Epilogue

It is 50 years since the discovery of the double helical structure of DNA, an event that marks the beginning of molecular biology. The structure of DNA represents the seed that germinated, grew rapidly, flowered and bore fruit. It has led to descriptions of the flow of information from gene to protein. Molecular biology, expanded from a small isolated research area into a major, all embracing, discipline. As this book is being published close to the 50th anniversary it is timely to reflect that during this period biochemistry has been marked by several defining discoveries based on the structure and function of proteins. The list of significant discoveries could provide the bulk of the content of another book but a brief and selective description of these events might include:

- *The elucidation of the structure of myoglobin and haemoglobin by Perutz and Kendrew using X-ray crystallography*. This work paved the way for all future crystallographic studies of proteins and established the basis for allostery.

- *The structure of the first enzyme, lysozyme, by Phillips*. Structural characterization defined an active site and the geometry of residues that facilitated biological catalysis and pointed towards molecular enzymology.

- *Protein folding is encoded entirely by the primary sequence*. Anfinsen proved that proteins could fold to reach the native state whilst in cells large macromolecular complexes known as chaperones were shown much later to assist folding by forming environments known as the Anfinsen cage that limit unfavourable protein interactions.

- *Crystallization of the photosynthetic reaction centre by Michel, Diesenhofer and Huber*. The helical structure of transmembrane segments was confirmed and showed that membrane proteins could be crystallized and subjected to the same high resolution methods applied previously to soluble proteins.

- *The architecture of the ribosome*. A daunting experimental problem revealed catalysis of the peptidyl transferase was performed by RNA and the ribosome is a ribozyme. The structure of the ribosome confirmed that biological catalysis could proceed in the absence of protein-based enzymes redefining our traditional view of nucleic acid and proteins.

- *p53 and the molecular basis of cancer*. The demonstration that over 60 percent of all tumours are associated with mutations in p53 elucidated a direct link between molecular defects in a protein and subsequent development of cancer.

- *The prion hypothesis*. Consequently the prion hypothesis showed that some proteins 'corrupt' native conformations promoting protein aggregation; a hallmark of many neurodegenerative disorders.

By reading the preceding 12 chapters, where these discoveries are described in more detail, I hope the reader will gain an impression of the rapidly expanding and advancing area of protein biochemistry. This area offers the potential to revolutionize treatment of human health and to eradicate diseases in all avenues of life. The next 50 years will see the complete description of

Proteins: Structure and Function by David Whitford

URL	Description
www.rcsb.org/pdb	The repository for the deposition of biomolecular structures mainly nucleic acids and proteins
www.hgmp.mrc.ac.uk	The human genome mapping project centre in the UK
www.nhgri.nih.gov	The human genome mapping research institute of the NIH
www.expasy.ch	The ExPASy (Expert Protein Analysis System) proteomics server of the Swiss Institute of Bioinformatics (SIB)
www.ebi.ac.uk	European Bioinformatics Institute containing access to databases and software for studying proteins
www.ncbi.nlm.nih.gov	A national resource for molecular biology information in USA
www.srs.ebi.ac.uk	Sequence retrieval system for a wide variety of databases
rebase.neb.com/rebase/rebase.html	Restriction enzyme database
bimas.dcrt.nih.gov/sql/BMRBgate.html	Biomolecular Nuclear Magnetic Resonance databank
tolweb.org/tree/phylogeny.html	Tree of Life web page
www.ncbi.nlm.nih.gov/Omim	On line Mendelian Inheritance in Man
www.biochem.ucl.ac.uk/bsm/biocomp/index.html	A collection biocomputing resources at University College London
www.ensembl.org	A database annotating sequenced genomes
www.embl-heidelberg.de/predictprotein/predictprotein.html	Protein prediction server for secondary structure
www-nbrf.georgetown.edu/pirwww/pirhome3	Protein Information resource centre
archive.uwcm.ac.uk/uwcm/mg/hgmd0.html/	Human gene mutation database
gdbwww.gdb.org/	Another genome database
www.ornl.gov/hgmis	US Human Genome Project Information

See home page of this book for latest web-based or on-line resources.

other proteomes and promises the possibility of equally devastating discoveries to match those of the previous 50 years.

The following universal resource locators (URL) represent web addresses of sites that offer very useful information of relevance to the subject of this book. The author is not responsible for their content and due to the transitory nature of the web these sites may not always be accessible, maintained or presenting the latest information. However, all (as of April 2004) had potentially useful information that provides an ideal learning resource.

