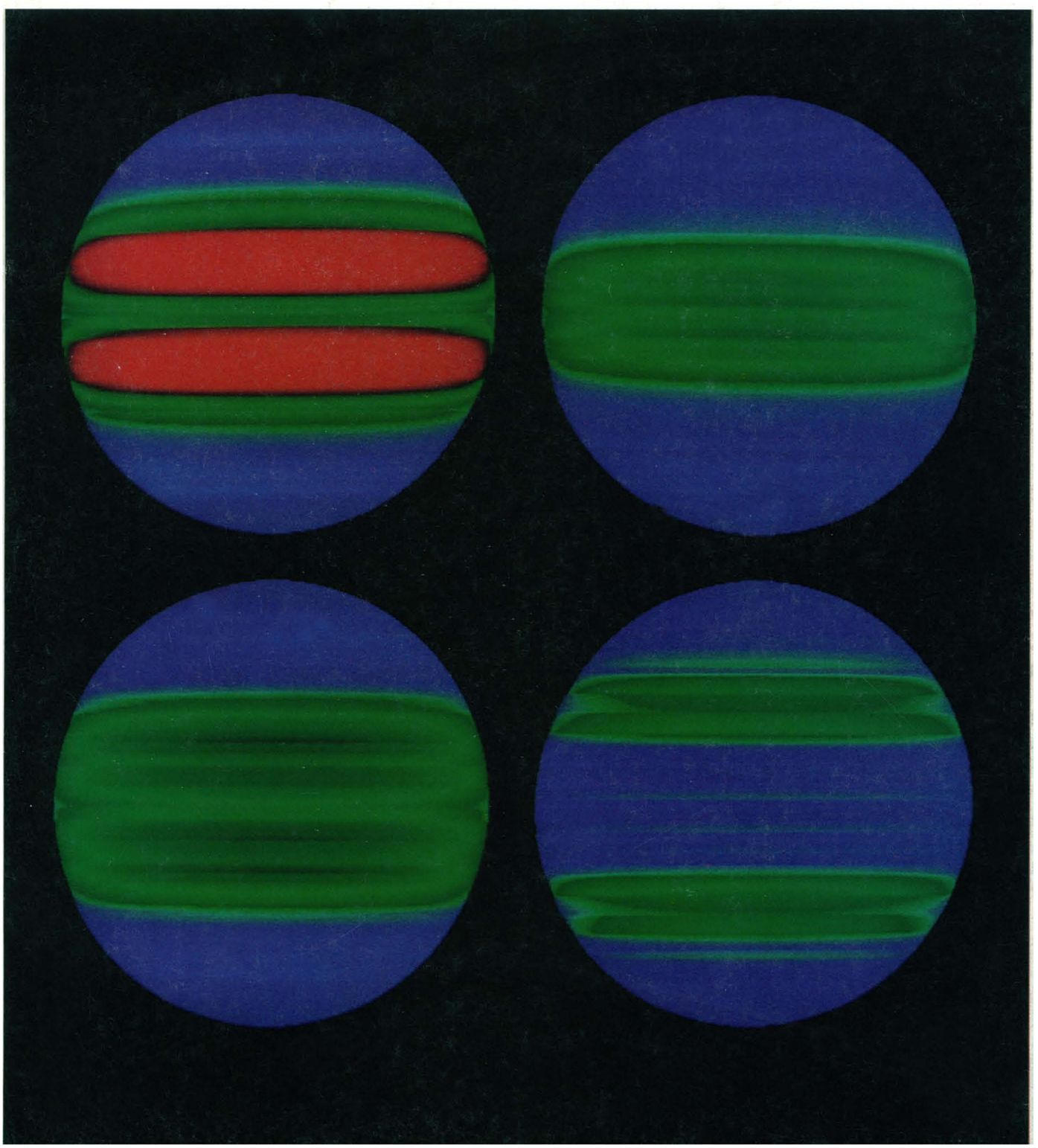

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COVER The effective surface temperature variation of the sun between 1983 and 1987 after removing the effect of bright solar faculae from the data. The temperature is calculated on the basis of solar limb data. The red regions are about 0.2% brighter, or 3°C hotter, than the blue areas. Starting in the upper left and moving down and then down in the right column, the images correspond to the sun in the summers of 1983, 1984, 1985, and 1987. See page 908. [J. R. Kuhn, Michigan State University, East Lansing, MI 48824; K. G. Libbrecht, Big Bear Solar Observatory, California Institute of Technology, Pasadena, CA 91125; and R. H. Dicke, Princeton University, Princeton, NJ 08544]

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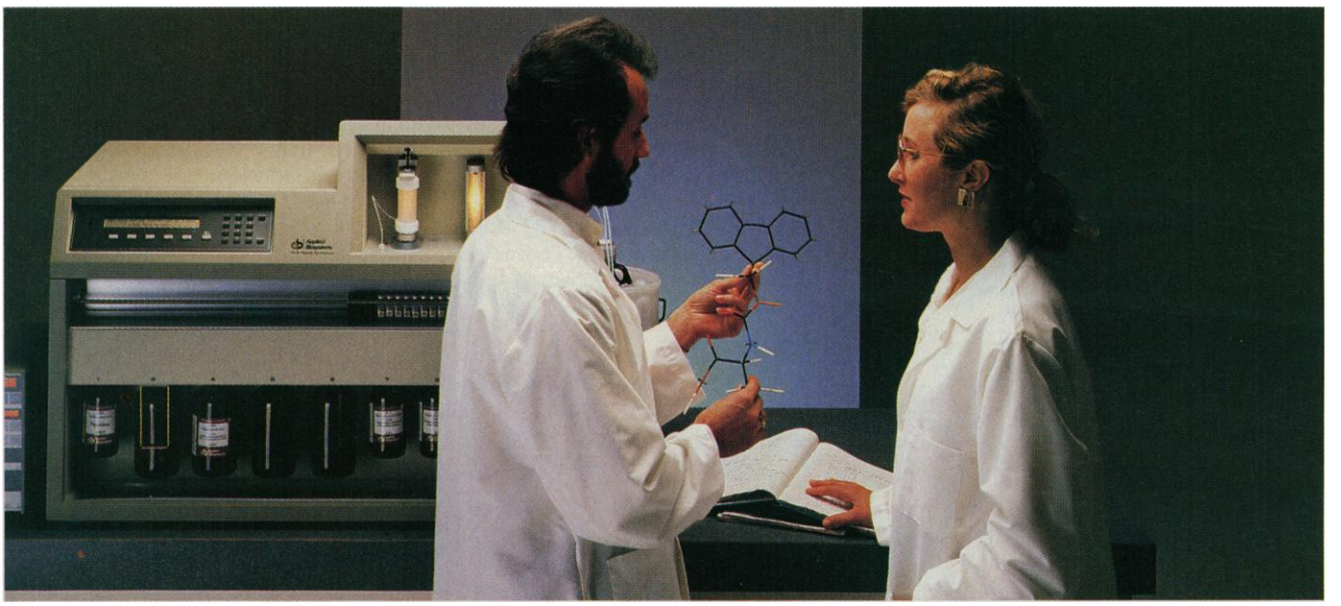

