PHYSICS OF PROTEINS

From the Editors: This book is a compilation of the notes that Prof. Hans Frauenfelder used in his pioneering course in Biological Physics at the University of Illinois at Urbana-Champaign with an emphasis on proteins and protein dynamics. We have tried to maintain as best we can the spirit of these lectures in these notes. This is not a conventional textbook, but rather a guide to the lectures which were written on something now sadly obsolete, the large chalkboard. Whenever possible, we have used Prof. Frauenfelder's hand-drawn figures as they would appear on the board. We believe that, while some may lack in detail, they more than make up for in their charm and elegance. Too bad we could not capture his unique Swiss-German accent! The editors (and Robert Austin) take no credit for the joy of these notes but take any blame for what is left unclear and possibly even found to be wrong.

Since these notes were compiled some years after Prof. Frauenfelder "retired" from Urbana, the editors recruited a few colleagues of Prof. Frauenfelder to fill in some gaps in the discussion. We also moved his wonderful notes on experimental techniques and ancillary topics to the end of the book so that the flow of ideas as Prof. Frauenfelder develops the concept of the protein's free energy landscape can move as smoothly as possible. We urge the reader to consult those chapters because, as Prof. Rob Phillips of Caltech likes to say, Biological Physics without numbers is Biology.

And now, Professor Frauenfelder speaks as we settle into our chairs in Loomis Laboratory of Physics:

Life is based on biomolecules. Biomolecules determine how living systems develop and what they do. They store and propagate information, build the systems and execute all processes, from transport of energy, charge, and matter to catalysis. A knowledge of the structure and function of biomolecules is essential for biology, biochemistry, biophysics, medicine, and pharmacology, and it even has technological implications.

The present course should provide a first introduction to the structure and function of biomolecules, particularly proteins. Emphasis is on aspects of interest to physicists. The number of unsolved problems is very large. Any new development in physical tools usually leads to exciting advances in our understanding of biomolecules. Tools and concepts of experiments will therefore be stressed.

In the present lectures we will discuss only a few of the physical tools, and we neglect chemical ones. We try to avoid techniques that are already well established and concentrate on those that may make major new steps possible. New tools appear regularly; laser, synchrotron radiation, muons, proton radiology, holography, gamma-ray lasers (?), and inner-electron spectroscopy are some of the ones that either have recently been introduced into biomolecular physics or are likely to become important.

Our approach is that of physicists. In recent years it has become customary to distinguish **biophysics** and **biological physics**. In biophysics, physics is the servant and the goal is unambiguously to understand the biology of living systems. In biological physics, the situation is not so clear, but one goal is to describe the physics of biological systems, to discover physical models, and possibly even to find new laws that characterize biological entities.

Progress in physics has often followed a path in which three areas are essential: structure, energy levels, and dynamics. Of course, progress is not linear and usually occurs in all three areas at once. Moreover, experimental results and theoretical understanding are both needed for progress. Nevertheless, the three steps can often be seen clearly and frequently they can be related to specific names. The present deep understanding of atoms and atomic structure is linked to a chain of discoveries and theories. Every student is familiar with the Balmer series, the Rutherford atom, the Bohr model, and the theories of Schrödinger, Heisenberg, Pauli, and Dirac. Similar discoveries, models, and theories have elucidated solids (Einstein, Laue, Debye, . . .), nuclei, and particles. We try to follow a similar path here. In Part I, we give a brief and superficial introduction to biomolecules. In Part II, we describe the structure of two main classes of biomolecules, proteins, and nucleic acids, and we treat the relevant methods. In Part IIII, we discuss the energy levels or, more properly, the energy landscape, of proteins. Since proteins are complex systems, their energy can no longer be described by a simple level diagram, but requires more general concepts. In Part IV, the heart of the book, we treat the dynamics of proteins. We show how in particular two types of fluctuations, alpha and beta, control protein motions and functions. We also apply the concepts to some selected biological problems. In Part V, we collect some of the background information which can be useful for understanding what has been described in the earlier parts.

The sequence structure–energy landscape–dynamics suffices for "simple" systems such as atoms and nuclei and for "passive" complex systems such as glasses and spin glasses. "Active" complex systems, such as biomolecules, computers, or the brain, perform functions. We do not discuss biological function in detail, but we consider some specific examples together with dynamics.

As we will describe briefly in Chapter 2, the number of biological molecules is extremely large, and indeed, the literature, while covering only a small fraction of existing systems, is vast. Since we are interested in concepts and general features, we cover only a very restricted set of biomolecules but hope to nevertheless cover many of the essential ideas.

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