Glossary

α helix regular unit of secondary structure shown by polypeptide chains characterised by 3.6 residues per turn in a right-handed helix with a pitch of 0.54 nm.

β sheet collection of β strands assembled into planar sheet like structure held together by hydrogen bonds.

$3d_{10}$ helix a form of secondary structure containing three residues per turn and hydrogen bonds separated by 10 backbone atoms.

Ab initio from the beginning (*Latin*).

Acid–base catalysis reactions in which the transfer of a proton catalyses the overall process.

Acidic solution a solution whose pH is less than pH 7.0.

Active site part of an enzyme in which the amino acid residues form a specific three-dimensional structure containing the substrate binding site.

ADP adenosine diphosphate.

Affinity chromatography. separation of proteins on the basis of the specific affinity of one protein for an immobilized ligand covalently attached to an inert matrix.

AIDS disease ultimately resulting from infection with HIV, sometimes called advanced HIV disease.

Allosteric effectors molecules which promote allosteric transitions in a protein.

Allostery with respect to proteins, a phenomenon where the activity of an enzyme's active site is influenced by binding of an effector to a different part of the enzyme.

Alzheimer's a disease characterized by formation of protein deposits with the brain and classified as a neurodegenerative disorder.

Amino acid an organic acid containing an amino group, carboxyl group, side chain and hydrogen on a central α carbon. The building blocks of proteins.

Amphipathic for a molecule, the property of having both hydrophobic and hydrophilic portions. Usually one end or side of the molecule is hydrophilic and the other end or side is hydrophobic.

Ampholyte a substance containing both acidic and basic groups.

Amyloid accumulation of protein into an insoluble aggregate often a fibre in tissue such as the brain.

Anabolism process of synthesis from small simple molecules to large often polymeric states.

Antigen a substance that can elicit a specific immune response.

Anaerobe organism capable of living in the absence of oxygen.

Antibody protein component of immune system produced in response to foreign substance and consisting of two heavy and two light chains.

Anticodon sequence of three nucleotide bases found in tRNA that recognizes codon via complementary base pairing interactions.

Antigenic determinant a specific part of an antigen that elicits antibody production.

Antiparallel running in opposite directions as in DNA strands or β sheets.

Apoprotein protein lacking co-factor or coenzyme. Apoprotein often show decreased or negligible activity.

Apoptosis programmed cell death.

Archae one of the two major groupings within the prokaryotes, also called archaebacteria.

Asymmetric centre a centre of chirality. A carbon atom that has four different substituents attached to it.

Proteins: Structure and Function by David Whitford

ATP adenosine triphosphate.

ATPase an enzyme hydrolysing ATP to ADP and Pi.

Association constant/Affinity constant given by 'K', in the oxygen binding reaction of myoglobin, K is calculated as the concentration of myoglobin bound to oxygen divided by the product of the free oxygen concentration and the free myoglobin concentration.

B cells lymphatic cells produced by B lymphocytes.

Backbone part of the polypeptide chain consisting of N–C_α–C portion (distinct from side chain)

Bacteriophage virus that specifically infects a bacterium.

Basic solution a solution whose pH is greater than pH 7.0.

BSE bovine spongiform encephalopathy, a prion-based disease first seen in cattle in the UK.

bp base pair, often used to describe length of DNA molecule.

Buffer a mixture of an acid and its conjugate base at a pH near to their pK. Buffer solution composed of an acid and conjugate base resist changes in pH.

Cahn–Ingold–Prelog system of unambiguous nomenclature of molecules with one or more asymmetric centres via a priority ranking of substituents. Also known as RS system.

Cap a 7-methyl guanosine residue attached to the 5′ end of eukaryotic mRNA.

Capsid protein coat or covering of nucleic acid in viral particles.

Catabolism metabolic reactions in which larger molecules are broken down to smaller units. Proteins are broken down into amino acids.

cDNA complementary DNA derived from reverse transcription of mRNA.

Chaotrope a substance that increases the disorder (chaos). Frequently used to describe agents that cause proteins to denature. An example is urea.

Chaperonins proteins which assist in the assembly of protein structure. They include heat-shock proteins and GroEL/ES of *E. coli*.

Charge–charge interactions interactions between positively and negatively charged side chain groups.

Chiral possessing an asymmetric center due to different substituent groups and exist in two different configurations.

Chloroplasts plant organelles performing photosynthesis.

