Preface

Physics is gaining a leading position in biology. This is not to be understood that physics is conquering biology and shoving biologists to the background. Simply, the science we used to call biology is evolving into physics, thereby confirming the view that natural science is passing through a period of reconstruction on a unified foundation.

Alexander Kitaigorodsky
I am a physicist (1971)

The contribution of physics-based techniques to biology had begun with the development of the microscope. It marked the beginning of the studies of cell structure—structural cell biology. Subsequently, with the discovery of the two most important macromolecules of the living cell—DNA and protein—biology had turned molecular. In order to understand how these molecules function, it became necessary to elucidate their structures.

Visible light-dependent microscopy has its limitations. Visualization of molecular structures at atomic resolution by such microscopes is not even a theoretical possibility. The problem has been addressed, in the last century, by the development of three powerful physical methodologies—X-ray crystallography, nuclear magnetic resonance (NMR), and electron crystallography. Within a span of less than ten years, the double helical structure of DNA and high-resolution structures of two proteins, myoglobin and hemoglobin, were published and, with these discoveries, the age of molecular structural biology had begun.

Physics has provided not only the techniques and tools for elucidation of the structure of biomolecules, but also concepts and laws for investigation of their dynamics. Based on physical laws it is possible to compute biomolecular interactions—as for example, how two molecules would bind, bend, and rotate each other—leading to mechanistic explanations for different biological processes.

Using the techniques mentioned above, more than 150,000 macromolecular structures have already been solved and deposited in the Worldwide Protein Data Bank (wwPDB). The number continues to grow at a rapid pace. These structures have been the basis for molecular biological investigations of various activities within and involving the cell.

Keeping pace with the scientific developments, institutional biology curricula have also been evolving. In 1965, the first edition of *Molecular Biology of the Gene* was published as "The field of molecular biology was ripe for its first textbook, defining for the first time the curriculum for undergraduate courses in this topic" (in Preface to the 7th edition of the book). Presently, there are molecular biology and related courses in universities across the world. These courses have been aptly supported by a number of popular textbooks written by renowned authors.

"Molecular biology" named courses, either introductory or advanced, mostly center around the "basic genetic mechanisms," namely, maintenance and expression of the genome and their regulation. Such courses are usually catered at the undergraduate level with due emphasis on biological and experimental aspects. However, the subject is transcending from its descriptive nature to a more mechanistic format. Even in the traditional molecular biology courses, explanation and understanding of the basic genetic mechanisms are becoming ever more dependent on macromolecular structure-function correlation. This is proving to be true not only for the graduate and upper-division courses, but also for the lower-division courses.

Looking at the graduate-level courses, we find titles such as structural biology, molecular interactions, molecular systems biology, biophysical methods, structural biochemistry, structure and function of biological macromolecules, macromolecular machines, techniques in structural biology, protein folding, molecular recognition and interactions, structure-function relationship of proteins, structural biology and proteomics, biophysical methods in life sciences, etc. Clearly and expectedly, these courses are interdisciplinary in nature with a judicious blend of physical and biological sciences. As such, it appears that no single textbook does or can cover all aspects of the above-named graduate level courses and no individual course can depend exclusively on one text.

During my tryst with molecular biology, first as a student and researcher and subsequently as a teacher, I have experienced how wonderfully the subject has evolved in the last five decades. Keeping pace with the developments, several landmark textbooks, written by world-famous authors, appeared one after another. My learning as well as my teaching have been enormously benefitted by these textbooks. Yet, particularly in my later years of teaching, I felt the need for a textbook going deeper into the structural aspects of molecular biology, at least as a supplement and not a substitute to the already available excellent textbooks.

It may be reasonable to consider that a textbook containing the words "molecular," "structural," and "biology" in its title should embrace macromolecular structures and interactions with the arms of conventional molecular biology featured by the "basic genetic mechanisms." Such a textbook would be useful for the interdisciplinary courses as well as the conventional molecular biology courses upgraded with the inclusion of macromolecular structures.

With all such considerations as outlined above, the present book is an attempt to cater to the fundamentals of molecular structural biology in a concise, yet comprehensive manner. The layout of the text has been stepwise. The historical perspective in the *Introduction* forms the philosophical basis of the entire book, for it is my personal belief that science bereft of philosophy produces technicians and not scientists. Chapters 1–4 provide the mathematical and physical concepts required for the subject. They are likely to be useful in a varying degree to the reader depending on his/her background. Based on these concepts, Chapters 5–7 deal with macromolecular structures—formation, determination, and representation. In Chapters 8–13, these structures are utilized to explain the basic genetic mechanisms. The chapters that follow discuss some advanced issues surrounding macromolecular structures, namely,

structural genomic/proteomics, cell signaling and systems biology, macromolecular assemblies, and computational molecular biology. Covering a wide spectrum, the book can be used as a reference as well as a text partially fulfilling the requirements of the related courses.

Needless to say, in science, every theory is preceded by experiments and observations. Accordingly, a number of published text books have elegantly described the experiments that have laid the foundation of different concepts and theories in molecular biology. The present book, though alluding to the results of many of these experiments, refrains from duplicating such efforts.

Instead, in order to do justice to the title, the book emphasizes the basic concepts and takes care not to overburden the reader with excessive information. Redundancy is avoided as much as possible. For example, it is mentioned in Chapter 11 that the enzyme aminoacyl-tRNA synthetase links an amino acid to a specific tRNA. Although, based on their active site architecture and consensus sequence elements, the family of aminoacyl-tRNA synthetases is divided into two classes, I and II, all these enzymes are united by a common aminoacylation reaction that occurs in two steps. The chapter highlights only one enzyme belonging to class I to understand the mechanism of the aminoacylation reaction.

In the same chapter, out of three release factors, bacterial RF1 and RF2 and eukaryotic eRF1, that are responsible for translation termination, only RF2 is selected for detailed discussion. The underlying expectation is that if the basic concepts are aptly conveyed, the interested reader is competent enough to explore the literature for mechanisms involving the other factors and identify the subtle differences.

It will be absolutely unwise to claim that the book is flawless. Critical comments and suggestions are most welcome to prompt the author to make necessary amends and improvements in subsequent editions, if and when opportunity arrives.

Subrata Pal