Preface

This book grew from a course in molecular biology for graduate students that I began at the University of Maine in the early 1970s. At that time the primary focus of the course was on the chemistry and biology of the nucleic acids. It also included a moderate dose of organic and physical chemistry because it was in those areas that many key explanations for various biological phenomena were provided at the molecular level. Since that time the subject has greatly expanded in detail and in new directions requiring that some material in the course, such as descriptions of analytical developments and model studies with synthetic polynucleotides and polypeptides,[1] be reduced to preserve a primary focus on biological information of more direct relevance. Important subjects that subsequently emerged: mechanistic details of replication, transcription and translation, noncovalent interactions, DNA primary sequences and their characteristics, sequence alignments and phylogenetic trees, protein-nucleic acid interactions, transcription factors, high-resolution DNA structures and interactions, protein folding, and most significantly, the important and exciting field of molecular evolution, all burst from interdisciplinary activities, requiring the advent of auxiliary special topics courses. Molecular biology now includes a significant emphasis on evolution and theories of life's origins, because they represent keystone topics in biology.

The consequence of such remarkable growth has been that basic and essential topics in molecular biology suitable for graduate students are scattered far and wide in the literature, and treated under the heading of different disciplines, often in journals that are not readily accessible. It has reached a state that I now feel the subject is probably best taught by a team consisting of members from the disciplines involved, so long as the team is like-minded with respect to the material covered and with the student's needs at heart.

I have attempted to include discussions of as many topics as possible together under the same cover and in a format that minimizes the distractions of methodologies while including important interdisciplinary and analytical topics and explanations. Of necessity, the meld may have some rough edges, and some discussions may seem superficial, yet in all cases the basic focus remains on the chemistry and biology of the nucleic acids, with a consideration of proteins as informational biopolymers to call attention to their associated biosynthesis and roles with the nucleic acids in gene expression, replication and maintenance but also in recognition of the complementary nature of their interactions and coevolutionary origins. Monographs and texts on nucleic acids generally lack a suitable treatment of proteins that would give better appreciation of their interaction with nucleic acids. Proteins are required in one capacity or another for virtually all molecular processes, and they are the principal products of living organisms. The minimal treatment of proteins in this volume is not designed as a substitute for excellent monographs on the subject.[2,3,4,5]

The goal has been to convey as complete a picture as possible of the nucleic acids and proteins, their structures, interactions, biological properties, origins and evolution at a level suitable for graduate and upper-level undergraduate students. Though it is somewhat

incidental to the chemical origins and evolution of the nucleic acids, the underlying picture is one of the unity of life, of which humans are a part. Brief discussions, footnotes, and asides designated by ruled borders, touch on analytical and physical topics, usually at an introductory level appropriate for upper-level biology students and in such a way that I hope leads to further exploration or that complements descriptive material in introductory texts in molecular and cellular biology. Methodologies and physical properties of the nucleic acids and proteins are covered authoritatively by Cantor and Schimmel,[6] Bloomfield *et al.*,[7] and Saenger.[8] Although it is far from a complete list, other texts useful in studies of the informational biopolymers include those by Adams *et al.*,[9] Alberts *et al.*,[10] Berry *et al.*,[11] Chang,[12] Chang,[13] Eigen,[14] Friedberg *et al.*,[15] Lewin,[16] Griffiths *et al.*,[17] Purves *et al.*,[18] and Mathews and van Holde.[19] These or comparable texts are prerequisites for the subjects discussed in this volume, and I recommend that students have access to them.

This volume contains more material than can be covered in the usual one-semester course, because it is designed to meet four requirements: to provide source material for a more comprehensive program of courses, to provide a clear and incisive treatment of nucleic acids at a level accessible to students in all fields of the biological sciences, to provide topics and questions for students coming into the course with specialized backgrounds and interests, and to provide topics together with original citations as a basis for student writing experiences. Although problems are included, the material covered is rich in unarticulated questions that advanced and serious students of the subject should be able to identify.