Clathrate structures hydrophobic molecules that dissolve in aqueous solutions form regular icelike structures called clathrate structures rather than the hydration shells formed by hydrophilic molecules.

Cloning process of generating an exact copy.

Coding strand analogous to sense strand.

Co-factor a small organic molecule or sometimes a metal ion necessary for the catalytic activity of enzymes.

Coiled coil arrangement of polypeptide chains where two helices are wound around each other.

Configuration arrangement of atoms that cannot be altered without breaking and reforming bonds.

Conformational entropy a protein folding process, which involves going from a multitude of random-coil conformations to a single, folded structure. It involves a decrease in randomness and thus a decrease in entropy.

Codon sequence of three nucleotide bases found in mRNA that determines a single amino acid.

Conformation proteins and other molecules occur in different spatial arrangements because of rotation about single bonds that leads to a variety of different, close related states.

Conservative amino acid changes Mutations in coding sequences for proteins which convert a codon for one amino acid to a codon for another amino acid with very similar chemical properties.

Cooperative transition a transition in a multipart structure such that the occurrence of the transition in one part of the structure makes the transition likelier to happen in other parts.

Covalent bonds the chemical bonds between atoms in an organic molecule that hold it together are referred to as covalent bonds.

Cristae invaginations of inner mitochondrial membrane involved in oxidative phosphorylation.

Cryo-EM cryoelectron microscopy a technique for the visualization of macromolecules achieved by rapid freezing of a suspension of the biomolecule without the formation of ice.

Cystine the amino acid cysteine can form disulfide bonds and the resulting structure is sometimes called a cystine, particularly in older textbooks.

Denaturation loss of tertiary and secondary structure of a protein leading to a less ordered state that is frequently inactive.

Da Dalton or a unit of atomic mass equivalent to 1/12th the mass of the ^{12}C atom.

Debye–Huckel radius a quantitative expression of the screening effect of counterions on spherical macro ions.

Dihedral angle an angle defined by the bonds between four successive atoms. The backbone dihedral angle ϕ is defined by C'–N–C_a–C'.

Dimer assembly consisting of two subunits.

Dipeptide a molecule containing two amino acids joined by a single peptide bond.

Dipolar ion term synonymous with zwitterions.

Dipole Moment molecules which have an asymmetric distribution of charge are dipoles. The magnitude of the asymmetry is called the dipole moment of the molecule.

Disulfide bond a covalent bond between two sulfur atoms formed from the side chains of cysteine residues, for example.

DNA deoxyribose nucleic acid – the genetic material of almost all systems.

Domain a compact, locally folded region of tertiary structure in a protein.

Elution removal of a molecule from chromatographic matrix.

Edman degradation procedure for systematically sequencing proteins by stepwise removal and identification of N terminal amino acid residue.

EF elongation factor, one of several proteins involved in protein synthesis enhancing ribosomal activity.

Enantiomers also called optical isomers or stereoisomers. The term optical isomers arises from the fact that enantiomers of a compound rotate polarized light in opposite directions.

Endergonic reaction process that has a positive overall free energy process ($\Delta G > 0$).

Enzymes catalytic proteins.

Electrophile literally electron-lover and characterized by atoms with unfilled electron shells.

Eubacteria one of the two major groupings within the prokaryotes.

Eukaryote a cell containing a nucleus that retains the genetic material in the form of chromosomes. Often multicellular and with cells showing compartmentation.

Exons a region in the coding sequence of a gene that is translated into protein (as opposed to introns, which are not). The name comes from the fact that exons are the only parts of an RNA transcript that are seen outside the nucleus of eukaryotic cells.

Fc fragment a proteolytic fragment of an antibody molecule

Fibrous proteins a class of proteins distinguished by a filamentous or elongated three dimensional structure such as collagen.

First order a reaction whose rate is directly proportional to the concentration (activity) of a single reactant.

FT Fourier transform.

FT-IR Fourier transform infrared spectroscopy.

g estimate of centrifugal force so that 5000 ***g*** is 5000 times the force of gravity.

G protein a protein that binds guanine nucleotides such as GTP/GDP.

Gel filtration chromatography also called size exclusion chromatography. Separates biomolecules such as proteins through the use of closely defined pore sizes within an innert matrix according to the molecular mass.

Globular proteins proteins containing polypeptide chains folded into compact structures that are not extended or filamentous and have little free space on the inside.

Heme prosthetic oxygen binding site of globin (and other) proteins. Is a complex of protoporphyrin IX and Fe (II). Carries oxygen in globin proteins

Henderson–Hasselbach equation describes the dissociation of weak acids and bases according to the equation $pH = pK_a + \log([A-]/[HA])$.

