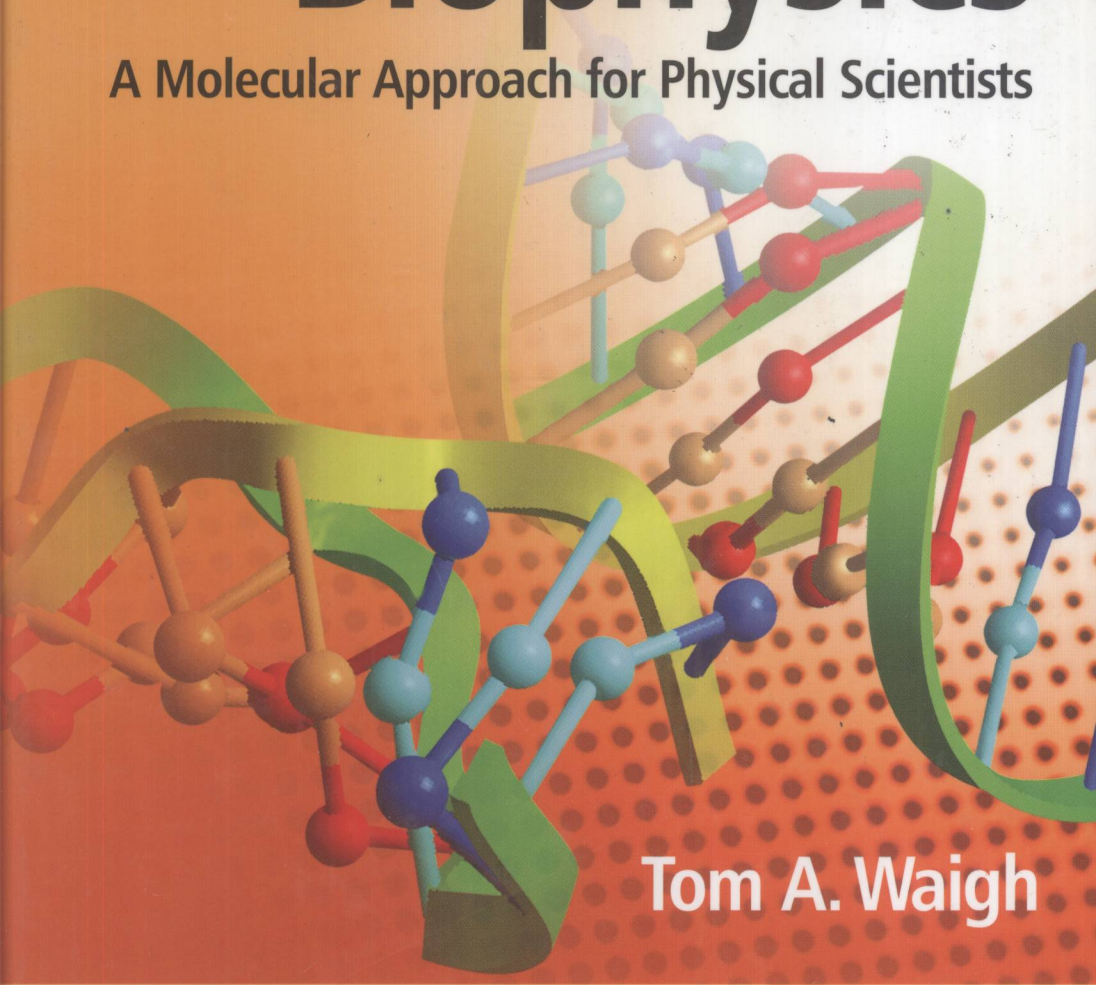
Applied Biophysics

A Molecular Approach for Physical Scientists



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Applied Biophysics
A Molecular Approach for Physical Scientists

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Applied Biophysics

Preface

The field of molecular biophysics is introduced in the following pages. The presentation focuses on the simple underlying concepts and demonstrates them using a series of up to date applications. It is hoped that the approach will appeal to physical scientists who are confronted with biological questions for the first time as they become involved in the current biotechnological revolution.

The field of biochemistry is vast and it is not the aim of this textbook to encompass the whole area. The book functions on a reductionist, nuts and bolts approach to the subject matter. It aims to explain the constructions and machinery of biological molecules very much as a civil engineer would examine the construction of a building or a mechanical engineer examine the dynamics of a turbine. Little or no recourse is taken to the chemical side of the subject, instead modern physical ideas are introduced to explain aspects of the phenomena that are confronted. These ideas provide an alternative, complementary set of tools to solve biophysical problems. It is thus hoped that the book will equip the reader with these new tools to approach the subject of biological physics.

A few rudimentary aspects of medical molecular biophysics are considered. In terms of the statistics of the cause of death, heart disease, cancer and Alzheimer's are some of the biggest issues that confront modern society. An introduction is made to the action of striated muscle (heart disease), DNA delivery for gene therapy (cancers and genetic diseases), and self-assembling protein aggregates (amyloid diseases such as Alzheimer's). These diseases are some of the major areas of medical research, and combined with food (agrochemical) and pharmaceutics, provide the major industrial motivation encouraging the development of molecular biophysics.