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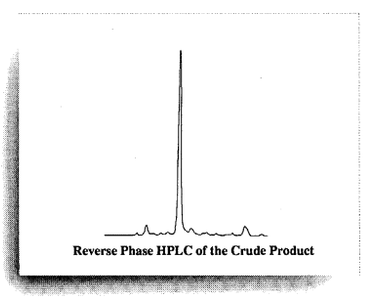

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Repressor-operator complexes

THE binding of a repressor protein to a specific site—an operator—on DNA is crucial to the regulation of gene expression. In bacteriophages such as lambda and 434, repressors bind to six operators in various combinations; the relative binding affinities control patterns of gene expression. The operators—all 17 base pairs long in lambda and 14 base pairs long in 434—have (approximately) twofold symmetry and the repressors bind as dimers. From biochemical, genetic, and crystallographic studies, much information has been obtained and deduced about the structures of these repressors and operators. Now, high-resolution crystallographic data—resolving the structures at 2.5 Å—elucidate further the complicated atomic interactions of repressors and operators. Jordan and Pabo prepared and studied co-crystals of the lambda repressor-operator complex (page 893); Aggarwal *et al.* studied those of 434 (page 899). Many differences, but also some similarities, are apparent when the systems are compared, both in the main protein-DNA interactions and in the secondary interactions that give the complexes stability. At this stage no simple "rules" have emerged that account for the specificity of recognition and binding.

Devonian bristletail

THE fossilized head and thorax of an insect that lived about 390 million years ago (during the Early Devonian) have been recovered from mudstone deposits along the Gaspé Bay in Québec (page 913). The three-dimensional specimen represents the earliest known terrestrial animal from North America and the oldest known member of the class Insecta. The eyes are large, compound, and bulging, the form of the mandible and presence of a lower lip-like structure suggest that relatively soft foods were procured and milled, there are numerous depressions (insertion sites) in the head cuticle for sensory hairs, and there are triangular bases in the thorax for the walking legs. Many of the features resemble those of bristletails (Archaeognatha) and some are diagnostic. Labandeira *et al.* point out that both bristletails, with their external mouthparts, and other hexapods that have internal mouthparts existed during the Early Devonian; thus, food-piercing and food-chewing hexapods may have been diverging from their common ancestor in the (earlier) Silurian period as were the primitive land plants that they ate.

Fungal-plant relations

AN understanding of how fungi interact with plants they infect may contribute to future efforts to interfere with the pathogenic process. When spores of pathogenic fungi land on a plant leaf, they bore through the leaf's protective cuticle layer: cutinase, an extracellular enzyme on the surface of the germinating fungus, begins to degrade the insoluble polyester cutin from which monomeric fatty acids are then released. Podila *et al.* show that these released monomers work synergistically with a soluble protein factor from the fungus to induce transcription of the cutinase gene in fungal nuclei (page 922). Cutinase production increases as more monomers become available. Thus, after the fungus has penetrated the cuticle and stimulatory monomers are no longer released, gene transcription and enzyme production should be shut off. Specific molecular events that are involved in the induction of transcription by monomer and protein may relate to the formation of a preinitiation complex before transcription gets under way.

Microtubule binding site

MICROTUBULES are substructures within cells that participate in cell division, cell motility, and other cellular processes, and help to maintain cell shape. Tubulins are their major constituents; large microtubule-associated proteins (MAPs) and smaller tau proteins are associated with the tubulin proteins. Characteristic determinants of MAP2 (a MAP protein detected only in the brain) and tau have been found in neurofibrillary tangles in the brains of patients with Alzheimer's disease. The complete amino acid sequence of MAP2 was determined by Lewis *et al.* from a series of overlapping cloned complementary DNAs; a polypeptide—the putative binding site—that is part of the carboxyl terminus of MAP2 was shown to associate strongly with microtubules, remaining attached during several cycles of polymerization (microtubule assembly) and depolymerization (disassembly) (page 936). When the MAP2 and tau sequences were compared, striking similarities were apparent, including three imperfect repeats of a stretch of 18 amino acids separated by 13 or 14 amino acids. If only one repeat segment is needed for binding to microtubules, the presence of three on a single MAP2 or tau molecule might ensure cross-linking. An understanding of how MAP2 and tau normally bind to microtubules may help clarify how or why these proteins disengage in Alzheimer's disease.

Peroxide trap

A protective "fertilization envelope" forms around sea urchin eggs minutes after they are fertilized. The powerful oxidant hydrogen peroxide (H_2O_2), which is produced by the egg, cross-links the envelope. The egg is protected by ovothiol C from the deleterious effects that would be caused if H_2O_2 were internalized; this amino acid reacts with and acts as a sink for H_2O_2 but then is regenerated by reduced glutathione (page 939). Turner *et al.* explain that ovothiol C may thus be an alternative to the enzyme glutathione peroxidase that, in other systems, controls H_2O_2 toxicity. Ovothiol C may also protect diverse marine organisms when, as a result of photochemical reactions, H_2O_2 reaches high concentrations in the sea. Because ovothiol C is so effective in controlling reactive oxygen species, it might have uses as a reagent in other cell systems in which dangerous oxidants are generated.

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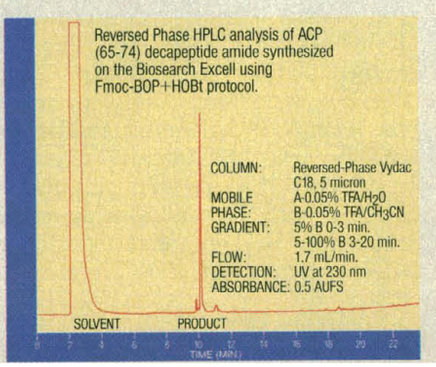

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Improved Efficiency of U.S. Copper Production

During the first two-thirds of this century, U.S. companies controlled most of the world's reserves of copper and the United States was the leading producer of the metal. But in the past two decades, U.S. companies have experienced traumatic blows, including nationalization of their profitable foreign holdings, competition from low-cost producers elsewhere, and impact of environmental regulations. For some years during the 1980s, operating losses of the companies were so large that it seemed possible that the U.S. copper industry would disappear. Such a development would have been a cause for concern. Copper has many uses and will have an increasing role as electricity is employed more intensively here and worldwide.