Heterodimer a complex of two polypeptide chains in which the two units are non-identical.

HIV human immunodeficiency virus; retrovirus responsible for AIDS.

HLH helix-loop-helix motif found in several eukaryotic DNA binding proteins.

Hormone molecule often but not exclusively protein that is secreted into blood stream and carried systemically where it elicits a physiological response in another tissue.

Hydrolysis cleavage of covalent chemical bond involving water.

Homeobox a DNA binding motif that is widely found in eukaryotic genomes where it encodes a transcription factor whose activity modulates the development, identity and fate of embryonic cell lines.

Homodimer a complex of two units in which both units are identical.

Hsp heat-shock protein – name given to a large group of molecular chaperone proteins.

HTH helix-turn-helix motif found in several DNA binding proteins in which the two helices cross at an angle of $\sim 120^{\circ}$.

Huntingtin the mutant protein contributing to Huntington's disease.

Hydrogen bond an attractive interaction between the hydrogen atom of a donor group, such as OH or =NH, and a pair of nonbonding electrons on an acceptor group, such as O=C. The donor group atom that carries the hydrogen must be fairly electronegative for the attraction to be significant.

Hydrophilic refers to the ability of an atom or a molecule to engage in attractive interactions with water molecules. Substances that are ionic or can engage in hydrogen bonding are hydrophilic. Hydrophilic substances are either soluble in water or, at least, wettable.

Hydrophobic the molecular property of being unable to engage in attractive interactions with water molecules. Hydrophobic substances are nonionic and nonpolar; they are nonwettable and do not readily dissolve in water.

Hydrophobic effect stabilization of protein structure resulting from association of hydrophobic groups with each other, away from water.

IF initiation factor involved in start of protein synthesis and ribosomal assembly and activation.

Ig immunoglobulin and another name for an antibody group such as IgG.

Importins generic group of proteins with homology to importin α and β that function as heterodimer binding NLS-proteins prior to import into nucleus.

In vitro normally means in the laboratory, but literally in glass.

In vivo in a living organism.

Integral protein a membrane bound protein that can only be removed from the lipid bilayer by extreme treatment. Also called intrinsic protein.

Intron(s) a region in the coding sequence of a gene that is not translated into protein. Introns are common in eukaryotic genes but are rarely found in prokaryotes. They are excised from the RNA transcript before translation.

Ionic strength an expression of the concentration of all ions. In the Debye–Huckel theory $I = 1/2\ \Sigma m_i z_i^2$

Isoelectric focusing a technique for separating ampholytes and polyampholytes based on their pI. Also used to determine pI.

Isoelectric point the pH at which an ampholyte or polyampholyte has a net charge of zero. Same as pI.

Isoenzymes also called isozymes. Represent different proteins from the same species that catalyse identical reactions.

kDa kilodaltons; equivalent to 1000 daltons or approximately 1000 times the mass of a hydrogen atom.

Keratins major fibrous proteins of hair and fingernails. They also compose a major fraction of animal skin.

Kinases enzymes that phosphorylate or transfer phosphorus groups to substrates including other proteins (e.g. protein kinases)

K_m the Michaelis constant. It is the concentration of substrate at which the enzyme-catalysed reaction proceeds with half maximal velocity

Leader sequence a short N-terminal hydrophobic sequence that causes the protein to be translocated into or through a membrane often called a signal sequence.

Mesophile an organism living at normal temperatures in comparison with a thermophile.

Module a sequence motif of between 40–120 residues that occurs in unrelated proteins or as multiple units within proteins.

Molten globule state intermediate structures of a protein in which the overall tertiary framework of the protein is established, but the internal side chains are still free to move about.

Mutation a change in the sequence of DNA.

NES nuclear export signal – a signal consisting of several leucine residues found in proteins and indicating export.

NLS nuclear localization signal – a short stretch of basic amino acid residues that targets proteins for import into the

nucleus. The sequence can have bipartite structure consisting of two short sequences of basic residues separated by #10 intervening residues.

NMR spectroscopy acronym for nuclear magnetic resonance spectroscopy, a technique useful in the elucidation of the three-dimensional structure of soluble proteins.

Non-covalent interactions attractive or repulsive forces, such as hydrogen bonds or charge–charge interactions, which are non-covalent in nature, are called non-covalent interactions.

