

Preface

My long and variegated career has spanned the period that has seen great advances in many areas of life science and my most recent activities have dealt with the founding and development of the new interdisciplinary field called neuroscience which thereafter developed explosively. This caused various friends to suggest that, for historical and scientific reasons, I should write an autobiographical account of my life. This was not the first time that the idea had been suggested to me. But on those occasions I explained that I simply could not remember in detail what had happened in the long time period since the publication of my first papers in 1924.

In 1982 it had been decided that the Neurosciences Research Program (NRP), with its many books, journals, and various kinds of records, would be sent to New York (Chapter XXIII). Meanwhile I had, for some days, been sorting out the large mass of records of various kinds that I had kept over the years. These were temporarily put in cardboard boxes, quite a few of them. At that point Kay Cusick and Fred Worden strongly suggested that my "papers" be put in the MIT Archives. At first I raised many objections to this plan, but in the end I agreed. My personal material filled 89 standard archival boxes and NRP-related material filled 26 boxes; these were brought to the MIT Archives. Thanks to the competent management of its director, Dr. Helen W. Samuels, and to library-trained personnel who arranged and cataloged the material in archival boxes, I was finally given a detailed list of the contents of all of these boxes, listed chronologically.

Now the major difficulty for me to write an autobiographical book had been removed. To obtain authentic information on items of significance for this book I had but to specify the particular box or boxes that contained the material; the requested boxes were then brought to my office. Meanwhile, my secretary and I were ensconced in the same quarters at MIT that I had especially designed when I had been appointed Institute Professor in 1955. In a sense I had returned to academia and my scientific activities began again.

Before turning to this project, however, my first scientific task was to formulate more clearly some ideas that had, in a preliminary form, been expressed in lectures in Texas (Chapter XXI), and during an NRP conference on molecular genetic neuroscience (Chapter XXII). This required a considerable amount of

data gathering and development of the idea before it was eventually published (Chapter XXIV).

In mid-1983 I received an invitation to write a prefatory chapter for the first volume of the *Annual Review of Biophysics and Biophysical Chemistry* (previously called *Annual Review of Biophysics and Bioengineering*). The editor specifically requested that this first chapter in the new series be strongly autobiographical. For this purpose it was necessary to review the relevant facts, mostly from reprints and books that had been collected over many years. The paper was written to show how, during my lifetime, "biophysical and biochemical methods have been developed and effectively applied to discover and characterize biological structures at the molecular level and thus to develop a comprehensive science of molecular biology." The title of the prefatory chapter is "Adventures in Molecular Biology."

The process of writing this prefatory chapter naturally focused my attention on autobiographical data which perforce had to be highly condensed; the published paper was only twenty-two pages long. However, this process, plus the fact that all the facts were now available in the boxes in the MIT Archives caused me, with the help of a small group of friends, to decide that I would undertake the task. Thus began the arduous work of planning and writing, through many versions, the story of my life from childhood to, and a bit beyond, my eighty-sixth birthday.

In the writing of scientific papers I, like many of my colleagues, would first write a detailed outline, then the text of the paper, and finally I would decide what the title should be. So it was in the case of this book. As the manuscript was nearing completion I decided on the title, "The Never-Ceasing Search." I think this well represents both my inherent tendencies from childhood onward and what actually occurred on endless occasions in my life's story.

This title also suggested what the dedication of the book should be: "Prove (test, search) all things, hold fast that which is good (true, beautiful)." This was the dedication used by Sir William Bayliss in his famous book *Principles of General Physiology*, first published in 1914. It was a quotation from Thessalonians, first epistle, chapter 5, verse 21. In his introductory remarks, Bayliss also said that, "Nowhere is this admonition of St. Paul to the Thessalonians more relevant than in research in general physiology" (which was the molecular biology of those years). I always began the first annual lecture in my course in general physiology at Washington University by saying that our motto in the lectures and lab exercises of this course would be this quotation from Thessalonians. This clearly made an impression on the students because many years later, some told me that they always remembered it and tried to conduct their research in keeping with it. It also reflects the inherent drive in my scientific life, as is recorded in the chapters of this book.

As the reader will discover, my major concern in the course of my professional

career, beginning in my senior year in college, was the study of living cells and life processes at, or as near as available techniques would permit, the level of molecules, frequently macromolecules. President Karl T. Compton called me to chair and to reshape the biology department at MIT for this very purpose. Although the term "molecular biology" was not widely used in those early years, it did apply to my scientific program. In more recent times the term is used synonymously with "molecular genetics." In the true sense of the word, many of us were molecular biologists long before the discovery that DNA, as a double helical structure, is the substance of genes.

From early college years I was well aware of the problems that arise when one attempts to deduce the properties of a system from a detailed knowledge of the properties of the components, particularly molecular components, a subject to which, as a molecular biologist, I have devoted most of my scientific life. Examples of this problem are the particle-system, the neuron-brain and the brain-mind dilemmas, the last of which is now of prime importance. In these there are philosophical as well as scientific aspects. Because philosophy and science differ categorically, differences of opinion have arisen which seem to defy solution. Some individuals have felt free to invoke vitalistic concepts, which implies that the phenomena are outside the domain of science as we now know it.

With the passage of time new techniques and concepts were developed that have brought with them solutions to some of these difficulties. For example, roughly at mid-century, developmental scientists found it difficult to understand how, if genes are the basic determiners of cell and tissue function, could genes determine the formation of characteristic patterns and colors at particular places in a bird's feathers. To say that this is an epigenetic as well as a genetic effect adds little to our knowledge. However, decades later, gene technology explained how the expression of genes may be affected by the immediate chemical environment which is characteristically different from one place to another in a developing organism; thus may the complex structure and appearance of the adult organism be determined.

Complex biological and biomedical problems may be investigated from the bottom up, from the level of molecules and their complexes to the behavior of the organism and eventually to the mind; or the process may go in the reverse direction, from the top down. Both methods are necessary if an integrated concept of the whole is to be determined. As the reader will discover, I am a bottom-to-top type; yet I am deeply interested in complex behavioral, even theological (Chapter XXV), problems.

In this autobiographical volume I have sought to accomplish the following desiderata: to relate primary events in my life in the temporal sequence in which they actually occurred, although for the purpose of assembling events into chapters, there has necessarily been some overlapping; to include, as in Chapter XVI,

experiences of a purely touristic sort, only to a limited extent and such as involve matters of general interest; to refer by name to as many as possible of those who were involved in this narrative although these can, perforce, be but a small fraction of the many hundreds of individuals who were actually involved. I hope that any whose names are not listed will understand my predicament in attempting to achieve brevity on the one hand and maximal name quotation on the other hand.

Although my life-long major concern was with science, I had, and continue to have, a keen interest in certain kinds of administrative matters. This is exemplified by my service as a Trustee of the Massachusetts General Hospital in Boston and of its mental division, the McLean Hospital in Belmont, Massachusetts for more than forty years (Chapter XI).

Finally, Chapter XXVI, called "Great Expectations," could have dealt with many more items. However, I chose to cite primarily those for which there was presently very substantial background and will predictably lead to great future developments.