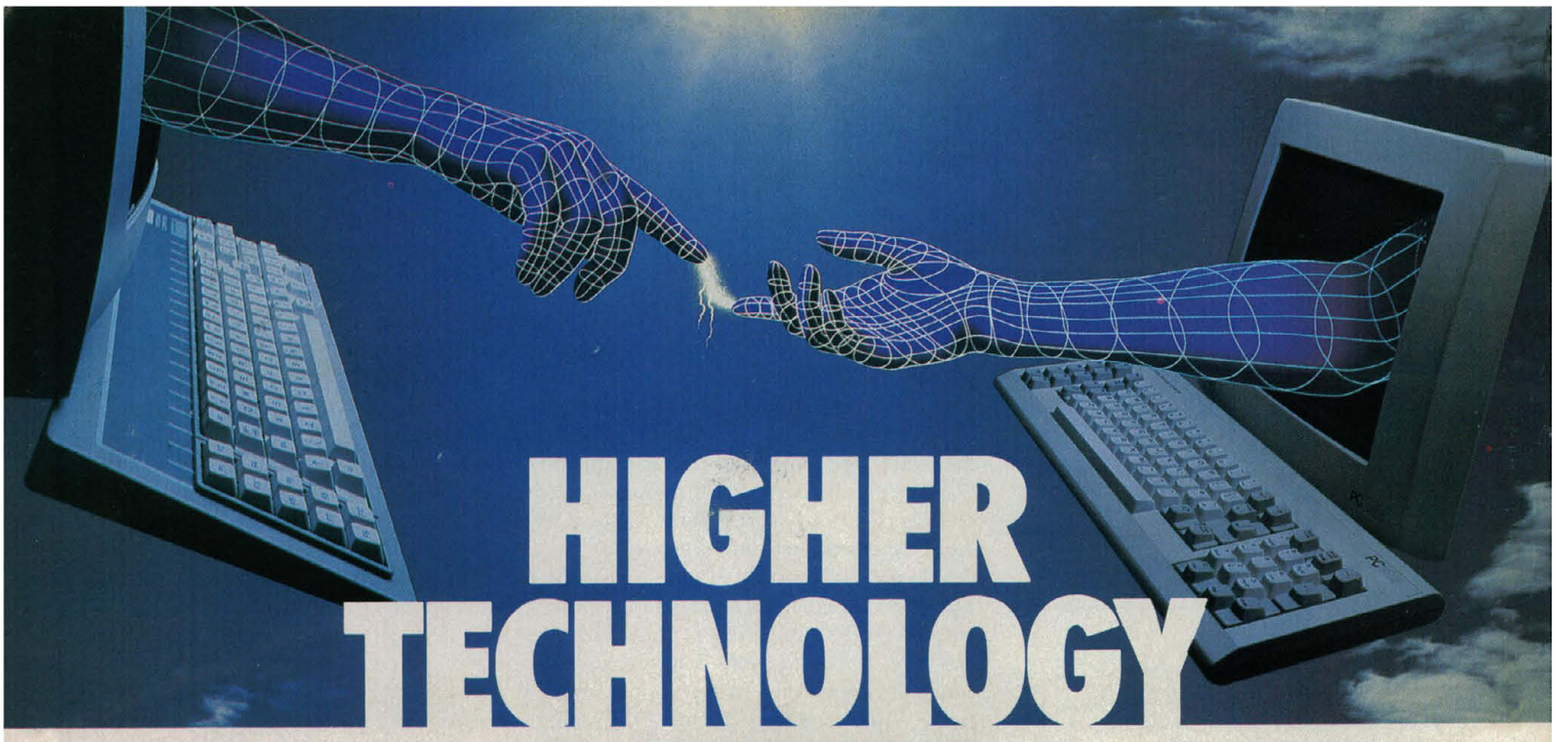
In part the problem of costs was due to failure of management to install state-of-the-art equipment in the huge open-pit mines that produce 85 percent of this nation's copper. In part the problem of costs was exacerbated by a slow decline in the grade of U.S. ore, which was and is considerably lower than that of foreign competitors. The financial and competitive problems of the copper industry were exacerbated by environmental regulations. While producers in most other countries continued to pollute, those in the United States were required to cut emissions of sulfur dioxide by 90 percent. As a result, substantial costs were incurred to achieve compliance, and some smelters were abandoned.

The period 1984 to 1986 was particularly trying as the producer price of copper hovered around 65 cents per pound. In terms of constant dollars, this was the lowest price since the great depression of the 1930s. Nevertheless, some companies did not give up on copper. Instead, they analyzed what needed to be done to be profitable even if the price of copper remained low. Looked at one way, the task of extracting each day the 0.8 percent copper from 77,000 tons of hard rock is enormous. But in principle, it is fairly simple. Boulders of the rock are blasted loose, transported to a mill, and ground into a fine powder. The powder is suspended in big vats that contain a detergent that sticks selectively to the copper values (mainly sulfides). Air bubbles rising in the vat bring to the surface a foam that contains most of the copper.

Major copper companies have found ways of reducing their costs. Phelps Dodge, the largest domestic producer (about 500,000 tons a year), achieved savings in a multiplicity of ways. It transferred its headquarters from New York to Phoenix and cut by half its white-collar staff. It will improve the efficiency of its transportation of rock by use of computer monitoring and by installing an in-pit crusher at its Morenci, Arizona, mine. This will permit cheaper transportation of rock to the mill on a moving belt. Phelps Dodge has improved the efficiency of its copper concentration process by employing analytic instrumentation, including x-ray fluorescence. The most effective move at Phelps Dodge has been to install equipment that permits inexpensive (less than 30 cents per pound) production of pure copper from leachates of wastes and tailings. Soon a third of its production will come from this source. The copper in the leachate is extracted by kerosene that contains a copper-binding organic chemical. The copper is later stripped from the kerosene by 1.5 molar sulfuric acid and then electroplated.

The mine at Bingham Canyon, Utah, is the largest man-made hole on Earth. It is shaped like a saucer, 2.5 miles in diameter and a half mile deep. Mining was stopped in March 1985 because of high costs and outmoded equipment. But by investing $400 million, British Petroleum, the owner, is achieving a cost reduction in production of copper of about 20 cents per pound. A 1000-car railroad has been replaced by a moving belt, and pipelines are being used to transport ore concentrates and tailings. The complex will annually produce 200,000 tons of copper, 300,000 ounces of gold, 2 million ounces of silver, and 12 million pounds of molybdenum.