NPC nuclear pore complex – a very large assembly of protein concerned with regulating flux of macromolecules between nucleus and cytoplasm.

Nucleophile atom or group that contains an unshared pair(s) of electrons and is attracted to electrophilic (electron deficient) groups.

Nucleoporins proteins found in the nuclear pore complex.

Oncogene a gene which in a mutated form gives rise to abnormal cell growth or differentiation.

Oncoprotein the product of an oncogene that fails to perform its normal physiological role.

Operator element of DNA at the transcriptional site that binds repressor.

Operon a genetic unit found in prokaryotes that is transcribed as a single mRNA molecule and consisting of several genes of related function.

Oxidative phosphorylation process occurring in mitochondria and bacteria involving oxidation of substrates and the generation of ATP.

Oxidoreductase catalyse redox reactions.

PAGE polyacrylamide gel electrophoresis – a technique for the electrophoretic separation of proteins through polyacrylamide gels.

PCR polymerase chain reaction – a method involving the use of thermostable DNA polymerases to amplify in a cyclic series of primer driven reactions specific DNA sequences from DNA templates.

PDI protein disulfide isomerase – an enzyme catalysing disulfide bond formation or re-arrangement.

Peptide molecules containing peptide bonds are referred to generically as peptides usually less than 40 residues in length.

Peptidase an enzyme that hydrolyses peptide bonds.

Peptide bond the bond that links successive amino acids in a peptide; it consists of an amide bond between the carboxyl group of one amino acid and the amino group of the next.

Peripheral protein also called extrinsic protein and refers to protein weakly associated with membrane.

pH the negative logarithm of the hydrogen ion concentration in an aqueous solution.

Phage shortened version of bacteriophage.

p*I* the isoelectric point or the pH at which an ampholyte or polyampholyte has a net charge of zero.

Pitch the spacing distance between individual adjacent coils of a helix.

p*K* a measure of the tendency of an acid to donate a proton; the negative logarithm of the dissociation constant for an acid. Also called pK_a

Polypeptide a polypeptide is a chain of many amino acids linked by peptide bonds.

Polyprotic acids acids which are capable of donating more than one proton.

Porphyrins a class of compounds found in chlorophyll, the cytochrome proteins, blood, and some natural pigments. They are responsible for the red color of blood and the green color of plants.

Prebiotic era the time span between the origin of the earth and the first appearance of living organism ($\sim 4.6 \times 10^9$–3.6×10^9 years ago)

Preinitiation complex the multiprotein complex of transcription factors bound to DNA that facilitates transcription by RNA polymerase.

Preproprotein a protein contain a prosequence in addition to the signal sequence.

Preprotein a protein containing a signal sequence that is cleaved to yield the active form.

Pribnow box prokaryotic promoter region located 10 bases upstream of the transcription start site with a consensus sequence TATAAT.

Primary structure for a nucleic acid or a protein, the sequence of the bases or amino acids in the polynucleotide or polypeptide.

Protoporphyrin IX a tetrapyrrole ring which chelates Fe(II) and other transition metals.

Primary structure or sequence the linear order or sequence of amino acids along a polypeptide chain in a protein.

Prions a class of proteins that causes serious disease without the involvement of DNA/RNA.

Procollagen a newly translated form of collagen in which hydroxylation and addition of sugar residues has occurred, but the triple helix has not formed.

Prokaryote a simple normally unicellular organism that lacks a nucleus. All bacteria are prokaryotes.

Prosequence region of a protein at the N terminal designed to keep the enzyme inactive. The pro sequence is removed in zymogen processing.

Prosthetic group a co-factor such as a metal ion or small molecule such as a heme group. It can be bound covalently or non-covalently to a protein and is usually essential for proper protein function.

Protease a generic group of enzymes that hydrolyse peptide bonds cleaving polypeptide chains into smaller fragments (the term proteinase is also used interchangeably). Often show a specificity for a particular amino acid sequence.

Proteasome assembly of proteins based on a core structure of four heptameric rings that functions to degrade proteins into small peptide fragments.

Proteins biomolecule composed of one or more polypeptide chains containing amino acid residues linked together via peptide bonds.

Proto-oncogene the normal cellular form of an oncogene with the potential to be mutated. Mutation of the gene yields an oncogene and may lead to cancer.

PrP the protein believed to be responsible for transmitting the disease of prions. The protein is encoded by the host's genome and exists in two forms, only one of which causes the disease.

Purine planar, heterocyclic aromatic rings with adenine and guanine being two important bases found in cells.

