Preface

We must be modest except in our aims.
— *Otto Loewi*

In an autobiographical article (1964),* Otto Warburg wrote: "The most important event in the career of a young scientist is personal contact with the great scientists of his time. Such an event happened in my life when Emil Fischer accepted me in 1903 as a co-worker in protein chemistry, which at that time was at the height of its development." On the first of the two statements made, Hans Krebs, himself a student of Warburg, wrote more extensively in *The Making of a Scientist*.† The second statement is my concern here. Emil Fischer's unifying theory of the manner of linkage of amino acids in proteins, proposed in 1902, was indeed a landmark, bringing together discoveries made since the 1740's. However, since then proteins have experienced a succession of climactic developments and the same must be true for other fields of active research. Indeed, every generation of scientists coming into a field asks its own questions, sets its own horizons and experiences its own excitements. In my own working experience, since the mid-forties I have observed organic chemistry develop into a mature mechanism-based experimentally predictive science. In the same period protein chemistry, as mentioned above, passed through revolutionary developments in amino acid analysis, amino acid sequence determination, then three-dimensional structures, followed by site-specific mutagenesis and, recently, extremely rapid structural analysis by mass spectrometry. Until the 1940's, the structural chemistry of nucleic acids was poorly understood and their biological functions were much contested. Yet, already in the early fifties clarification of nucleic acid structures had uncovered the chemical basis of heredity. Furthermore, concurrent developments in the two areas, the nucleic acids and the proteins, had culminated in the birth of molecular biology. The importance of biological phosphorylation began to be recognized at the beginning of the twentieth century. Energy-rich phosphate compounds were identified as the intermediaries in cell metabolism. By the 1950's, the golden age of intermediary metabolism had arrived. Currently, we seem to be entering the golden age of integral membrane proteins, molecular neurobiology and the all-pervading theme of signal transduction.

In several of the chapters that follow, I have attempted to bring out the landmarks in the development of the fields covered in this book, with the hope of bringing the reader to

*O. Warburg, *Ann. Rev. Biochem.* **33**, 531–544 (1964).
†H. A. Krebs, *Nature* **215**, 1441–1445 (1967).

the stage where my own research contributions began. I hope that this way I have conveyed the intellectual background and excitement in the fields in which I have worked.

The selection of my published papers had to be extremely restricted. Therefore, in the individual chapters, I have tried to give background to the experimental work that was pursued. Furthermore, comprehensive lists of publications from my laboratory have been included on all the topics; these precede the selected papers in the individual chapters. I have also provided in a later section a list of reviews written by me and some lectures given at different periods that were published.

From 1952, when I started my own laboratory, to 1960, I worked at the British Columbia Research Council, located on the campus of the University of British Columbia. During the next ten years (1960–1970), I worked at the Institute for Enzyme Research of the University of Wisconsin at Madison. Since 1970 I have been at the Massachusetts Institute of Technology. To all these three institutions I owe infinite gratitude. I was essentially left completely free to do my research as I wished. The work in British Columbia began with initial support from the National Research Council of Canada, made possible through the efforts of an able and visionary administrator, Gordon M. Shrum of the University of British Columbia. During a part of that period, even though working in Canada, I received support also from the National Institutes of Health, U.S. Public Health Service. Since my move to Madison in 1960 and all through the subsequent years, my major support has continued to come from the National Institutes of Health. In addition, the National Science Foundation provided support for many years while I also received support for some years from the Office of Naval Research.

In my own scientific development, I was most fortunate in coming under the influence of a number of very great scientists: Vladimir Prelog made me see beauty in chemistry, work and effort. Later, in biochemistry, I came under the influence of Fritz Lipmann, who was so gifted in integrating ideas, and Arthur Kornberg, who taught me stringency in biochemical experimentation. Association with Francis Crick during and since work on the genetic code has been intellectually stimulating and inspiring. Much later, Efraim Racker introduced me to membrane biochemistry.

Experimental work in my laboratory most often demanded group effort. In the fifties and sixties, the nucleic acid field held great attraction for the young generation of chemists and biochemists, as does the field of signal transduction at the present time, the field I work in now. Colleagues came to my laboratory from all over the world. They were stimulating and not only made experimental contributions but created decisive impacts on the directions of work. A very large proportion of my colleagues have attained high stature in science through their own contributions. This has been a major source of fulfillment in my scientific life. Further, my associations with a large number of my colleagues have evolved into lifelong friendships. It is to all the colleagues with whom I have shared all the ups and downs in research for more than 45 years that I wish to dedicate this book.

On the personal side, my wife, Esther, gave me unfailing support throughout my scientific career. Taking care of all matters outside of the lab, she left me completely free to pursue my scientific work.

I wish to thank my daughter, Julia, for all the artwork in this book. Finally, I am grateful to my longtime assistant, Judy Carlin, for her untiring efforts in the preparation of the book.

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