At the moment, the price of copper is above $1 per pound, and essentially all producers are making a profit. History teaches that in time there will be new mines elsewhere, overproduction, and low world prices. But at least some of the U.S. production will have costs that will be among the lowest anywhere. We will probably continue to import about 25 percent of our copper for consumption, but expanded imports of copper will not add a further burden to our trade deficit.—PHILIP H. ABELSON



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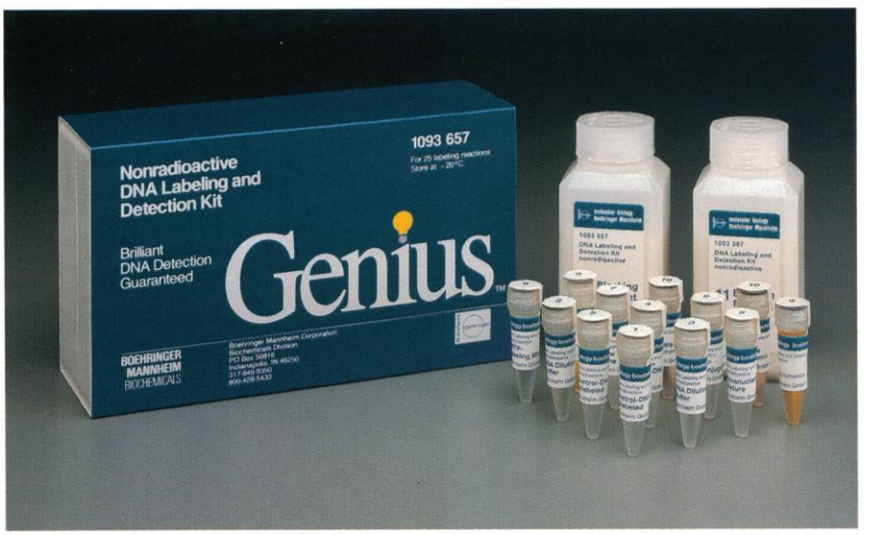

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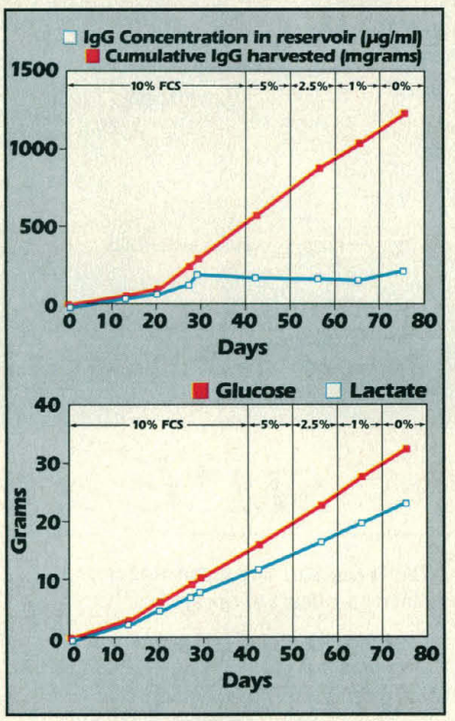

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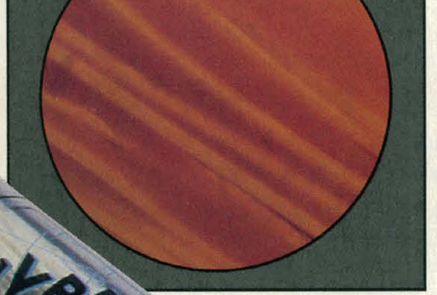

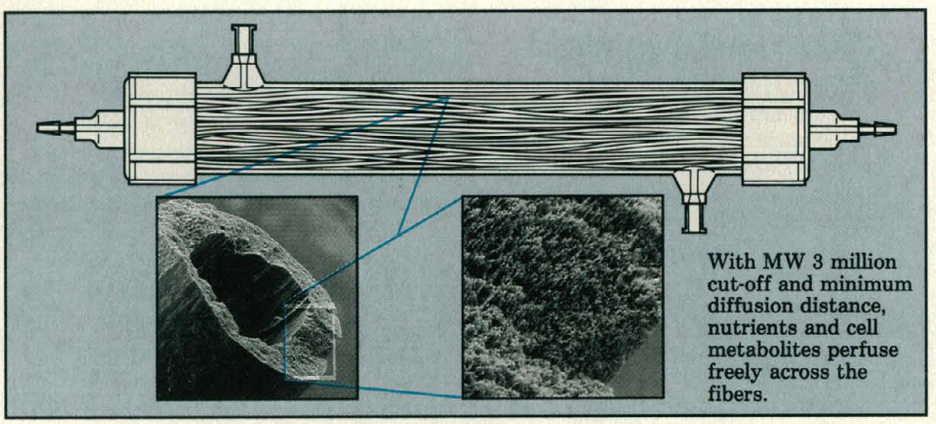

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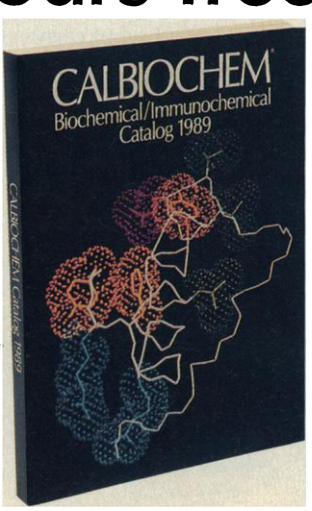

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other companies make reagents for it. Hoffmann–La Roche has now begun to market an FPIA device of its own. The rate cited for the Hitachi machine was misquoted: it should have been 1500 to 1800 results an hour.—ELIOT MARSHALL

Pork Barreling

In his editorial, "Regularizing 'pork' " (12 Aug., p. 769), M. Granger Morgan suggests capitulating to the political forces that more and more are diverting research funds away from merit review and straight into the pork barrel. Morgan states: "If 'pork barrel' science and engineering cannot be stopped politically, and arguably serves positive social ends, we should be trying to regularize the practice in a formal program, not terminate it." I feel this a dangerous concession and one that will invite more players to join in the pork barrel game.

Recently, academic pork barreling took a turn for the worse in both the House and the Senate. On 20 June, for example, the Senate subcommittee for rural development, agriculture, and related agencies of the Committee on Appropriations earmarked $8.25 million in the U.S. Department of Agriculture (USDA) competitive grants program for research at the University of Arkansas, Kansas State University, Iowa State University, the University of Iowa, a Midwest plant biotechnology consortium, and the city of Cedar Rapids, Iowa. While the objectives in the appropriations may have been meritorious—food safety, alternative pest control, and biotechnology among them—it is a disservice to the nation for Congress to designate the location of research, particularly when it includes handing over nearly a quarter of the $40.8 million originally appropriated for competitive grants.

Widespread circumvention of the merit review process is eroding the foundation of our system for federally supported research. This system depends on a delicate balance between federal funding of research and federal control of research. Further, it entrusts the scientific community with determining the nature of our research and with ensuring its quality. Pork barreling by the scientific community compromises our objectivity and integrity. Consequently, we stand to forfeit our right to play a significant role in federal resource decision-making.

