Book Reviews

Honoring Kamen

From Cyclotrons to Cytochromes. Essays in Molecular Biology and Chemistry. Papers from a symposium, La Jolla, Calif., 1978. NATHAN O. KAPLAN and ARTHUR ROBINSON, Eds. Academic Press, New York, 1982. xvi, 888 pp., illus. $64.

This book is more than a collection of lectures; it is a record of a celebration by people who have known Martin Kamen intimately for many years and who admire him. In the prologue, following a foreword by the two organizers of the symposium, one encounters a photocopy of a letter of congratulations to Kamen from an old friend, Hugo Theorell, then a page of delightful and appropriate doggerel by a musician friend, Henry Temianka, and a warm recollection by S. J. Singer of a chance encounter at a violin and piano recital. The final contribution to the prologue, by Melvin Calvin, brings the reader back to considerations of science and technology and their social consequences.

Like the object of the celebration himself, the symposium covers a wide range of subjects. The papers are grouped into five sections: Isotopes; Cytochromes: Chemistry and Structure; Phosphorylation, Oxidation, and Photosynthesis; Protein Structure; and Regulatory Mechanisms and Metabolic Miscellany.

The section on isotopes is a rich mixture of history and science. A paper by E. M. McMillan sets the stage by describing the atmosphere and the research in E. O. Lawrence's Radiation Laboratory in Berkeley in the 1930's and early 1940's. McMillan describes the synthesis of isotopes in the chamber of the cyclotron. Everything was home-made, nothing was automated. Simple-seeming methods were used to detect dozens of new isotopes, and the excitement in the laboratory must have been enormous. Although the laboratory was devoted to physics, there were serious attempts to develop biological applications, such as methods to study the absorption, uptake by tissues, and excretion of the radioactive materials in animals and in humans (some of those attempts are frightening, in hindsight). The medical implications were clearly seen, as is shown by the investigation of ^{32}P as a possible cure for leukemia. In all, 46 isotopes were synthesized and identified in Berkeley in the years 1934 to 1940, and Kamen was involved in four of those events.

Several authors in this section give insights into the discovery of ^{14}C and note the impact it had on biology and on physics, as well as on Kamen. Mildred Cohn relates that she was present when Harold Urey was explaining to Lawrence his conviction that the stable isotopes (^{2}H, ^{13}C, ^{15}N, and ^{18}O) would be more generally useful in biology than would the radioactive isotopes. At the time, Lawrence had no basis for a rebuttal but "on returning to Berkeley, he informed his research team, which included Kamen, that they had to find a long-lived radioisotope that would be useful as a biological tracer." A. A. Benson, who was there at the time, insists that because of Lawrence's request Kamen and Ruben invented (rather than discovered) ^{14}C. They knew it could be done, and they used every plausible trick to do it. They "spent a year trying to make it from ^{13}C"; "the less likely reaction of ^{14}N with neutrons finally led to success." Benson notes that, for various reasons, the inventors had no opportunity to exploit their new isotope.

An unexpected property of ^{14}C is its very long (about 5700 years) half-life. Henry Primakoff, a theoretical physicist, refers to early calculations that predicted half-lives for ^{14}C between 1.3 days and 5 years. He proposes a different mechanism for the β-decay, one that gives a result close to the experimental value. Cohn explains why two isotopes are better than one, giving as examples the combination of ^{14}C and ^{32}P in the study of phosphoglucomutase and the combination of ^{32}P and ^{18}O in the study of oxidative phosphorylation. Combinations of stable isotopes, including the inexpensive, naturally abundant ones, which can be studied by NMR spectroscopy, are useful in establishing chemical reaction mechanisms. Cohn cites the simultaneous use of ^{2}H and ^{13}C in a stereochemical study and of ^{31}P and ^{18}O in mechanistic studies of nucleotides. Benson tells briefly of the earliest studies of the photosynthetic pathway. H. A. Barker describes a number of the earliest studies of photosynthesis, in which the Ruben-Kamen-Hassid-Barker combination was involved in experiments with ^{11}C. He tells also of some political troubles that beset Kamen and led to his becoming more deeply involved in biological studies and to the application of ^{14}C to those studies.