Quantum a packet of energy

Quaternary structure the level of structure that results between separate, folded polypeptide chains (subunits) to produce the mature or active protein.

R group one of the 20 side chains found attached to the backbone of amino acids.

R state the relaxed state describing the activity of an allosteric enzyme or protein.

Ramachandran plot usually shown as a plot of dihedral angle ϕ against ψ.

Random coil refers to a linear polymer that has no secondary or tertiary structure but instead is wholly flexible with a randomly varying geometry. This is the state of a denatured protein or nucleic acid.

Redox reduction–oxidation reactions.

Renaturation refolding of a denatured protein to assume its active or native state.

RER rough endoplasmic reticulum – characterized by ribosomes attached to this membrane involved in cotranslational targeting.

Residue a name for a monomeric unit with a polymer such as an amino acid within a protein.

Reverse turn a short sequence of 3–5 residues that leads to a polypeptide chain altering direction and characterised by occurrence of certain amino acid residues with distinct dihedral angles. Also called a β bend.

Ribozyme a enzyme based on RNA capable of catalysing a chemical reaction.

S Svedburg unit of sedimentation with the units of 10^{-13} s. An example is the 30S ribosome particle. It is an estimate of how rapidly a protein or protein complex sediments during ultracentrifugation.

Salting in the effect of moderate amounts of ions, which increases the solubility of proteins in solution.

Salting out the effect of an extreme excess of ions which makes proteins precipitate from solution.

Scurvy a condition that occurs with vitamin C deficiency and reflects deficiency in connective tissue and collagen cross linking.

Secondary structure the spatial relationship of amino acid residues in a polypeptide chain that are close together in the primary sequence.

Serpin serine protease inhibitor.

Sheet a fundamental protein secondary structure (ribbon-like) discovered by Linus Pauling. It contains two amino acid residues per turn and forms hydrogen bonds with residues on adjacent chains.

Site-directed mutagenesis technique for altering the sequence of a DNA molecule. If the alteration occurs in a region coding for protein, the amino acid sequence of the protein may be altered as a consequence.

Snurps proteins found in spliceosomes with small nuclear RNAs.

SRP signal recognition particle. A ribonucleoprotein complex involved in cotranslational targeting of nascent polypeptide chains to membranes.

Stereoisomers molecules containing a center of asymmetry that possess same chemical formula but exist with different configuration or arrangement of atoms.

Substrate a reactant in an enzyme catalysed reaction that binds to active site and is converted into product.

T cells cells of the immune system derived from the thymus and concerned with fighting pathogens based on two types killer: T cells and helper T cells.

TATA box A/T rich region of genes that is involved in the binding of RNA polymerase to eukaryotic DNA sequences.

Tertiary structure large-scale folding structure in a linear polymer that is at a higher order than secondary structure. For proteins and RNA molecules, the tertiary structure is the specific three-dimensional shape into which the entire chain is folded.

Thermophile bacteria capable of living at high temperatures sometimes in excess of 90 °C.

Thermosome name given to the proteasome in thermophiles such as *T. acidophilum.*

Tic analogous system to Tim found in chloroplast inner membrane

Tim translocation inner membrane – a collection of proteins forming a protein import pathway in the inner mitochondrial membrane.

TMV tobacco mosaic virus.

Toc analogous system to Tom found in chloroplast outer membrane

Tom translocation outer membrane – a collection of proteins forming a protein import pathway in the outer mitochondrial membrane.

Torsion angle also known as dihedral angle.

Transcription the process of RNA synthesis from a DNA template performed by RNA polymerase and associated proteins known as transcription factors.

Transition state all reactions proceed through a transition state that represents the point of maximum free energy in a reaction coordinate linking reactants and products.

Transition state analogue a stable molecule that resembles closely the transition state complex formed at the active site of enzymes during catalysis.

Translation the process of converting the genetic code as specified by the nucleotide base sequence of mRNA into a corresponding sequence of amino acids within a polypeptide chain.

Transmembrane a protein or helix that completely spans the membrane.

Tropocollagen basic unit of collagen fibre. It is a triple helix of three polypeptide chains, each about 1000 residues in length.

TSE transmissible spongiform encephalopathy – any agent causing spongiform appearance in brain.

UV region of the electromagnetic spectrum extending from ∼200 to ∼400 nm.

van der Waals interactions weak interactions between uncharged molecular groups that help stabilize a protein's structure.