Fortunately, through the combined efforts of the scientific community, academic and agency administrators, and congressional leaders, the location-specific earmarks on the USDA competitive grant funds were removed when the Senate passed the fiscal year 1989 Rural Development, Agriculture, and Related Agencies Appropriations Bill in the beginning of August. It is important, though, that the participants who pressed for this reversal remain vigilant until the Senate-House Conference Committee acts on the bill. This example shows how collective protest against pork barreling can bring it to a halt, at least in its most extreme cases. We do not have to "regularize" a practice we know is fundamentally unacceptable just because it "shows no sign of abating." Certainly not when there is evidence that we can bring about the abatement.

I also disagree that pork barrel science and engineering "arguably serves positive social ends." First, while the goals of upgrading the quality of science and engineering throughout the country and of enhancing the economic viability of particular regions are noble, such social and economic engineering should not be funded with monies allocated for fundamental research and research facilities. These monies must be awarded on the basis of research performance, intrinsic merit, and relevance of the research. To do otherwise when research dollars are scarce will result in spreading

resources so thinly that the quality of research in the United States would fall to a common level of mediocrity. Attempts to upgrade the research activities and economy in a particular region by pulling the rug out from under research that meets objective criteria for deserving funding is woefully shortsighted. In the long run, it weakens our strongest research and undermines our economic competitiveness. Equating federal research monies with "vital regional development resources" is bad mathematics—we would not like the numbers we would end up with.

At a time when funding for research is becoming scarce while scientific opportunities are increasing, we should be helping set priorities, not climbing into the pork barrel. We should also work together to convince Congress of the great need to improve the research infrastructure in U.S. universities and colleges. There is growing recognition of that need, as Morgan indicates, with the introduction of the University Research Facilities Revitalization Act (H.R. 1905) and in the fact that similar language was included in the trade bill passed by Congress but vetoed by the President. We need these improvements to take advantage of new opportunities in science, to provide better training for students, and to improve our ability to address the nation's problems that require scientific solutions. We should redouble our efforts to ensure that adequate funds are provided to conduct good science rather than resorting to pork barrel politics.

CHARLES E. HESS*
Dean, College of Agricultural and Environmental Sciences, University of California, Davis, CA 95616

*Past member and vice chairman of the National Science Board.

Response: I share Hess's belief in the value of peer review in allocating scientific R&D resources. There is, however, strong empirical evidence that Congress is unprepared to accept peer review as the sole basis for allocation and believes that other considerations, such as regional economic development, ought to figure substantially in at least some decisions. Hess argues that the answer lies in persuading Congress that they are wrong.

Both as individuals and in various groups, leaders of the nation's research establishment have made this argument repeatedly. I have myself made it with my own congressman who chairs the science, research, and technology subcommittee of the House Committee on Science and Technology. The clear evidence is that Congress does not find the argument persuasive. Members have strong political and philosophical reasons for believing that factors other than peer review should figure in at least some R&D allocation decisions. The steadily growing volume of pork barrel R&D provides strong evidence that our arguments are going nowhere.

In the face of this evidence I have concluded that the most effective defense is to "regularize" the process. Force the Congress to make a few explicit decisions that limit the overall level of R&D resources that can be allocated on a basis broader than conventional peer review. Then hold the line. Hess may not like this approach, but I believe it is better than risking the growing erosion of the peer review process that results from large numbers of individual congressional decisions, most of which are not being as effectively countered as the one Hess outlines in his letter.