Though ^{11}C, with its 20-minute half-life, was superseded by ^{14}C for tracer studies of metabolism, it has another useful property; it emits positrons when it decays, and in recent years positron-emitters have found uses in nuclear medicine because compounds labeled with such isotopes give rise to γ-rays as a result of positron annihilation. Morris Friedkin describes a number of uses for such isotopes in the study of cellular proliferation and of infiltration by neoplastic cells. The new field of positron-emission tomography is another application of these isotopes to human medicine.

The last two contributors to the section, Harland G. Wood and David Shemin, were among the earliest and most successful exponents of isotopes in the study of biosynthesis and metabolism. Wood and C. H. Werkman had discovered in 1936 that heterotrophic microorganisms can fix CO_2. Soon thereafter they used $^{13}CO_2$ to study the pathways involved. They found ^{13}C in the carboxyl groups of succinate formed during a microbial fermentation of glycerol and went on to other work. Wood recalls his shock on reading a report from the group at Berkeley that in the presence of $^{11}CO_2$ the propionate formed in such a fermentation was labeled in all three carbons; it seemed likely that the propionate was synthesized de novo from CO_2 rather than by a simple transformation of glycerol without rearrangement of the carbon skeleton. Wood had saved propionic acid from his experiments with $^{13}CO_2$; he proceeded to purify it and selectively degraded each position. He had been right after all; the CO_2 was incorporated only into the carboxyl group. Five years later, however, Barker and Kamen found that when *Clostridium thermoaceticum* ferments glucose in the presence of $^{14}CO_2$ radioactivity is incorporated and labels both positions of the product, acetate. Wood has continued to try to unravel the mechanism by which these organisms accomplish this reaction, and he describes some of his recent work in the rest of his contribution.

In the last paper in this section, Shemin describes the role that isotopes played in Rudolf Schoenheimer's laboratory in the early 1940's. Schoenheimer had introduced the use of isotopes for studying metabolism and had developed the concept of the dynamic state of body constituents. Shemin had undertaken a study of the turnover of plasma proteins by feeding ^{15}N-glycine (which he synthesized himself) to a rat. Next, he administered the glycine to himself, swallowing a 1-gram sample every hour for 66 hours. Blood was withdrawn at intervals, and the ^{15}N concentration in various proteins was measured. The data were consistent with Schoenheimer's concept, and the half-life of the total plasma proteins was found to be about five days. The hemoglobin was isolated also; the ^{15}N content of the hemin reached a maximum about 20 days after the start of the experiment and stayed constant for nearly 80 days, in total disagreement with the concept of the dynamic state. The experimenters accused each other of mixing up the samples and of using the mass spectrometer incorrectly. Finally, when they analyzed the data they deduced that the half-life of the erythrocyte is about 127 days and that glycine is the nitrogenous precursor of heme. Next they turned their attention to the carbon skeleton and found that 2-^{14}C-glycine labeled the heme as expected. While this work was in progress, Kamen's laboratory reported that carboxyl-labeled glycine did not label heme. From these and some other results, Shemin was able to formulate a biosynthetic pathway for heme.

This section occupies about one-seventh of the book and is neatly balanced by an appendix of about the same length in which 15 of Kamen's papers are reproduced. As one progresses through these papers, including the one that influenced Shemin, one goes, indeed, from cyclotrons to cytochromes. The earliest papers are from *Physical Reviews* in 1937, 1938, and 1941. For biological scientists, the most interesting of the three is a six-page article "Long-lived radioactive carbon—^{14}C." All of the "biological" papers merit the description "quantitative." Perhaps the most remarkable of these is a paper with Hershey, Kennedy, and Gest on the mortality of bacteriophage containing radioactive phosphorus, which combines nuclear chemistry, virology, statistics, and excellent experiments.