Variable domain a part of an immunoglobulin that varies in amino acid sequence and tertiary structure from one antibody to another.

vCJD new variant CJD that arose from BSE and is a transmissible spongiform encephalopathy.

V_{max} the maximal velocity in an enzyme-catalysed reaction.

v_o the initial velocity associated with an enzyme-catalysed reaction

Zwitterion a molecule containing both positively and negatively charged groups but has no overall charge. Amino acids are zwitterionic at ∼pH 7.0.

Zymogen an inactive precursor (proenzyme) of a proteolytic enzyme.

Appendices

Appendix 1
The International System (SI) of units related to protein structure

Physical quantity	SI unit	Symbol
Length	Metre	m
Time	Second	s
Temperature	Kelvin	K
Electric potential	Volt	V
Energy	Joule	J
Mass	Kilogram	Kg

Appendix 2
Prefixes associated with SI units

Prefix	Power of 10 (e.g. 10^n)
Tera	12
Giga	9
Mega	6
Kilo	3
Milli	−3
Micro	−6
Nano	−9
Pico	−12
Femto	−15
Atto	−18

Frequently when discussing protein structure bond lengths will be expressed in nanometres (nm). For example, the average distance between two carbon atoms in an aliphatic side chain is ∼0.14 nm or 0.14×10^{-9} m. Occasionally a second (non SI) unit is used and is named after the Swedish physicist, Anders J Ångström. It is called the Ångström (Å) and is equivalent to 0.1 nm or 10^{-10} m. Both units are widely and interchangeably used in protein biochemistry and in this textbook.

Appendix 3
Table of important physical constants used in biochemistry

Planck constant	h	$6.6260755 \times 10^{-34}$ J s
	$h/2\pi$	$1.05457266 \times 10^{-34}$ J s
Boltzmann constant	k	1.380658×10^{-23} J K^{-1}
Elementary charge	e	$1.60217733 \times 10^{-19}$ C
Avogadro number	N	6.0221367×10^{23} particles/mol
Speed of light	c	2.99792458×10^{8} ms^{-1}
^{1}H gyromagnetic ratio		2.67515255×10^{8} T s^{-1}
Atomic mass unit	amu	1.66057×10^{-27} kg
Gas constant	R	8.31451 J mol^{-1} K^{-1}
Faraday constant	F	96485.3 C mol^{-1}

Proteins: Structure and Function by David Whitford

Appendix 4
Derivation of the Henderson–Hasselbalch equation concerning the dissociation of weak acids and bases

The Henderson–Hasselbalch equation reflects the logarithmic transformation of the expression for the dissociation of a weak acid or base.

$$HA \leftrightarrow A^- + H^+$$

$$K = [H^+]\ [A^-]/[HA]$$

Rearranging this equation leads to

$$[H^+] = K\ [HA]/[A^-]$$

and by taking negative logarithms this leads to

$$-\log\ [H^+] = -\log K - \log\ [HA]/[A^-]$$

Since $pH = -\log\ [H^+]$ and we can define pK as $-\log K$ this leads to the following equation

$$pH = pK - \log\ [HA]/[A^-]$$

that is related to the Henderson–Hasselbalch equation by a simple changing of signs

$$pH = pK + \log\ [A^-]/[HA]$$

Expressed more generally and using the Bronsted Lowry definition of an acid as a proton donor and a base as a proton acceptor this equation can be re-written as

$$pH = pK + \log\ [\text{proton acceptor}]/[\text{proton donor}]$$

The Henderson–Hasselbalch equation is fundamental to the application of acid–base equilibria in proteins or any other biological system. It is used to calculate the pH formed by mixing known concentrations of proton acceptor and donor whose pK_a's are known. Alternatively this equation can be used to calculate the molar ratio of donor and acceptor given the pH and pK, or to calculate the pK at a particular pH given the concentrations relative or absolute of proton donor and acceptor.

Appendix 5
Easily accessible molecular graphic software

1. Koradi, R., Billeter, M., and Wüthrich, K. (MOLMOL: a superlative program for display and analysis of macromolecular structures. (obtainable from http://www.mol.biol.ethz.ch/groups/Wuthrichgroups/software/) *J. Mol. Graphics* 1996, **14**, 51–55.
2. Roger Sayle developed Rasmol although no formal citation exists. Rasmol is a very suitable introduction to molecular visualization software. An adaptation of Rasmol for use in web browsers called Chime is available from http://www.mdli.com or http://www.mdli.co.uk.
3. Kraulis, P.J. MOLSCRIPT: A Program to produce both Detailed and Schematic Plots of Protein Structures. *J. Appl. Crystallogr.* 1991, **24**, 946–950.
4. Molecular graphic software such as VMD produced by the Theoretical Biophysics group, an NIH Resource for Macromolecular Modeling and Bioinformatics, at the Beckman Institute, University of Illinois at Urbana-Champaign.
5. Guex, N. and Peitsch, M.C. SWISS-MODEL and the Swiss-PdbViewer: An environment for comparative protein modeling *Electrophoresis* 1997, **18**, 2714–2723. Official site for software http://www.expasy.ch/spdbv.