M. GRANGER MORGAN
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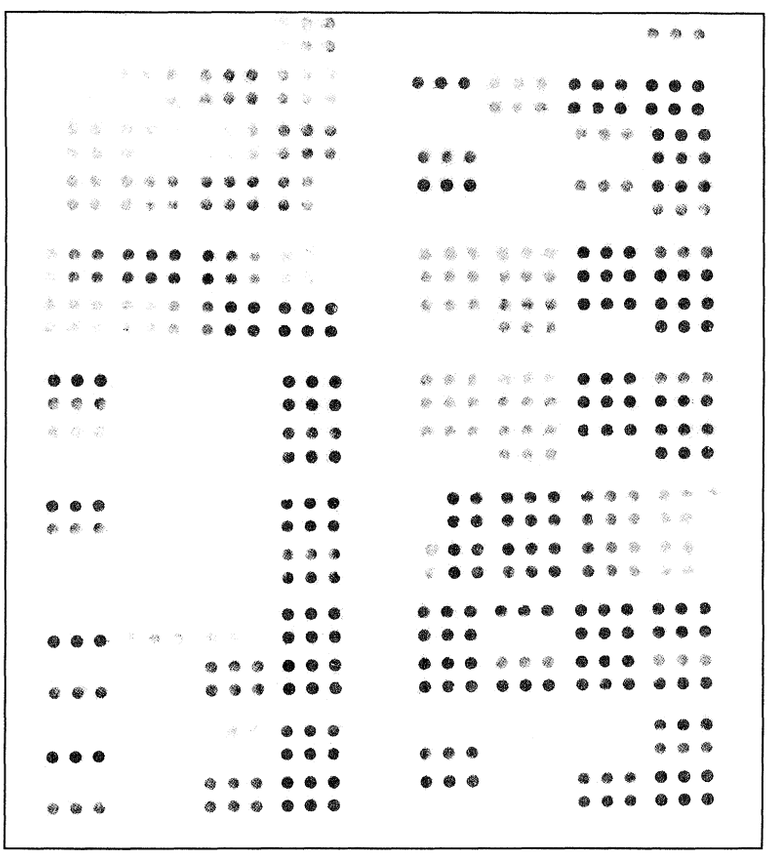

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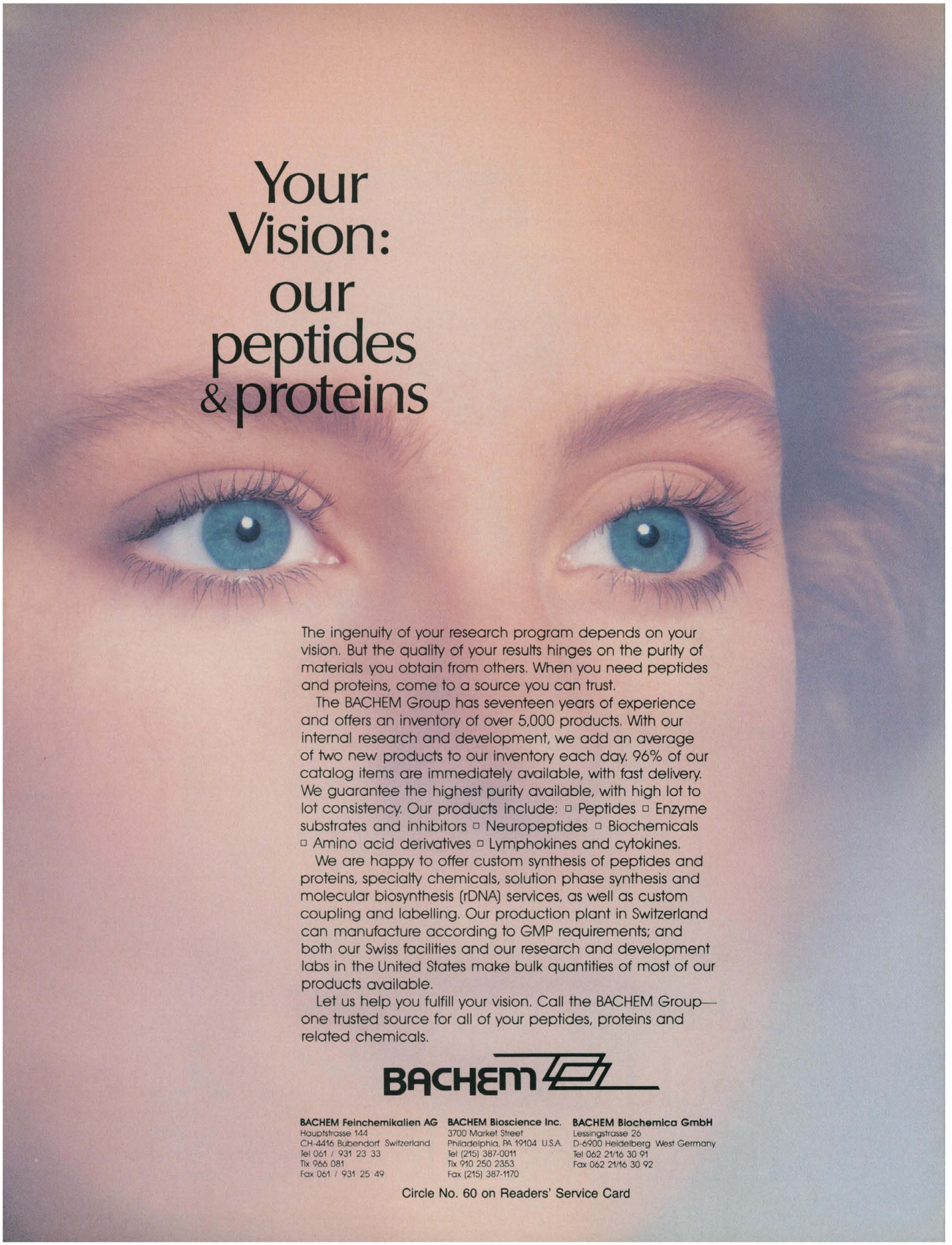

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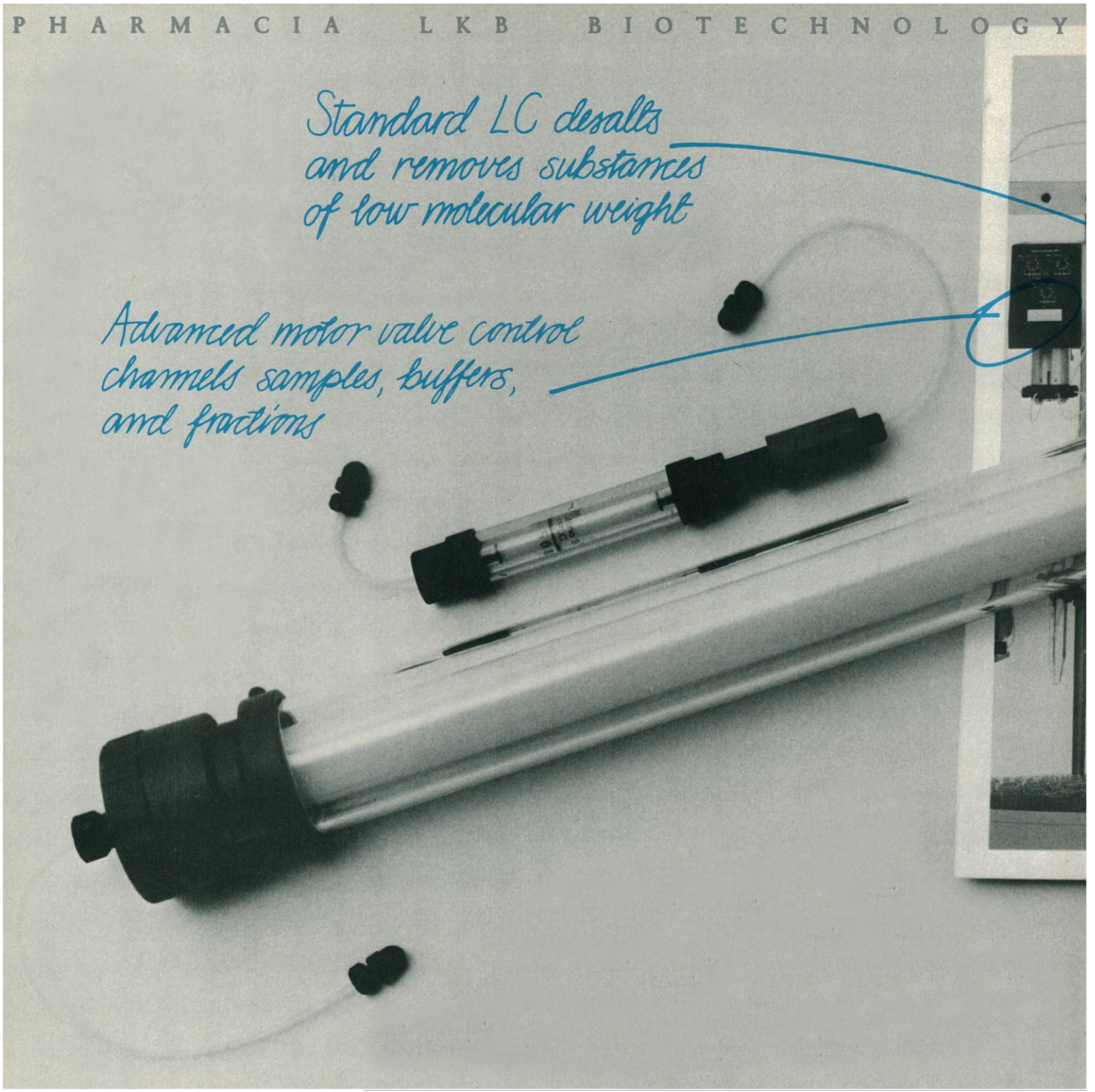

