Book Reviews

Honoring Hans Krebs

Biological Cycles. Papers from a symposium, Dallas, March 1980. RONALD W. ESTABROOK and PAUL SRERE, Eds. Academic Press, New York, 1981. xxii, 574 pp., illus. $59.50. Current Topics in Cellular Regulation, vol. 18.

This volume diverges from the pattern set by its predecessors in a distinguished series in being the report of a symposium held in honor of the late Hans Krebs on his 80th birthday. It therefore contains many more papers of considerably shorter average length than others in the series.

It is possible to define the word "cycle" broadly enough that nearly all biological events may be considered cyclic. In its catalytic action, for example, every enzyme alternates between different conformations and different enzyme-substrate, enzyme-intermediate, and enzyme-product complexes. If, however, "cycle" is defined narrowly as denoting a cyclic sequence of reactions that occur simultaneously in one cell and have a biologically useful result, there are far fewer examples, and perhaps only three of large magnitude. It is impressive that two of these three were discovered by Krebs during his, and the century's, fourth decade.

The urea cycle is responsible for the largest-scale net synthesis in the adult mammal. It disposes of excess end-product ammonia, and because it consumes large amounts of bicarbonate, the conjugate base of the primary blood buffer system, it must also profoundly affect acid-base balance. In addition to the intrinsic importance of this cycle, its formulation in 1932 introduced the concept of metabolic cycles in the strict sense. The citrate cycle supplies electrons for use in the generation of most of the adenosine triphosphate produced in aerobic organisms. Its description in *Enzymologia* in 1937 (after the manuscript had been rejected by *Nature*) is one of the most important and best-recognized events in the history of biochemistry.

Photosynthesis completes the trio of major cycles. Other cycles of this type include the Kornberg-Krebs glyoxylate cycle (1957) and the histidine biosynthetic cycle, as well as a host of others that may be more localized or specialized. Having little in common with these except the word "cycle," but also of fundamental importance, are the regulatory cycles in which an enzyme is covalently modified with resulting modulation of its catalytic function. Several such regulatory cycles are discussed in the book.

Discussion of selected papers would reflect in part the interests of the reviewer and in any case would necessitate invidious omissions. I will therefore refer only to papers by four great contemporaries or near-contemporaries of Krebs's. Cori briefly describes the discovery of the glycogen-lactate cycle, which, although dispersed both in time and in place (muscle and liver), is a valid and metabolically important cycle. Lipmann recalls the development of the concept of a very different kind of cycling that underlies all metabolic activities—that between the different forms of transducing or coupling systems such as ATP-ADP and NAD^+-NADH. Leloir discusses activation of sugars for polysaccharide synthesis and other metabolic purposes, with brief historical comments. Wood's paper on bacterial fermentations is prefaced by some recollections that should be particularly valuable to students. Among the triumphs of the exciting early days of isotope availability were the apparent proofs that citrate is not an intermediate of the citrate cycle and that the citrate cycle is not important in microorganisms, including yeast as well as bacteria. Each of these proofs blended excellent experimentation with a plausible but faulty premise. The story of Ogston's recognition of the weak premise in the exclusion of citrate from the cycle and of Potter's subsequent experiments that put it back in is still sometimes included in textbooks. The equally important recognition by Krampitz of a possible flaw in the proof that microorganisms have no citrate cycle, and his elegant experimental demonstration that they do after all resemble the rest of us in that regard, are nearly forgotten. Both episodes illustrate the perhaps surprising possibility that new techniques may provide results that mislead even the most astute of investigators; in each of these cases the whole biochemical community accepted false conclusions on a fundamentally important point for several years. It behooves us to realize that such things have happened, are happening, and will happen again.

The quality of the papers in the book is high. I would judge that as many as 25 of the 31 would be well worth reading for young biochemists—certainly a high yield for a symposium-derived volume. The wide range of topics covered must have made for an exciting symposium, but, as in all such collections, it may limit the usefulness of the book. The title will not serve as a useful guide, and many papers may be read less than they deserve.

Since the purpose of the symposium and of the volume is to celebrate the distinguished career and contributions of Krebs, it seems appropriate to close a review with an especially apt comment from the paper by Leloir, "People with no research experience underestimate the feat of adding even a small new idea to our intellectual heritage." Facts are easy to acquire and to add to the sum of human knowledge; ideas are quite different. Krebs not only originated very important ideas, he was unusual if not unique among leading biochemists in specifically urging the importance of ideas. In a short lecture (published in *Bull. Johns Hopkins Hosp.* **95**, 45 [1954]), he discussed cogently the importance of biological thinking in biochemical research. The lecture could be read profitably by all young scientists, and I wish that it could have been reprinted in the present volume. As Leloir comments, "When new knowledge reaches the textbooks, the ideas appear obvious and the fact of having dispelled previous ignorance appears less momentous. . . . The ideas on the urea and the citric acid cycles were a very important landmark in our understanding of intermediary metabolism. They will remain as an everlasting homage to a great man of biochemistry, Sir Hans Krebs."

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