A wide range of commercial software has also been produced.

Appendix 6 Enzyme nomenclature

Enzyme classes and subclasses

EC 1 Oxidoreductases

EC 1.1 Acting on the CH-OH group of donors
EC 1.2 Acting on the aldehyde or oxo group of donors
EC 1.3 Acting on the CH-CH group of donors
EC 1.4 Acting on the CH-NH_2 group of donors
EC 1.5 Acting on the CH-NH group of donors
EC 1.6 Acting on NADH or NADPH
EC 1.7 Acting on other nitrogenous compounds as donors
EC 1.8 Acting on a sulfur group of donors
EC 1.9 Acting on a heme group of donors
EC 1.10 Acting on diphenols and related substances as donors
EC 1.11 Acting on a peroxide as acceptor
EC 1.12 Acting on hydrogen as donor
EC 1.13 Acting on single donors with incorporation of molecular oxygen (oxygenases)
EC 1.14 Acting on paired donors, with incorporation or reduction of molecular oxygen
EC 1.15 Acting on superoxide radicals as acceptor
EC 1.16 Oxidising metal ions
EC 1.17 Acting on CH_2 groups
EC 1.18 Acting on reduced ferredoxin as donor
EC 1.19 Acting on reduced flavodoxin as donor
EC 1.97 Other oxidoreductases

EC 2 Transferases

EC 2.1 Transferring one-carbon groups
EC 2.2 Transferring aldehyde or ketonic groups
EC 2.3 Acyltransferases
EC 2.4 Glycosyltransferases
EC 2.5 Transferring alkyl or aryl groups, other than methyl groups
EC 2.6 Transferring nitrogenous groups
EC 2.7 Transferring phosphorus-containing groups
EC 2.8 Transferring sulfur-containing groups
EC 2.9 Transferring selenium-containing groups

EC 3 Hydrolases

EC 3.1 Acting on ester bonds
EC 3.2 Glycosylases
EC 3.3 Acting on ether bonds
EC 3.4 Acting on peptide bonds (peptidases)
EC 3.5 Acting on carbon-nitrogen bonds, other than peptide bonds
EC 3.6 Acting on acid anhydrides
EC 3.7 Acting on carbon-carbon bonds
EC 3.8 Acting on halide bonds
EC 3.9 Acting on phosphorus-nitrogen bonds
EC 3.10 Acting on sulfur-nitrogen bonds
EC 3.11 Acting on carbon-phosphorus bonds
EC 3.12 Acting on sulfur-sulfur bonds

EC 4 Lyases

EC 4.1 Carbon–carbon lyases
EC 4.2 Carbon–oxygen lyases
EC 4.3 Carbon–nitrogen lyases
EC 4.4 Carbon–sulfur lyases
EC 4.5 Carbon–halide lyases
EC 4.6 Phosphorus–oxygen lyases
EC 4.99 Other lyases

EC 5 Isomerases

EC 5.1 Racemases and epimerases
EC 5.2 *cis-trans*-isomerases
EC 5.3 Intramolecular isomerases
EC 5.4 Intramolecular transferases (mutases)
EC 5.5 Intramolecular lyases
EC 5.99 Other isomerases

EC 6 Ligases

EC 6.1 Forming carbon–oxygen bonds
EC 6.2 Forming carbon–sulfur bonds
EC 6.3 Forming carbon–nitrogen bonds
EC 6.4 Forming carbon–carbon bonds
EC 6.5 Forming phosphoric ester bonds

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INDEX

Entries are arranged alphabetically with page numbers in italic indicating a presence in a figure whilst bold type indicates appearance in a table. Greek letters and numbers are sorted as if they were spelt out; β sandwich becomes beta-sandwich, 5S rRNA appears where *five* S rRNA is normally located in listings. Positional characters are ignored; so 2-phosphoglycolate appears under phosphoglycolate.