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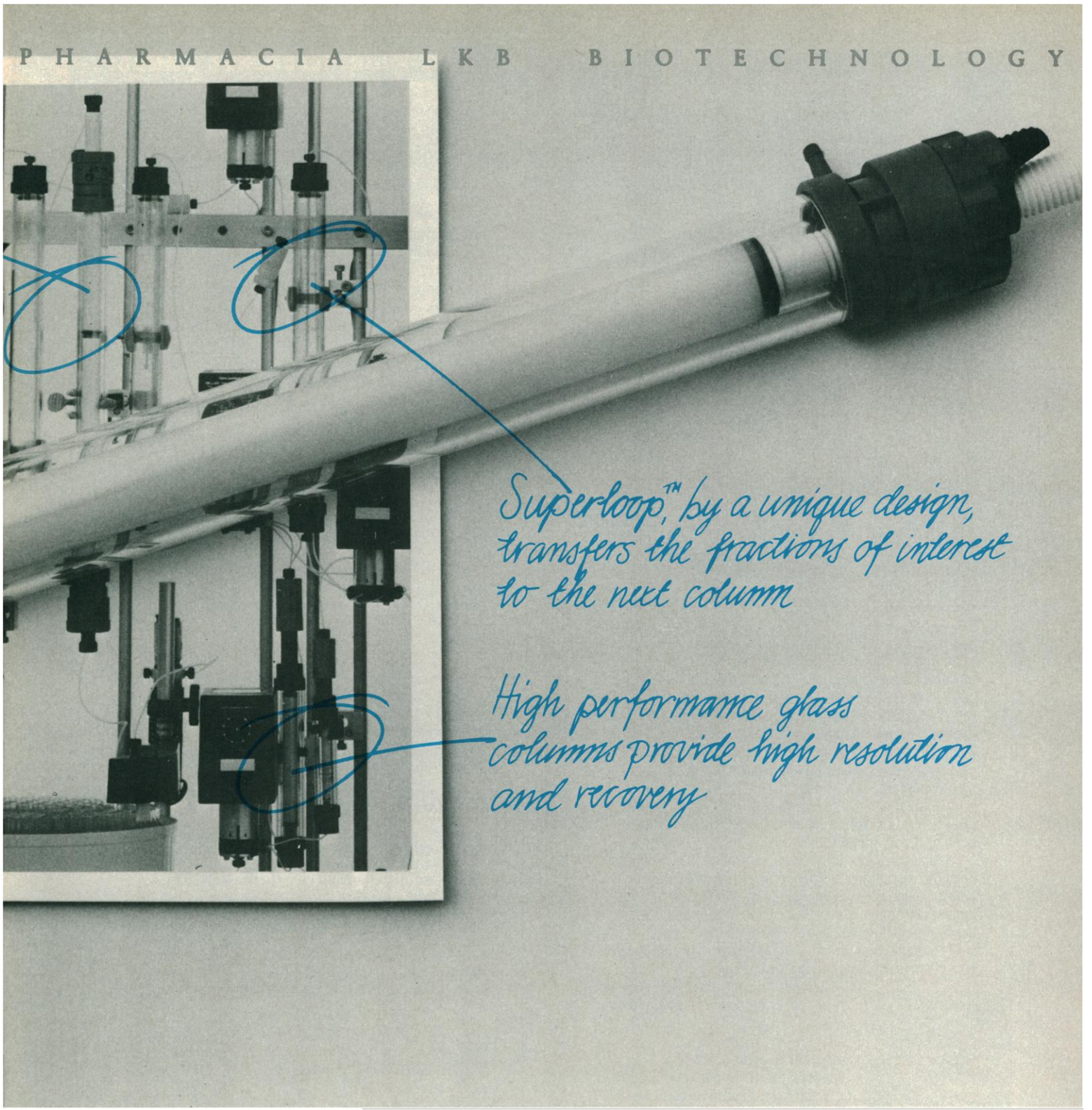

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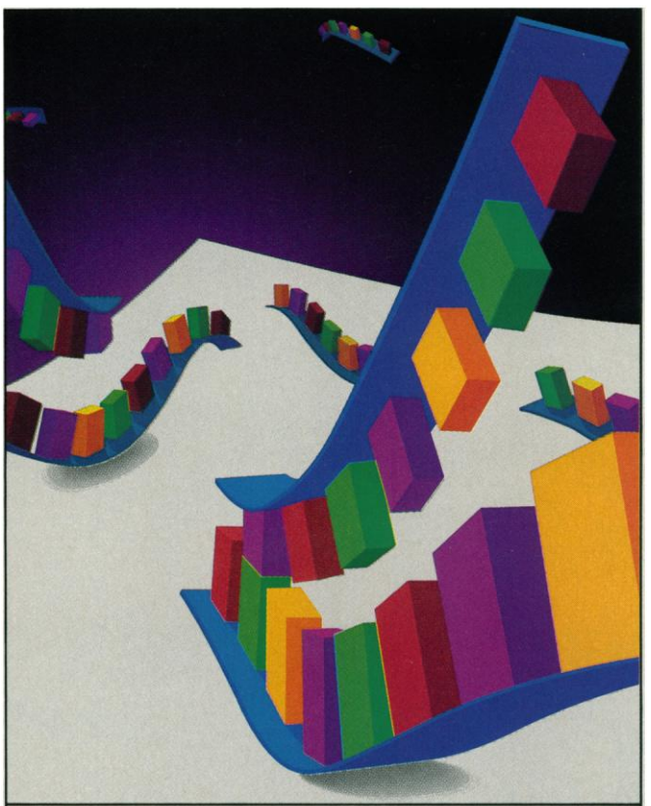

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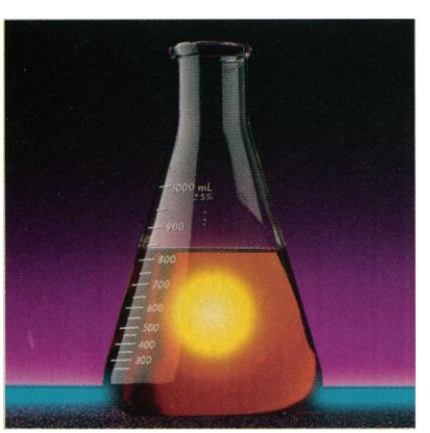