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Please try to read some of the highlighted books, they will prove invaluable to bridge the gap between undergraduate studies and active areas of research science.

TOM WAIGH
Manchester, UK
February 2007

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1

The Building Blocks

It is impossible to pack a complete biochemistry course into a single introductory chapter. Some of the basic properties of the structure of simple biological macromolecules, lipids and micro organisms are covered. The aim is to give a basic grounding in the rich variety of molecules that life presents, and some respect for the extreme complexity of the chemistry of biological molecules that operates in a wide range of cellular processes.

1.1 PROTEINS

Polymers consist of a large number of sub-units (monomers) connected together with covalent bonds. A protein is a special type of polymer. In a protein there are up to twenty different amino acids (Figure 1.1) that can function as monomers, and all the monomers are connected together with identical peptide linkages (C–N bonds, Figure 1.2). The twenty amino acids can be placed in different families dependent on the chemistry of their different side groups. Five of the amino acids form a group with lipophilic (fat-liking) side-chains: glycine, alanine, valine, leucine, and isoleucine. Proline is a unique circular amino acid that is given its own separate classification. There are three amino acids with aromatic side-chains: phenylalanine, tryptophan, and tyrosine. Sulfur is in the side-chains of two amino acids: cysteine and methionine. Two amino acids have hydroxyl (neutral) groups that make them water loving: serine and threonine. Three amino acids have very polar positive side-chains: lysine, arginine and histidine. Two amino acids form a family with acidic

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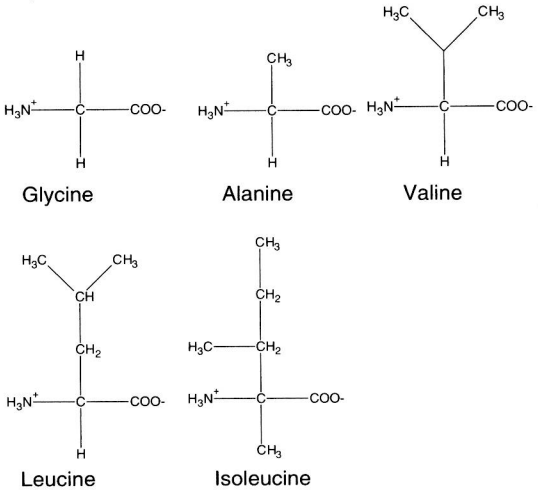
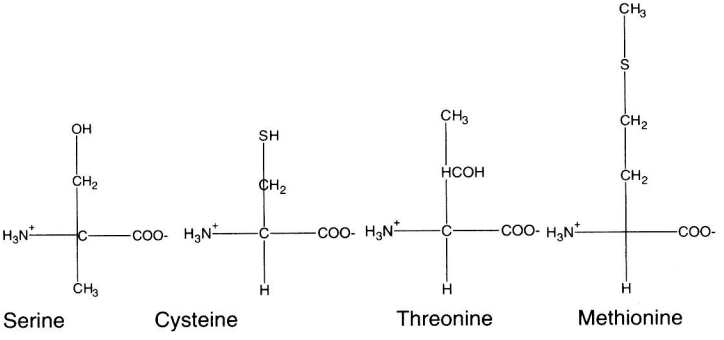
Aliphatic amino acids



Amino acids with hydroxyl or sulfur containing groups



Aromatic amino acids

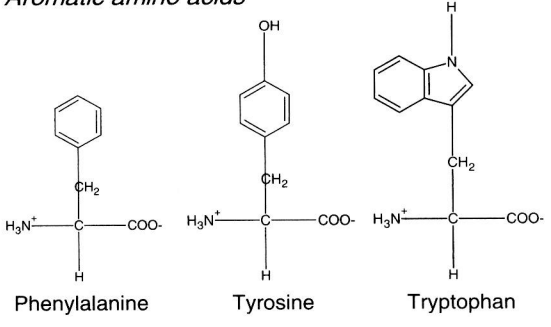
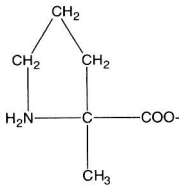


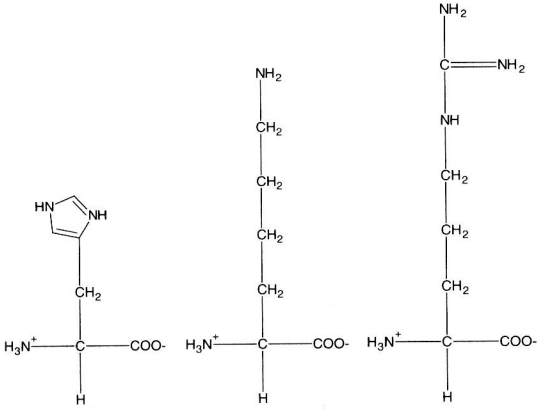
Figure 1.1 The chemical structure of the twenty amino acids found in nature