The broad spectrum of topics is a good basis for the practice students need in scientific writing, since it allows them to indulge their interests in an array of subjects not necessarily covered in class. For this reason I have included citations that oftentimes represent different perspectives on specific topics using different methods of analysis. Besides recognizing the pioneers, the older references are often easier to read where they lack the specialized and abbreviated vocabulary that characterizes much of contemporary literature. The extensive bibliographies that follow each chapter are therefore mainly for the benefit of students in their research and writing requirements. The experience of writing five, six, or ten papers per semester-course is not sufficient, of course, for students to become proficient in recognizing important questions, organizing their thoughts and mastering the craft at a level required for the submission of acceptable manuscripts, but it is at least a contribution.

If the emphasis of the course is to be on the chemistry of the informational biopolymers, the core chapters are Chapters 1 through 4, plus the first half of Chapter 5, all of Chapter 6, first three-quarters of Chapter 7, and all of Chapters 8 and 9. A number of sections and topics can be expanded with material cited or abridged or omitted if deemed unsuitable to a particular group of students without breaking the flow of argument. If the emphasis is to be on the molecular biology of the informational biopolymers, the core material is from Chapters 1, 3 through 7, and 9 through 12. The format of the book is also suitable for specific discussion and special topics courses for students and instructors with particular interests. Thus, molecular evolution can be covered with selected sections of the core chapters, together with Chapters 7, 10–13, while a course on the origin of life can be presented with the core chapters together with Chapters 7, 11, and 13. A special topics course on protein-nucleic acid interactions can be assembled from material in Chapters 3, 5, 9, 10, and 12.

Over the years the majority of students who enrolled in my courses were from the biological sciences, but it was not unusual to find a significant number of students from physics, chemistry, the computer sciences and engineering, and in this regard I suspect that my experience is not unusual. Although these students often lack the prerequisites expected of students of biology, they are more proficient in areas that students of biology are often not exposed to, bringing skills in physics and physical chemistry that have been most responsible

for our understanding of biology at the molecular level. It is important to these students that they find biological phenomena discussed in a way they can quickly appreciate and readily explore. It is, of course, no less important for students of the biological sciences to have detailed explanations of molecular phenomena.

Many of the images in this book can be viewed in color on the accompanying website. Adopting professors may also wish to download color versions of the figures to use as lecture slides. To access the color images, go to *http://www.uscibooks.com* and click on this book's web page. Additionally, many color figures are available in high resolution by contacting the author.

I have had the encouragement and assistance of many colleagues, but I make special mention of my wife Jeanne, and of my closest longtime collaborator Jon Blake. Despite an extraordinarily active academic career, Jon has always accepted my calls for help and comment on matters of science and computers. A more knowledgeable, effective and patient teacher is unimaginable. He has maintained my computers, introduced me to the Linux operating system, and installed and coached me in the use of the molecular modeling program Molscript,[20,21] which together with Raster3D[22,23] has been used to display many of the molecular structures in this book from coordinates in the Protein Data Bank at the Research Collaboratory for Structural Bioinformatics (RCSB)[24] or in the Nucleic Acid Database.[25] Besides several well-known, UNIX-based modeling programs running on Sun and SGI machines, the vector postscript outputs of NUCPLOT[26] and RASMOL[27] have been particularly useful. I recommend that students acquire a good-quality adjustable 3D viewer for viewing the many stereo images in this book. Not everyone has that easy ability to separate what each eye is seeing, taught to me by an old colleague of mine who makes his living primarily in the area of molecular graphics.

I owe a special debt of gratitude to J. R. Fresco and S. D. Delcourt for many wonderful years of collegial discussions of science and for their expert advice and encouragement when I needed it. Thanks also to R. Cochrane for her help in collating many thousands of references from my collection of the early literature. The following people read sections of the book and provided me with excellent comments and suggestions: N. L. Allinger, R. F. Doolittle, R. Chang, J. Ellis, J. R. Fresco, G. F. Joyce, A. McGuire, W. K. Olson, L. E. Orgel, K. E. van Holde, J. Völker, and P. H. von Hippel. They have my sincere thanks. Thanks also to members of the Chemistry Department and Schow Science Library at Williams College and the Science Library at SUNY Albany for their kind hospitality.

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