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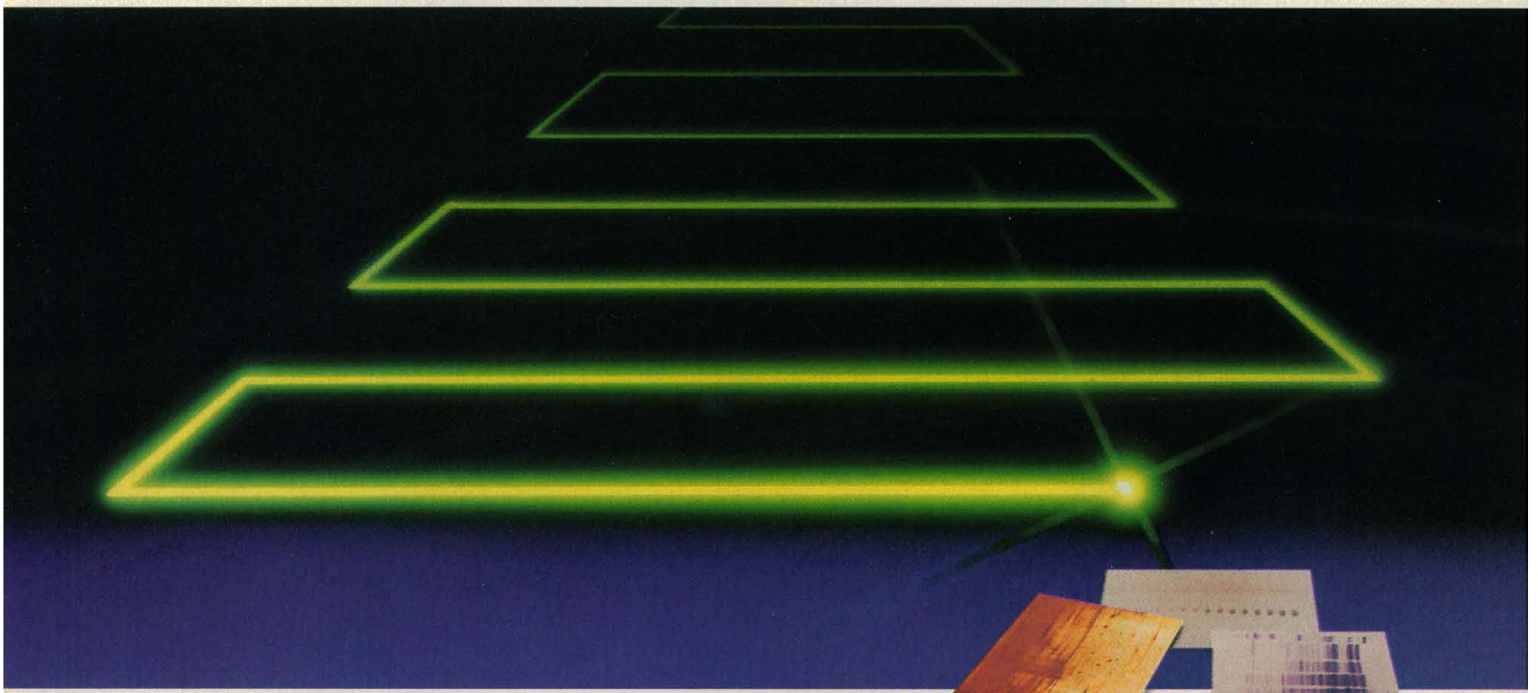

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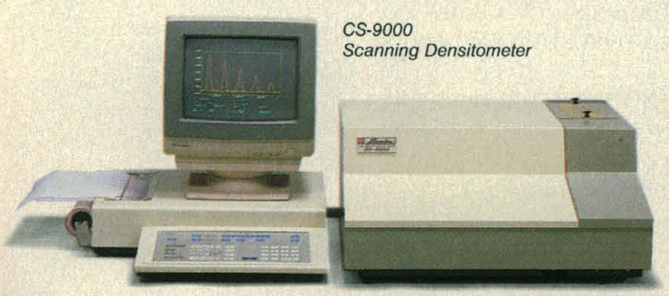

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activation of key intermediates that serve as group donors: "groups, such as phospho-, acetyl-, and amino-, are brought by metabolic mechanisms intermediately into positions from which they can easily be carried into desired places." Examples and corollaries of this generalization that underlie the organization of metabolism were discussed, among them the central role of ATP: by virtue of formation of ATP from ADP in catabolic sequences and of ADP from ATP in energy-requiring processes, the ATP-ADP couple serves as the central energy-transducing system by which metabolic sequences are functionally interrelated; thus biological energy transfer is stoichiometric and quantized.

To emphasize the metabolic importance of activation, which he compared to the use of such organic reagents as acetyl chloride, Lipmann spoke of "biologically interesting linkages designed to transfer groups with loss of energy," which are " 'weak' linkages based on the usual chemical nomenclature," as energy-rich bonds and proposed that they be distinguished by the special symbol ~. That symbol and some ambiguous statements about "concentration" of energy in such bonds were promptly adopted by biochemists. They proved a mixed blessing. On the one hand, by emphasizing the central role of ATP, they established the pervasive interdependence of sequences and the quantized nature of those relationships, and thus contributed importantly to the development of a functional view of metabolism. On the other, they led to wide acceptance in biochemistry and biology of such chemically illiterate concepts as bonds into which energy can be packed and which release energy on cleavage. Since cleavage of any bond necessarily requires, rather than releases, energy, that terminology confused students and estranged metabolic chemistry from mainstream chemistry for several decades. That estrangement was as unnecessary as it was unfortunate, since if defined appropriately the ~ symbol could have emphasized the importance of activation and quantization in metabolism without doing violence to the fundamental meaning of activation. In this book Slater remarks rather condescendingly that although the discussion of energy-rich bonds "upset the chemists somewhat, since it seemed to run counter to their concepts of bond energy," biochemists always clearly understood that it referred to the standard Gibbs free energy of hydrolysis of the bond. If Slater really believed that in 1987, he should have reread nearly any biochemistry textbook, or nearly any review treatment of metabolic energetics, published between about 1945 and 1970.

From 1941 onward, Lipmann's interests were focused on metabolic activation. His research group discovered the carbamoyl donor carbamoyl phosphate and the sulfate donor PAPS, and (in the work for which he received the Nobel Prize) contributed to the discovery of coenzyme A, which is involved in the activation of acyl groups. It was his curiosity as to the mode of activation of amino acids for formation of peptide bonds that led to the very important contributions to understanding of protein biosynthesis that his group made during the last decades of his career.

Several contributors to this volume mention the strangely parallel careers of Lipmann and Hans Krebs. Born within a few months of each other, both attended medical school. They met at the beginning of their research careers in the Kaiser Wilhelm Institute laboratories at Berlin-Dahlem, where Lipmann worked with Meyerhof and Krebs with Warburg. Both left Germany to escape the Nazis, Krebs going to Britain and Lipmann to the United States. Their research careers were complementary. Krebs's most important contributions were the discovery of the urea cycle (and with it the concept of metabolic cycles) and the citrate cycle. Lipmann's most important contribution was the concept of the importance of metabolic activation, with emphasis on the role of ATP, which in aerobic cells is regenerated primarily as a consequence of Krebs's citrate cycle. He discovered the donor of carbamoyl groups to the urea cycle and contributed to the discovery of the donor of acetyl groups to the citrate cycle. They shared the Nobel Prize in 1953.

It is the contrast between the temperaments of Lipmann and Krebs that intrigues several of the authors of this volume. Krebs was hard-driving, highly organized, logical, quick-witted, and fluent in lectures and discussions—all characteristics to be expected in a major scientist. Lipmann seemed the opposite in all these respects. These two men, so different in temperament, were the most important metabolic biochemists of their generation. One could not ask for a better illustration of the wide range of personal characteristics that may underlie high achievement in science.

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