Cyclic amino acid



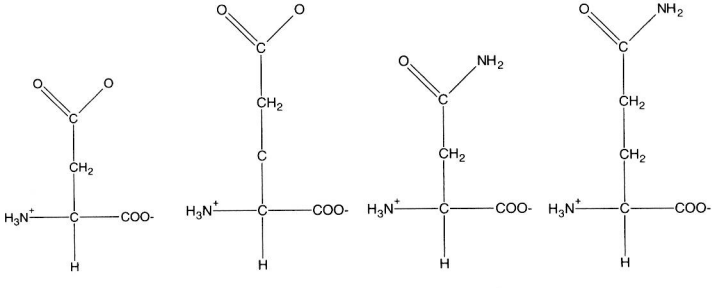
Proline

Basic amino acids



Histidine Lysine Arginine

Acidic amino acids and amides



Aspartic acid Glutamic acid Asparagine Glutamine

Figure 1.1 (*Continued*)

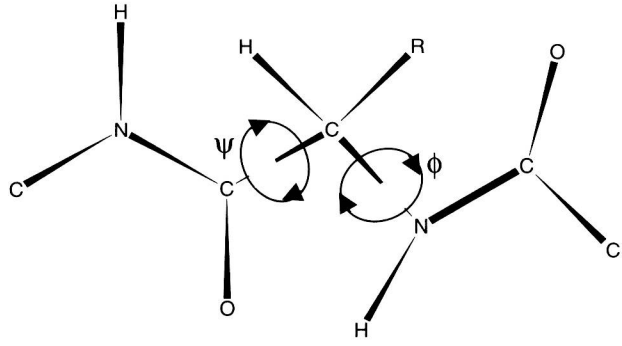


Figure 1.2 All amino acids have the same primitive structure and are connected with the same peptide linkage through C–C–N bonds
(O, N, C, H indicate oxygen, nitrogen, carbon and hydrogen atoms respectively. R is a pendant side-group which provides the amino acid with its identity, i.e. proline, glycine etc.)

side-groups and they are joined by two corresponding neutral counterparts that have a similar chemistry: aspartate, glutamate, asparagine, and glutamine.

The linkages between amino acids all have the same chemistry and basic geometry (Figure 1.2). The *peptide linkage* that connects all amino acids together consists of a carbon atom attached to a nitrogen atom through a single covalent bond. Although the chemistry of peptide linkages is fairly simple, to relate the primary sequence of amino acids to the resultant three dimensional structure in a protein is a daunting task and predominantly remains an unsolved problem. To describe protein structure in more detail it is useful to consider the motifs of secondary structure that occur in their morphology. The motifs include *alpha helices*, *beta sheets* and *beta barrels* (Figure 1.3). The full three dimensional *tertiary structure* of a protein typically takes the form of a compact globular morphology (the globular proteins) or a long extended conformation (fibrous proteins, Figures 1.4 and 1.5). Globular morphologies usually consist of a number of secondary motifs combined with more disordered regions of peptide.

Charge interactions are very important in determining of the conformation of biological polymers. The degree of charge on a polyacid or polybase (e.g. proteins, nucleic acids etc) is determined by the pH of a solution, i.e. the concentration of hydrogen ions. Water has the ability to dissociate into oppositely charged ions; this process depends on temperature

$$H_2O \rightleftarrows H^+ + OH^- \qquad (1.1)$$

The product of the hydrogen and hydroxyl ion concentrations formed from the dissociation of water is a constant at equilibrium and at a fixed temperature (37 °C)

$$c_{H^+}c_{OH^-} = 1 \times 10^{-14}M^2 = K_w \tag{1.2}$$

where c_{H^+} and c_{OH^-} are the concentrations of hydrogen and hydroxyl ions respectively. Addition of acids and bases to a solution perturbs the equilibrium dissociation process of water, and the acid/base equilibrium

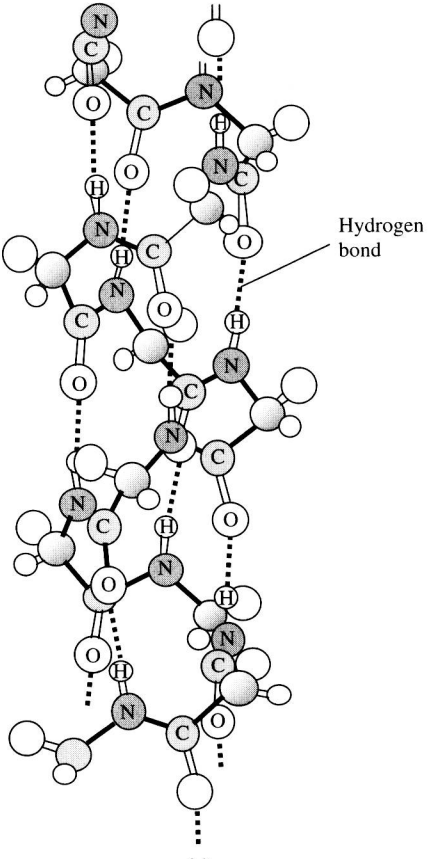


Figure 1.3 Simplified secondary structures of (a) an α-helix and (b) a β-sheet that commonly occur in proteins
(Hydrogen bonds are indicated by dotted lines.)

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