Since science is the result of human endeavor, one ought to consider the scientist along with the science. It is unlikely that an industrial designer would start his planning for a leader in many branches of science with an avid fan of the Chicago White Sox who worked in a laboratory called the "Rat House," who knew the words of many rather obscure Methodist hymns, and whose discussions with his colleagues are described thus: "They treated each other's ideas with brutal respect, replete with the strong language of Comiskey Park." Another recollection refers to the handling of ^{11}C and other, short-lived radioisotopes: "I seem to remember that Kamen wore gloves for some of these manipulations, although pictures . . . that have survived do not show this. As additional protection, Kamen wore an old and rather dirty lab coat. [His clothing] was so heavily contaminated . . . that he was not permitted in the lab . . . until the counting was finished."

In the fall of 1944 Kamen, Barker writes, "in a state of shock and bewilderment . . . told us that he had just been summarily dismissed from his position . . . because he had had dinner in a San Francisco restaurant with a Russian consular official under circumstances that an overzealous FBI agent considered to be suspicious." In spite of the official banishment, Lawrence continued to have confidence in Kamen and permitted him to visit and work in nonsensitive areas of the Radiation Laboratory. Consequently, he spent much of his spare time with Barker, applying ^{14}C to the investigation of several bacterial fermentations. The dinner in San Francisco continued to haunt Kamen. During the McCarthy era, he had booked passage for a trip to Europe, but when he went to board the ship he was not allowed to do so and his passport was taken away from him. He instituted legal action to recover the passport, which was restored only after several years. Kamen often played his viola at musical gatherings at FASEB meetings, and on one such occasion I was able to ask him some questions about his continuing problems. He explained that the Russian consular official had asked to talk to him because a relative was suffering from leukemia and he wanted to know about the possible use of ^{32}P as a treatment. A delightful vignette of the centrality of music in Kamen's life is presented by Jekisiel Szulmajster in his paper "Saint Agnes, music, and sporulation."

Carlyle's dictum that "the true university of these days is a collection of books" is no less true a century and a half after he wrote it. This book should be on the shelves of every college, university, and research institute that is engaged in the training of scientists and science educators.

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Insect Biology

Bark Beetles in North American Conifers. A System for the Study of Evolutionary Biology. JEFFRY B. MITTON and KAREEN B. STURGEON, Eds. University of Texas Press, Austin, 1982. xii, 528 pp., illus. Cloth, $30; paper, $17.50. Corrie Herring Hooks Series, no. 6.

Ecologists and evolutionary biologists are becoming increasingly aware of the problems associated with attempts to test theory using species whose basic ecological and genetic properties have been only superficially examined. In addition, pest management specialists have become more aware of the importance of a detailed understanding of population, genetic, and community processes for the development of management programs. Because such knowledge does not usually come to us without a considerable investment of time and money, it is a pity that applied ecologists and population biologists have shown so little interest in cutting their costs by studying the same organisms.

Lack of communication may be one factor in this situation. Mitton and Sturgeon must therefore be complimented for their attempt to bridge the communication gap. In this book, they and 11 colleagues with a variety of backgrounds present a coherent summary of the enormous literature on bark beetle species. Seven of the 10 chapters describe the general ecology and taxonomy of bark beetles, their hosts, mutualists, and natural enemies. One chapter addresses pest management, and in two chapters the editors explore some of the evolutionary aspects of bark beetle life systems. The reference list of over 1000 publications, mostly dealing with the ecology of economically significant bark beetle species, can be used as a rough index of the effort that has already been invested in this system. Population biologists could argue about the lack of analytical rigor in some of the studies described or the limited understanding of concepts such as group selection and coevolution displayed by some authors. On the other hand, one cannot help but be impressed by the detailed descriptions of interactions between biotic components of bark beetle life systems, which are as complex as they are intriguing. To illustrate this point, let me use the biotic interactions involved in initial host attack by *Dendroctonus pseudotsugae* as described by Borden. The first female that begins boring into a tree releases a number of "aggregation" pheromones. Some of these pheromones are unaltered secondary plant com-